THE IOWA ORTHOPAEDIC JOURNAL

2012 • Volume 32

EDITORS
Julian O. S. Carlo, MD
Jaron P. Sullivan, MD

STAFF ADVISERS
Joseph A. Buckwalter, M.D.
Jose A. Morcuende, M.D.

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INSTRUCTIONS FOR AUTHORS, 2013 EDITION


PLEASE NOTE: October of 2013, marks the 100th Anniversary of the Department of Orthopaedics and Rehabilitation. The 33rd edition of the Iowa Orthopaedic Journal (June, 2013) will celebrate this important milestone.

Any original article relevant to orthopaedic surgery, orthopaedic science or the teaching of either will be considered for publication in The Iowa Orthopaedic Journal. Articles will be enthusiastically received from alumni, visitors to the department, members of the Iowa Orthopaedic Society, residents, and friends of The University of Iowa Department of Orthopaedics and Rehabilitation. The journal is published every June. The deadline to receive articles for the June 2013 edition is Monday, January 7, 2013.

Published articles and illustrations become the property of The Iowa Orthopaedic Journal. The journal is peer reviewed and referenced in Index Medicus and MEDLINE. Articles previously published will not be accepted unless their content has been significantly changed. The IOJ receives approximately 30,000 internet hits per month.

When submitting an article, send the following:

1. The original manuscript with illustrations and Abstract.
2. The corresponding author must be clearly identified with mailing address, telephone/fax numbers and e-mail address. Manuscripts will not be returned unless requested.
3. The bibliography must list references in the order of their appearance, and be double-spaced. References must be presented in the text by superscript numbers.
4. Legends for all illustrations should be listed in order of appearance and single spaced.
5. Illustrations/Images:
   a. Color illustrations may not be used unless it is the opinion of the journal that they convey information not available in black and white.
   b. Each image should be sent to diana-johannes@uiowa.edu as an individual .tif or .jpg file. All images must have resolution of 600 pixels per inch (ppi). Web page images are to be avoided. Set digital cameras to their highest quality (ppi) setting for photographs.
   c. When submitting an illustration that has appeared elsewhere, give full information about previous publication and credit to be given, and state whether or not permission to reproduce it has been obtained.
6. Send electronic copies of all items to diana-johannes@uiowa.edu. Special illustrations and photographs may be exempted from this electronic requirement and should be mailed to the address below.

       ++++++

Preparation of manuscripts: Manuscripts must be typewritten and double spaced. Write out numbers under 10 except percentages, degrees or numbers expressed as decimals. Direct quotations should include the exact page number on which they appeared in the book or article. All measurements should be given in SI metric units. In reporting results of surgery, only in rare instances can cases with less than two years of follow-up be accepted.

Additional copies of these instructions may be obtained at http://www.uiortho.com/index.php/education/iowa-orthopaedic-journal.html or by writing to Diana Johannes, University of Iowa Hospitals and Clinics, Department of Orthopaedics and Rehabilitation, 200 Hawkins Drive – 01006 J.P.P., Iowa City, Iowa, 52242-1088 or by emailing diana-johannes@uiowa.edu.

Printed on acid-free paper effective with Volume XV, 1995.

The Iowa Orthopaedic Journal
2012 IOJ EDITORS’ NOTE

It is with great pleasure that we present the 32nd edition of The Iowa Orthopaedic Journal (IOJ) in 2012.

As in previous years, this edition represents work and contributions from countless faculty, support staff and residents from the University of Iowa. Submissions were received from within our department and from across the nation and globe. The impact of the IOJ continues to increase, as the articles are freely available via Pub Med. A recent analysis demonstrated that more than 1,000 articles from the IOJ are downloaded from Pub Med on an average day. We are hopeful that the Pub Med exposure will continue to increase the IOJ readership and result in continued growth.

As per tradition, we would like to recognize the departing senior residents Drs. Boyer, Campion, Herickhoff, Lack, Nystrom, and Teusink. They have led by example and inspired younger resident classes to high achievement. We wish them well as they leave the department and embark on the next stage of their careers. We hope that their Iowa Orthopaedic roots will serve them well and keep them connected to the department throughout their promising careers.

Speaking of Iowa roots, it is appropriate to introduce the recipient of this year’s dedication: Dr. Randy N. Rosier. After completing an Iowa residency, Randy Rosier has gone on to have a truly exceptional career as a musculoskeletal oncologist and researcher. His career is an inspiration to all residents and reflects glowingly on Iowa. We are delighted to recognize him.

The IOJ would not be possible without the help of certain people. Diana Johannes continues to be a driving force behind the creation of the IOJ. We would also like to thank Catherine Fruehling-Wall for her assistance this year. They have the tremendous task of ensuring the journal comes to fruition, and were deeply involved in all facets of the journal, including organizing articles for review, proofreading manuscripts, and coordinating with the publisher. They have kept us on track in our efforts to produce the highest quality publication possible. We would like to thank Paul Elte for his guidance throughout the process. Jonathan Peterson deserves recognition for working tirelessly securing corporate sponsorships, all while being a brand new daddy.

Next, we would like to recognize the faculty who have overseen various projects, cases, and other efforts that have resulted in works that find themselves in this journal. Finally, we would like to thank our faculty adviser, Dr. Jose Morcuende, whose guidance continues to make the IOJ possible. We are indebted to him for his input, leadership, and service.

We would also like to thank our corporate sponsors for continuing to generously support our publication efforts with integrity in spite of increased industry scrutiny.

We hope this year’s edition of the IOJ continues in the same high standard as previous editions. It has been an honor to serve as the editors for the IOJ for 2012.

Last, we would like to mention that the next edition of the IOJ in 2013 will celebrate the 100-year anniversary of the Department of Orthopedics and Rehabilitation at the University of Iowa. We look forward in the coming year to the submission of many excellent studies that continue to reflect a tradition of excellence in scientific study and clinical practice that will advance the field of orthopedics.

Julian Carlo MD
Jaron Sullivan MD
Co-Editors
Iowa Orthopedic Journal
Department of Orthopedics and Rehabilitation
University of Iowa Hospitals and Clinics

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IOWA ORTHOPAEDIC JOURNAL
EDITORS EMERITI

1981
Frederick R. Dietz
Randall F. Dryer

1982
John J. Callaghan
Randy N. Rosier

1983
Don A. Coleman
Thomas J. Fox

1984
Fred G. McQueary
Nina M. Njus

1985
Patrick M. Sullivan
Mark D. Visk

1986
John J. Hugus
Randall R. Wroble

1987
Thomas C. Merchant
Mark C. Mysnyk

1988
Richard A. Berger
David M. Oster

1989
James L. Guyton
Peter M. Murray

1990
Craig G. Mohler
Joseph E. Mumford

1991
Devon D. Goetz
Thomas K. Wuest

1992
Robert L. Bass
Brian D. Mulliken

1993
Kenneth J. Noonan
Lacy E. Thornburg

1994
George J. Emodi
James C. Krieg

1995
Steven M. Madey
Kristy L. Weber

1996
Jay C. Jansen
Laura J. Prokuski

1997
James S. Martin
Todd M. Williams

1998
R. Dow Hoffman
Darron M. Jones

1999
Matthew B. Dobbs
Dennis P. Weigel

2000
Gregory N. Lervick
Jose Morcuende
Peter D. Pardubsky

2001
Daniel Fitzpatrick
Erin Forest
Rola Rashid

2002
Karen Evensen
Stephen Knecht

2003
Mark Hagy
Christopher Sliva

2004
Timothy Fowler
Michael Sander

2005
Kirk D. Clifford
Anthony V. Mollano

2006
Mohana Amirtharajah
Christina M. Ward

2007
Michael S. Chang
Matthew R. Lavery

2008
Jaren M. Riley
Christopher J. Van Hofwegen

2009
Jonathan Donigan
Ryan Ilgenfritz

2010
Christopher E. Henderson
Bryan A. Warme

2011
William D. Lack
Matthew J. Teusink

2012
Julian Carlo
Jaron Sullivan
Each year we dedicate the Iowa Orthopaedic Journal to an individual who has been a member of the Iowa orthopaedic family and has made exceptional contributions to the specialty of orthopaedics. It is with great pleasure that we present this honor to Randy Rosier.

Randy received his M.D. from the University of Rochester in 1978 and his Ph.D. in Biophysics in 1979 from the University of Rochester. It was Iowa’s great good fortune that we recruited Randy to our orthopaedic residency in 1978. He proved to be an exceptional clinician and a skilled surgeon. His mentors and his peers alike recall him as an amazingly brilliant resident. He is remembered as one of the greatest residents the University of Iowa Orthopaedics Department has ever had. All of us who worked with Randy appreciated his talent, creativity, natural warmth, and unique sense of humor.

During his residency, in addition to becoming a master orthopaedic surgeon, he conducted innovative basic science investigations of the role of mitochondria in endochondral ossification. He patented the digital electroneurometer, a portable nerve conduction velocity measurement device. Randy also has the distinction of serving as Associate Editor of the first edition of The Iowa Orthopaedic Journal and as Editor for the second edition. Randy’s commitment to pursuing a career as a clinician-scientist inspired two of his fellow residents, John Callaghan and Fred Dietz, who are current members of our faculty.

Dr. John Callaghan described the following about Dr. Rosier:

During intern year we were all busy with clinical tasks, but Randy was also in the midst of writing and then defending his PhD thesis. Randy is unbelievable in part because of his enthusiasm. He can take some of the topics that are boring to the rest of us, and bring out the fascinating science behind them that is accessible to the lay public as well as the most educated in that area – he truly has an infectious enthusiasm. Randy demonstrated little to no interest in the finance and business of medicine, yet when this was needed he became a chairman and not only educated himself in the topics needed, but excelled in his leadership. Randy was the type of guy that just wanted to get the work done rather than have the high profile status, accumulate a set of awards, or obtain prestigious leadership positions. His interests and skills were not limited to academics. He built a harpsichord during residency and was an excellent pianist. His classmates and friends benefited from his desire to live life to the fullest at work and play. He talked all of his ABC fellowship mates into bungee jumping in New Zealand! He always carried with him a great sense of humor, was a great researcher, and an excellent surgeon.

After finishing his residency in 1984, Randy returned to the University of Rochester to become an assistant professor of Orthopaedics, Oncology, and Biophysics. Less than ten years later, he became a full professor in each of those three departments. He has had an exceptionally active and productive research career, and has helped collect over $50 million in grant funding.

In addition to being a stellar investigator and clinician he has served the University of Rochester as the Founding Director of the Center for Musculoskeletal Research, Chairman of the Department of Orthopaedics and Rehabilitation, and Senior Associate Dean for clinical research. He has held leadership positions in multiple national professional and scientific organizations, including the American Academy of Orthopaedic Surgeons, the American Board of Orthopaedic Surgery, the American Orthopaedic Association, and the National Institutes of Health. Currently, he co-directs the Pilot and Collaborative Clinical and Translational Studies Program for the University of Rochester Clinical and Translational Science Institute.

Though we wish Randy had continued his career here at Iowa, we are glad he has put his talent and skills to extraordinary use at Rochester and that he continues to further the field of Orthopaedics. The University of Iowa Orthopaedics Department is honored to claim Randy Rosier as one of its own. Randy makes us all proud.
2012-2013
DEPARTMENT OF ORTHOPAEDICS AND REHABILITATION
SCHEDULE OF LECTURESHEIPS AND CONFERENCES

(Larson Conference Room, 01090 JPP, unless otherwise noted)

Carroll B. Larson Shrine Memorial Lecture
May 4-5, 2012
James G. Wright, MD, MPH, FRCSC
Surgeon-in-Chief and Chief of Perioperative Services
Department of Surgery
The Hospital for Sick Children
Toronto, Ontario, Canada
Spring 2013 to be arranged. Contact Nancy Love at (319) 356-1872

2012 Senior Resident’s Day
June 8-9, 2012
Dr. Benjamin Alman
Head, Division of Orthopaedics
Hospital for Sick Children
Toronto, Ontario, Canada

Dr. Robert Trousdale
Professor, Orthopaedic Surgery
Mayo Clinic
Rochester, Minnesota
Contact Gloria Yorek, (319) 356-3523

2013 Senior Residents Day
June 7-8, 2013 (Fri/Sat)
Discussants to be arranged.

Ponseti Clubfoot Treatment Symposium
International Meeting October 3, 4, and 5, 2012
The Ponseti Races will be held on Saturday, October 6, 2012
Discussants to be arranged
Contact Gloria Yorek at (319)356-3469

28th Annual Hawkeye Sports Medicine Symposium
December 6-7, 2012 (Thurs/Fri)
Marriott Hotel and Conference Center
300 East 9th Street, Coralville

K. Donald Shelbourne, MD
Shelbourne Knee Center
Indianapolis, IN
Contact Kris Kriener @ (319) 353-7954
Department of Orthopaedics

Mederic Hall  
2011-present
Carolyn Hetrich  
2011-present

Arthur Steindler  
1912-1949
Theodore Willis  
1917-1918

Matthew Karam  
2011-present
Matthew Bollier  
2010-present

Joseph Milgram  
1926-1932
Ernest Freund  
1932-1936

Benjamin Miller  
2010-present
Christina Ward  
2008-2009

Thomas Waring  
1932-1939
James Vernon Luck  
1936-1939

Heather Bingham  
2008-present
Phinit Phisitkul  
2008-present

Ignacio Ponsetti  
1946-2009
Eberly Thornton  
1946-1952

Nicolas O. Noiseux  
2007-present
Robert Yang  
2007-2010

Robert Newman  
1948-1956
Michael Bonfiglio  
1950-1995

Erika Lawler  
2006-present
John E. Femino  
2005-present

Carroll Larson  
1950-1978
Adrian Flatt  
1956-1979

Joseph D. Smucker  
2005-present
Jin-soo Suh  
2004-2005

Reginald Cooper  
1962-present
Howard Hogshead  
1964-1965

Neil A. Segal  
2004-present
Brian Wolf  
2003-present

Maurice Schnell  
1964-1965
Richard Johnston  
1967-1970;

John E. Femino  
2005-present
Joseph Chen  
2000-present

1998-present
Todd McKinley  
1999-present

Michael O'Rourke  
2003-2007
Sergio Mendoza  
2003-present

Donald Kettelkamp  
1968-1971
Gerald Laros  
1968-1971

Jose Morcuende  
2001-present
Annunziato Amendola  
2001-present

Richard Stauffer  
1970-1972
John Albright  
1971-present

Anjali Vivek  
2008-present
Joseph Buckwalter  
1979-present

2000-present
Todd McKinley  
1999-present

Stuart Weinstein  
1976-present
Thomas Lehmann  
1976-present

R. Kumar Kadiyala  
1998-2004
Leon Grobler  
1996-1999

Erika Lawler  
2006-present
John E. Femino  
2005-present

Charles Saltzman  
1991-2005
John Callaghan  
1990-present

78-1987

R. Kumar Kadiyala  
1998-2004
Leon Grobler  
1996-1999

Brian Adams  
1993-present
Charles Saltzman  
1991-2005

David Tearse  
1989-2000
Ernest Found  
1987-present

Lawrence Marsh  
1987-present
Curtis Steyers  
1985-2006

1984-present
Fred Dietz  
1984-present

James Nepola  
1984-present
James Weinstein  
1983-1996

William Pontarelli  
Charles Clark  
1980-present

William Blair  
1980-1997
Barbara Campbell  
1982-1984

1980-present
William Blair  
1980-1997
Barbara Campbell  
1982-1984

1980-present
William Blair  
1980-1997
Barbara Campbell  
1982-1984

The University of Iowa  
Roy J. and Lucille A. Carver College of Medicine

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Jeff Boyer

Jeff is the fifth of six children born to Wayne and Sue Boyer in Denver, Colorado. His family moved to Idaho Falls, Idaho when he was 13 years old. While growing up in these places, he spent much of his free time involved in various sports and outdoor activities. Jeff attended Brigham Young University and earned his degree in biochemistry. After his first year of college, he served a two-year mission for the Church of Jesus Christ of Latter-day Saints in Connecticut and Rhode Island. He returned to BYU after his mission, and met Holly, a California beauty. They soon fell in love and were married.

Jeff and Holly were both excited to have Jeff start medical school at the University of Washington as part of the WWAMI program, which provides medical education and training to students, residents, and practicing physicians in Washington, Wyoming, Alaska, Montana, and Idaho. They were able to travel around the Northwest for different rotations and enjoy the outdoors. During medical school, Claire and Ethan came into their family, and are a source of constant joy and laughter.

It was a great honor for Jeff to match into orthopaedic residency at The University of Iowa. He has felt fortunate to be trained at one of the top academic programs in the world. Holly, Claire, and Ethan have loved living in Iowa and became Hawkeye fans while fostering many friendships. The family will now move to St. Louis while Jeff trains in a fellowship in hand surgery at Washington University. Then, they plan to move back west to be closer to family and the mountains.

Jeff thanks all the faculty and staff for their guidance and mentorship in career development, as well as the residents he has worked with. His parents and siblings have also been a great support for him throughout his life. Most importantly, he thanks Holly, Claire and Ethan for putting up with him and giving him perspective on what is most important in life.

Heather Campion

Heather was born in Eugene, Oregon, the second daughter of Jim and Carla Hoffman, on what we can only guess was a rainy night because it is Oregon after all. From an early age, Heather knew she wanted to be a physician. Her grandfather was one of the first general surgeons in Eugene, which may have prompted her to declare to her first-grade class that she was going to be a “stomach doctor” someday. The doctor part stuck, but today she is very thankful that her area of interest transitioned from the digestive tract to the musculoskeletal system.

Growing up, Heather’s social calendar revolved around whichever sport was in season. Between soccer, basketball, softball, track, and cheerleading, very few sports were left un-played by young Heather. The pinnacle of her athletic career came her senior year in high school when her Marist High School Lady Spartans basketball team claimed the Oregon Division 3A state title. Finding that Oregon had temporarily run out of challenges for her, she left to attend college in South Bend, Indiana at the University of Notre Dame. Seeking a well-rounded college experience, Heather joined the cheerleading team at the end of her freshman year. This began a journey that included cheering for a women’s basketball national title and a men’s basketball Sweet 16 run, a trip to the Gator Bowl, and meeting her best friend, Dan, who has been at her side ever since.

After graduation, Heather attended medical school at Loyola University in Chicago where she met some amazing people and enjoyed a wonderful city for four years. She was ecstatic on Match Day in 2007 when she learned that she would receive her training in orthopaedics at the University of Iowa. Heather feels truly blessed to have worked with the finest fellow residents and faculty in the country. Iowa City has been a great place for both professional and personal growth. Dan and Heather welcomed Marcella Anne into the world on December 2nd, 2011 and life has never been more exciting! The five years in Iowa have gone by in a flash. As Heather departs for further training in hand and upper extremity surgery in Oklahoma City next year, she would like to thank her mentors for their support and guidance. She will always be grateful for the opportunities that the University Iowa Orthopaedics Department has provided her.
Paul Herickhoff

Paul was born and raised in Garden City, Minnesota, the second of Bob and Penny Herickhoff’s three boys. While he was growing up, his parents taught him the value of hard work, empathy and integrity, and he is forever grateful for their unwavering love and support. His brothers, John and Carl, with whom everything was a competition as children, are now his closest friends.

After graduation from Lake Crystal-Wellcome Memorial High School, Paul completed his undergraduate studies at Creighton University in Omaha, Nebraska where he majored in chemistry. Paul then took a year off to teach biology and chemistry at an inner city high school in Baltimore through the Teach For America program before applying for medical school. Educating teenagers living in a culture of poverty, drugs, violence, and broken families proved to be an in-your-face experience that stays with Paul to this day. The best part of his teaching experience, however, was his introduction to a sweet and sassy first-grade teacher, Juliana Barbalunga. Juliana is the most lovely and incredible woman (and now mother) he could ever have asked for, and they were married in 2006. Paul also became a step-father to Juliana’s black cat Jinx – since he was informed that was part of the “package deal.” Five months after the wedding, Paul and Juliana adopted their first child, Oscar, an easy-going black Labrador who is always the first one to the door to greet Paul when he comes home from work.

Paul graduated from Johns Hopkins University School of Medicine in 2007 and was elated to match at Iowa for residency. At the beginning of his second year, Paul and Juliana were blessed with their first (human) child, Anna (now three-and-a-half) and two years later with their son Benjamin (now one-and-a-half). Paul treasures his evenings and weekends at home with Juliana and the kids. Popular activities at the Herickhoff household include wrestling, reading books, and going on walks to the playground.

After residency, Paul will start his orthopaedic career in Beaufort, South Carolina as a lieutenant in the United States Navy. Paul is convinced there is no better place to learn orthopaedic surgery and raise children than Iowa City, and would like to wish all his friends and colleagues the very best in the future.

William Lack

Will was born in Mason City, Iowa and moved among several towns in Northern Iowa (Rockford, Cedar Falls and Mason City) before age nine. He is the youngest child in his family, and has five older siblings; Tony, Tanya, Heidi, Ben and Adam. His father, Gary, was a welder - his parents met at work at the Lehigh Portland Cement plant in Mason City, Iowa (both were card-carrying members of the AFL-CIO). Neither parent had a college degree until his mother, Veronica, went back to school later in life and acquired her bachelor’s degree in education. They both impressed on their children the importance of education. All their children completed college, two at Ivy League schools. Several now hold graduate degrees.

Will’s family moved to Buffalo, Wyoming when he was in fourth grade, after his parents bought a small business, the Z-Bar Motel. This was a great success for the family, but everyone moved back to northern Iowa several years later when his mother’s diagnosis of breast cancer made running the business more difficult. Fortunately, she remains a breast cancer survivor to this day.

After the move back to Iowa, Will attended Osage High School where he enjoyed football and wrestling. After high school he attended the University of Iowa where he earned his biomedical engineering degree and met Brandi, with whom he remains very close. As an undergraduate, Will worked at the Orthopaedic Biomechanics Laboratory part-time in the spring and summer for four years, between classes and football practice. He was a walk-on member of the football team at Iowa for four years, and in his senior year the team won the Big Ten Championship and went to the Orange Bowl. (This was not only the first time he had seen the ocean, but coincidentally, was also the first time he nearly drowned in the ocean).

Will graduated two weeks before the Orange Bowl; two weeks after, he began attending Harvard Medical School in Boston. There he became a Red Sox fan, and confirmed his interest in orthopaedics. During his fourth year of medical school he was very happy to match into the orthopaedics residency program at The University of Iowa.

His father, Gary, passed away from cancer while Will was in medical school. His brother, Adam, passed away in a motor vehicle accident during Will’s second year of orthopaedic residency. They were both lifelong role models for Will and they are always in his heart.

Over the last five years, Will has enjoyed working alongside a tremendous group of residents and faculty at The University of Iowa. He will begin a fellowship in orthopaedic trauma at the Carolina’s Medical Center upon completion of residency. Will wishes to thank Brandi, his family and good fortune for the opportunities life has afforded him.
Matthew Teusink

Matt was born and raised in Fremont, a small town in Western Michigan. He attended Hope College in Holland, Michigan. During a spring break mission trip to Kentucky, he had a conversion with another student about his plans to attend medical school and become an orthopaedic surgeon. She mentioned he should consider Iowa, because her uncle was an orthopaedist there (Dr. Marsh), and she had heard it was a pretty good place. Matt interviewed and agreed; so, he decided to attend the University of Iowa for medical school. During medical school he had the opportunity to work with many of the outstanding faculty and residents, which made the decision to stay for orthopaedic residency a no-brainer.

During his first year of medical school Matt was lucky enough to meet his wife, Jen, at a Super Bowl Party hosted by friends. They lived apart - with Matt in Iowa City and Jen in Williamsburg, Virginia and then Chicago - before they were married just prior to Matt starting residency. They have enjoyed Iowa City with all that it has to offer, including Hawkeye football games, as well as the multiple local triathlons during the summer months.

After completion of residency, Matt and Jen will move to Tampa, Florida where Matt will perform a fellowship in shoulder and elbow surgery at the Florida Orthopaedic Institute. They are excited to welcome their first child this fall.

Matt wishes to thank his parents, Jim and Kathy, his fellow residents, and the distinguished orthopaedic surgery faculty for their support. Most of all, he is grateful to his wife Jen for her patience and understanding during the past five years.

Lukas Nystrom

Luke was born and raised in the Twin Cities area of Minnesota. He was an avid baseball player, but those who saw him play encouraged him to do well in school. He grudgingly agreed, and attended St. Olaf College where he majored in chemistry, and played only intramural sports.

Despite the endless excitement offered by balancing chemical equations, Luke decided to go a different route with his career and apply to medical school. He entered the class of 2007 at the University of Minnesota, immediately after graduating from college. It was between his third and fourth years that he met the love of his life, Katrina, who was in law school at the time. They were engaged six months to the day after meeting and will celebrate their five year wedding anniversary in August.

After performing a visiting rotation on the orthopaedic trauma service at the University of Iowa, Luke was intent on matching there for a residency position, and was fortunate enough to do so. He considers himself lucky to have been educated by such a wonderful group of orthopaedic leaders.

During his fifth year of residency, Luke and Katrina welcomed a son, Henrik, who has provided endless joy and entertainment. Next year, the family will move to Gainesville for a one-year fellowship in orthopaedic oncology at the University of Florida. After that, he will join the faculty at Loyola University Medical Center in Chicago.

Luke wishes to thank his residency classmates for being so easy and fun to work with, and all of the Iowa residents for making the last five years so memorable. He thanks his parents, Mike and Jaana, for their constant love and encouragement. Lastly, he wishes to thank Katrina who has loved and supported him every day: Good, bad, and late.
2012 GRADUATING FELLOWS

Sami Abdulmassih, M.D.

Sami was born and raised in Damascus, Syria. He attended the medical school at Damascus University and then moved to Beirut, Lebanon where he did his orthopedic residency at the American University of Beirut Medical Center. He was interested in sports medicine and joint arthroscopies from the first day of his residency.

He had the chance to visit The University of Iowa Hospitals and Clinics and work with Dr. Amendola for one month during the last year of his residency. He admired the way of teaching and the diversity of exposure in the orthopedic department and the sports division. After he finished his residency, he decided to come to Iowa to achieve his dream of specializing in sports medicine and joint arthroscopy.

Sami worked under the supervision of his mentor, Dr. Amendola, during the last year. He was also interested in adding more knowledge in the foot and ankle field and sports-related foot-and-ankle injuries, and ended up doing a foot and ankle fellowship at The University of Iowa. Sami is planning to return to Syria at some point, but he will have great difficulty leaving Iowa and the orthopedic department, especially his godfather, Dr. Amendola.

Christian L. Sybrowsky, M.D.

Christian is the University of Iowa Sports Medicine fellow for 2011-2012. He was born and raised in the Salt Lake City area, where much of his family still resides. He received his undergraduate degree from the University of Utah, and then stayed on to complete his medical training at the University of Utah School of Medicine. He completed his residency training at the University of Washington Department of Orthopaedics and Sports Medicine in Seattle, Washington.

Christian and his wife, Mandy, have three children: James (8), Adam (6) and Jonas (born at the University of Iowa on Christmas Eve, 2011). Christian would like to give special thanks to Drs. Albright, Amendola, Bollier, Hettrich, Nepola, and Wolf for their patience, wisdom, mentorship and friendship.
Jacqueline Vanderzanden, M.D.

Jacqueline was born and raised in New Hampshire. She graduated from the Peabody Conservatory of Music of the Johns Hopkins University in Baltimore, Maryland, with a Bachelors of Music in Violin Performance. She spent some additional time in the Baltimore-DC area while she applied to medical school. During that time, she completed the pre-medical requirements at Hopkins, worked as a research technician at the Centers for Biologics Evaluation and Research and in a virology lab at the National Institutes of Health, taught private violin lessons and worked as a freelance musician, including frequent performances with the Maryland and Annapolis Symphony Orchestras.

She then moved to Albany, New York, to start her medical training. She attended Albany Medical College and then stayed at AMC for her residency in orthopaedic surgery. She is now completing her fellowship in Hand and Upper Extremity Surgery at UIHC, where she has fallen in love with the Iowa Hawkeyes and the Midwest. Jackie would like to thank Drs. Adams and Lawler for their patience, support, and wisdom. She also thanks her family and husband, Matthew Roland, who have been supporting her from a distance during this year. Jackie is looking forward to joining New England Orthopaedic Surgeons in Springfield, Massachusetts, later this summer.
NEW ORTHOPAEDIC FACULTY

**Mederic Hall**
Mederic Hall was raised in rural Illinois, obtained his Bachelor of Science degree from the University of Notre Dame and attended medical school at the University of Illinois at Chicago. He completed his Internal Medicine internship, Physical Medicine & Rehabilitation residency and Sports Medicine Fellowship at the Mayo Clinic in Rochester, Minnesota. He joined the University of Iowa Institute for Orthopaedics, Sports Medicine and Rehabilitation in 2011. His primary interests are in diagnostic and interventional musculoskeletal ultrasound, treatment of tendon and muscle injuries and the care of endurance athletes.

**Matthew Karam, M.D.**
For Matt, joining the orthopaedic trauma team at The University of Iowa Hospitals and Clinics was the culmination of a long-held interest in the management of both adults and children who sustain traumatic musculoskeletal injuries. Matt grew up in Cedar Rapids, Iowa and attended the Chicago Medical School. He was fortunate enough to complete orthopaedic residency here at The University of Iowa. After spending a snowy (but wonderful) year at Hennepin County Medical Center in Minneapolis, Minnesota, he was thrilled to come home again! Matt is pleased to finally settle down with his lovely wife, Chenelle, and their two beautiful children Mason (5) and Evalynn (2).

**Carolyn Hettrich**
Carolyn Hettrich joined the University of Iowa Sports Medicine team in 2011. She was born and raised in Portland, Oregon. She completed her undergraduate degree from Pomona College in Los Angeles, and attended medical school at the University of Washington in Seattle. She completed residency in orthopaedic surgery at the Hospital for Special Surgery in New York, and her Sports Medicine and Shoulder Surgery fellowship at Vanderbilt University. In addition, she obtained her Masters of Public Health from Columbia University while a resident. Her clinical interests are in conditions affecting the shoulder, elbow, scapula, SC and AC joints. Dr. Hettrich’s research interests include tendon-to-bone healing, the role of genetics in orthopaedic conditions, and comparative-effectiveness research and clinical outcomes research on shoulder, elbow, and knee injuries.
The UI Sports Medicine Center offers sport injury prevention, treatment and rehabilitation for competitive and recreational athletes of all ages. The staff at the center is also responsible for team coverage and taking care of all Hawkeye student athletes. The clinic is conveniently located off-site from the University of Iowa Hospitals and Clinics and offers an array of faculty and staff, including orthopaedic surgeons, family practitioners, pediatricians, internists, athletic trainers and physical therapists all specializing in sports medicine. In addition, American Prosthetics and Orthotics provides professional orthotist consultations for custom and off-the-shelf bracing, custom orthotics, athletic shoe modification and post-operative needs.

Since opening in the fall of 2009, UI Sports Medicine has continued to grow by adding new faculty and developing new services. Dr. Carolyn Hettrich joined the center in August 2011 after completing her orthopedic training at the Hospital for Special Surgery and an orthopedic sports medicine fellowship at Vanderbilt. Carolyn is involved in clinical care and is also highly involved in departmental research activities. Dr. Mederic Hall also joined the sports medicine group in August 2011. Mederic completed his physiatry and sports medicine training at the Mayo Clinic in Rochester. In addition to providing primary care and physiatry expertise, Mederic utilizes ultrasound imaging of sports injuries for diagnostic and therapeutic applications. This imaging technique has enhanced the current digital imaging and MRI services we provide, particularly for soft tissue problems.

Over this past year, we have also added an additional physical therapist, Jonathan Lueth, and physical therapy assistant, Auriel Luna, to our sports rehabilitation team. These two individuals have helped accommodate increased rehabilitation volumes and share our team's passion for providing high-level care in a collaborative, team environment.

Educational programs within UI Sports Medicine also
continue to expand, and two new programs accepted their first candidates during the past year. The Primary Care Sports Medicine Fellowship Program under the direction of Dr. Kyle Smoot increases our educational offerings in addition to our previously existing Orthopedic Sports Medicine Fellowship. The first post-professional athletic trainer was also accepted into the Athletic Training Physician Extender Residency Program. This program provides specialized training for athletic trainers who seek positions as physician extenders, a rapidly growing employment area. The UI Orthopaedic Sports Medicine Fellowship continues to excel and attract the best candidates from orthopaedic surgery.

Two new services that started within the last year include outreach programming and a concussion specialty clinic. The UI Sports Medicine Outreach Program focus is providing education and service to athletes involved in scholastic and recreational programs in the community. Members of UI Sports Medicine are providing educational programming emphasizing prevention and treatment of sports related injuries, and providing services at sporting events, including sports medicine care for high schools in the community. The addition of a concussion clinic to the UI Sports Medicine services also provides athletes in eastern Iowa with a high level of expertise in managing this common sport-related problem, and has been an early focus of outreach educational programming as well.

At the UI Sports Medicine Center we continue to excel in delivering exemplary clinical care and academic excellence through a synergistic multidisciplinary team approach. We continuously search for ways to improve, and strive to become a regional and national resource for sports medicine expertise.
The University of Iowa Department of Orthopaedics and Rehabilitation, along with the Iowa Orthopaedic Society, sponsors two research awards involving medical students.

The Michael Bonfiglio Award originated in 1988 and is named in honor of Dr. Bonfiglio who had an avid interest in students, teaching and research. The award is given annually at the medical convocation and consists of a plaque and a stipend. It is awarded to a senior medical student in the Carver College of Medicine who has done outstanding orthopaedic research during his or her tenure as a medical student. The student has an advisor in the Orthopaedic Department. However, the student must have played a major role in the design, implementation and analysis of the project. He or she must be able to defend the manuscript in a public forum. The research project may have been either a clinical or basic science project, and each study is judged on the basis of originality and scientific merit. The winner presents their work at the spring meeting of the Iowa Orthopaedic Society as well as at a conference in the Department of Orthopaedics and Rehabilitation.

The Iowa Orthopaedic Society Medical Research Award for Musculoskeletal Research is an award for a student in the Carver College of Medicine who completes a research project involving orthopaedic surgery during one of his or her first three years of medical school. The award consists of a $2000 stipend, $500 of which is designated as a direct award to the student and $1500 of which is designated to help defray continuing costs of the project and publication. The student must provide an abstract and a progress report on the ongoing research. The aim is to stimulate research in the field of orthopaedic surgery and musculoskeletal problems. This award is also presented at a medical convocation. In addition, the student presents his or her work at the spring meeting of the Iowa Orthopaedic Society and at a conference in the Department of Orthopaedics and Rehabilitation. This award is supported through the generosity of the Iowa Orthopaedic Society.

This year the selection committee consisted of Dr. Edward Law, the president of the Iowa Orthopaedic Society, and Drs. Charles R. Clark, Joseph A. Buckwalter, Jose Morcuende, John Femino, and Carolyn Hettrich, all members of the Department of Orthopaedics and Rehabilitation. They recommended that Andrew Odlund, M4, receive the 2011 Michael Bonfiglio Student Research Award. Andrew’s award was based on his project, “Wear Lysis is the Problem in the Modular TKA in the Young OA Patient at 10 Years”. His advisor was Dr. John Callaghan. The selection committee recommended that The Iowa Orthopaedic Society Medical Student Research Award be given to Jacob Elkins, M3, for his research titled “Choices and Compromises in Metal-on-Metal Total Hips. A Transitional Biomechanical Study”. His advisor was also Dr. John Callaghan.

The Michael Bonfiglio Award and the Iowa Orthopaedic Society Medical Student Research Award for Musculoskeletal Research are very prestigious, recognizing student research on the musculoskeletal system. These awards have indeed attained their goal of stimulating such research and have produced many fine projects over the years.

Charles R. Clark, M.D.
The Michael Bonfiglio Professor of Orthopaedic Surgery
From left to right: Charles R. Clark, M.D., Michael Bonfiglio Professor of Orthopaedic Surgery; Joseph A. Buckwalter, M.D., Department Chair, Department of Orthopaedics and Rehabilitation. Jacob Elkins, M3, winner of the 2012 Iowa Orthopaedic Society Medical Student Research Award for Musculoskeletal Research; Andrew Odlund, M4, winner of the 2012 Michael Bonfiglio Student Research award. John Callaghan, M.D., Distinguished Lawrence and Marilyn Dorr Endowed Chair for Hip Reconstruction and Research, advisor to both Jacob Elkins and Andrew Odlund.
ABSTRACT
Background: Anterior ankle impingement with and without ankle osteoarthritis (OA) is a common condition. Bony impingement between the distal tibia and talus aggravated by dorsiflexion has been well described. The etiology of these impingement lesions remains controversial. This study describes a cam-type impingement of the ankle, in which the sagittal contour of the talar dome is a non-circular arc, causing pathologic contact with the anterior aspect of the tibial plafond during dorsiflexion, leading to abnormal ankle joint mechanics by limiting dorsiflexion.

Methods: A group of 269 consecutive adult patients from the University of Iowa Hospitals and Clinics who were treated for anterior bony impingement syndrome were evaluated as the study population. As a control group, 41 patients without any evidence of impingement or arthrosis were evaluated. Standardized standing lateral ankle radiographs were evaluated to determine the contour of the head/neck relationship in the talus. Two investigators made all the radiographic measurements and intra- and inter-observer reliability were measured.

Results: 34% of patients were found to have some anterior extension of the talar dome creating a loss of the normal concavity at the dorsal medial talar neck. A group of 36 patients (13%) were identified as having the most severe cam deformity in order to assess any correlation with coexisting radiographic abnormalities. In these patients, a cavovarus foot type was more commonly observed. Comparison with a control group showed much lower rates of anterior-medial cam-type deformity of the talus.

Conclusions: Cam type impingement of the ankle is likely a distinct form of bony impingement of the ankle secondary to a morphological talar bony abnormality. Based on the findings of this study, this form of impingement may be related to a cavovarus foot type. In addition, there may be long term implications in the development of ankle OA.

Level of Evidence: Level III

INTRODUCTION
Anterior ankle impingement syndrome presents with pain during ankle dorsiflexion. This is thought to be due to hypertrophy of soft tissues or bone surrounding the tibiotalar joint. This condition is commonly thought to develop in response to repetitive trauma and torsional stresses to the joint, having been originally identified by Morris and McMurray in European footballers. Repetitive forced dorsiflexion can result in anterior compression of the tibiotalar joint, and repeated direct contact at the tibiotalar junction has been shown to induce osteophyte development. Over time, attempted repair, including fibrosis and fibrocartilage proliferation, leads to osteophyte development. These osteophytes can limit ankle dorsiflexion and increase irritation of nearby soft tissues. Radiographs are commonly obtained for these patients and are usually diagnostic. Conservative approaches to treatment, including rest, physical therapy, and anti-inflammatory treatment, are effective for many patients. Surgical treatment for these patients is reserved for cases where conservative measures fail. Both open and arthroscopic debridement procedures have high success rates for treating anterior ankle impingement. Most patients return to full activity, including athletics, following either type of treatment. Tol et al. found recurrence of some osteophytes in two-thirds of patients with grade-I OA following arthroscopic debridement for impingement. A possible cause of failure in these patients is a more significant or different type of impingement.

This study attempts to identify a cam-type impingement of the ankle, similar to what has been described in the hip femoral neck, in which the sagittal contour of

1 University of Iowa Hospitals and Clinics, Iowa City, IA
2 Chiang Mai University, Chiang Mai, Thailand
Disclosures: Ned Amendola, MD – royalties (Arthrex, Inc.); stock options (Arthrosurface)
Corresponding author - Ned Amendola, MD
Professor and Director
UI Sports Medicine Center
Department of Orthopaedics and Rehabilitation
University of Iowa Hospitals and Clinics
2701 Prairie Meadow Dr.
Iowa City, IA 52242
Ned-amendola@uiowa.edu
the talar dome forms a non-circular arc with an anterior flattening that causes loss of the normal concavity of the talar neck and pathologic contact with the anterior aspect of the tibial plafond in dorsiflexion, and abnormal loading of the talar dome cartilage (Fig.1). This anatomic relationship could also lead to the formation of reactive osteophytes and soft tissue hypertrophy but specifically differs from anterior impingement syndrome in that there appears to be an underlying anatomical bony deformity of the talar body-neck junction (Fig. 2). Sarrafian described the normal talus as having a medial extension facet of the talar body articular surface in 36% of 100 specimens.11

A parallel scenario in cam impingement of the hip has been previously identified by Notzli et al.10 In this condition, an aspherical portion of the femoral neck causes pathologic contact with the acetabulum, leading to decreased mobility and pain on internal rotation.12 Acetabular morphology in this condition is normal.13 Contact at the femoral neck with cam impingement causes inflammation of the surrounding tissues and mimics typical impingement.10, 12 Cam impingement is found in 40% of patients who develop osteoarthritis at the hip and typically leads to progressive degeneration of joint stability.12 Cam impingement of the hip is generally treated with arthroscopic or open surgery to remove the skeletal deformities causing impingement.14 Patients who undergo surgery to resect the cam lesion have better range-of-motion and less pain than those who undergo physical therapy alone.14 Although long term results are not available yet, it is believed that this procedure is also beneficial in preventing future development of arthritis in the joint.12

Although ankle impingement has been a well-described condition, there is a notable incidence of failure and recurrence with current surgical treatment of anterior impingement. This may be in part due to the surgical removal of osteophytes only without addressing the bony deformity. Medial impingement has been described in gymnasts with some unique characteristics.15 Hamilton may have described this as the “unrecognized osteophyte.”15 This form of cam impingement and ankle deformity has been observed by the senior author (AA) in numerous cases. We feel that the impingement we describe in this paper is a unique form of bony ankle impingement which has not previously been identified and have termed it cam-type impingement.

Arthroscopic or open debridement of the osteoarthritic ankle has been shown to have much less success in alleviating symptoms than in ankles with impingement without OA.6 Most arthritis observed in the ankle is secondary, meaning that it is incited by a traumatic event or other pathology.16, 17 Primary OA of the ankle is likely multifactorial, however, the ankle seems resistant against primary (idiopathic) osteoarthritis by having articular cartilage that is more resilient to sheer stress than articular cartilages found in the hip and knee.16, 18 There is no comprehensive treatment for this condition, although some measures can be taken to alleviate pain and improve joint flexibility.16 This study proposes cam-type impingement of the ankle as a distinct form of bony impingement that may have implications for long-term function of the ankle and as a possible etiology for ankle OA. We hypothesize that this cam-type
A deformity would frequently accompany ankles anterior bony impingement, posttraumatic arthritis (PTA), or idiopathic osteoarthritis (OA) compared to ankles in the general population. In addition, due to clinical and surgical observations, a correlation between cam-type impingement and varus hindfoot alignment has also been explored.

MATERIALS AND METHODS

This study was conducted at the University of Iowa Hospitals and Clinics in the Department of Orthopaedics and Rehabilitation. IRB approval was obtained from the university for both the patients for the study and control patients. Subjects for this study consisted of 269 consecutive patients (149 men and 120 women) with preoperative standing lateral ankle radiographs who had surgical diagnoses of: anterior ankle impingement (120 patients), idiopathic osteoarthritis (61), or posttraumatic arthritis (88) from 2004-2009 at the University of Iowa Hospitals and Clinics. The mean age of patients was 45 years (12 to 81). A control group was composed of 41 (35 women and 6 men; ages 16-69, mean 40) consecutive patients from July-August of 2009 with asymptomatic ankles, who had radiographs taken for other conditions. All patients were collected from one of four surgeons to eliminate possible inter-operator discrepancies.

Lateral ankle radiographs were obtained using a standard protocol (55 KV, 2.5 MAS, 45° distance, no grid and small focal spot) with the patients being instructed to place the lateral side of the affected foot against the digital receiver with the malleoli perpendicular to the receiver surface, placing equal weight on each foot. Images were templated and measured using OrthoView software (Meridian Technique Ltd.).

Measurements were made on each lateral ankle radiograph using the following protocols:

Cam ratio- a line was drawn parallel to the superior surface created by the navicular, cuneiform, and metatarsal bones. This line is then translated over the subtalar joint space, just beneath the lateral process of the talus. From this line, measurements are taken on a perpendicular axis to the widest and narrowest aspects of the talus, with the latter generally occurring at the neck. Both measures must be taken anterior to the apex of the talar dome. The cam ratio is the narrow (neck)/wide (body) calculation (Fig. 3).

α Angle- the α angle was measured by first identifying the largest circle that matches the curvature of the inferior tibial articular surface. This circle was then matched and overlayed with the curvature of the talar dome both medially (anterior dome) and laterally (posterior dome). A positive α sign is generated if the radius of the talar dome exceeds the radius of the circle anteriorly as part of a normal continuation of the talus. To quantify this measurement, a straight vertical line is made to bisect the circle. From the center of the circle, a straight line is drawn to the anterior point at which the radius is exceeded as part of a normal continuation of the talus (non-osteophytic bone and no gutter between). The angle between these two lines is the angle α (Fig. 4). If only one dome is distinguishable, the same measure is recorded for both domes. Measurements larger than 50 degrees (Mean-2SD for all control ankles) are considered negatives (no measurement recorded). The medial and lateral talar dome of the talus is identified by their outline location on the lateral xray. This was verified on 3D CT scan on 5 of the patients to confirm that the medial dome was the prominent and most anterior one on the impingement cases (Fig. 5a,b,c).
FIGURE 5. Lateral view of the ankle demonstrating the cam impingement and the difference between the medial outline of the dome (white arrow) and the lateral (black solid arrow). The medial border extends more anteriorly than the lateral (a). The frontal view for the 3D CT scan (b) and the lateral view (c) demonstrate the difference between the medial border (arrows) and the lateral extend of the talar dome and neck of the talus.

FIGURE 6. Lateral view showing the standard measure of the calcaneal pitch angle (a) and arch height (b).

Calcaneal Pitch (Calcaneal inclination angle) (Fig. 6a) - as described by Thomas et al., the angle created between the supporting surface and a line from the most anterior plantar point of the calcaneal tubercle to the most anterior plantar point of the calcaneus at the calcaneal cuboid joint.¹⁹

Arch Height - arch height was measured from a horizontal line from the inferior-most point of the calcaneus to the inferior bony surface of the great toe sesamoids. The distance from this line to the inferior-most aspect of the medial cuneiform bone is the arch height (Fig. 6b).

Distal Tibial Articular Angle - the distal tibial articular angle was measured from a straight line that bisects the tibia and a straight line that crosses the inferior surfaces of the anterior and posterior tibial plafond. The angle between these two lines is the distal tibial articular angle (Fig. 7).
These measures were performed by two of the investigators (DN) and (TV). Both individuals received standard instruction on how to make the radiographic measures prior to the study. Both inter- and intra-observer reliability were tested for this study. Tests for both were completed on 15 patients (selected using random number generator) with the recorders blind to one another and to previous results. Measures were taken two additional times for these patients per observer, with 48 hours between studies.

For reliability data, intraclass correlation coefficients were calculated (ICCs) for each measure. A Student’s t-test was used to determine significance of all other measurements. A p value <0.05 was determined to be statistically significant.

Source of Funding
Funding for this study was provided in part by the Bryan and Nancy Den Hartog Foot and Ankle Sports Medicine Research Fund, through the University of Iowa Foundation.

RESULTS
Intra-observer testing for both investigators for these measures showed high reliability using ratings based on two published reports.20, 21 Inter-observer reliability is shown in Table 1. Each measurement has a good level of agreement, with arch height and calcaneal pitch scoring as the most reliable.20 Measurement of angle α was the least reliable numerically, but raters were unanimous in identifying ankles as positive or negative. Average differences between measurers were as follows: medial α angle – 8.9 degrees, distal tibial articular angle – 1.01 degrees, calcaneal pitch – 0.0033 degrees, arch height – 0.025 cm, cam ratio – 0.0308.

In this study, 91 of the 269 (34%) total population (impingement, OA, and PTA ankles) generated a positive α angle measurement on the medial talar dome, and 47 (17.4%) measured positively on the lateral dome. Medial α angles, if positive, averaged 36.46 degrees (range 15-50) while lateral α angles averaged 38.62 degrees (range 19-50). Table 2 shows average measurements for ankles with and without positive medial α signs. Among the control ankles, 1 (2.4%) was measured to have a positive α sign on both the medial and lateral talar dome according to the guidelines we created.

Control ankles carried an average α angle of 65 (64.77 medial, 65.23 lateral) with a standard deviation of 7.616. Averages for distal tibial articular angle, calcaneal pitch, and arch height were 84.15 degrees, 21.76 degrees, and 1.98 cm, respectively. The average cam ratio for control ankles was 0.8638 with a standard deviation of 0.1057.

Patients with differing diagnoses were also compared. Angle α measures, distal tibial articular angle and calcaneal pitch did not differ significantly based on diagnosis. Patients with PTA were found to have a significantly higher arch height (2.53 cm) than those with primary OA (2.20 cm) or impingement (2.30 cm) as well as a significantly higher cam ratio (0.8487 versus OA – 0.8019, impingement – 0.8039). Positive medial α signs were not significantly linked to diagnosis, with each patient pool yielding similar percentages of positive ankles.

A population of 36 patients within this study was selected based on measurements (29 males, 7 females) believed to be prototypical or obvious of cam impingement (medial α angle ≤ 40, cam ratio ≥ 0.875). 10 total patients with PTA (11% of all PTA patients measured), 9 with OA (15%), and 17 with impingement (14%) were included in this group. These patients were analyzed with the rest of the population to determine whether cam impingement may be correlated with cavus foot

<table>
<thead>
<tr>
<th>TABLE 1. Inter-observer reliability for the measures described.</th>
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<tr>
<td><strong>Radiographic measure</strong></td>
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<tr>
<td>Medial α angle</td>
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<td>Lateral α angle</td>
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<td>Distal Tibial Articular Angle</td>
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<td>Calcaneal Pitch</td>
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<td>Arch Height</td>
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<td>Cam ratio</td>
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<th>Table 2. Measurements for ankles with (positive) and without (negative) medial α signs. Two-tailed t-tests were performed to generate p values.</th>
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<td><strong>Positive (n)</strong></td>
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<td><strong>Significance</strong></td>
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The results are shown in Table 3. None of the patients from the control group qualified for these values. The group of control patients was also compared to these patients to demonstrate the difference of cam ratios found between patients with the prototype cam deformity and those with no ankle complaints (Table 4).

### DISCUSSION

This study identifies a percentage of patients with anterior ankle complaints who demonstrate a specific type of talar bony morphometry. These patients appear to have either flattened talar domes which extrude into the anterior gutter space, reducing the amount of curved articular surface with which the tibia can articulate, or a thicker anterior neck just distal to the talar body articular surface creating the cam impingement effect. Standing lateral radiographs were investigated as a means for identifying patients with this particular anatomy. The most significant deformities were defined as patients with medial $\alpha$ measure less than 40 degrees and a cam ratio of .875 or higher (13% of all patients with PTA, OA, or anterior impingement). Images 5 and 6 depict ankles with this anatomy.

Prototypical cam-type ankles were found to have a significantly higher cam ratio than those with no $\alpha$ sign. The results were similar when these patients were compared to a control group with no ankle complaints. These control ankles had a very low incidence of a positive $\alpha$ sign and elevated cam ratio. This finding demonstrates a correlation between extraneous anterior talar bone presence and a decreased head/neck discrepancy in the talus. Patients from each diagnosis were equally represented among patients who generated a positive $\alpha$ sign on the medial dome as well as among the patients with the highest degree of cam-type deformity. These results indicate that this anatomy is not isolated to certain patient pools and that it may play a role in the development of osteoarthritis, as indicated previously.

Age, obesity, gender, type of fracture and procedure performed have all previously been identified as risk factors for the development of PTA. Between 70-75% of ankle arthritis is posttraumatic in origin and the average latency time between injury and development of arthritis has been shown to be around 20 years. Treatment for this condition is both difficult and controversial, with some studies suggesting total ankle replacement (TAR) and others more conservative measures. Elimination of an abnormal talar process like the one described in this study may be beneficial in treating patients with ankle impingement, may reduce the treatment failure rate, and may also reduce a patient’s risk for degenerative arthritis. Another hypothesis proposed by this study is that abnormal talar morphology can lead to increased pathologic contact between the tibia and talus, increasing the chances of fracture and later PTA. Similar risk factors exist for the development of idiopathic OA, with age being the strongest risk factor. One study has shown that any abnormal joint mechanics can have long-term detrimental effects, specifically leading to an increase in arthritis. By this logic, cam-type impingement of the ankle may be related to development of idiopathic OA. It is unclear if this process is reversible, but restoration of

<p>| TABLE 3. Measurements for ankles with medial $\alpha$ angles smaller than 40 degrees and cam ratios greater than 0.875 degrees compared to those without. Two-tailed t-tests were performed to generate p values. |
|---------------------------------|----------------|----------------|----------------|</p>
<table>
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<tr>
<th>Med. $\alpha \leq$ 40, cam ratio $\geq$ 0.875 (n)</th>
<th>Distal Tibial Articular Angle (degrees)</th>
<th>Calcaneal Pitch (degrees)</th>
<th>Arch Height (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>36</td>
<td>Averages</td>
<td>80.97</td>
<td>22.42</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>4.837</td>
<td>4.959</td>
</tr>
<tr>
<td>Other ankles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>233</td>
<td>Averages</td>
<td>83.67</td>
<td>20.09</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>5.176</td>
<td>5.860</td>
</tr>
<tr>
<td>Significance</td>
<td>p=0.0036</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| TABLE 4. Measurements for ankles with (positive) medial $\alpha$ signs of 40 degrees or less and cam ratio of 0.875 or larger from pathologic patients compared to those with no ankle complaints (control). Two-tailed t-tests were performed to generate p values. |
|---------------------------------|----------------|----------------|
| Medial $\alpha \geq$ 40, cam ratio $\leq$ .875 (n) | Cam Ratio |
|---------------------------------|----------------|----------------|
| 36                              | Average        | 0.9062         |
|                                 | SD             | 0.0342         |
| Control                         |                |                |
| 41                              | Average        | 0.8638         |
|                                 | SD             | 0.1057         |
| Significance                    | p=0.0002       |                |
normal joint mechanics can often allow the joint to heal.\textsuperscript{25}

Previous research has shown that the distal tibial articular angle in relation to the tibial axis is related to anterior articular stress in the ankle.\textsuperscript{26} Ankles with a positive medial $\alpha$ sign had a significantly different distal tibial articular angle, and those with the most serious cam-type tali (med. $\alpha \leq 40$, cam ratio $\geq 0.875$) had a much smaller anterior angle than those without. This position may play a role in the severity of cam impingement, as it is likely that these patients would have more pathologic contact at the tibio-talar joint than those with larger angles.

The data in this study also indicate a strong correlation between cam-type deformity and pes cavus. Thomas et al. found an average calcaneal pitch among patients over the age of 31 with no history of ankle complaints to be 20.6 degrees, with males and females carrying the same average.\textsuperscript{19} These results are supported by the control ankles in this study, which carried an average pitch of 21 degrees. This study suggests that these results may be typical of ankles with a history of pathology as well, which averaged 20.4 degrees in our measures. However, ankles with a positive medial $\alpha$ sign were significantly higher-arched than those without (Table 2). Furthermore, patients with a prototypical cam lesion (med. $\alpha \leq 40$, cam ratio $\geq 0.875$) were found to have a more cavus foot compared to those without, with an average pitch 2 degrees larger and arch 3 mm higher than all pathological ankles measured. This correlation may be causative, as increased arch height leads to external rotation of the tibia and reduced joint space within the tibio-talar junction.\textsuperscript{27, 28, 29} Due to the limitations of only viewing standing lateral radiographs for this study, it is also possible that these patients, who were experiencing some ankle pathology at the time of image collection, were under-loading their affected foot during the procedure, causing an increase in arch height to be perceived laterally.

The reliability results for this study indicate that for each individual, a high level of consistency can be expected when making these measurements. Inter-rater reliability is slightly lower when measuring $\alpha$ angles and cam ratios. This is likely due to the slightly subjective nature of determining these measurements and experience in reading radiographic images. These measures are all considered to have a good level of inter-rater reliability according to an objective metric.\textsuperscript{20} Based on average differences, we can expect to calculate $\alpha$ angles within 10 degrees of one another and cam ratios within 0.03 (unitless) reliably with this method. This finding demonstrates that the cam ratio may be a more reliable means of measuring the degree of cam impingement in these patients. Ultimately, the cam ratio may be a better clinical tool as a measure of cam impingement when compared to the $\alpha$ angle, based both on reliability of measurements between observers and the ease of completing this metric.

This study is limited in its scope in several ways. Primarily, the retrospective nature of this study leaves many variables uncontrollable. Secondly, the use of standing lateral radiographs exclusively limits the total understanding of ankle morphology that may be present. Lateral ankle radiographs are also subject to rotational effects, although attempts were made to eliminate any possible rotational alterations by using ratios and angles for the majority of measurements.\textsuperscript{26, 30} The use of a standard protocol for collection of the images also served to eliminate this bias. A similar study using 3D CT reconstructions would be more useful in determining the entire bony anatomy present with this deformity. Further follow-up should include prospective research following patients with these measurements to determine surgical outcomes, clinical presentations, and demographic trends. A pediatric study of this anatomy would be useful to confirm its developmental nature. It is also unknown whether more significant measurements of the angle $\alpha$ and cam ratio lead to more severe clinical outcomes.

REFERENCES


COMPARISON OF TWO MANUAL TESTS FOR ANKLE LAXITY DUE TO RUPTURE OF THE LATERAL ANKLE LIGAMENTS

Tanawat Vaseenon, MD; Yubo Gao, PhD; Phinit Phisitkul, MD

ABSTRACT

Background: Assessment of ankle laxity can be both subjective and difficult, especially in less-experienced hands. The commonly-practiced anterior drawer test can mislead practitioners in the diagnosis of ankle instability due to subtalar joint motion. A manual stress test, focusing on tibiotalar translation, may be required.

Objective: To evaluate the validity, reliability, and diagnostic accuracy of the modified manual stress test - the anterolateral drawer test (ALDT) - compared with the original anterior drawer test (ADT) in two groups of examiners with different levels of experience.

Methods: A cadaveric study was performed at University Research Laboratory. Nine below-the-knee specimens were randomized into three groups to simulate different degrees of lateral ligament injury. Two groups of examiners (Group A was four athletic training students; Group O was four senior orthopaedic trainees) performed ADT and ALDT while direct anatomical measurement (DAM) of tibiotalar translation was used as a reference under controlled load (Telos device). Ankle translation from DAM, ADT, and ALDT was recorded in millimeters. Measurements were compared using a paired t-test. Pearson correlation was used to determine linear relationship between groups. Inter- and intra-rater reliability was identified using ICC (intraclass correlation coefficient). The diagnostic threshold was determined by a receiver operating characteristic curve.

Results: Both groups of examiners demonstrated excellent intra-observer reliability (0.94 for ADT and 0.80 for ALDT) and fair-to-good inter-observer reliability (0.52 for ADT and ALDT). There was no difference in the mean of measurement between group A and group O except for the ALDT on intact specimens ($P = 0.01$) and the ADT on the ATFL+CFL cut specimens ($P = 0.02$). Correlation with the DAM was superior in the ALDT ($r = 0.73$) compared to the ADT ($r = 0.57$). When using 4 mm or more as a diagnostic threshold, sensitivity and specificity (respectively) were found to be 100% and 66.67% for the ADT and 100% and 66.67% for the ALDT.

Conclusion: For diagnosis of ankle ligament injuries, this cadaveric study demonstrated high sensitivity, reliability and correlation with the gold standard using ADLT, regardless of the examiner’s experience.

Keywords: Ankle instability, anterior drawer test, anterolateral drawer test, ankle ligament, ankle laxity.

The Authors received no financial support for this study.

INTRODUCTION

Chronic ankle joint instability can develop in 19% to 72% of patients following lateral ankle sprains. The common presenting complaints are pain, fear of giving way, actual instability symptoms, and/or swelling that interferes with daily living and/or sport activities. After an acute injury, adequate diagnosis and treatment are important to expedite recovery and to prevent chronic ankle joint instability. In addition, it is important to assess the degree of ankle laxity in order to determine the presence of mechanical instability which may not improve following rehabilitation or the use of orthotics.

On a subacute or delayed basis, laxity of the ankle joint is also a key factor in guiding further treatments and as an indication for surgical repair or reconstruction of the lateral ankle ligaments.

Instability of the ankle joint after a sprain can be evaluated by manual examination or instrumented stress testing, with or without radiographic or ultrasonographic assistance. Stress radiographs have been used for this
purpose; however, these have not been very helpful in deciding treatment because of their lack of reliability. While the use of ultrasonography has shown promising results, the technique is operator-dependent and may not be widely available. Different ankle testers have been designed to measure displacement between the calcaneus and the tibia under controlled loading without radiography. However, the validity of the testers has been questioned due to possible false laxity through the subtalar joint. In a clinical setting, the anterior drawer test (ADT) is generally used as a manual test to evaluate ankle instability. The test is usually performed with one hand stabilizing the distal tibia and the other hand pulling the foot anteriorly without any attempt to isolate the displacement from only the tibiotalar joint. Determination of instability by this technique can be subjective, has a lack of sensitivity, and is difficult, especially in less-experienced hands. In addition, the test can only evaluate the total combined laxity across both tibiotalar and subtalar joints. Due to the need for a better test for clinical use, the anterolateral drawer test (ALDT) was developed and has been routinely used by the senior author (PP) since 2006. This technique is a modification of one described by Mann et al, regarding specific positioning of the hands and fingers to allow appreciation of isolated laxity of the lateral ankle joint by direct palpation of the tip of the fibula and the lateral talus as anterolateral rotatory subluxation occurs.

In a previous study, we found that the ALDT demonstrated high sensitivity and accuracy in determining lateral ankle laxity in cadaver specimens. That study also demonstrated the ALDT had superior linear correlation with the Telos stress device when compared to the ADT. The promising initial results of this technique warranted further validation in larger groups of examiners with differing levels of experience.

In this present study, we evaluated the reproducibility and sensitivity of two ankle laxity tests (ADT and ALDT) for lateral ankle ligament instability as performed by a group of senior orthopaedic trainees and by a group of athletic training students. We hypothesized that the ALDT would show higher correlation with directly measured talar displacement and provide higher accuracy for the diagnosis of lateral ankle ligament rupture than the ADT for both groups of examiners.

MATERIALS AND METHODS

Nine fresh-frozen human ankle specimens (four pairs and a single ankle) were obtained from two male and three female donors with a mean age of 55 years (range, 48 to 70 years). The number of specimens was determined by the availability of cadavers. Each specimen was thawed at room temperature for 24 hours before testing. Specimens with limited range of motion or any evidence of prior surgery were excluded. Three groups, each containing three specimens, were blindly assigned: intact ligaments, anterior talofibular ligament (ATFL) cut, and anterior talofibular ligament and calcaneo-fibular ligament (ATFL+CFL) cut. Each specimen had the same lateral curvilinear incision, regardless of the ligament transection. Bone pins were placed on the center of the fibular and talar attachments of the ATFL. The distance between the pins was measured using a vernier caliper with 0.01 mm precision as a baseline distance. The distance between the same pins was again measured while the ankle was under anteriorly directed force of 15 kilopascals (143 Newton) on the Telos stress device (Austin & Associates, Inc., Telos Medical, MD, USA) with the same position of the ankle, 20 degrees of plantar flexion. This difference between the measured distance and the baseline distance was recorded as a direct anatomic measurement (DAM). The DAM was considered the gold standard for the ankle laxity tests. The skin was meticulously closed. Two investigators (TV and PP) who were not involved in the manual testing prepared all specimens.

Two groups of examiners with differing experience levels were selected. Group A included four athletic training students with an average of 2.25 years clinical experience. Group O included four senior orthopaedic trainees (three fourth-year orthopaedic residents and one foot-and-ankle fellow) with an average of 4.5 years clinical experience. Each group applied both ankle laxity tests to all specimens. All examiners were instructed in ADT and ALDT using a video demonstration provided by a fellowship-trained foot-and-ankle surgeon (PP). All were allowed to practice with a plastic ankle model for up to one hour before actual specimen testing. The ADT was performed with one hand stabilizing the leg just above the ankle joint; the heel was then grasped from behind with the opposite hand, and an anterior force was used in an effort to produce forward translation (Figure 1B). The ALDT was performed with one hand stabilizing the leg just above the ankle joint. The index and middle fingers of the opposite hand were then pressed firmly against the posterior aspect of the heel to provide a gentle anteriorly directed force. The palm supported the sole of foot to stabilize the ankle in slight plantar flexion. The thumb was placed along the lateral aspect of the talar dome and the anterior aspect of the lateral malleolus. Anterior translation was applied at the posterior aspect of the heel while the foot was allowed to rotate internally. Any step-off was palpable by the thumb (Figure 1A).

Each of the nine specimens was randomly arranged at testing stations with the tibia secured in a vertical...
position while the foot and ankle were free of any constraint. The manual tests were performed twice on each specimen on separate occasions, using different specimen arrangements. All specimens were randomly placed using a random-number table. Without the use of a measuring device, the displacement of the talus was manually appreciated by each examiner from each test session and was recorded in millimeters.

The laxity data between the two groups of examiners were compared using a paired t-test. Pearson’s correlation coefficient was used to determine the linear relationship between the DAM and the two laxity tests. The correlation coefficients (r) were interpreted as weak (0.1-0.29), moderate (0.3-0.49), and strong (0.5-1.0). Inter-observer and intra-observer reliabilities of the examiners were identified using ICC (intraclass correlation coefficient). ICCs were interpreted to be poor-fair at ICC ≤ 0.4, fair-good at 0.4 < ICC < 0.75, and excellent at ICC ≥ 0.75. A post hoc analysis with a receiver operating characteristic (ROC) curve was used to determine a proper diagnostic threshold. The sensitivity and specificity of each laxity test was evaluated. All tests were performed with use of the SAS procedure (SAS 9.1.3; SAS Institute, Cary, NC) and using a significance level of alpha set at 0.05.

**TABLE 1. The mean and standard deviation (mm) from different measurement techniques for all specimens categorized by the degree of ligamentous destabilization**

<table>
<thead>
<tr>
<th></th>
<th>Intact</th>
<th>ATFL cut</th>
<th>ATFL+CFL cut</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAM</td>
<td>0.4 ± 0.1</td>
<td>5.7 ± 1.7</td>
<td>9.4 ± 2.7</td>
</tr>
<tr>
<td>ADT (O+A)</td>
<td>3.9 ± 1.6</td>
<td>5.4 ± 1.7</td>
<td>5.3 ± 2.1</td>
</tr>
<tr>
<td>O</td>
<td>3.2 ± 1.4</td>
<td>6.5 ± 1.5</td>
<td>6.8 ± 1.2</td>
</tr>
<tr>
<td>A</td>
<td>4.5 ± 1.6</td>
<td>4.3 ± 1.1</td>
<td>3.8 ± 1.6</td>
</tr>
<tr>
<td>ALDT (O+A)</td>
<td>3.4 ± 0.7</td>
<td>5.2 ± 1.7</td>
<td>5.8 ± 2.0</td>
</tr>
<tr>
<td>O</td>
<td>2.8 ± 0.5</td>
<td>5.0 ± 1.8</td>
<td>6.1 ± 1.5</td>
</tr>
<tr>
<td>A</td>
<td>4.0 ± 0.4</td>
<td>5.5 ± 1.7</td>
<td>5.4 ± 2.6</td>
</tr>
</tbody>
</table>

“O+A” = data from all examiners
“O” = data from group O (orthopaedic trainees)
“A” = data from group A (athletic training students)
“DAM” = direct anatomical measurement

The mean and standard deviation of the joint translation from different measurement techniques for all specimens, categorized by the degree of ligamentous destabilization, are shown in Table 1. The results from the ALDT showed significant differences in average measurements between group A and group O in specimens with the ligament intact (p=0.0083), and no significant difference in both the specimens with ATFL cut, or those with ATFL+CFL cut (p=0.6776 and p=0.6363, respectively, Figure 2A). However, for the ADT, the average measurement was statistically significantly different between group A and group O in the specimens.
with ATFL+CFL cut ($p=0.0247$). We found no significant differences between the two groups of examiners in the specimens with the intact ligament ($p=0.2485$) and ATFL cut ($p=0.0585$; Figure 2B).

Using Pearson’s correlation coefficient to analyze a linear relationship between the DAM and ankle laxity tests, we found that the correlation between ALDT and DAM ($r=0.7656$, strong) was comparable to that between ADT and DAM ($r=0.7621$, strong) in group O (Figure 3). However, these two $r$’s were not significantly different. Meanwhile, in group A the correlation between ALDT and DAM ($r=0.6129$, strong) was much higher than the correlation between ADT and DAM ($r=0.0208$, weak). The two $r$’s were significantly different ($p=0.0442$).

Moreover, to evaluate the overall effects, we averaged the ADT and ALDT values over the two groups. The correlation between averaged ALDT and DAM ($r=0.7332$, strong) was higher than that between the averaged ADT and DAM ($r=0.5704$, strong). All of the results showed that ALDT was consistently more accurate in the diagnosis of a lateral ankle ligament rupture than ADT, over different groups of practitioners.

Intra-observer reliabilities identified using ICC were 0.9443 (excellent) for the ADT and 0.8017 (excellent) for the ALDT. Moreover, inter-observer reliability values for the ADT were 0.5274 (fair-good), and 0.5230 (fair-good) for the ALDT.

The best cut points with highest sensitivity and specificity to identify ankle ligament ruptures for the ADT and the ALDT were 3.81 and 3.97 mm, respectively, in ROC curves. When using 4mm or more of the displacement value as a threshold to diagnose lateral ankle ligament rupture for both manual tests, the sensitivity and the specificity, respectively, were found to be 100% and 66.67% for the ALDT, and 100% and 66.67% for the ADT (Figure 4).

**DISCUSSION**

The ALDT demonstrated its ability to diagnose lateral ankle laxity well in both groups of examiners, even with different experience levels. In the more experienced group of examiners, group O, we recorded a trend: Laxity values from both the ADT and the ALDT increased continuously with the severity of ankle ligament injuries (Figure 2). In addition, this strongly correlated with the gold standard DAM (Figure 3). This suggested the possibility that both ankle laxity tests were clinically applicable for examiners with more experience. However, in the less-experienced group A, we noted a different trend: Only the ALDT was useful in differentiating ankles with lateral ligament injury from intact ankles. In addition, correlation with the gold standard was sig-

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**Figure 2.** The charts show the average degree of displacement from the anterolateral drawer test (ALDT, graph A) and anterior drawer test (ADT, graph B) in group O, orthopaedic trainees (O) and group A, athletic training students (A). The DAM (direct anatomical measurement) is shown in each graph as a control. The dispersion bars indicate standard deviations.
Comparison of Two Manual Tests for Ankle Laxity due to Rupture of the Lateral Ankle Ligaments

Figure 3. Charts demonstrate Pearson's correlation between direct anatomical measurement and tests of ALDT and ADT, in orthopaedic trainees (A and B) and athletic training students (C and D). The correlation with the gold standard (DAM) was significantly higher in the ALDT as compared with the ADT.

As in previous studies, a laxity of 4 mm or more was found to be the best diagnostic threshold for lateral ankle ligament rupture. This was slightly higher than the value from our prior study (3 mm). We believe that this effect occurred because of the difference in experience levels, and the number of examiners. In practice, the difference between the laxity of uninjured and injured limbs should be noted; however, a recommendation on the optimum number as a threshold cannot be made from our information.

Despite the fact that ankle sprains are well recognized as the most common sports injury, effective clinical evaluations of the degree of joint laxity are lacking.
Multiple classification systems have been proposed for acute ankle sprains using the combination of pain, swelling, anatomical ligament disruption, manual stress testing and stress radiographs. While the degree of injury and instability have been overlooked, functional treatments are generally applied to most athletes who sustained an ankle sprain. This may, in part, explain the relatively high incidence of subacute or chronic symptoms in athletes. In an epidemiologic study of 639 patients with ankle arthritis by Saltzman et al., 70% was post-traumatic in origin. Single-incident and recurrent ankle sprains, interestingly, accounted for 28% of the entire post-traumatic group. The diagnosis of ankle instability in both acute and chronic settings may have been less than optimal.

Investigations into the evaluation of ankle instability have not been clinically successful despite extensive research. While some ankle stressors and ultrasound techniques may have shown some promising results, their use can be limited due to availability and their operator-dependent characteristics. It has been the senior author’s impression that a slight modification of the manual examination technique significantly improves the accuracy of the anterior drawer test, as we report. The ALDT required simultaneous palpation of the step-off while applying translational force to the ankle. Both groups of examiners, with different backgrounds and experience levels, were able to be trained in this technique.

We recognize that the present study has several limitations. The training period prior to manual testing was relatively brief. This may have affected test performance for the less experienced examiners. However, both groups of examiners repeated their tests in a blinded fashion, and intra-observer and inter-observer reliabilities were excellent and moderate (ICC > 0.8 and ICC > 0.5, respectively). While we used millimeters for the threshold point of diagnosis, other commonly used instability grading systems e.g. mild/moderate/severe, absent/present, or same/different compared to the contralateral side, may yield different results in diagnostic accuracy. Unfortunately, there is no anatomically validated grading system for the anterior drawer test currently available. In addition, the degree of instability may not reflect the true degree of ligament disruption due to the inherent stiffness in cadaveric specimens. Also, a pain inhibition mechanism is absent in cadaveric studies, and associated soft tissue injuries such as capsular rupture and tendon damage are important factors which can complicate interpretation of the physical examination in a clinical setting. Finally, the small number of cadavers and evaluators might weaken the present results. Therefore, larger numbers of specimens and additional clinical studies are necessary to establish the efficacy of the ALDT.

For the diagnosis of ankle ligament injuries, this cadaveric study demonstrated the high sensitivity, reliability, and correlation with the gold standard of the ALDT, regardless of the examiners’ experience. Further studies in clinical settings with larger sample sizes are warranted to establish the efficacy of the ALDT and its potential use as a diagnostic and screening tool.
REFERENCES


ABSTRACT

Dislocation remains a serious concern for total hip arthroplasty (THA). Impingement, typically between the implant femoral neck and the acetabular cup, remains the most common dislocation impetus. Wear reductions from recent bearing technology advancements have encouraged introduction of substantially increased femoral head diameters. However, there is some evidence that range of motion with larger head sizes is limited by bone-on-bone, rather than hardware, impingement. While all impingement events are of course undesirable, currently little is known biomechanically if these two impingement modes differ in terms of generation of potentially deleterious stress concentrations or with regard to dislocation resistance. Finite element (FE) analysis was therefore used to parametrically investigate the role of head diameter on the local biomechanics of bone-on-bone versus component-on-component impingement events. Of several dislocation-prone patient motion challenges considered, only squatting consistently resulted in bone-on-bone (as opposed to hardware) impingement. Implant stress concentrations arising from hardware impingement during squatting were greater than those from bony impingement, for all head sizes considered. Additionally, dislocation resistance was substantially greater for instances of bony impingement versus hardware-only impingement. These findings suggest that hardware impingement may still be a/the predominant mode of impingement even with the use of larger femoral heads, for sub-optimally positioned cups. Additionally, the data indicate that, should impingement occur, impingements between the implant neck and cup are (1) more likely to dislocate, and (2) have a greater propensity for causing damage to the implant compared to impingement events involving bony members.

INTRODUCTION

Owing to recent adoption of advanced low-wear bearings, as of 2009, instability had surpassed osteolysis as the leading diagnosis requiring revision surgery in total hip arthroplasty (THA) 1. The risk factors for dislocation in THA are numerous and varied 2-10. Many of these factors involve damage to the periarticular soft tissues, or they involve the geometrical design and surgical orientation of the implant. Regardless of the underlying risk factor, impingement is the proximate mechanism for the overwhelming majority of dislocations 11. In this situation, the femur (either native or implant) impinges on bone, on soft tissue, or on the acetabular component of the implant, constituting a fulcrum about which there is tendency for levering-out of the femoral head from the cup. Widely recognized mechanisms to reduce the incidence of impingement include meticulous component positioning and the use of larger diameter femoral heads. Larger femoral head sizes have been statistically associated with improved implant stability in most 5, 10, 12, 13 (but not all 14) clinical studies.

In conventional-sized THAs (22-32mm), impingement typically occurs between the implant femoral neck and acetabular cup. Therefore, the vast majority of experimental studies of THA impingement and range-of-motion have used THA hardware components tested in isolation. Additionally, from the viewpoint of experimental practicality, hardware-only studies are substantially more practical to execute. However, both cadaveric 15 and mathematical 16 studies have suggested that bone-on-bone impingement predominates for femoral head diameters greater than about 32mm to 36mm. To date, large-head impingement mechanics studies have been limited by (1) only reporting impingement-free range of motion, and (2) only utilizing simplified joint motions. To clarify the different consequences of bone-on-bone versus hardware impingement as regards instability and/or potential implant damage, a dynamic finite element (FE) model of THA impingement was developed to investigate the role of femoral head size and impingement modality for large-diameter total hips.
MATERIALS & METHODS

The study utilized a previously validated FE model of a widely used contemporary THA implant (Summit stem, 36mm M-spec head, 36mm x 56mm Pinnacle cup, DePuy Orthopaedics, Warsaw, IN) generated from manufacturer-provided engineering CAD files. Implant geometry was pre-processed using TrueGrid (v. 2.3 XYZ Scientific Applications, Inc., Livermore, CA) and Mathcad (v. 14.1, PTC, Needham, MA) software. Seven distinct femoral head diameters were considered (32mm to 44mm, in 2mm increments, Fig. 1). The models were generated by projecting the outer surface of the femoral head mesh onto correspondingly scaled surfaces representing the outer diameter of the implant femoral head. Appropriate mesh densities for each model were determined from prior convergence studies. Bony anatomy of the pelvis and femur was determined by manual segmentation of the Visible Human data set (National Library of Medicine, Bethesda, MD). The bony anatomy was registered to the pelvic reference frame of the FE model. Virtual femoral osteotomy and pelvic reaming were performed using Geomagic Studio (v. 12, Geomagic Inc., Research Triangle Park, NC). The acetabular components were then positioned in a consensus neutral orientation (40° inclination and 15° acetabular anteversion).

The implants were modeled as linearly elastic metal-on-metal, (CoCr, elastic modulus = 210 GPa, Poisson’s ratio = 0.3), with 0.029 mm of radial clearance and with a friction coefficient of 0.19. To economize computational run time, the bony anatomy, cup backing, and distal regions of the femoral component were assigned rigid body definitions. In all cases, the femoral component was positioned in 10° of anteversion.

Two separate FE series were conducted (Fig. 2). The first was undertaken to determine the impingement propensity for various impingement-prone patient motions. The second series investigated differences between hardware and native bony impingement events, for different cup orientations. For the first series, nine candidate impingement challenge motions were considered: pure flexion, as well as six posterior dislocation maneuvers (sit-to-stand from a low chair, sit-to-stand from a normal height chair, seated leg crossing, seated leaning, stooping, and deep squatting) and two anterior dislocation challenges (rolling over in bed, and standing exorotation/pivoting), for a 42mm implant in consensus-neutral cup orientation. Of these various dislocation challenges, only pure flexion and squatting consistently resulted in bone-on-bone impingement for the neutrally-oriented cup (Fig. 3).

After identifying that squatting was the most discriminational motion challenge leading to bone-on-bone impingement, a second (larger) FE series was undertaken (Fig 2). For this second series, the effect of head size on bone impingement was investigated by considering all seven femoral head sizes for the squatting challenge with a neutral (40° abduction) cup orientation, a situation for which bone impingement occurred between the bony members (referred to as “B-B”). Seven additional FE models were generated with a more horizontal cup orientation (30°), resulting instead in implant neck-on-cup impingement, also for the squatting challenge (referred to as “I-I”). To then eliminate cup orientation as
Bone-on-Bone versus Hardware Impingement in Total Hips: A Biomechanical Study

For neutrally-positioned cups, of the nine candidate challenge motions, only pure flexion and deep squatting resulted in impingement, and that impingement was bone-on-bone. None of the other candidate challenges resulted in either form of impingement. Pure flexion resulted in impingement between the bony femoral neck and the anterior acetabular rim, at approximately 100° of flexion. Squatting resulted in bone impingement between the bony femoral neck and a region near the anterior inferior iliac spine, which occurred at about 105° of hip flexion.

For the component-on-component (I-I30) simulations, impingement events during the squatting challenge generated significantly higher impingement-associated edge loading implant stresses than occurred for either of the two bony impingement situations (Fig. 4). Both situations of bony impingement (B-B40 & B-B30) involved generally similar stresses. Edge loading stresses for all three impingement conditions decreased with increased head diameter, the effect being most pronounced for the hardware impingement events. Peak resisting moments developed for the two B-B impingement situations were, on average, 5.5- and 2.6-fold higher than for hardware impingement, and tended to increase with increased head size (Fig 5).

**RESULTS**

For neutrally-positioned cups, of the nine candidate challenge motions, only pure flexion and deep squatting resulted in impingement, and that impingement was bone-on-bone. None of the other candidate challenges resulted in either form of impingement. Pure flexion resulted in impingement between the bony femoral neck and the anterior acetabular rim, at approximately 100° of flexion. Squatting resulted in bone impingement between the bony femoral neck and a region near the anterior inferior iliac spine, which occurred at about 105° of hip flexion.

For the component-on-component (I-I30) simulations, impingement events during the squatting challenge generated significantly higher impingement-associated edge loading implant stresses than occurred for either of the two bony impingement situations (Fig. 4). Both situations of bony impingement (B-B40 & B-B30) involved generally similar stresses. Edge loading stresses for all three impingement conditions decreased with increased head diameter, the effect being most pronounced for the hardware impingement events. Peak resisting moments developed for the two B-B impingement situations were, on average, 5.5- and 2.6-fold higher than for hardware impingement, and tended to increase with increased head size (Fig 5).
DISCUSSION

Impingement of the implant neck on the implant liner (I-I impingement) is commonplace, with corresponding liner rim damage being reported in a majority of explanted conventional-sized THAs \(^1\), \(^2\), \(^3\). However, the recent shift toward advanced low-wear bearing couples has enabled the use of larger diameter femoral components, that theoretically better protect against I-I impingement by allowing for increased angular excursion prior to such contact. It has been previously suggested, however, that the theoretical range of motion in these new larger components actually many not be achieved in practice, due to bone-on-bone impingement first occurring. Using a cadaveric model, Bartz et al. \(^4\) contended that I-I impingements constituted only 50% of impingements for 28mm femoral heads, and only 30% of impingements for 32mm head diameters, the remainder of impingements being B-B. However, that study was limited in terms of the motion analyzed (only pure hip flexion, ostensibly simulating chair rising), and it involved only a single cup position (neutral). Reports of a similar transition from I-I impingement to B-B impingement with increasing head sizes considered, the impingement-associated edge loading stresses induced by implant neck-on-liner impingement approached or exceeded the yield strength of cobalt-chrome alloy. Altogether, this suggests that, should impingement occur, events of impingement involving the implant neck and cup are (1) more likely to dislocate, and (2) more prone to result in hardware damage, as compared to bone-on-bone impingements.

It has oftentimes been suggested (based on purely geometrical considerations) that bone-on-bone impingement is the limiting factor for joint range of motion in large-diameter THAs. However, the present investigation provides convincing evidence that hardware-only impingement is physically very possible for various dislocation-prone motions, if the implant components are sub-optimally positioned surgically. Additionally, while B-B impingement was found to occur with pure flexion as well as with deep squatting for neutrally positioned cups, it did not occur for the other motion challenges. This suggests that while B-B impingement may in fact be the predominant limiting factor in certain situations for larger diameter THA, B-B impingement is still a rather unusual occurrence, even for high-risk patient motions.

This investigation has a number of limitations. First, only a single bony geometry was used. While this particular “standard” Visible Human geometry has been very widely used in a host of scientific investigations, it is a reasonable assumption that individual variants in bony geometry could directly influence both the occurrence of bony impingement, and the kinetics of impingement-associated edge loading contact stress generation. However, given the large difference in the intrinsic dislocation resistance and surface stresses between instances of bone-on-bone versus implant-on-implant impingement, it is likely that specific normal-range variants in bony anatomy would have a only a minor/modest effect on impingement dynamics. Secondly,
while several impingement-prone kinematic challenges were considered, these obviously still represent only a small subset of possible impingement scenarios. Nevertheless, the selection of motions considered in the present study represents a much more comprehensive sampling than for any other impingement study conducted to date.

In summary, should impingement occur, contact between the bony femur and pelvis is substantially less detrimental than contact between the implant neck and cup. Larger femoral heads, regardless of impingement location, result in less impingement-associated implant edge loading stress and have greater dislocation resistance.

ACKNOWLEDGMENTS
We thank the NIH (AR46601 and AR53553), the Veterans Administration and the National Center for Resource Resources (UL1 RR024979) for financial assistance.

REFERENCES
SURGEON AGE AS THE MAJOR FACTOR IN RECOMMENDATION OF UNI-COMPARTMENTAL KNEE REPLACEMENT VERSUS HIGH TIBIAL OSTEOTOMY A CASE STUDY IN ORTHOPAEDIC DECISION MAKING

Frederick R. Dietz*, MD and Mark G. Kelman#

ABSTRACT
This case report concerns surgical decision making. The subject is a 59 year old male orthopaedic surgeon with medial compartment knee arthritis. Both high tibial valgus osteotomy and uni-compartmental knee replacement would be appropriate with similar outcomes reported in the literature. Surprisingly, almost all young surgeons recommended a uni-compartmental knee replacement and almost all older surgeons recommended a high tibial osteotomy. We discuss the reasons that surgeon age, which is clearly irrelevant to the optimal decision, is the dominant determinant of surgical recommendation for this patient.

INTRODUCTION
Little has been written on decision making in orthopaedic surgery. It is generally assumed that treatment decisions are made by the physician and a properly informed patient in consultation. The orthopaedic literature generally addresses how best to measure desirable outcomes and how specific treatments affect these outcomes. The desirable outcomes are almost always a limited number of aspects of physical functioning. There are many more general models of how to optimize medical decision making. For example, classical economic utility analysis assesses the worth of a medical procedure by attempting to ascertain what a person would give up in other goods or services for a certain amount of health, then adjusting that sum to account for the objective probability of reaching the desired outcome and for the risk proclivity of the patient and comparing that figure to the full cost of the procedure (in resources, in time, and in other health risks). Capability analysis emphasizes not so much how patients subjectively value, at the time they must decide what steps to take, the changes in health status they will experience as it emphasizes the need to take whatever steps maximize human potentials over a lifespan. However, all evaluation approaches include physical functioning as a major component. Therefore, it may seem that such decision making analysis is not very relevant to orthopaedic surgery in which the goal is most often to maximize physical functioning. We discuss specific decision making difficulties in a specific, common orthopaedic surgical problem.

The literature does not often address how a surgeon should decide whether to recommend to a patient one particular procedure as opposed to another designed to meet broadly similar aims. Optimally, for a specific problem in a specific patient, there exists a combination of sufficient evidence, surgeon experience and patient characteristics that allows a surgeon to recommend a single procedure as the “best” choice given typical patient desires or uncontroversial ideas about capability maximization—evidence based medicine. Many times the evidence is lacking, even when looked at for a large group of patients. Not uncommonly, too the patient has characteristics that are unusual, so that the “best” procedure for the particular patient may not be the procedure that would more typically be superior.

What we want to address here is the surgeon’s decision making biases in a specific case. Multiple biases in medical decision making have been identified. Anchoring bias (excessive reliance on one trait or piece of information), attribution bias (substitution of a simple characteristic(s) as representative of a complex problem), availability bias (over estimating the likelihood of an outcome based on the vividness of examples of the outcome which make them more memorable) and confirmation bias (tendency to interpret data so that it confirms one’s preconceptions) are several that have been well described. Most of these biases have been described in the context of medical errors, most commonly misdiagnosis. The type of bias we are considering here is a bias in the statistical sense of a systematic alteration in what would be expected to be randomly distributed data or, in this case, surgical recommendations. It is not to be interpreted as a distortion due either to prejudice or to the use of a decision making procedure that always leads to systematic, unambiguous error, although those possibilities will be discussed.

The critical point we address is that the age of the surgeon making a recommendation alters the surgical
recommendation, though the surgeon’s age (though not the patient’s) is quite transparently irrelevant to the correct choice of procedure. (This would be true except in the unlikely situation, not germane here, that a surgeon’s age is a good proxy for his competence in distinct procedures: hypothetically, it might, for instance be appropriate for younger, more recently trained surgeons to recommend a recently developed operation they are more familiar with rather than an older operation that older surgeons might still feel will lead to superior outcomes should they perform the operation, given their skill with the more traditional method.)

There is no discussion in the medical literature of the effect of surgeon age on decision making of which we are aware.

We will accept that maximizing physical function is the main goal of most orthopaedic surgery and will examine a specific case in which surgeon age predicts the procedure the surgeon recommends.

We address the following questions. Does the age of the surgeon relative to the age of the patient influence or even determine his/her surgical recommendation between two essentially equivalent operations? If so, why does the age of the surgeon determine which of two operations he/she recommend? Furthermore, should a surgeon’s age affect his/her choice if his/her training is identical for all of the surgeons making the recommendation? This is a report of the effect of surgeon age and stage in career on the recommendation for either a high tibial osteotomy (HTO) or a uni-compartmental knee replacement in a specific patient.

CASE REPORT

The patient is a 59 and ½ year old male orthopaedic surgeon with a chief complaint of left medial knee pain.

Present Illness

The knee pain came on relatively acutely after playing 5 hours of tennis one day. Swelling was present the next day, but resolved rapidly. Activity related pain at the medial joint line persisted. The pain has been present for 8 months. The patient is unable to run. The pain is present with every step—usually mild when walking and severe with attempted running. No pain at rest. The knee pain is localized to the medial joint line and has not improved with PT, rest, NSAID’s, lidocaine/corticosteroid joint injection (although this temporarily completely relieved the symptoms.) He is somewhat better with an “un-loader” brace when walking, but it does little for running symptoms. He is very sore after standing for a day in the operating room. He wishes to remain active.

Past Medical History

He has had previous bone-patellar tendon-bone ACL grafts in both knees and both knees have had one or two meniscal partial resections for symptomatic tears. These resulted from sports injuries. He has mild/moderate hypertension and elevated cholesterol that are well controlled medically.

Physical Examination

He is moderately overweight. He has mild varus alignment of the legs. He has a stable knee to examination.

Imaging

Anterior-posterior lower extremity alignment films show mild varus (Fig. 1). Posterior-anterior flexion radiograph shows loss of medial joint space (Fig 2). MRI shows loss of medial joint cartilage (Fig 3). Valgus stress anterior-posterior radiograph showed a normal lateral joint space.

Impression

Medial joint osteoarthritis in a stable knee in a nearly 60 year old physically active man; unresponsive to conservative measures.

Recommendation

High tibial osteotomy (HTO) or uni-compartmental knee replacement.

CAVEATS

At the University of Iowa, where the patient sought treatment, orthopaedic residents are taught that the literature does not show a clear difference in outcomes between these two procedures in patients of this age. Although individual faculty has opinions as to which procedure is better, they are not presented as evidence based. Furthermore, at this institution, all HTO’s are done as opening wedge procedures whereas most of the literature deals with closing wedge osteotomies. All the uni-compartmental knee replacements at this institution are Oxford Partial Knee Replacement, though the literature includes other uni-compartmental knee replacement devices. This allows speculation that between opening wedge HTO and Oxford uni-compartmental replacements there may in fact be a significantly better choice. But no compelling comparison of these two specific options has been done. If relying on the existing literature, a surgeon should be expected to be at equipoise with respect to the two operations. In practice surgeons may have opinions about which procedure is preferable due to an imperfect literature.

METHODS

The above history and physical and imaging studies were sent to all the resident/fellow orthopaedic surgeons and faculty orthopaedic surgeons by the patient in what he thought would be an interesting educational exercise. He asked them to make a recommendation for his surgery between these two procedures. Some
FIGURE 1. Bilateral antero-posterior full leg radiograph showing varus alignment and interference screws from prior patellar bone-tendon-bone ACL reconstructions.

FIGURE 2. Posterior-anterior flexed knee radiograph showing medial joint space narrowing.

FIGURE 3. MRI STIR sagittal image of medial knee showing absent articular cartilage.
facult y recused themselves due to lack of familiarity with the treatment issues of medial knee joint compartment osteoarthritis in late middle age/early elderly patients. No hand surgeons offered an opinion, for example. Some residents did not answer, either because they were too junior to have been exposed to all the issues or for other reasons. What is critical to note is that if residents (younger) differed from faculty (older) in their recommendations, it was not because they had been trained by people who may have different beliefs about the superiority of one procedure to the other for patients of this age, given this set of indications. They had all been trained by the faculty whose opinions were also being solicited. If residents are making different recommendations from faculty, they are certainly not simply doing so because they were instructed to believe something different than the faculty believed about appropriate treatment.

RESULTS

The total possible response groups include 29 residents and fellows (interns were excluded) and 22 clinically active faculty. Thirteen residents/fellows responded (45%) and 12 faculty responded (50%).

Of the residents and fellows, eleven recommended uni-compartmental knee replacement and two recommended HTO. Of the faculty, nine recommended HTO and three recommended uni-compartmental knee replacement. The difference between resident/fellow and faculty recommendations was assessed by Fisher exact test and was significantly different with a P value=0.0048. Faculty age averaged 49 years and 3 months (range 33-70 years). Resident/fellow age averaged 31 years and 4 months (range 29-36 years). The youngest faculty member, 33 years of age, recommended a uni-compartmental and the oldest resident/fellow at 36 years old recommended an HTO.

DISCUSSION

Why did the residents/fellows and faculty choose different operations for this patient? Looking at the existing literature, it would appear that either option seems reasonable for patients from approximately age 55-65. One could reasonably expect all surgeons to be at equipoise with respect to the two options. Nearly all of the respondents would recommend an HTO for a 30 year old active person, since a uni-compartmental replacement would not be expected to last his lifetime. Similarly, all would recommend a uni-compartmental knee (some a TKR) for medial knee arthritis in a 75 year old as it can be anticipated to be a definitive procedure with more rapid recovery than an HTO.

Nonetheless, all the respondents did have a preference. None said, "I really can't make a recommendation; the patient should decide." This might be because all respondents were very familiar with the particular patient and were asked to pick a single choice. But even in a more typical clinical setting, the response to a statement that there are two equivalent operations for a problem by most patients would be "what would you do?" so it is likely that the recommendations elicited here mirror those that would be elicited in a more typical setting.

For a few respondents, obvious sources of bias can be identified. One faculty recommending the HTO is a sports medicine physician who only does HTO's. The 2 faculty who recommended uni-compartmental knee replacement are both joint arthroplasty surgeons who do not perform HTO's. However, excluding the responders with a clear bias based on their familiarity with only one procedure in their practice would only increase the statistical significance of the distinction in responses between faculty and residents. The one faculty member, who performs both HTO and uni-compartmental in his practice, recommended HTO. Both residents recommending HTO have played sports with the patient. But several resident/fellows who played sports with the patient recommended uni-compartmental knee replacement.

Perhaps a single strong faculty personality has convinced the residents/fellows that uni-compartmental is the best option? This seems implausible because only one junior arthroplasty surgeon performs uni-compartmental knee replacements regularly and the head of sports medicine service is a strong advocate of HTO.

A parsimonious explanation for the results may be that both groups of surgeons are, in the first instance, using a heuristic, attending only to a single, readily processed cue (patient age), to circumvent the need to make a complex judgment that accounts for a multitude of potentially relevant traits. Heuristics users typically make decisions lexically – that is, if one choice is superior to another along a single most significant dimension, they make that choice and attend to a second differentiating factor only if there is a tie along the first dimension, and to a third only if there are ties along the first two etc. (Think about comparing the size of numbers, which we do lexically: 812 is a larger number than 798 because the “8” in the hundreds column is bigger than the “7,” and we need not compare differences in the tens and ones.) Those using conventional, non-heuristic based rational choice methods typically process cues in a what is generally dubbed a compensatory fashion, balancing virtues (of greater or lesser magnitude) in some domains against flaws (of greater or lesser magnitude) along others.

Thus, a heuristic user may only note that a patient is above or below some threshold of “old” rather than attending to a host of other variables that would seem to affect the decision, such as the patient’s activity level, life expectancy, probability of experiencing distinct complications associated with each procedure, desire with
respect to recovery time, and anticipation of surgery for another joint. Essentially this heuristic substitutes a simple question for a complex question. Instead of asking “what is the better of two similar procedures for this particular complex human being?” one substitutes the question “is he old?” This bias is a type called “attribution substitution”. Attribution substitution is attending to an easily processed cue as a substitute for considering more complex information. It is common to observe this sort of heuristic decision making process. When people engage in “stereotyping,” another common form of attribute substitution, they use an easily processed cue – age, gender, race – as a proxy for more complex traits that are actually of interest (vulnerability to disease, trust-worthiness, stamina, etc.). We can readily imagine how using the attribution substitution heuristic was adaptive in an evolutionary sense if the error costs of use were lower than the costs of obtaining and processing greater amounts of information. Using the heuristic can misfire when the single attribute selected is poorly representative of the individual or group at issue.

But the question that remains, if all surgeons recommend HTO for the “young” and replacement surgery for the “old,” is why residents/fellows see a 60 year old man as being old, with limited life expectancy and limited physical capacity, while faculty sees the patient as not-old, with a lot of good life left and plenty of physical capacity. It would have been possible to find that patient age is the only cue that surgeons attend to in deciding between these procedures, but that they all agree that when a patient reaches a particular chronological age, he is now “old enough” that replacement is appropriate, and not until then. Instead, what we observe is the use of what seems like a second-order heuristic to implement the heuristic that assigns one procedure to the old and a different one to the young. At this second level, the residents/fellows might “stereotype” all people “roughly” 30 or more years older than they are as old and the faculty may “stereotype” people “near” their own age as not old. Perhaps only one group of respondents is using a stereotyping heuristic. The faculty may have a more accurate view of the life of a 60 year old, and this is not “stereotyping.” Alternatively, the residents may more accurately understand the remaining years and quality of physical activity of a 60 year old and the faculty are engaging in a form of denial—“no one my age should have an elderly person’s operation.” What is curious, though, is that the use of a “relative age” heuristic to determine whether a patient “is” old does not serve information-economizing functions: chronological age is just as immediately perceived and easily processed as relative age. So if the surgeons are using some sort of “relative age” heuristic, it is not one readily explained in the most conventional terms (as a strategy to make use of readily available and easily recognized information to make a judgment that typically meets the subject’s ends.)

Thus, we seem to have observed is something like a physician/patient relative age evaluative bias. This bias has not been discussed to our knowledge in medical decision making but the psychological underpinnings of this bias are well studied. Humans value years in the future differently based on their present age. Simply stated, the years from 70 to 80 are more highly valued by a 50 year old than a 30 year old. This has been demonstrated, for example, by asking people how many years of life they would exchange for something else, such as a painless death or a disability free elderly period. The older one is, the more one values the remaining years.

It is also possible that humans intuitively, and much more effortlessly, perceive age in relative, not absolute terms. People are indeed quickly classified as “old” or “young” based on relative age because only those relative judgments typically matter—whether in terms of evolutionary imperatives or for more immediate functional reasons that have little bearing on inclusive fitness. A person we see is too old (or young) to mate with; old enough to be owed deference in hierarchical communities or young enough to be owed protection or guidance, etc. Of course, even if it is generally appropriate to make quick judgments of age based on relative age, it may well be inapt in this setting: the young surgeon is not being asked to judge whether the patient is an apt mate, for instance, and if the surgeon is using an age judgment metric designed for that task, rather than for the task of evaluating which operation is apt, he will be displaying a bias in the pejorative sense of the word.

Physician/patient relative age bias is type of inter-temporal bias. This may be relevant for many orthopaedic decisions. For example, there may be a major difference in how a 16 year old with aseptic necrosis of the hip values the hip mobility and relatively normal function for the next 10 to 20 years of their life compared to a 50 year old surgeon’s assessment of the importance of those years. The surgeon may be concerned about the inability to replant a multiply replaced or infected total hip replacement as the patient ages and recommend a hip arthrodesis to be converted to a total hip replacement when the patient is older. The teenager, though, might reasonably contend that the years from 15 to 30 are critical in establishing career and mate and status and that having a visible disability might compromise his ability to optimize along these dimensions. The surgeon can reasonably contend that there is a long full life after fifty that might be compromised by an unstable, un-re-implantable failed total hip. It seems clear that there is not a technical or literature based way to adjudicate between these opinions.
The question remains whether surgeons would make more similar recommendations— and perhaps more defensible ones—if they were to take a more nuanced history and perform a more patient-specific evaluation, rather than relying on a “patient age” heuristic. What factors might be left out if doctors attend only to chronological age? The life expectancy for a patient born in 1951? The particular patient’s expectation of longevity? The patient’s expectations about his level of continued physical activity? The patient’s risk averseness to certain types of complications, e.g., artificial joint infection vs. HTO non-union? Patient’s beliefs concerning ease of revision to TKR if needed? Other limiting musculoskeletal issues, particularly this patient’s expectations for his multiply operated contralateral knee? Does it matter that the patient recently took up triathlons? Does it matter that the patient still hopes to play softball on the departmental team and expects to do well in his age group at USTA tennis tournaments? These are factors that might allow a more nuanced recommendation by the surgeon and choice by the patient. They are often unstated. A checklist of such factors—expected longevity, activity level, etc.—might result in more reasoned judgments, though the general literature on heuristics shows many instances in which efforts to make people consider additional factors simply fail. Certainly, though, the surgeon’s age is irrelevant to the choice.

Whether it is ultimately sensible or not, rather than merely economical in terms of decision-making resources, to use patient age lexically, rather than attempt to assess each particular patient’s needs and condition with greater particularity is a question we won’t really address. (It is worth noting, though, that there are psychologists, associated with what is generally dubbed the “fast and frugal heuristics” school,12,13, who believe that lexical methods, or decision-making procedures that rely on a very small number of cues if not a single differentiating one, are often superior, in the medical context, to multi-factor balancing tests, without regard to information-processing costs; and others, associated with the “heuristics and biases” school, e.g., Tversky and Kahneman, who sharply criticize these claims, but this dispute is outside the bounds of this paper (For a fuller discussion of the dispute, see reference 14). It is certainly possible that at the first level recommending between uni-compartmental knee replacement and HTO based simply on age might be a “good enough” heuristic. Nuances of health, activity level, expected longevity might augment the decision making process, but age is the single most important variable.

Should surgeons be aware of their changing biases as they age? If so, who is right—the young or the old surgeons? What can or should a surgeon do about this bias? Since the operations’ outcomes are nearly equivalent, does it even matter? We think it is possible that being aware of potential stereotyping might prompt a surgeon to take a more nuanced history and explore with the particular patient of his/her expectation in determining the choice between two operations with similar outcomes in more general populations. Simply being aware of potential biases might then help the surgeon give better advice.

REFERENCES
CT SCANS FOR PULMONARY SURVEILLANCE MAY BE OVERUSED IN LOWER-GRADE SARCOMA

Benjamin J. Miller, MD1, Emily E. Carmody Soni, MD2, John D. Reith, MD3, C. Parker Gibbs, MD3, Mark T. Scarborough, MD3

ABSTRACT

Chest CT scans are often used to monitor patients after excision of a sarcoma. Although sensitive, CT scans are more expensive than chest radiographs and are associated with possible health risks from a higher radiation dose. We hypothesized that a program based upon limited CT scans in lower-grade sarcoma could be efficacious and less expensive. We retrospectively assigned patients to a high-risk or low-risk hypothetical protocol. Eighty-three low- or intermediate-grade soft tissue sarcomas met our inclusion criteria. Eight patients had pulmonary metastasis. A protocol based on selective CT scans for high-risk patients would have identified seven out of eight lesions. The incremental cost-effectiveness ratio for routine CT scans was $731,400. A program based upon selective CT scans for higher-risk patients is accurate, spares unnecessary radiation to many patients, and is less expensive.

INTRODUCTION

The identification of pulmonary metastatic disease is important, as its presence or absence affects treatment and prognosis.1-14 The two primary imaging options are chest roentgenograms and computed tomography (CT). Radiographs are quick, relatively inexpensive and accessible, and they minimize radiation exposure.15 CT scans expose the patient to higher doses of radiation and are more expensive.16-20 However, the detail and information provided in a CT scan is superior to a radiograph.15, 21, 22 The preferred method of pulmonary surveillance in soft tissue sarcoma remains controversial.23-31 Elimination of unnecessary CT scans would be beneficial to patient safety and cost savings. Recent reports in the literature have raised concerns about a causative effect with excessive radiation exposure from CT scans and subsequent development of malignancy.16, 19 In this tumultuous era of health care reform, there is continuing pressure to eliminate superfluous diagnostic studies and interventions. It is an appropriate time to make a real effort in determining the most effective form and frequency of monitoring post-resection sarcoma patients.

Our hypothesis was that CT scans are over utilized in low-risk patients. We questioned whether CT scans could be used selectively while retaining overall efficacy. We determined risk factors for pulmonary metastasis to aid in the hypothetical implementation of selective CT scans. Any reduction in CT scans would be expected to result in a cost benefit.

MATERIALS AND METHODS

We identified 139 low- and intermediate-grade soft tissue sarcomas resected for cure and monitored postoperatively at our institution from March 1994 to April 2008. Patient charts, including clinical notes, operative notes, pathology reports, and radiology reports were reviewed for completeness of documentation. All included patients required an official pathology report from our institution stating the diagnosis, grade, and margin. When a grading system was reported, grades 1-2/3 and 1-2/4 were allowed into the study. Two years of radiographic follow-up were required. We excluded patients with high-grade sarcoma, metastatic disease at diagnosis, absent pathology reports, retroperitoneal location, and primary bone sarcoma. Patients with local recurrence or distant metastasis after their initial surgery were included regardless of length of follow-up. This study was approved by our Institutional Review Board.

The algorithm for pulmonary surveillance currently used at our institution for low- and intermediate-grade lesions is a CT scan at baseline and every four months for years 1 and 2, every six months for years 3 through
CT Scans for Pulmonary Surveillance May Be Overused in Lower-Grade Sarcoma

5, and a chest radiograph annually after five years. The primary outcome measures were evidence of local recurrence, distant lung metastasis, distant non-lung metastasis, or no evidence of disease. All local recurrences were confirmed histologically. Lung and non-lung metastases were either confirmed histologically or had progressed with serial imaging studies consistent with metastatic disease.

We compared patients with pulmonary metastases to those without, to determine corresponding risk factors. Chi-square or Fisher’s exact test were used for statistical analysis for nominal variables depending on the group size. Continuous variables were analyzed using t tests. Logistic regression was performed in an attempt to elucidate further associations between independent variables.

Factors from our outcome analysis that had p values < 0.05 were considered characteristics that placed patients at high risk for developing pulmonary metastasis. We then retrospectively “assigned” our cohort into a low-risk, chest radiograph-based protocol, or a high-risk, routine chest CT-based protocol (Fig 1). We then re-analyzed the patients with pulmonary metastases to see if their lesions would have been accurately identified using hypothetical selective CT scans. A low-risk protocol based upon chest radiographs was selected for comparison simply because it is the most reasonable alternative to chest CT scans. We did not attempt to compare the diagnostic ability of chest CT scans and chest radiographs.

We performed a cost analysis by using the Incremental Cost-Effectiveness Ratio (ICER). This tool has previously been implemented for comparisons such as this. It is calculated by dividing the difference in the costs of the test per patient by the gain in diagnostic yield. This value represents the spending required to identify each additional lesion in the higher-yield protocol. Our institution’s current hospital and professional fees for a chest CT without contrast is $1,571. The cost for a PA/lateral chest radiograph is $191. We also performed a sensitivity analysis to look at the change in ICER given two separate assumptions. The first assumption is that the cost of a chest CT is half as much as it is currently; the second, that the yield of the selective CT protocol is only half as much as with routine CT scans for all patients.

**RESULTS**

We initially found 139 low- and intermediate-grade soft tissue sarcomas that met our inclusion criteria. Twenty-two patients had dermatofibrosarcoma protuberans (DFSP) and 30 had well-differentiated liposarcoma. None of these had pulmonary metastases. The documented pulmonary metastatic rates of these tumors are so low that we did not think it appropriate to include them in our analysis. Four patients died of non-oncologic processes at less than two years, leaving a cohort of 83 patients for analysis.

There were 47 females and 36 males. The median age was 52.1 years (range 11-86 years). The median radiographic follow-up was 4.4 years (range 0.6-14.9 years) with a minimum of two years in patients without local recurrence or distant metastasis. There were 46 low-grade and 37 intermediate-grade lesions. The histologic diagnoses consisted of liposarcoma (28), fibrosarcoma (27), malignant fibrous histiocytoma (8), leiomyosarcoma (8), spindle cell sarcoma (3), hemangiopericytoma (3), hemangioendothelioma (2), malignant giant cell tumor of soft parts (2), and malignant peripheral nerve sheath tumor (2). Both of the hemangioendotheliomas were isolated lesions. For purposes of analysis, “lipomatous and fibrous tumors” included any histologic diagnosis of liposarcoma, fibrosarcoma, malignant fibrous histiocytoma, and their variants.

In our cohort of 83 patients, we noted local recurrence, distant metastases, and/or nodal spread in 20 patients. Twelve patients had low-grade tumors and eight had intermediate-grade. Eight patients had pulmonary metastases (9.6%) (Table 1). The median time to pulmonary metastasis was 13.2 months (Table 2). All of the pulmonary metastases were discovered during routine surveillance and none of the patients were symptomatic.

We analyzed various tumor and patient characteristics in an attempt to quantify risk factors for pulmonary metastasis in order to determine when a selective CT scan should be performed (Table 3). Notable differences were found with regard to the presence of local recurrence (p = 0.013), non-lung metastasis (p = 0.002), and histology (p = 0.002). Patients with these clinical attributes were considered at high risk for metastases and placed into the selective CT limb of our hypothetical analysis. Although patients with local recurrence or distant metastasis would initially be started on the low-risk protocol.
### TABLE 1. Oncologic recurrence and spread by histology

<table>
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<th>Histology</th>
<th>Total number</th>
<th>Local recurrence</th>
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<th>Non-lung distance metastasis</th>
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<td>3</td>
</tr>
<tr>
<td>Fibromyxoid sarcoma</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>DFSP transformation</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Myxoinflammatory fibroblastic sarcoma</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Myofibrosarcoma</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
<td>8</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Spindle cell sarcoma</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Hemangiopericytoma</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Hemangioendothelioma</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Malignant giant cell tumor of soft parts</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>MPNST</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>All</td>
<td>83</td>
<td>12</td>
<td>8</td>
<td>5</td>
<td>3</td>
<td>20</td>
</tr>
</tbody>
</table>

MFH – malignant fibrous histiocytoma, DFSP – dermatofibrosarcoma protuberans, MPNST – malignant peripheral nerve sheath tumor

### TABLE 2. Details of patients with pulmonary metastasis

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Other disease(^1)</th>
<th>Time to metastasis (mo)(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Spindle cell sarcoma</td>
<td>Yes</td>
<td>7.0</td>
</tr>
<tr>
<td>2</td>
<td>Myxoid liposarcoma</td>
<td>Yes</td>
<td>9.3</td>
</tr>
<tr>
<td>3</td>
<td>Myxofibrosarcoma</td>
<td>Yes</td>
<td>20.0</td>
</tr>
<tr>
<td>4</td>
<td>Malignant giant cell tumor of soft parts</td>
<td>No</td>
<td>3.4</td>
</tr>
<tr>
<td>5</td>
<td>Hemangiopericytoma</td>
<td>Yes</td>
<td>11.2</td>
</tr>
<tr>
<td>6</td>
<td>Malignant giant cell tumor of soft parts</td>
<td>Yes</td>
<td>56.4</td>
</tr>
<tr>
<td>7</td>
<td>MPNST</td>
<td>Yes</td>
<td>73.6</td>
</tr>
<tr>
<td>8</td>
<td>Hemangiopericytoma</td>
<td>No</td>
<td>15.2</td>
</tr>
</tbody>
</table>

\(^1\)Local recurrence or non-lung metastasis  
\(^2\)Measured from date of primary tumor resection  
MPNST – malignant peripheral nerve sheath tumor

Our current algorithm of routine CT scans identified eight patients with pulmonary metastasis. Our hypothetical selective CT protocol would have identified all but one of these lesions. Seven of these patients would have been labeled high-risk, six for unusual histology and one for a nodal metastasis prior to pulmonary dissemination. In the remaining patient (patient 3), selective CT scans would not have been implemented. In reality, a surveillance CT scan showed diffuse pulmonary and abdominal metastases without a concurrent radiograph, and success or failure of our algorithm in this patient is unclear.

Using institution-specific administrative claims data from 2009, the cost per patient of the CT-based protocol was $15,289, compared to the selective CT protocol of $6,477. The yield of metastatic detection of the CT-based protocol was 9.6% (8/83), compared to 8.4% for selective CTs (7/83). This results in an incremental cost-effectiveness ratio of $731,400. This is the cost to identify an additional case of pulmonary metastasis us-
TABLE 3. Patient and tumor characteristics for pulmonary metastasis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pulmonary metastasis</th>
<th>No pulmonary metastasis</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Median (range)</td>
<td>51.6 (39-86)</td>
<td>52.1 (11-80)</td>
</tr>
<tr>
<td></td>
<td>Mean (std dev)</td>
<td>57.7 (16.0)</td>
<td>50.1 (17.9)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>5</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>3</td>
<td>44</td>
</tr>
<tr>
<td>Grade</td>
<td>Low</td>
<td>6</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>Intermediate</td>
<td>2</td>
<td>35</td>
</tr>
<tr>
<td>Size</td>
<td>&gt;5 cm</td>
<td>6</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>≤5 cm</td>
<td>2</td>
<td>36</td>
</tr>
<tr>
<td>Depth</td>
<td>Deep</td>
<td>7</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>Superficial</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>Location</td>
<td>Axial</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Lower extremity</td>
<td>5</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td>Upper extremity</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Proximal limb/trunk</td>
<td>4</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td>Distal limb</td>
<td>4</td>
<td>22</td>
</tr>
<tr>
<td>Margins</td>
<td>Intralesional</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Marginal</td>
<td>2</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>Wide</td>
<td>5</td>
<td>43</td>
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<tr>
<td>Outside excision</td>
<td>Yes</td>
<td>2</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>6</td>
<td>43</td>
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<tr>
<td>Procedure</td>
<td>Primary excision</td>
<td>6</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>Tumor bed re-excision</td>
<td>2</td>
<td>33</td>
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<tr>
<td>Recurrence on presentation</td>
<td>Yes</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>6</td>
<td>68</td>
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<td>1</td>
<td>37</td>
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<tr>
<td>Local recurrence</td>
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<td>8</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>4</td>
<td>67</td>
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<tr>
<td>Non-lung metastasis</td>
<td>Yes</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>4</td>
<td>71</td>
</tr>
<tr>
<td>Histology</td>
<td>Lipomatous / Fibrous</td>
<td>2</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>6</td>
<td>14</td>
</tr>
</tbody>
</table>

TABLE 4. ICER calculation and sensitivity analysis

<table>
<thead>
<tr>
<th>Assumption</th>
<th>Cost per patient ($)</th>
<th>Yield</th>
<th>ICER ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current data (Routine CT)</td>
<td>16,860</td>
<td>0.096</td>
<td>731,400</td>
</tr>
<tr>
<td></td>
<td>Selective CT</td>
<td>8,048</td>
<td>0.084</td>
</tr>
<tr>
<td>CT half as expensive</td>
<td>Routine CT</td>
<td>9,298</td>
<td>0.096</td>
</tr>
<tr>
<td></td>
<td>Selective CT</td>
<td>5,502</td>
<td>0.084</td>
</tr>
<tr>
<td>Selective CT yield decreased</td>
<td>Routine CT</td>
<td>16,860</td>
<td>0.096</td>
</tr>
<tr>
<td></td>
<td>Selective CT</td>
<td>8,047</td>
<td>0.048</td>
</tr>
</tbody>
</table>

Although recommendations pertaining to pulmonary surveillance after sarcoma excision exist, no uniform regimen is agreed upon. In higher-grade sarcoma, where tumor progression can be quick and relentless, close monitoring is warranted. This is not necessarily the case in low-grade lesions. We retrospectively separated our cohort of patients with lower-grade sarcoma into a low-risk or high-risk protocol in an attempt to minimize the number of CT scans. Our goals were to compare the diagnostic yield of selective and routine CT scans, and to calculate the incremental cost-effectiveness ratio. This would provide greater insight into the implications of limiting the number of CT scans for pulmonary surveillance.

We found an overall rate of pulmonary metastasis of 9.6%. There have been several investigations documenting the incidence of metastatic disease in soft tissue sarcoma with rates of 22-40%. When low-grade (grade 1) sarcomas are observed individually, the reported rates are 6-9%. Several authors have advocated minimal surveillance in low-grade sarcoma. Whooley et al concluded that chest radiographs were sufficiently effective for pulmonary surveillance and questioned whether early detection with CT results in any survival benefit. Kane et al felt that chest x-rays annually were sufficient for the monitoring of low-risk lesions. Lord et al actually questioned the necessity of any radiographic follow-up for low-grade tumors. The concern with an all-radiograph based protocol is the potential to miss relevant lesions that would be detected by CT scan.
A counter argument is that CT scans are overly sensitive. Reportsedly, 80% to more than 90% of non-calcified nodules on screening studies are felt to be benign.\textsuperscript{17, 21} At least, these findings warrant follow-up examinations - at most, an invasive procedure. Even in lesions that are felt to be worrisome enough to mandate biopsy or resection, 18-55\% are found to be false positives.\textsuperscript{18} In patients with sarcoma, Rissing et al reported that only 28\% of those with indeterminate nodules on CT had eventual evidence of metastatic disease, and that patients with lesions <5 mm had equivalent survival to those with completely normal scans.\textsuperscript{29} Although worrisome nodules in sarcoma patients should be addressed with suspicion, there is still a possibility of subjecting someone to the inherent risks of pulmonary resection or biopsy for an otherwise benign entity.

The consequences of radiation exposure from screening CT scans are becoming significant concerns in the literature and media. A generally accepted, although still debatable, means to assess low-dose radiation risk is the linear non-threshold model,\textsuperscript{20} in which the risk of radiation-induced malignancy increases incrementally with dose exposure.\textsuperscript{16} Brenner and Hall estimated that as many as 1.5-2.0\% of all cancers in the United States may be caused by radiation exposure from CT scans.\textsuperscript{19} The risks are cumulative and more pronounced in children.\textsuperscript{16, 19} The radiation dose from a chest CT scan is estimated to be nearly 100 times greater than a standard posterior-anterior and lateral chest radiograph.\textsuperscript{19} Although the risk of undetected cancer spread is greater than the risk of radiation-induced malignancy in these patients, it is sound practice to minimize unnecessary radiation when possible.

Monetary considerations should never be the sole reason to determine appropriate diagnostic or therapeutic intervention. However, as health care is continually becoming a more limited resource, it is responsible to ensure that we are at least being cost-conscious in our decision-making. Using current pricing, we estimated that it costs over $700,000 to find each additional case of pulmonary metastatic disease with our current routine CT protocol rather than one which utilizes selective CT scans for high-risk patients.

Weaknesses of this study include the heterogeneity in diagnosis and treatment inherent in most studies analyzing outcomes in rare conditions. The grading of tumors is a subjective art, and it is possible that the histologic appearance was initially misinterpreted in the clinically aggressive lesions. However, all slides were reviewed at the time of recurrence or metastasis and the retrospective grading remained consistent even with knowledge of the subsequent clinical course.

The small sample size limits the conclusions we can draw. The number of subjects was somewhat restricted by the nature of our institution as a large referral center requiring a substantial amount of travel for patients in many cases. As some patients elected to be monitored closer to their residence after surgery, our investigation was limited to those who agreed to be monitored under the guidance of our institution. We are not attempting to propose a protocol for generalized acceptance, but simply suggesting that the number of diagnostic CT scans in lower-grade sarcoma may potentially be decreased with few adverse consequences. Again, the lack of definitive conclusions is primarily attributable to the rarity of the condition and cannot be easily overcome in a single institutional study. As there is a paucity of literature on this subject, our hope is that our preliminary data will evoke thought and act as an impetus for continuing efforts to address this important issue with further investigations.

The goal of pulmonary surveillance is to detect lesions in a timely manner so that an intervention that changes the natural history of the disease may be implemented. A secondary goal is to comment on disease status and prognosis. An ideal algorithm would be able to predictably detect metastases, yet minimize the number of studies needed to accomplish these objectives. This is a complex topic which will require well-designed multi-institutional prospective studies to adequately address it. Larger studies will also help to better define criteria for designating high-risk patients. We found that implementation of selective CT scans could reduce unnecessary radiation exposure, accurately detect pulmonary lesions, and decrease the cost of monitoring lower-grade sarcoma.

CONFLICT OF INTEREST STATEMENT
We declare that we have no conflicts of interest relevant to this investigation. Dr. Gibbs is a consultant for Zimmer.

ACKNOWLEDGMENTS
The authors wish to thank Wei Hou, PhD for assistance with the statistical analysis.

REFERENCES


LIPOSCLEROSING MYXOFIBROUS TUMOR (LSMFT), A STUDY OF 33 PATIENTS: SHOULD IT BE A DISTINCT ENTITY?

Jonathan Dattilo, BSa and Edward F. McCarthy, MDb,c

ABSTRACT

Liposclerosing myxoid fibrous tumor (LSMFT) is a recently described bone lesion site specific to the proximal femur. We have studied the radiographs and clinical features of 33 patients with this disorder. Histologic material was available for study in 18 of these patients. Histologic study revealed that 12 of these 18 had an underlying fibrous dysplasia and these had an underlying intraosseous lipoma. Because of this histologic evidence as well as the radiographic spectrum of the other lesions, we conclude that LSMFT is not a specific lesion and use of the term should be discontinued.

INTRODUCTION

Neoplasms are classified by specific histologic and histochemical features. In bone, many neoplasms may be more specifically classified by their radiologic features. For example, low grade fibroblastic osteosarcomas may be classified based on whether they are surface or intraosseous lesions. In recent years, molecular genetics has altered the way we classify neoplasms. Many lesions, including those in bone, are classified based on their genetic signature.1, 2 For example, an XP-11 translocation is found in neoplasms occurring in numerous areas such as the kidney, soft tissue, and bone.3 This translocation defines this group of neoplasms more specifically than any histologic pattern.

It is rare for a distinct bone tumor to occur in only one site. Exceptions are adamantinomas, which occur almost exclusively in the tibia, and chordomas, which are found almost only in the spine. Both of these neoplasms have very specific histologic features. To suggest that a lesion with non-specific histologic and radiographic features is a new entity because it occurs in one location in bone is controversial.

However, this suggestion has been the case with a new lesion described in 1998 by Ragadale, et al. which they called liposclerosing myxofibrous tumor (LSMFT).4 This lesion was site specific for the proximal femur and had non-specific histologic features. Ragadale further characterized this lesion in 1993 using his experience with ninety five lesions.5 Then in 1999, Kransdorf, et al. from the Armed Forces Institute of Pathology, described 39 patients with LSMFT.6 They recommended that this lesion be accepted as a distinct bone tumor entity. Although this lesion is often diagnosed by radiologists,7, 8 careful pathologic study has suggested that LSMFT should not be regarded as a distinct entity. More likely, this entity represents degenerative changes in other well-defined bone lesions such as fibrous dysplasia and intraosseous lipoma.

This paper reports our study of 33 patients with lesions in the proximal femur that met the radiographic criteria suggestive for LSMFT. Histologic study was possible on 18 of these cases. In these eighteen cases, careful histopathologic study revealed that there was evidence of an underlying well defined bone lesion. Radiographic features in some of the other lesions also suggested underlying well-established bone lesions.

METHODS

These thirty-nine cases were collected and reviewed from the IRB approved database of the senior author. Clinical history and radiographic images were present on all 33 patients. Histologic material was available on 18 patients.
There were 20 male patients and 13 female patients. The age range was from 19 years to 80 years (mean age was 46 years). Ten patients presented with vague upper-leg pain. Two patients presented with a pathologic fracture. The remainder of the patients were asymptomatic, and their proximal femoral lesions were discovered incidentally during studies for other medical issues.

**RADIOGRAPHIC FEATURES**

All lesions occurred in the proximal femur, and all were centered in the inter-trochanteric region. Lesions were well defined, geographic luencies often with a sclerotic rim and varying amounts of interlesional radiodensity (Fig. 1). Bone contour was usually normal.

**HISTOPATHOLOGIC FEATURES**

Eighteen cases were studied histologically. Needle aspiration biopsies were performed on five cases. However, these biopsies were non-diagnostic and were followed by open biopsies. 13 cases were treated by curettage followed by bone grafting with or without internal fixation.

All cases showed areas of fibrosis, myxoid change, and reactive bone, the features described for LSMFT (Fig. 4). However 12 cases showed areas of spindle cell proliferation with woven bone. These areas would be diagnostic of fibrous dysplasia in any other bone (Fig. 5). Three cases showed adipose tissue with fat necrosis.
and calcification of the necrotic fat. This calcification corresponded to areas of central radiodensity seen on radiographs (Fig. 6). This pattern was diagnostic of interosseous lipoma.

The remaining 3 cases showed no diagnostic areas of fibrous dysplasia or interosseous lipoma; they only showed areas of degenerative change that was seen in varying amounts in the diagnostic lesions. This degenerative change consisted of myxomatous transformation, fibrosis, and reactive bone and calcification. We feel this suggests that, in these 3 cases, the degenerative changes completely obscured the underlying lesion.
The histologic study of the cases in this series suggests the idea that LSMFT is not a distinct entity. Fifteen of the cases studied showed an underlying well known bone entity with varying degrees of secondary degenerative change. These degenerative changes consisted of myxoid transformation of fibrous tissue, fat necrosis, reactive bone and calcification. Eight of the cases showed clear evidence of an underlying fibrous dysplasia and five showed histologic features of interosseous lipoma. Fibrous dysplasia is a fibro-osseous proliferation due to an activating mutation in the Gsα codon.9 Lesions may be focal or multi-focal, and the proximal femur is a frequent location. Long standing fibrous dysplasia undergoes secondary changes which may obscure the typical fibro-osseous histology. This is especially true in the proximal femur where stress fractures producing histologic features similar to those described in LSMFT.10 In the present series, evidence for fibrous dysplasia elsewhere in the skeleton of two patients strongly suggested that the proximal femoral lesion was also fibrous dysplasia. Furthermore, Matsuba et al. found mutations in two patients with LSMFT identical to the mutations as identified in all cases of fibrous dysplasia.11 These observations conclude that many cases of LSMFT are manifestations of fibrous dysplasia.

Interosseous lipoma is another lesion that has been included in the LSMFT entity. These lesions may occur in any bone, and they have a distinctive radiographic pattern. The proximal femur is a common location, and its radiographic presentation in this area has a distinctive pattern identical to that described for LSMFT.12 Interosseous lipomas frequently undergo fat necrosis. This results in fibrosis and calcification of the necrotic fat, and changes which cause the central radiodensity frequent seen on plain radiographs of interosseous lipomas in any location. Both radiographic and histologic evidence of interosseous lipoma were present in three of our cases histologically. Two of our cases which were not examined histologically had radiologic features of intraosseous lipoma.

Two other well defined lesions possibly included in the LSMFT category are healing solitary bone cysts and fibromyxoma of bone. Unicameral bone cysts are often asymptomatic, but in the healing process they undergo fibrous tissue proliferation with reactive bone. Similarly fibromyxoma of bone has also been described in the proximal femur. These lesions are identical to those published as LSFMT.13 Excluding patients with fracture or stress fractures, lesions in our study have been asymptomatic or had vague upper leg pain. Many were found incidentally when patients were studied for other reasons. Asymptomatic lesions with these radiographic features should not be biopsied or treated. This would be the standard of care in patients with asymptomatic fibrous dysplasia or interosseous lipoma. However, using the diagnostic category of LSMFT complicates decision making and often leads to unnecessary procedures. This problem has been exaggerated by reports of malignancy associated with LSMFT.14 These reports imply that lesions should be biopsied to rule out an aggressive neoplasm. However, these reported cases are most probably primary myxofibrosarcomas in bone and are not secondary malignant change in a previous existing benign lesion. Also, fibrous dysplasia may show degenerative atypia and may be misdiagnosed as a malignant tumor.15

This study suggests that LSMFT may not be a distinct entity. Lesions are almost always either fibrous dysplasia or interosseous lipoma with varying degrees of degenerative change. Since pathology was only performed on 18 of our 33 cases, it is possible that other pathologic findings may underlie this radiographic pattern. Use of the term as a diagnostic entity may lead to a poor understanding of the patient’s disease process and possibly lead to unnecessary treatment. We feel that the use of this diagnostic term should be ended.

REFERENCE LIST
Liposclerosing Myxofibrous Tumor (LSMFT), A study of 33 patients: Should it be a distinct entity?


ABSTRACT
Objective: Our goal was to document the presentation, location, diagnostic modalities, preoperative embolization status, treatment, histology, complications, and recurrence rates for aneurysmal bone cysts of the mobile spine.

Methods: We reviewed our institution’s database to identify patients diagnosed with aneurysmal bone cysts of the mobile spine (excluding the sacrum) from 1995 through 2006. Of those 17 patients, three were treated elsewhere and 14 underwent surgical treatment at our institution. Of those 14 patients, the nine (mean age at presentation, 17.2 years; range, 5–32 years) with at least 2 years of follow-up (average, 49.6 months; range, 24–88 months) formed our study group. For those nine patients, we tabulated the presentation, location, diagnostic modalities, preoperative embolization status, treatment, histology, complications, and recurrence rates.

Results: Pain was the presenting symptom in all nine patients. The lesion most commonly occurred in the cervical spine (five); two occurred in the lumbar spine, and two occurred in the thoracic spine. Patients underwent resection and combined anterior and posterior spinal arthrodesis (six) or resection and posterior spinal arthrodesis (three). There were four complications: one iliac crest donor site infection, one incidental durotomy, and two neurologic deficits. We noted two recurrences (both within 3 months).

Conclusions: Aneurysmal bone cysts of the spine can be successfully treated with surgical resection and instrumentation.

Keywords: aneurysmal bone cyst, spinal element, surgery, treatment, complications

INTRODUCTION
Aneurysmal bone cysts (ABCs) are rare (1% of primary bone tumors), benign, highly vascular pseudotumors of unknown cause.1 Approximately 6% to 22% of ABCs develop in the mobile spine; 13% to 21% occur in the sacrum.2-6 ABCs can be classified as primary (no underlying lesion) or secondary (associated with bone tumors such as giant cell tumors, telangiectatic osteosarcoma, osteoblastoma, or chondroblastoma).1 ABCs in the spine usually affect the posterior elements. The cervical spine is involved in 30% to 41%, the thoracic spine in 25% to 30%, and the lumbar spine in 40% to 45% of cases.2,7 Treatment options include selective arterial embolization (SEA), radiotherapy, curettage, and en bloc excision with reconstruction.

The purpose of our study was to document the presentation, location, diagnostic modalities, preoperative embolization status, treatment, histology, complications, and recurrence rates for ABCs of the mobile spine.

SUBJECTS AND METHODS
With approval from our institutional review board, we searched our histologic database for patients diagnosed with ABCs of the mobile spine (excluding the sacrum) from 1995 through 2006. Of those 17 patients, three were treated elsewhere, and were excluded from our study. Of the remaining 14, nine had at least 2 years of follow-up (average, 49.6 months; range, 24–88 months) and formed our study group. At presentation, the mean age of the three male and six female patients was 17.2 years (range, 5–32 years).

We tabulated the presentation, location, diagnostic modalities, preoperative embolization status, treatment, histology, complications, and recurrence rates for their ABCs of the mobile spine.

RESULTS

Presenting Symptoms
All patients presented with pain localized to the site of the lesion for an average of 5.9 months’ duration (range, 1–18 months) (Table 1). Neurologic deficits were present in three patients, one of whom presented with signs and symptoms of cauda equina syndrome secondary to mass effect from the ABC at the L4-L5 level and underwent urgent decompression and reconstruction.
Lesion Location

The lesions were most often located in the cervical spine (cervical, five; lumbar, two; thoracic, two); one lesion extended from C6 to T1. The lesions were found in the following portions of the spine: anterior (vertebral body), one; posterior (lamina, spinous process, pedicle, transverse process), three; and anterior and posterior, five.

Diagnostic Modalities

Imaging consisted of radiographs (eight patients), magnetic resonance imaging (MRI; eight patients), computed tomography (CT; seven patients), and a combination thereof (eight patients). CT scans typically showed a lytic lesion with a thin rim (Fig. 1a), whereas T2-weighted MRI showed multiple fluid levels (Fig. 1b).

Biopsy

Biopsies were obtained in eight patients (open, five; CT-guided, three); the type was at the surgeon’s discretion. An intraoperative pathology specimen was obtained from the patient who presented with the signs and symptoms of cauda equina syndrome and underwent surgical intervention.

Preoperative Embolization

Preoperative embolization was ordered at the surgeon’s discretion. Preoperative angiograms were obtained for three patients, two of whom underwent successful embolization with 350 to 500 µ of polyvinyl alcohol particles (Boston Scientific, Natick, MA, USA). Two other patients had recurrence and underwent preoperative embolization; one embolization was successful.

Surgical Treatment

Surgery was performed by orthopaedic surgeons (seven patients) and neurosurgeons (two patients). During the index procedure, resection of the lesions and combined anterior and posterior spinal fusion were...
performed in six patients. Of the five patients with cervical spine ABCs, three underwent lesion resections and combined anterior and posterior spinal fusion (Figs. 1c, d). One of the two lesions in the lumbar spine and two of the lesions in the thoracic spine were treated with corpectomy and combined anterior and posterior spinal fusion. Complete intralesional excision was performed in eight patients; one patient had partial intralesional excision.

One patient with an ABC of the cervical spine (C7) had posterior cervical fusion only and was disease free at 2 years after surgery. One patient with an ABC of the lumbar spine (L4-L5) underwent posterior resection/laminectomy with in situ fusion and was disease free at 51 months after surgery. One patient with an ABC of the cervical spine (C3) initially underwent anterior fusion only and had a recurrence of the lesion within 3 months; during revision, combined anterior and posterior fusion was performed. Estimated blood loss averaged 1368 ml (range, 100–2700 ml).

Autograft was used in eight patients (iliac crest, four; rib, three; fibula, one). Allograft was used in two patients. Resected tumor-free bone was used as autograft in two of the eight patients without any recurrence.

Somatosensory-evoked potentials and motor-evoked potentials were used in all patients. There was one case of intraoperative loss of motor signals in the lower extremities (after corpectomy of a T8 ABC). A wake-up test was performed, and the patient was able to move her lower extremities. No neurologic changes were present after surgery.

Postoperatively, seven patients were immobilized.
in a halo, thoracolumbosacral orthosis brace, cast, or cervical collar.

Hospital stay averaged 8.1 days (range, 2–17 days). This time included: (1) an international patient who underwent an open biopsy and lesion resection during the same admission, with a total of 17 days in the hospital; and (2) a patient with a postoperative cerebrospinal fluid leak requiring a return to the operating room for durotomy repair during the same admission, who spent a total of 14 days in the hospital. Excluding these two patients, hospital admission averaged 6 days.

**Histology**

All biopsy (Fig. 1e) and intraoperative specimens were evaluated by one musculoskeletal pathologist. All patients with a preoperative biopsy were diagnosed with ABCs based upon the pathology. One preoperative biopsy was initially read as an ABC and was later determined to be a giant cell tumor with a secondary ABC based upon the intraoperative pathology specimen.

**Complications**

We noted four postoperative complications in three patients within 4 weeks of the index procedure. One patient required surgery for closure of an incidental durotomy; one developed an infection at the iliac crest bone graft harvest site requiring irrigation, debridement, and intravenous antibiotics; and one with a secondary ABC and primary giant cell tumor developed two neurologic changes (Horner’s syndrome and right upper extremity weakness) secondary to tumor recurrence that required surgical decompression.

**Tumor Recurrence**

Two patients had tumor recurrence. One had a giant cell tumor with a secondary ABC at C6 and T1. This patient required four revision anterior and posterior spinal fusions during a 28-month span after the index procedure. She also underwent a trial of radiation therapy (unsuccessful in preventing recurrence) and a preoperative embolization before the second revision. The patient has been disease free for 81 months after the last resection. The second patient had a C3 lesion that was treated with corpectomy, anterior-only spinal fusion, and anterior partial intradiscal excision. The tumor recurred in the posterior elements within 3 months. The patient underwent repeat resection and combined anterior and posterior spinal fusion and has been disease free for 27 months.

**DISCUSSION**

We report our experience with the surgical management of ABCs of the mobile spine over an 11-year period at our institution. The initial description of an ABC is attributed to Van Arsdale,8 who in 1893 reported a case of ossifying hematoma of the humerus that arose 6 weeks after a traumatic episode. The term “aneurysmal bone cyst” was first used in 1942 by Jaffe and Lichtenstein9 when they reported two cases of ABCs in male patients 18 years old and younger, one of which was in the posterior elements of the spine. The incidence of ABCs has been reported to be 1.4 of 100,000 and comprises 1% of bone tumors.10

**Presentation**

Pain is the most common presenting symptom of ABCs. Neurologic symptoms present if the lesion encroaches on nerve roots or the spinal cord. A palpable mass may be present in the posterior elements, and tenderness may be elicited. In our nine patients, the average duration of symptoms before presentation was 5.9 months (range, 1–18 months). This finding is consistent with the slow and gradual onset of pain described in the literature.1,2,6

Diagnosis is confirmed via biopsy, and imaging modalities (radiograph, CT, MRI) should be part of the work-up. Enneking11 classified ABCs as three types: I (latent), II (active), and III (aggressive). ABCs of the spine are not common in patients more than 20 years old; the incidence in large series (>20 patients) of such patients is 14% to 19%.1,2,6,12 It is conceivable that certain ABCs that develop in the second decade can remain clinically silent until the third decade, as seen in 33% of our patients. ABCs can also cause vertebra plana, and it is important to consider ABCs in the differential for vertebra plana.13 An open or closed CT-guided biopsy can be performed preoperatively.

**Lesion Location**

In our series, the cervical spine was the most common location. Other series1,2,6 have reported cervical spine involvement in 11% to 41%, thoracic spine involvement in 25% to 41%, and lumbar spine involvement in 17% to 50% of cases. In their epidemiologic study, Cottalorda et al10 reported on 161 ABCs in the mobile spine. They found 30% of the ABCs in the cervical spine, 30% in the thoracic spine, and 40% in the lumbar spine. Lesions were found in the anterior and posterior elements of the spine in 56% of our patients; 33% had lesions in the posterior elements only, and 11% had lesions in the anterior portion only.

**Management**

Surgical resection en bloc has the lowest recurrence rate when treating ABCs of the spine.1,6 For ABCs of the mobile spine, we recommend surgical resection en bloc when possible or an aggressive complete intradiscal excision and stabilization with instrumentation and bone graft. Several reports also advocate en bloc resection for the cervical spine.14,20 Although the en bloc resection is technically challenging,1 this technique minimizes the
risk of recurrence.

Other management options for ABCs include SEA, intralesional injection of calcitonin/steroids, radiotherapy, and curettage alone without fusion or instrumentation. Radiotherapy has been used in sites that are inoperable. However, its risk of postirradiation sarcoma, neurologic damage, scoliosis, and damage to surrounding structures has decreased its use for ABCs. Recent reports have advocated the use of SEA for definitive management of ABCs. The benefits are its minimally invasive nature, which reduces damage to the pediatric spine. Coils, coposed material such as polyvinyl alcohol, and liquid material such as n-butyl cyanoacrylate (Cordis, Miami Lakes, FL, USA) have been used during SEA. The risks of SEA include recurrence of the lesion and spinal cord ischemia. Multiple embolizations may also be needed to eradicate the lesion. Intralesional curettage with or without bone grafting has been described. Boriani et al have advocated SEA as the first-line treatment for spinal ABCs except in the presence of pathologic fractures or neurologic deficit. However, in their series of 41 patients, SAE was used as primary treatment for only four patients.

Lesion Recurrence and Complications

Two of our patients had disease recurrence, both within 3 months of excision. One recurrence was in a patient with a secondary ABC. Although this patient’s preoperative biopsy was thought to be a primary ABC, the intraoperative biopsy showed a giant cell tumor and a secondary ABC. Our experience with this patient, who required four revisions, led us to recommend an aggressive resection of the primary lesion in secondary ABCs during the index procedure. The role of aggressive initial surgical resection has been emphasized in a recent study reporting a 36% recurrence rate of giant cell tumors with secondary ABCs. Our second recurrence was in a patient with a C3 lesion who underwent only anterior partial intralesional excision and reconstruction. Because of the incomplete resection, the lesion recurred in the posterior elements, and a combined anterior and posterior lesion resection and reconstruction was performed; the patient remains disease free at 27 months.

The four complications (incidental durotomy, iliac crest donor site infection, and two neurologic deficits) occurring in three patients were treated successfully with no permanent sequelae.

The largest study to date examining ABCs of the spine (excluding the sacrum) was by Papagelopoulos et al. In that study spanning 83 years, 41 of 52 patients had a lesion involving the mobile spine, and all were treated with surgical excision; 30 patients with primary occurrences were treated surgically with various modalities. There was a 13% recurrence rate and five cases of secondary ABCs with primary giant cell tumors. It is unclear whether the recurrences occurred in patients with secondary ABCs. There was a 31% complication rate, including two deaths. One patient was treated with radiation for an ABC with subsequent development of a postirradiation sarcoma and another had massive intraoperative blood loss resulting in cardiac arrest.

In another large series, Boriani et al reported on 41 patients with ABCs of the mobile spine (excluding the sacrum) treated over a 44-year period, 32 of whom were treated surgically. However, only six patients had a fusion performed, three of whom had fusion with instrumentation. A 5% recurrence rate was reported; one was attributed to an incomplete curettage and one was in a patient treated only with SEA. A 17% complication rate, including five surgical wound complications and one urethral compression, was reported.

In another large series, de Kleuver et al reported on 31 patients with ABCs of the spine (28 in the mobile spine) over a 45-year period. Surgical excision was used in 93%; a variety of surgical procedures was used. The recurrence rate was 21% (six in 28 patients, attributed to incomplete excision). Complications included angular kyphosis in the thoracic spine after laminectomy without fusions or instrumentation.

Study Limitations

The limitations of our study are the small sample size and the multiple surgeons involved in the treatment of the patients. However, the oncologic principle of aggressive excision and reconstruction with fusion and instrumentation to maintain stability of the spinal column (except one case) was uniform among all of the surgeons. The rarity of these tumors and the 11-year study span account for the small sample size. Series with larger patient numbers have spanned an average of 57 years (range, 44–83 years). However, the shorter study period is beneficial because surgical management techniques did not change much in comparison to studies spanning several decades. We also ensured adequate follow-up by limiting our study to patients with at least 2 years’ follow-up. Two of the larger series included patients with 6 to 12 months’ follow-up.

CONCLUSION

In our series, successful treatment of ABCs of the spine was achieved with aggressive lesion excision or en bloc resection with combined anterior and posterior spinal fusion with instrumentation. We continue to use this technique at our institution. SEA was used for preoperative embolization but not as a definitive treatment. Radiation therapy was not used as primary treatment for ABCs of the spine.
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SWARM RAT CHONDROSARCOMA CELLS AS AN IN VIVO MODEL: LUNG COLONIZATION AND EFFECTS OF TISSUE ENVIRONMENT ON TUMOR GROWTH

Jose A. Morcuende a, *, Jeff W. Stevens a, Todd E. Scheetz b, Maria de Fatima Bonaldo c, Thomas L. Casavant b, Jesse E. Otero a, and Marcelo B. Soares c

ABSTRACT
Swarm rat chondrosarcoma cells have been used extensively for biochemical studies of extracellular matrix metabolism in cartilage. However, these cells also possess tumor-like behavior in vivo and are useful in investigation of chondrosarcoma biology. The current study was designed to develop a metastatic model using Swarm rat chondrosarcoma cells, and to assess the effect of tissue-environment on tumor behavior in vivo. Tumors were implanted subcutaneously or into bone, and animals were assessed radiographically and microscopically for tumor growth and metastasis. The subcutaneous tumor grew to an average mass of 35 g, while tumor implanted into bone grew 75 mg. Transplantation of the cells into the bone led to extensive bone remodeling with invasion of the medullary cavity and destruction of the bone cortex. Light microscopy demonstrated no significant differences in the number of mitoses, cellular atypia or extracellular matrix staining between the two sites of tumor implantation. Interestingly, lung colonization was observed in none of the animals in the subcutaneous tumor injection group, while tumors colonized the lungs in 95% of the rats with tumor injected into bone. Analysis of cDNA libraries from subcutaneous and bone-transplanted tumors demonstrated a complex and diverse array of expressed transcripts, and there were significant differences in gene expression between tumors at different sites. The results of this study suggest Swarm rat chondrosarcoma is a model that resembles human chondrosarcoma mimicking its ability to infiltrate and remodel local bone and to colonize the lungs. Furthermore, the interaction between host-tissue and tumor cells plays a major role in the tumor behavior in this model. Identifying these interactions will lead to further understanding of chondrosarcoma and contribute to therapeutic targets in the future.

Key words: chondrosarcoma, Swarm rat chondrosarcoma, metastasis, animal model, gene expression

INTRODUCTION
Metastasis, the spread and growth of tumor cells to distant organs, represents the most devastating attribute of cancer. In chondrosarcoma, the 5-year survival for patients with metastatic disease is less than 10%. An incomplete understanding of the molecular and cellular mechanisms underlying chondrosarcoma progression and metastasis hinders the development of effective therapies that would improve survival rates in these patients.

Although chondrosarcoma is the most common primary skeletal tumor in adults, its incidence is relatively small (about 800 to 1000 cases per year) when compared to other cancers. The low incidence makes the design of clinical and pathology-based studies exceptionally challenging. The establishment of a chondrosarcoma animal model that resembles human chondrosarcoma would greatly improve our understanding of the biology of this tumor.

The Swarm rat chondrosarcoma, first described as an osteogenic tumor with chondrogenic differentiation potential arising spontaneously in a Sprague-Dawley rat, has been maintained for decades by serial subcutaneous injections. The main utility of Swarm rat chondrosarcoma in research has been provision of cells for in vitro biochemical studies of cartilage extracellular matrix metabolism. Despite the ability of the tumor to grow in vivo, few studies have taken advantage of this system as a model of chondrosarcoma disease. Two studies have reported that transplantation of Swarm rat chondrosarcoma cells into bone results in tumors with a biological behavior similar to human chondrosarcoma. Kenan and Steiner reported extensive invasion of the marrow and cortex, but rare distant dissemination (1 of 24 rats at 14 weeks after implantation).
colleagues reported bone remodeling and tumor grade modifications induced by interactions between the bone and Swarm rat chondrosarcoma cells, but no metastases were observed. The objectives of the current study were to develop a model using Swarm rat chondrosarcoma cells that results in distant tissue colonization, and to evaluate the effects of tissue-environment on tumor behavior. In addition, cDNA libraries from these tissues were generated which could be useful for future studies.

**MATERIAL AND METHODS**

**Swarm rat chondrosarcoma transplantation and normal growing rat cartilage tissue isolation**

We have established a procedure whereby Swarm rat chondrosarcoma cells are isolated, frozen and upon thawing, transplanted subcutaneously into rats for propagation of the tumor line, JWS. This procedure eliminates the need to maintain a rat colony and allows the use of the same cells for many experiments. Animal usage was institutionally reviewed and approved. Animals were obtained from Harlan laboratories and were pathogen free. Animals were housed three per cage in a temperature-controlled room with a 12hr/12hr light/dark schedule and allowed water and rat chow ad lib.

Briefly, male Sprague-Dawley rats (75 grams, 3-week-old) with transplanted Swarm rat chondrosarcoma tumor cells in the subcutaneous tissue were euthanized. The tumors were removed and then cut into 1-cm³ pieces. These pieces were pressed through a 1-mm² wire screen and 50 grams of tumor were processed for cell isolation using a procedure based on Kimura et al. Samples were treated with 0.25% trypsin, 1 mM EDTA in Hank’s Balanced Salt Solution without calcium or magnesium, and 25 mM HEPES buffer at 37° C for 30 minutes. Following washing with trypsin, a collagenase digestion (6 mg/ml) was performed (37° C for 30 minutes). The liberated cells were passed through a 25 μm Nitex membrane. A yield of 4.6 x10⁸ cells was usually obtained from 50 grams of tumor. Cells were immediately frozen in 10% dimethyl sulfoxide and 90% fetal bovine serum at 1-2 x 10⁶ cells per ml for later subcutaneous injection and tumor growth.

For this study, thawed and washed tumor cells were injected subcutaneously in both sides of the lumbar spine at 1 x 10⁶ cells in 0.5 ml of Dulbecco’s Modified Eagle Medium. Thirty-four days post-injection the rats were euthanized, and the tumors were removed. The tumor tissue was screened as described above, drawn into a syringe, and then used for new subcutaneous and bone transplantations (n=20 per group). In the subcutaneous groups, tumor transplantation was performed by injection or by making a skin incision and injecting the cells in the wound before closure. For the bone transplantation group, a longitudinal skin incision in the anterior aspect of the knee was performed, the muscles were dissected and the proximal tibia was exposed. Using a 16-gauge needle, a small hole was created in the proximal tibial metaphysis. The bone marrow was aspirated and approximately 10 μl of tumor slurry was transplanted using a 24-gauge needle. The bone opening was closed with bone wax to prevent early escape of tumor cells. The skin was closed in a standard fashion. Limb amputations were performed at time 0 (just after implantation), 3 days, 7 days and 21 days to evaluate tumor growth in bone.

To evaluate lung colonization, animals were euthanized at 34 days. The primary tumors were removed, measured and weighed, immediately frozen in liquid nitrogen and stored at -80°C. A necropsy was performed to identify metastasis. When metastases were identified, they were counted and isolated from the host tissue under a dissecting microscope (Olympus SZ60 with a FOSTEC/EKE 8375 light source). The metastatic nodules were then measured and weighed, and immediately frozen in liquid nitrogen and stored at -80°C.

**Radiographic analysis**

Animals were anesthetized following standard protocols. Radiographs were obtained using an Ultima-CD, Model WFL-MC125 (Sinyo Shoko Co., Ltd). Settings were constant at 40 KVP, 1 mAS, with a source distance of 132.5 cm. Bony changes were recorded including osteopenia, osteolysis, and sclerosis.

**Histochemical analysis**

For light microscopy examination, samples were fixed in 10% phosphate-buffered formalin (pH 7.0). Bone samples were decalcified with EDTA, processed, and embedded in paraffin using standard methods. Five-micrometer sections were stained with hematoxylin and eosin, or Safranin O (specific for proteoglycan staining).

**In vitro Invasion Assays**

Swarm rat chondrosarcoma cells (1 x 10⁵) were seeded into the upper wells of the MICS (membrane invasion culture system) chamber onto collagen IV/laminin/gelatin-coated polycarbonate membranes containing 10-µm pores (Osmonics, Livermore, CA) in RPMI 1640 with 1X MITO+ (Collaborative Biomedical). After 24 hours of incubation at 37°C, the cells that invaded each membrane were collected, stained and counted as previously described. Percent invasion was corrected for...
proliferation and calculated as: (Total number of invading cells X 100) : Total number of cells seeded.

RNA isolation

Total RNA from subcutaneous and bone tumors, and rat normal growing cartilage was extracted by a modified method of Smale and Sasse\textsuperscript{11}. Briefly, frozen cartilage was powdered in a Spex Freezer Mill (SPEX, Metuchen, NJ). A TRIZOL/chloroform extraction was then performed followed by an isopropanol/ high salt precipitation. DNase I digestion was performed at 22°C for 15 min and terminated by adding EDTA. The CsTFA working solution was prepared with a density of 1.51 g/ml in 100 mM EDTA, pH7.0. The DNase I-treated RNA solution was mixed with 18 ml of 5.5M guanidinium thiocyanate solution (with 1% fresh beta-mercapto-ethanol). Nineteen ml of CsTFA working solution was added into cyanate solution (with 1% fresh beta-mercapto-ethanol). After ultracentrifugation was performed in a Beckman SW28 rotor and centrifuged at 22°C for 15 min and terminated by adding EDTA. The CsTFA working solution was prepared with a density of 1.51 g/ml in 100 mM EDTA, pH7.0. The DNase I-treated RNA solution was mixed with 18 ml of 5.5M guanidinium thiocyanate solution (with 1% fresh beta-mercapto-ethanol). Nineteen ml of CsTFA working solution was added into a Beckman centrifuge tube (25 x 89 mm). The sample was then applied to the top of CsTFA working solution. Ultrasound was performed in a Beckman SW28 rotor at 25,000 rpm for 24 hr at 15°C. After ultracentrifugation, the liquid in the tube was aspirated to within 1 cm of the bottom, and the remaining liquid was decanted. The tube was then inverted to drain on paper for 5 min. The bottom of the tube was cut off and placed on ice. The RNA pellet was dissolved in 400 µl of TE. RNA was precipitated with 10 µl of 1 M acetic acid and 300 µl of 100% ethanol and chilled at -70°C for 20 min. The RNA was pelleted by centrifugation at 4°C. RNA was dissolved in TE, and precipitated with 20 µl of sodium acetate (3 M, pH 7.0) and 600 µl of 100% ethanol, and chilled at -20°C overnight or at -80°C for 20 min. After precipitation, the RNA was dissolved in 100 µl of TE and stored at -80°C. Poly(A)+ RNA was isolated by chromatography on oligo (dT)-cellulose (New England Biolabs) according to manufacturers’ instructions, except that two rounds of purification were performed.

cDNA library construction

High-quality poly (A)+ RNA isolated from Swarm rat chondrosarcoma and rat normal growing cartilage was used for construction of the cDNA libraries. cDNA library construction was essentially as described previously by Bonaldo et al\textsuperscript{11}. Briefly, 1 µg poly(A)+ RNA was annealed at 37°C with a twofold mass excess of a Not I-tag-(dT)\textsubscript{18} primer and reverse-transcribed at 37°C. The tag sequence is a sequence of 10 nucleotides that is unique for each library and thus serves as an identifier. As a primer for first-strand cDNA synthesis, we used the oligonucleotide 5’-AACTGGGAAGAATTCCGGCCGCGCNNN NNNNN (T) 18-3’, which contains a Not I site (underline) and a tag sequence (N10), specific for each library. Double-stranded cDNAs were size-selected by gel filtration. After ligation to EcoRI adaptors, the cDNAs were digested with Not I and cloned directionally into the EcoRI and Not I sites of the pIT73-Pac vector. This vector is essentially the same as pIT73-Pac with a modified poly-linker and flanking sequences. Library normalization was performed as previously described by Bonaldo et al\textsuperscript{11}.

DNA sequencing and Data analysis

Double-stranded plasmid DNA templates were prepared using the 96-well microwave protocol and sequenced from the 3’ end using Rhodamine dye terminator chemistry (Applied Biosystems) with universal M13 primers. Sequencing reactions were assembled with a Robbins Scientific Hydra-96 Microdispenser and then transferred to a MJ Research PTC-222 Peltier thermal cycler for cycle sequencing. Reaction products were ethanol precipitated, resuspended in formamide, and electrophoresed on an ABI Prism 3700 DNA Analyzer (Applied Biosystems). Nucleic acid database searches were performed locally using the BLAST family of programs.

RESULTS

Swarm rat chondrosarcoma cells show local invasion potential

Invasion assays were performed after isolation of cells from subcutaneous tumors, bone tumors, soft-tissue extension of the bone tumor and metastases. Cells from both the subcutaneous and bone tumors had a 12 % +/- 0.7% invasion, compared to 9% +/-0.56% in the soft-tissue tumor extension, and 9 % of the lung metastasis (p= 0.2) (Table I).

Site of transplantation affects tumor growth

All animals in both the subcutaneous and tibia groups developed tumors. Tumors injected subcutaneously grew up to an average of 35 grams (range: 8 to 66 g). Histologically, tumors demonstrated nodular...
Swarm Rat Chondrosarcoma Cells as an in vivo model

Proliferation containing chondroid material (positive for Safranin O). Nodules were delimited by fine fibrous septae. There was hypercellularity and mild atypia with neo-vascularization (thin arrows) from the host-tissue. Mitoses were present as well as many cells with prominent nucleoli.

In the tibia, tumors grew to an average of 75 mg (range: 23 to 116 mg) with cells expanding until the majority of the bone marrow cavity was replaced by tumor (Figure 2). Radiographic changes were evaluated at 4 weeks post-transplantation and demonstrated extensive osteolysis and periosteal reaction of the proximal tibia where the cells were transplanted (now shown). Histologically, the tumor appeared similar to the subcutaneous group with hypercellularity and mild atypia. The cells in bone invaded the cortical bone and the Harvesian system and expanded outside the bone (Figure 3). No evidence of tumor ossification or change in tumor grade was observed during these experiments. In 16 animals (80%), there was soft-tissue tumor extension occurring on the third week after transplantation. The tumors grew to an average size of 3.5 x 2 cm (range: 0.7 x 0.7 to 4 x 7 cm).

Lung colonization by Swarm rat chondrosarcoma cells

When the animals were euthanized at 34 days after transplantation, lung metastases were observed in 0% of animals in the subcutaneous group (including subcutaneous and sub-incision groups), and in 2% - 98% in the bone group ($p=0.001$) (Figure 4). Interestingly, the presence of metastases was related to the method of bone
tumor transplantation. When the tumor was implanted as a 1 mm³ tissue block, lung lesions were identified in 2% of animals. However, when the tumor was passed throughout a 1 mm size screen pre-implantation, the observed incidence of lung colonization was 60%. This percentage increased to 98% when a 0.25 mm screen was used. Necropsy demonstrated that this colonization happened around the time of the tumor injection since chondrosarcoma cells were seen in animals sacrificed immediately after injection.

The number of lung nodules ranged from 1 to 43 (median: 14) with an average size of 1 x 2 mm. The nodules were localized in all lungs fields. One case demonstrated a metastatic nodule into the heart. No metastases were observed in the liver, spleen, kidneys, abdominal cavity or retro peritoneum.

Sequencing and Analysis of ESTs
In order to analyze gene expression in rat normal growing cartilage and Swarm rat chondrosarcoma, approximately 24,000 random ESTs were sequenced from the 3' end (3'ESTs). To aid in the analysis of expressed genes, overlapping ESTs corresponding to the same gene were grouped into clusters. A representative member from each cluster was then compared against public gene databases.

5,024 ESTs were sequenced from the tibia tumor library and grouped into 3,791 clusters. The number of known rat genes and novel homologs to known genes was 1,752. Similarly, out of 7,871 ESTs sequenced from the subcutaneous tumor library, a total of 4,918 clusters were obtained. The number of known rat genes and novel homologs to known genes was 1,465. A total of 6,640 ESTs were sequenced from the rat normal growing cartilage library and grouped into 3,981 clusters. The number of known rat genes and novel homologs to known genes was 965. A subtraction library was also constructed and sequenced including samples from the 3 tissues (tumor in the subcutaneous tissue and tibia, and normal cartilage). Together, there were 5,686 ESTs grouped into 4,093 clusters. (Table II).

Analysis of the most abundant transcripts
Table III shows the most abundant transcripts in Swarm rat chondrosarcoma (subcutaneous and tibia) and rat normal growing cartilage libraries. This list shows the cDNA of interest and the corresponding number of ESTs identified in each of the three libraries. There is a clear difference in gene expression in these tissues. For example, biglycan, articular superficial zone protein (Prg4), and collagen type X are highly expressed in normal cartilage, but not in chondrosarcoma. On the other hand, vimentin, N-myc downstream-regulated protein, chondromodulin-1, and ferritin light chain 2, are highly expressed in both Swarm rat chondrosarcoma libraries. COL2-A1 is the most highly expressed gene in all three libraries (Table III).

| TABLE II: Analysis of ESTs from Swarm rat chondrosarcoma and rat normal growing cartilage. |
|-------------------------------------------------|-------------------------------------|------------------|
| Swarm rat chondrosarcoma                        | Total ESTs  | Total Clusters | Total Genes |
| Subcutaneous                                    | 7,871       | 4,918           | 1,752       |
| Tibia                                           | 5,024       | 3,791           | 1,465       |
| Rat normal growing cartilage                    | 6,640       | 3,081           | 965         |
| Subtraction library (sc+tib+norm)               | 5,686       | 4,093           |             |
| TOTAL                                           | 24,221      | 15,883          |             |

Figure 4: Lung colonization of Swarm rat chondrosarcoma after injection into tibia
Multiple discrete nodules of chondroid tumor proliferating in the lung 34 days after injection of tumor cells into the proximal tibia of rats.
DISCUSSION

This study describes the use of Swarm rat chondrosarcoma cells as an in vivo model for chondrosarcoma biology using inbred rats as a host.

Metastasis is the ultimate step in the multistage process of tumor progression. Development of metastases requires tumor cells to complete a complex sequence of events, including penetration into the lymphatic or circulatory systems, dissemination, binding to specific molecules in particular organs or tissues, and recruiting vascular supply to proliferate. In the current model, we observed lung colonization in rats in which the tumor was strained before implantation. Necropsy suggested that this colonization occurred around the time of the implantation, since tumor cells were histologically identified in lungs on day zero of implantation. Fewer lung metastases were identified in rats into which blocks of tumor tissue were implanted. Lung colonization was not observed after subcutaneous implantation of tumor. The frequency of lung colonization we observed after implantation of blocks of tumor into bone is consistent with previous observations. Kenan and colleagues identified 1 out of 24 animals with lung metastases after implantation of tumor into bone. In the current model, we observed lung colonization in rats in which the tumor was strained before implantation. Necropsy suggested that this colonization occurred around the time of the implantation, since tumor cells were histologically identified in lungs on day zero of implantation. Fewer lung metastases were identified in rats into which blocks of tumor tissue were implanted. Lung colonization was not observed after subcutaneous implantation of tumor. The frequency of lung colonization we observed after implantation of blocks of tumor into bone is consistent with previous observations. Kenan and colleagues identified 1 out of 24 animals with lung metastases after implantation of tumor into bone. Straining the tumor through a 0.25 mm screen yields a slurry of cancer cells in solution. We hypothesize that the slurry of cells is easily disseminated into the circulation through the highly dense network of bone marrow capillaries which lack a basement membrane. It is remarkable that the cells which metastasized to the lung formed clinically detectable macroscopic lung metastases that maintained an invasive phenotype. Further study is required to delineate the factors which are necessary for the survival of chondrogenic tumors in the lung.

This study also describes the use of a large-scale EST sequencing approach to identify genes that are expressed in Swarm rat chondrosarcoma and rat normal growing cartilage. Until recently, efforts to identify changes in gene expression relied on focused studies of known genes of interest. Large-scale EST sequencing offers a powerful tool for investigating the gene expression pattern of a large number of genes simultaneously, allowing the global analysis of complex biologic systems.

Our study broadly confirms previously published data on the many characteristic genes in cartilage. Analysis of the gene expression profiles from both normal and tumor libraries revealed a complex pattern of gene expression, including many genes not yet reported to be expressed by chondrocytes, which suggests that the biochemical characterization of cartilage reported to date has only begun to unravel the complexity of this tissue.

Many cartilage matrix components were found in both of these libraries. Several types of collagen were expressed including type II, IX, X, XI, and XV. The most abundant proteoglycans present in the rat normal growing cartilage were biglycan, articular superficial zone protein, and aggrecan. Other proteoglycans include the cell surface glypican, the small leucine-rich proteoglycans fibromodulin and chondroadherin, and the basement membrane proteoglycan, perlecan. Interestingly, decorin expression was not observed, which is in contrast to published data in cultured hu-

<table>
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<th>Rank</th>
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<th>Swarm rat chondrosarcoma</th>
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<td>Polyubiquitin</td>
<td>Ferritin 1</td>
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<td>COL11-A1</td>
<td>Fibronecin</td>
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<td>eEF2</td>
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<td>Fibromodulin-1</td>
<td>Vimentin</td>
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man chondrocytes, normal adult articular cartilage and in osteoarthrosis where it is the most prevalent mRNA. Age-dependent or species-specific expression may contribute to this discrepancy, and will require further investigation.

Differences in cartilage matrix gene expression were observed among transplantation locations. There was minimal expression of collagen X and XI, and no expression of the articular superficial zone protein in tumors. These molecules are associated with specific features of differentiation in chondrocytes, and those aspects may be altered in chondrosarcoma cells. Interestingly, there was no evidence of expression of lysyl oxidase—the enzyme that catalyzes the conversion of lysine or hydroxylysine to aldehyde residues and leads to cross-linking in collagen. Loss of heterozygosity and mutations on lysyl oxidase have been implicated in aberrant tumor suppression and cell growth regulation in several tumor models.

Several proto-oncogenes and oncogene-associated proteins were found including c-raf, RAB-1, RAN, Fyn proto-oncogene, a gene over-expressed in astrocytoma, and Jun co-activator Jab-1. The kinase suppressor of ras, Mas proto-oncogene, p53-associated cellular protein and N-mycc downstream-regulated protein were only expressed on Swarm rat chondrosarcoma. In addition, a high level of expression of vimentin was observed in Swarm rat chondrosarcoma. High expression of vimentin has been observed in high-grade prostate tumors; however, its significance in chondrosarcoma is not known. Whether proto-oncogene expression in Swarm rat chondrosarcoma tumors is involved in their pathogenesis remains to be determined.

There was also differential expression of growth factors and membrane receptors, including TGF beta, growth hormone receptor, PTH receptor, IGF2 receptor, IGFBP3, and retinoic acid receptor. These molecules are known to modulate cartilage matrix synthesis, chondrocyte proliferation, and chondrocyte differentiation. We also identified in tumors the expression of connective tissue growth factor. This protein is believed to play a role in various cellular processes such as cell adhesion, mitogenesis, and cell-matrix interactions, and it is also involved in skeletal development. This growth factor has also been identified in human osteoarthritic cartilage.

We have discussed only a fraction of the expressed genes identified in our Swarm rat chondrosarcoma libraries. Future investigations will aim to determine the significance of the expression of these genes in the biology of Swarm rat chondrosarcoma. Ultimately, we anticipate that these studies will unravel the molecular pathways and networks that are altered in chondrosarcoma. We anticipate that this information will lead to a deeper understanding of the pathogenesis of chondrosarcoma resulting in the development of effective targeted therapies.

ACKNOWLEDGEMENT

This study was supported by NIH 99SX131A.

REFERENCES

ABSTRACT:
Study Design/Setting: Randomized, Controlled study in a laboratory setting. Blinded observations/assessment of study outcomes.

Objective: The purpose of this study is to determine the performance characteristics of PROGENIX® DBM putty as a bone graft extender, enhancer, and substitute in a rabbit posterolateral spine fusion model.

Summary of Background Data: The rabbit posterolateral fusion model is an established environment for testing of fusion concepts. It offers the opportunity to obtain radiographic, histological, and biomechanical data on novel fusion materials.

Methods: Forty rabbits were entered into the study with 37 used for analysis. Bilateral posterolateral lumbar intertransverse fusions were performed at L5-L6. The lateral two thirds of the transverse processes were decorticated and covered with graft material: autograft only (1.5 or 3.0 cc/side), a combination of PROGENIX® (1.5cc) + autograft (1.5cc), PROGENIX® (1.5cc) + autograft (3.0cc), or PROGENIX® only (3.0cc/side).

Results: Radiographic Fusion: At 8 weeks the 3.0cc autograft group had a 67% fusion rate and the 1.5cc autograft group fused in 25%. The extender group (1.5cc autograft + 1.5cc PROGENIX®) had an 88% fusion rate at 8 weeks. In the enhancer group (3.0 cc autograft + 1.5cc PROGENIX®) 86% of the spines were fused. The substitute group (PROGENIX® only) had a fusion rate of 38%. Manual Palpation: The 3.0cc autograft group had a 67% fusion rate and the 1.5cc autograft group fused in 38%. The extender group had an 88% fusion rate. In the enhancer group 86% of the specimens fused. The substitute group had a 50% fusion rate.

Conclusions: In a rabbit posterolateral fusion model, PROGENIX® DBM Putty in an autograft extender or enhancer mode produced manual palpation and radiographic fusion rates equivalent or slightly better than autograft fusion (3cc) alone. The results from the two autograft groups demonstrate the need for adequate graft volume to achieve high radiographic and mechanical fusion rates.

INTRODUCTION
Iliac crest autograft is considered the gold standard graft material despite limitations in the quantity available and complications associated with the harvesting procedure. These disadvantages have motivated clinicians and investigators to seek alternative graft materials to extend, enhance and/or substitute for autograft. Examples of such alternatives include: allografts, synthetic materials and recombinant human bone morphogenetic proteins (BMPs).

Many such products have been in clinical use in various forms for a number of years. Evidence for methods of use, appropriate volume/percentages of graft material, and local biocompatibility/fusion has sometimes been lacking despite incorporation of these technologies into clinical practice. As more technologies become available, scientific investigations have the opportunity to contribute to the understanding of efficacious and safe use.

The current study was performed to assess a de-mineralized bone matrix (DBM)-based graft material (PROGENIX® DBM Putty) as an autograft extender, enhancer, and substitute in the rabbit posterolateral fusion model. Fusion rates of iliac crest autograft in two separate volume-based groups were compared to lesser...
amounts of autograft extended or enhanced with the investigational material and the investigational material alone.

**PURPOSE**

The purpose of this study was to determine the performance characteristics of PROGENIX® DBM putty (Spinal Graft Technologies) as a bone graft extender, enhancer, and substitute in a rabbit bilateral posterolateral spine fusion model.

**MATERIALS AND METHODS**

Skeletally mature New Zealand White Rabbits weighing 4.5-5.5 kg were obtained from Myrtal Rabbitry (Thompson, TN) and entered into the study. All procedures were approved by the Institutional Animal Care Use Committee (#0612251) and conducted at the Bone Healing Research Lab, Iowa Spine Research Center. Throughout the study, animals were individually caged and monitored daily for signs of pain and discomfort.

The test article used in this study was PROGENIX® Putty in which the human DBM (demineralized bone matrix) component was replaced by rabbit DBM. This was done to avoid the potential for cross-species incompatibility. The procedures used for preparation of this material modeled the clinical manufacturing process. The alginate, collagen and PBS (phosphate buffered saline) were identical to those used in the clinical product.

A single level posterolateral intertransverse process fusion was performed in 40 rabbits (Table 1), bilaterally at L5-L6, with autogenous bone graft (3.0cc or 1.5cc/side) from the iliac crest, PROGENIX® DBM putty (3.0cc/side), or a combination of PROGENIX® DBM putty + autograft. The PROGENIX® DBM Putty + autograft combination groups were either 3.0cc autograft + 1.5cc PROGENIX® (enhancer) (4.5 cc / side), or 1.5cc autograft + 1.5cc PROGENIX® (extender) (3.0cc / side).

**SURGICAL PROCEDURE**

All operative procedures were performed in a surgical suite using inhalation anesthesia and aseptic techniques. A preanesthetic dose of Ketamine HCL 26mg/kg, Aperpromazine Maleate 0.15mg/kg, and Xylazine HCL 0.78 mg/kg was administered intramuscularly. Surgical anesthesia was maintained with 1.5-2.5% isoflurane delivered in O₂. Cardiorespiratory monitoring was continued throughout the procedure.

A parenteral dose of cefazolin (13 mg/kg) was administered for infection prophylaxis preoperatively and then BID for 48 hours post-op.

Rabbits were placed prone on the operating table and surgically prepped with 70% Betadine solution. A dorsal midline incision, approximately 15 centimeters long, was made from L1 to the sacrum. A full-thickness flap of skin and subcutaneous tissue was developed and retracted on both sides. Approximately 1.5-2.0 cm lateral to the midline at the L5–L6 level, a 4- to 6-cm longitudinal incision was made through the lumbar fascia. Through the fascial incision, the iliacostalis muscle was divided exposing the underlying longissimus muscle. The transverse processes were exposed through blunt dissection along the lateral border of the longissimus muscle. A small self-retaining retractor was used to maintain exposure of the two transverse processes and the intertransverse ligament.

The surgical sites were packed with gauze after completing the surgical approach. After exposure and packing of the contralateral fusion site, small self-retaining retractors were placed in the surgical site to allow exposure for the decortication of the transverse processes. Decortication of the fusion site was performed with a high-speed 3.0mm round burr. Decortication was performed only until bleeding bone was achieved and was limited to the lateral transverse processes with no decortication of the medial boney structures. This technique has previously been validated to provide autograft fusions in approximately 50-70% of animals when using 3.0cc of autograft per side. This provides a challenging model and allows for comparison of test articles to autograft.

Approximately 3.0 cc of corticocancellous bone graft from each iliac crest was obtained as needed depending on randomization – a volume considered to be the maximum amount which can be harvested from the rabbit iliac crest without significant animal morbidity13-18. The
morselized cancellous bone graft, PROGENIX® DBM putty, or the combination of PROGENIX® DBM Putty + autograft was placed between the transverse processes in the paraspinal bed. Fascia and skin were closed with 3-0 Vicryl and then the skin was stapled with 35W surgical staples. Butorphanol (1-7.5 mg/kg IM q4) and Flunixin Meglumine (1.1mg/kg IM q12) were given daily for 48 hours post-op.

All the rabbits were radiographed at 3, 4 and 8 weeks post-operatively. Animals were humanely euthanized at 8 weeks post surgery, a time point consistent with the published literature of this model\textsuperscript{16,18-22}. Following necropsy, high resolution Faxitron radiographs were obtained of the explanted spines. A random specimen from each group was also subjected to 3D computerized tomography (CT).

Three (3) rabbits were omitted from the study due to post-op complications (2 Pasteurella infections and 1 GI inflammation). Two of the animals were in Group 4 (resulting in n=6), and 1 in Group 2 (n=7). This finding supports prior evidence that harvesting the full autograft volume of 3cc’s from both iliac crests has significant mortality.

**RESULTS**

**Radiographic**

Radiographic fusion (Figure 1) was judged by continuous trabecular continuity between the affected transverse processes. At least one side of the spine had to have continuous bridging bone between the transverse processes to be classified as fused.

At 8 weeks the 3.0cc autograft group had a 67% fusion rate (4/6) and the 1.5cc autograft group fused in 25% (2/8) of the rabbits. In the enhancer group (3.0 cc autograft + 1.5cc PROGENIX®), 85% (6/7) of the spines were fused. The extender group (1.5cc autograft + 1.5cc PROGENIX®) had an 88% (7/8) fusion rate at 8 weeks. The substitute group (PROGENIX® only) had a radiographic fusion rate of (38%, 3/8). Individual results are listed in the Table 2.

**3D-CT**

Computerized tomography (CT) images were obtained from one animal from each group for investigator’s use as a possible imaging tool to determine fusion across the transverse processes (Figure 1). No qualitative or quantitative analyses were performed with these images. Therefore, CT images in this manuscript are only a visual tool to see the graft characteristics (size, shape, etc.) in a limited number of animals.

**Manual Palpation**

Stiffness of the fused motion segment was assessed by manual palpation\textsuperscript{13}. The fusion was graded by three independent blinded observers as “solid” if no detectable motion at the disc space was detected in flexion and extension. The fusion was graded as “not solid” if motion was present. Final results were determined by agreement of at least 2 of the 3 observers.

The 3.0cc autograft group had a 67% fusion rate (4/6) and the 1.5cc autograft group fused in 38% (3/8) of the rabbits. In the enhancer group (3.0 cc autograft + 1.5cc PROGENIX®), 86% (6/7) of the spine were fused. The extender group (1.5cc autograft + 1.5cc PROGENIX®) had an 88% (7/8) fusion rate. The PROGENIX® only
group (substitute) had a 50%, (4/8) fusion rate when tested mechanically.

Manual palpation results (Table 2) correlated with the radiographic assessment with the exception of 1 animal from the PROGENIX® alone group and 1 from the 1.5 cc autograft group. In each of these groups, no motion was evident by manual palpation although they were graded as ‘not fused’ radiographically.

### TABLE 2: Faxitron Radiographic Results

<table>
<thead>
<tr>
<th>Animal #</th>
<th>Group</th>
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<th>Manual Palpation Fusion</th>
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<td>1</td>
<td>Pseudarthrosis</td>
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<tr>
<td>2</td>
<td>1</td>
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<td>Solid</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
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<td>Not Solid</td>
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</tr>
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<tr>
<td>6</td>
<td>1</td>
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<td>Solid</td>
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<tr>
<td>7</td>
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</tr>
<tr>
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<tr>
<td>37</td>
<td>5</td>
<td>Pseudarthrosis</td>
<td>Not Solid</td>
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**FIGURE 2: Histology Examples**
Photomicrographs (50µm section @ 1X) of Group 1-PROGENIX® Putty (3.0cc/side), Group 2-PROGENIX® Putty (1.5cc/side) + Autograph (3.0cc/side), Group 3-PROGENIX® Putty (1.5cc/side) + autograph (1.5cc/side), Group 4- Autograph (3.0cc/side), and Group 5- Autograph (1.5cc/side).

from the PROGENIX® alone group and 1 from the 1.5 cc autograft group. In each of these groups, no motion was evident by manual palpation although they were graded as ‘not fused’ radiographically.

**Histology (Figure 2)**
There were no adverse inflammatory reactions to the PROGENIX® DBM Putty regardless of volume of test article. The PROGENIX® DBM Putty treatment groups tended to have more histological evidence of mature/immature bone development across the inter-transverse process spaces than did the autograft controls. In all groups except the 1.5cc/side autograft, most new bone
growth was regularly seen adjacent to the transverse processes and variably extended across intertransverse process space.

These results suggest that treatment groups had enhanced bone formation and fusion over the control groups. Results also demonstrated that the PROGENIX® Putty material was remodeled into host bone with little residual graft material remaining after 8 weeks. The extent of remodeling also was greater than that observed for the autograft, likely due to the difference between the mineral content of the materials (autograft is mineralized whereas PROGENIX® Putty is composed primarily of demineralized bone).

**DISCUSSION**

This study demonstrates the efficacy of PROGENIX® DBM Putty in separate autograft extender/enhancer applications and as a stand-alone bone graft substitute in a rabbit model (Table 3). Similar models have been used to verify autograft extenders/enhancers with reproducible results. The manual palpation fusion rate of 67% observed in the autograft control group is consistent with the rate demonstrated in prior studies performed in this laboratory as well as other published studies. PROGENIX® DBM Putty + autograft, regardless of concentration of autograft, demonstrated increased fusion rates compared to the autograft controls. The ability of the PROGENIX® DBM Putty to homogenously mix with the morselized autograft allowed a continuous mixture of substrate with minimal void within the graft site for new bone to develop and fuse the motion segment.

The results from the autograft groups also demonstrate the need for adequate graft volume to achieve increased fusion rates in this model, confirming a concept that has been previously proposed to affect fusion rates in the rabbit model. When 3cc was used 67% fused, whereas 1.5cc resulted in only 25% radiographic and 38% palpation fusions. This is good evidence of why the need for graft extenders is important - as autograft availability is limited and harvesting is associated with morbidity, increased operative time and blood loss in patients, and also mortality in rabbits.

In this rabbit model, PROGENIX® DBM Putty did not appear to function favorably as a stand-alone graft material. Histological sectioning of the stand-alone group showed no evidence of negative graft characteristics other than diminished bone-forming in comparison to the 3.0cc Autograft, extender, and enhancer groups. While we did not attempt to further characterize the diminished fusion activity of the stand-alone group, this may present an opportunity for further investigations with PROGENIX® DBM as a carrier for materials such as bone-marrow-aspirate or synthetic BMP’s in this or other experimental models.

Our Faxitron-based radiographic fusion assessment and histologic analysis concurred with the manual palpation results. The addition of CT-based imaging in this study adds a novel assessment of fusion that is one of the options available for similar assessments in humans. Although there is some controversy with regard to CT-based assessment of fusion in humans, many of the options that are available for fusion assessment remain in the radiology realm. While the present study did not make attempts to fully characterize fusion rates based upon the CT-based imaging, this may be a relevant and timely assessment for future studies. Such assessments would need to be compared to other standards of assessment in this model (faxitron radiographs, manual palpation, and histological evaluation) for such a method to become further validated. Yet, this idea has been previously proposed as an acceptable adjunct to plain radiographic assessment in the rabbit model.

The results of this rabbit study suggest that PROGENIX® DBM Putty is effective in producing a posterolateral fusion by radiographic and manual palpation criteria in an extender and enhancer mode. While animal models cannot be translated into clinically successful human applications, the results of this study suggest that further investigation into use of PROGENIX® DBM Putty as an autograft extender or enhancer in a human clinical setting may be appropriate.

**CONCLUSIONS:**

In this commonly used rabbit posterolateral fusion model, PROGENIX® DBM Putty in an autograft extender or enhancer mode produced manual palpation and radiographic fusion rates slightly better than autograft fusion (3cc) alone. When a lower volume of autograft was used, the PROGENIX® Putty was able to extend the autograft and improve fusion rates in comparison to the less than optimal autograft volume. These results were also slightly better than the full 3cc autograft volume.

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**Table 3: Summary of Results**

<table>
<thead>
<tr>
<th>Group</th>
<th>Test Article</th>
<th>Radiographic Fusion</th>
<th>Manual Palpation</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>PROGENIX® Putty 3cc (Substitute)</td>
<td>38%</td>
<td>50%</td>
</tr>
<tr>
<td>2</td>
<td>PROGENIX® Putty 1.5cc + Auto 3.0cc (Enhancer)</td>
<td>86%</td>
<td>86%</td>
</tr>
<tr>
<td>3</td>
<td>PROGENIX® Putty 1.5cc + Auto 1.5cc (Extender)</td>
<td>87%</td>
<td>87%</td>
</tr>
<tr>
<td>4</td>
<td>Autograft 3cc (Control)</td>
<td>67%</td>
<td>67%</td>
</tr>
<tr>
<td>5</td>
<td>Autograft 1.5cc (Control for Extender Group)</td>
<td>25%</td>
<td>38%</td>
</tr>
</tbody>
</table>
demonstrating enhancer capability. These findings indicate that PROGENIX® Putty was able to both extend (overcome inadequate autograft volume) and enhance (improve fusion rates over adequate volume of autograft) performance of autograft – as per the prior definitions of these terms. This finding has important clinical implications in that autograft volume is often limited and harvest is associated with morbidity, additional surgical time and blood loss.

It is hypothesized that PROGENIX® Putty mixed with autograft has the ability to improve fusion performance by creating a homogeneous graft construct that provides a contiguous lattice between the osteogenic autograft particles. It appears to have the ability to act as both an osteoconductive and osteoinductive bone graft that works to improve the autograft construct. The material properties of this construct subjectively improved the handling characteristics in comparison to autograft alone, and objectively resisted migration intraoperatively and during the bone formation process.

PROGENIX® Putty when used alone or in combination with autograft induced de novo bone formation and remodeled into host bone as evidenced by histologic and radiographic appearance. The rate of remodeling also was greater for the PROGENIX® Putty material than for the autograft, likely due to the mineral content (mineralized vs. demineralized bone).

Although the rabbit posterolateral model is well characterized and provides a challenging bone healing environment, results cannot be extrapolated to the human clinical environment. Further studies would be necessary to determine how the results observed in this study correlate to those that may be observed with similar use in humans.

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ABSTRACT:
Study Design/Setting: Randomized, controlled study in a laboratory setting. Blinded observations/assessment of study outcomes.
Objective: The purpose of this study is to determine the performance characteristics of MASTERGRAFT® STRIP with bone marrow aspirate (BMA) as a bone graft extender in a rabbit posterolateral spine fusion model.

Summary of Background Data: The rabbit posterolateral fusion model is an established environment for testing of fusion concepts. It offers the opportunity to obtain radiographic, histological, and biomechanical data on novel fusion materials.

Methods: Thirty six rabbits were entered into the study with 34 used for analysis. Bilateral posterolateral lumbar intertransverse fusions were performed at L5-L6. The lateral two thirds of the transverse processes were decorticated and covered with graft material: autograft only (2.5 - 3.0 cc/side), 75% MASTERGRAFT® STRIP + 5.0cc BMA / 25% autograft (3.0cc total per side), or 50% MASTERGRAFT® STRIP + 5.0cc BMA and 50% autograft (3.0cc total per side). Animals were humanely euthanized at 8 weeks post surgery.

Results: The autograft group had a 60% radiographic fusion rate (6/10) and a manual palpation fusion rate of 50% (5/10). The 50% MASTERGRAFT® STRIP group had a 75% radiographic and manual palpation fusion rate (9/12). The 75% MASTERGRAFT® STRIP group demonstrated a 58% (7/12) radiographic and manual palpation fusion rate. Histologically, no adverse inflammatory reactions of significant size were present. The two MASTERGRAFT® STRIP groups demonstrated a tendency towards more bone development across the fusion bed.

Conclusions: In this commonly used rabbit posterolateral fusion model, MASTERGRAFT® STRIP with BMA in an autograft extender mode produces biomechanical and radiographic results similar to autograft fusion alone.

INTRODUCTION
Iliac crest autograft is considered the gold standard graft material despite limitations in the quantity available and complications associated with the harvesting procedure. These disadvantages have motivated investigators to seek alternative graft materials to extend, enhance, and/or substitute for autograft. Examples of such alternatives include: allografts, synthetic materials, and recombinant human bone morphogenetic proteins (BMPs).

Many such products have been in clinical use for years. As the number and complexity of these options grow, so does the need for scientific studies that examine evidence for methods of use, appropriate volume/percentages of graft material, and local biocompatibility/fusion results. Such studies have the opportunity to add to the collective knowledge of safe and efficacious use.

The current study was performed to assess MASTERGRAFT® STRIP as an autograft extender in the rabbit lumbar posterolateral fusion model. Fusion rates of iliac crest autograft (approximately 3cc/side) were compared to lesser amounts of autograft extended with the investigational “STRIP.”
TABLE 1: Experimental Design

<table>
<thead>
<tr>
<th>Group</th>
<th>Graft Type</th>
<th>Manual Palpation</th>
<th>Radiographic Fusion</th>
<th>Histology</th>
<th>Sacrifice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autograft</td>
<td>Autograft (3.0 cc)</td>
<td>12</td>
<td>12</td>
<td>3</td>
<td>8 Weeks</td>
</tr>
<tr>
<td>STRIP 50:50</td>
<td>STRIP 50% (1.5 cc) soaked with 1.5 cc BMA + Autograft 50% (1.5 cc)</td>
<td>12</td>
<td>12</td>
<td>3</td>
<td>8 Weeks</td>
</tr>
<tr>
<td>STRIP 75:25</td>
<td>STRIP 75% (2.25 cc) soaked with 1.5 cc BMA + Autograft 25% (0.75 cc)</td>
<td>12</td>
<td>12</td>
<td>3</td>
<td>8 Weeks</td>
</tr>
</tbody>
</table>

METHODS

The rabbit fusion model is a well accepted tool for evaluating bone graft performance. The surgical procedure involves exposure of the transverse processes between L5/L6, limiting decortication to the lateral regions and grafting with the same material bilaterally. Autograft is harvested from the bilateral iliac crests yielding between 2.5-3.0 cc’s per crest, such that approximately 3 cc’s of graft is placed on each posterolateral graft bed. This procedure typically results in fusion rates around 65%. To evaluate MASTERGRAFT® STRIP as an extender, two groups were compared to autograft alone, STRIP 50:50 (1.5 cc STRIP + 1.5 cc autograft) and STRIP 75:25 (2.25 cc STRIP + 0.75 cc Autograft). Each volume of MASTERGRAFT® STRIP was soaked with the same amount of bone marrow aspirate (BMA) which was acquired from the rabbit’s proximal tibia.

Skeletally mature New Zealand White Rabbits weighing 4.5-5.5 kg were entered into the study. All procedures were approved by the Institutional Animal Care Use Committee (#0708172) and conducted at The University of Iowa Department of Orthopaedics, Bone Healing Research Lab-Iowa Spine Research Center. Throughout the study, animals were individually caged and monitored daily for signs of pain and discomfort.

Surgical Procedure

All operative procedures were performed in a surgical suite using inhalation anesthesia and aseptic techniques. A preanesthetic dose of Ketamine HCL 26 mg/kg, Acepromazine Maleate 0.15 mg/kg, and Xylazine HCL 0.78 mg/kg was administered intramuscularly. Surgical anesthesia was maintained with 1.5-2.5% isoflurane delivered in O₂. Cardiorespiratory monitoring was continued throughout the procedure.

A parenteral dose of cefazolin (13 mg/kg) was administered for infection prophylaxis preoperatively and then BID for 48 hours post-op.

Rabbits were placed prone on the operating table and surgically prepped with 70% Betadine solution. A single level posterolateral intertransverse process fusion was performed in 36 rabbits (Table 1). A dorsal midline incision, approximately 15 centimeters long, was made from L1 to the sacrum and the soft-tissues overlying the transverse processes (TP) were dissected via separate bilateral fascial incisions. The transverse processes were decorticated with a high-speed burr. At no time were the vertebral bodies decorticated in the gutter of the motion segment.

Approximately 3.0 ml of corticocancellous bone graft from the iliac crest was obtained bilaterally as needed depending on the study group. This volume of graft is the maximum amount which can be harvested from the rabbit iliac crest without significant animal morbidity. Investigational implant preparation of the MASTERGRAFT® STRIP was done by hydrating the STRIP with corresponding amounts of BMA. In the BMA groups, a 1 mm hole was drilled in the tibial tuberosity. An 18g needle and syringe were used to obtain 5.0 cc of BMA. The hole was then filled with surgical bone wax and the surgical incision closed in a routine manner.

The morselized cancellous bone graft or the combination of STRIP/BMA + autograft was then placed between the transverse processes in the paraspinous bed (3.0 ml per side). The lateral two thirds of the transverse processes were covered with the graft. The MASTERGRAFT® STRIP + autograft combination was 75% MASTERGRAFT® STRIP / 25% autograft or 50% MASTERGRAFT® STRIP and 50% autograft. In each of these groups, the autograft was implanted first in the paraspinous bed and the MASTERGRAFT® STRIP placed over the autograft.

Animals were housed and monitored throughout the study. Animals were humanely euthanized at 8 weeks post surgery, a time point consistent with the published literature of this model.

Manual Palpation

The primary outcome used to determine fusion was manual palpation. After removing the spines, fusion was graded by three independent blinded observers as “fused” if no detectable motion was present at the treated segment when tested in flexion and extension. The fusion was graded as “not fused” if motion was present. Final results were determined by agreement of at least 2 of the 3 observers.
Assessment of MASTERGRAFT® STRIP with Bone Marrow aspirate AS A GRAFT EXTENDER

Radiographic Assessment
At time of euthanasia, high resolution images of removed spines were judged by three 'blinded' observers for radiographic fusion by evaluating for continuous trabecular bridging between the grafted transverse processes. Density of the grafts limited observers from accurately grading the fusion sites and false positive grades of union was prevalent.

Histology
Three specimens from each group were randomly selected for histological evaluation (Figures 1-3). Non-decalcified slides were prepared and stained with hematoxylin and eosin. Slides were evaluated for presence of inflammation, extent of graft remodeling, and general observations relevant to bone formation activity. New Bone Formation (NBF) was scored on a 0-3 scale (0 = none detected, 1= small uncommon foci, 2= moderate sized, multiple foci, and 3 = extensive multiple foci). Fusion was scored using a 1-10 scale where a score of 10 was complete bridging of the TPs with mature bone (Table 2).

Complications
Two (2) rabbits were omitted from the study due to complications.
The rabbits tolerated the surgery and study period well and regained normal activity within 24 hours of surgery. Two (2) rabbits were omitted from the study due to post-op complications associated with graft harvest. Necropsy of the animals was unremarkable regardless of treatment. Macroscopic analysis of the paraspinal bed area demonstrated healthy tissue with no apparent adverse effects such as inflamed, necrotic, or decreased vascularized tissue.

Animals were evaluated by manual palpation, radiographic and histological criteria (Tables 3 & 4). The autograft group had a 60% radiographic fusion rate (6/10) and a 50% (5/10) fusion rate when scored by manual pal-
Assessment of MASTERGRAFT® STRIP with Bone Marrow aspirate AS A GRAFT EXTENDER

pation. The STRIP 50:50 group had a 75% fusion rate by manual palpation and radiographic scoring. The STRIP 75:25 group had a 58% fusion rate by manual palpation and radiographic assessment.

**Histology**

Blinded histological assessments were made on each histological specimen by a board-certified veterinary pathologist (Table 4, Figures 1-3). There were no adverse inflammatory reactions to the MASTERGRAFT® STRIP regardless of volume of test article. In sections where a mild inflammatory response was noted (2 autograft and 1 MASTERGRAFT® STRIP 50%/autograft 50%), there were uncommon, locally extensive foci devoid of new bone formation with fibrous or loose connective tissue often in an unusual stromal pattern suggestive of resolving or chronic inflammation.

The STRIP treatment groups tended to have more

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**FIGURE 3: 75%/25% Histological Analysis**

A.) Microradiograph of 500 µm section. Ceramic granules are in white and new bone formation is in light grey.

B.) Stained section (50 µm 1 x) with ceramic in black and new bone in pink.

C.) Bone in direct apposition to the ceramic granule (10 x).
### TABLE 2: Histologic Scoring Scale for Fusion

<table>
<thead>
<tr>
<th>Fusion</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Union of TPs by mature bone; complete bridge</td>
<td>10</td>
</tr>
<tr>
<td>Union of TPs by immature bone and cartilage; complete bridge</td>
<td>9</td>
</tr>
<tr>
<td>Union of TPs by cartilage with little fibrocartilage</td>
<td>8</td>
</tr>
<tr>
<td>Partial union with more bone (&gt; 75%) than cartilage and fibrocartilage</td>
<td>7</td>
</tr>
<tr>
<td>Partial union with more bone (50%-75%) than other tissues (i.e., cartilage, fibrocartilage and fibrous tissue)</td>
<td>6</td>
</tr>
<tr>
<td>Partial bridge; equal amounts of bone (45%-55%) and other tissues (i.e., cartilage, fibrocartilage and fibrous tissue)</td>
<td>5</td>
</tr>
<tr>
<td>Minimal bridge with less bone (25%-44%) than other tissue (i.e., cartilage, fibrocartilage and fibrous tissue)</td>
<td>4</td>
</tr>
<tr>
<td>Minimal bone (&lt;25%) with predominantly other tissue (i.e., fibrocartilage, predominantly fibrous tissue)</td>
<td>3</td>
</tr>
<tr>
<td>Little new bone with predominantly fibrous tissue</td>
<td>2</td>
</tr>
<tr>
<td>Fibrous tissue only between TPs; full (across the defect)</td>
<td>1</td>
</tr>
</tbody>
</table>

### TABLE 3: Fusion Results

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Manual Palpation Fusion Rate</th>
<th>Radiographic Fusion Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autograft</td>
<td>50% (5/10)</td>
<td>60% (6/10)</td>
</tr>
<tr>
<td>STRIP 50:50</td>
<td>75% (9/12)</td>
<td>75% (9/12)</td>
</tr>
<tr>
<td>STRIP 75:25</td>
<td>58% (7/12)</td>
<td>58% (7/12)</td>
</tr>
</tbody>
</table>

### TABLE 4: Histological assessment of NBF, inflammation and fusion

<table>
<thead>
<tr>
<th></th>
<th>New bone formation (NBF)</th>
<th>Inflammation</th>
<th>Fusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>MASTERGRAFT® STRIP / Autograft 50/50</td>
<td>2.33</td>
<td>3.83</td>
<td>7.00</td>
</tr>
<tr>
<td>MASTERGRAFT® STRIP / Autograft 75/25</td>
<td>2.17</td>
<td>4.00</td>
<td>7.00</td>
</tr>
<tr>
<td>Autograft</td>
<td>2.17</td>
<td>3.67</td>
<td>6.50</td>
</tr>
</tbody>
</table>

NBF was scored on a 0-3 scale. Inflammation was scored on a 0-4 scale, where a score of 4 indicated no inflammatory response. Fusion was scored using a 1-10 scale where a score of 10 was complete bridging of the TPs with mature bone.

DISCUSSION:

Optimal bone graft substitutes should demonstrate biocompatibility, be of consistent quality, be able to promote osseous formation, be cost-effective, and be readily available. MASTERGRAFT® STRIP is a resorbable, malleable, osteoconductive scaffold composed of biphasic calcium phosphate (hydroxyapatite and beta-tricalcium phosphate) ceramic granules and purified fibrillar bovine type I collagen. It is designed to create a favorable environment for bony ingrowth. The objective of this study was to evaluate the efficacy of MASTERGRAFT® STRIP as a bone graft extender in a rabbit bilateral lumbar posterolateral spine fusion model.

This study demonstrates the efficacy of MASTERGRAFT® STRIP with BMA in two separate autograft extender ratios in a commonly used rabbit spinal fusion model. The ability of MASTERGRAFT® STRIP with BMA to be combined with lesser amounts of autograft and achieve similar fusion rates as autograft alone meets the definition for an autograft extender in this model. The fusion rate of 50% (manual palpation) observed in the Autograft group is consistent with prior studies performed in this laboratory as well as other published studies. The manual palpation fusion rates for both investigational STRIP + BMA extender groups demonstrated similar or slightly better results when compared to Autograft control. As with other radiodense calcium-based bone void fillers, the initial, interval, and final radiographs could over predict the rate of biomechanical fusion as the density of non-remodeled graft material may cause the appearance of fusion by typical radiographic criteria in this model. This finding has been noted in other studies with some calcium-based filler formulations in our lab. CT-based assessments (not performed in the current study) and/or histological assessment may have the potential to be more consistent with the final biomechanical status of the fusion.

Histological evidence of mature/immature bone development across the inter-transverse process spaces than did the autograft controls. In all groups, most new bone growth was regularly seen adjacent to the transverse processes and variably extended across intertransverse process space.

The histologic scores suggested the STRIP 50:50 group had similar bone formation and fusion compared to the STRIP 25/75 group, while both implant groups had increased fusion scores over autograft.
Histologically, the results between the 3 groups were similar and not significantly different from one another, remodeling was underway in all groups, and that there was no evidence of adverse inflammatory reactions. The results of this rabbit study suggest that MASTERGRAFT® STRIP with BMA is effective in producing a posterolateral fusion by radiographic and manual palpation criteria in an extender mode. While animal models cannot be translated into clinically successful human applications, the results of this study suggest that further investigation into use of MASTERGRAFT® STRIP with BMA as an autograft extender in a clinical setting may be appropriate.

CONCLUSIONS:
In this well-established rabbit lumbar posterolateral fusion model, MASTERGRAFT® STRIP with BMA was an effective extender of autograft, allowing reduction of autograft by up to 75% while achieving fusion rates equal to or slightly better than autograft alone.

REFERENCE LIST


THE TIME OF THE INSULT/TRIGGERING EVENT IN LEGG-CALVÉ-PERTHES’ DISEASE DETERMINED BY INCUBATION PERIOD MODELING AND THE AGE DISTRIBUTION OF CHILDREN WITH PERTHES’

Randall T. Loder, MD*, Richard H. Browne, PhD^, Andrew Millis, MD*, Wook-Cheol Kim, MD, PhD$,
Hitesh Shah, MS (Ortho.)#, Aidan P. Cosgrove, MD, FRCS (Orth.)^&; Ola Wiig, MD, PhD&

INTRODUCTION

Legg-Calvé-Perthes’ disease (LCPD) is an idiopathic osteonecrosis of the proximal capital femoral epiphysis in children which typically presents between 4 and 8 years of age. Except for children from southern India1,2 and Nigeria3, all other areas of the world and ethnicities demonstrate a similar average age at diagnosis (5 to 7 years)4-7. The etiology of LCPD is unknown, but there is significant data that indicates a triggering event or insult occurs somewhere in the prenatal or early years of life16-21. Although the symptoms and subsequent diagnosis occur much later. If the age/time when such a triggering event occurs can be determined, then the number of potential etiologies in LCPD can be narrowed. This could provide further insight into the etiology of LCPD and perhaps avenues for prevention22.

An estimation of the time/age when such a triggering event occurs can be obtained using incubation period modeling. Incubation period modeling was first used with infectious diseases23,24. An infectious disease occurs when an organism is exposed to an infectious agent. The pathogen infects the organism, the host later develops clinical symptoms, and is then diagnosed with the disease. The incubation period is the time from exposure to clinical manifestation of the disease. Different members of a population afflicted with an infectious disease demonstrate different incubation periods. The natural variation in incubation periods can be characterized by a frequency distribution, with the x axis representing the time of the incubation period and the y axis the number of organisms infected (frequency) during that particular incubation period. The area (integral) under a particular portion of the frequency distribution denotes the proportion of the entire population spanning that particular portion of the x axis.

A well known frequency distribution is the normal distribution, a bell shaped curve characterized by its arithmetic mean x and standard deviation s (Addendum D), commonly expressed as x ± σ. Although normal distributions are often used in statistical analyses in medicine, many populations are better evaluated with skewed distributions. Skewed distributions are particularly common when values cannot be negative, as with incubation periods. Infectious diseases are better modeled using a logarithmic normal distribution24,25.

*Department of Orthopaedic Surgery, School of Medicine, Indiana University; James Whitcomb Riley Children’s Hospital, Indianapolis, Indiana rloder@iupui.edu, andrew.millis.md@gmail.com;
^Texas Scottish Rite Hospital for Children, Dallas, Texas Richard.Browne@tsrh.org;
#Department of Orthopaedics, Kasturba Medical College, Manipal, Karnataka, India hiteshshah12@gmail.com;
$Department of Orthopaedic Surgery, Musgrave Park Hospital, Belfast, Northern Ireland, UK aidan.cosgrove@doctors.org.uk
&Orthopaedic Centre, Ullevål University Hospital, Oslo, Norway ola.wiig@ullevaal.no;

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where the frequency of the log of the x value is normally distributed (Addendum I). Incubation period modeling has subsequently been applied to chronic diseases 22, 26, 27 and malignancies 28-31.

Incubation period modeling is the epidemiologic tool that first determines the best frequency distribution for a data set of an entire population afflicted with the disease/syndrome in question. When y = 0, (frequency distribution is zero), no cases of the disease have yet occurred. The x which corresponds to y = 0 represents the moment in time when the host was exposed to the infectious/triggering/causeative agent(s) (defined as xₜ in this study). Many frequency distributions are mathematically undefined when y = 0 due to the particular mathematical expression (e.g., division by zero or logarithm of 0). In such instances the y corresponding to an x when only 0.1-1% of the population has been diagnosed with the disease is used as xₜ. Similarly, the area under the curve for all x > xₜ is 99-99.9% respectively.

In 1984 Hall et al. 21 modeled the age distribution of LCPD with the lognormal distribution and noted an excellent fit (Figure 1A). This was interpreted as LCPD having a single etiologic agent before 2 years of age (Figure 1B). There have been no further studies of incubation period modeling and LCPD. Recent authors have suggested that other frequency distributions are better models for chronic as well as infectious diseases 22, 32, 33. With the advent of computers it is easy to fit a data set to many frequency distributions, both simple and complex. It was the purpose of this study to examine the fit of many distributions to children with LCPD and determine the best one(s). From this, xₜ and incubation periods are calculated to give further insight into the etiology of LCPD and perhaps avenues for prevention 22.

MATERIALS AND METHODS

This is a retrospective study of children with LCPD from institutions where the age at diagnosis of LCPD in increments of 1 year had been recorded for an entire cohort of children (Table 1). Studies with pre-selected age ranges were excluded. This study was classified as exempt research by our local Institutional Review Board.

There were two data sources. The first was published series where the age distribution data was either tabulated or could be extrapolated from a published graph/figure. Hall’s original 1984 manuscript was reviewed 21 as well as any subsequent publications. Studies with < 50 children were excluded to ensure an adequate number of children in each year of age to allow for acceptable frequency distributions. Six studies met these criteria 5, 7, 11, 15, 34, 35.

The second source was a comprehensive PubMed literature review for publications of large series of children with LCPD where the incremental ages were not stated in the manuscript but must have been known to the original authors because an average age and standard deviation was reported. Incremental age data was requested from these locations, and were Ireland 6, Japan 16, Norway 39, and Karnataka State, India 1, 2, 40.

The data were analyzed using TableCurve® 2D, version 5.01 software (SYSTAT Software Inc., Richmond, CA, 2002) which fits over 6,000 potential mathematical equations. We wished to find a single peak model that accurately fit the lower age frequencies, as that is the portion of the distribution that is used to determine xₜ in incubation period modeling. The ideal model should have an r² ≥ 0.99 to indicate a close fit, and one comparatively simple in form.
After finding the optimum model, \( x_t \) was calculated using the 99% criteria. When the area under the distribution density curve is 0.99 for \( x > x_t \), only 1 out of 100 children with LCPD will have presented before that particular \( x_t \). Such value of \( x_t \) is then a plausible value for the age of “insult” or “exposure” to the causative event/agent(s) in LCPD. Numerical integration employing the trapezoidal method was used to determine the area under the curve for \( x > x_t \) and the median age for the distribution (the \( x \) at which the area under the curve is 50%). The median incubation period (\( IP_m \)) = median age – \( x_t \).

### RESULTS

There were 2,911 children from 10 different sources (Table 1). All groups demonstrated a similar age except those from India. We created two groups: those not from India (2,406 children, avg age = 5.8 ± 2.2 years) and those from India (505 children, avg age = 8.1 ± 2.3 years). This age difference was statistically significant (Mann-Whitney U = 9.19 x 10^5, \( P < 10^{-6} \)). An excellent fit to the distribution of age at diagnosis was the relatively simple distribution \( \ln(y) = a + bx + c\ln(x) \), where \( y \) is the proportion of children with LCPD at age of diagnosis \( x \) (\( r^2 = 0.959 \) and 0.994 for the Indian and non-Indian groups respectively) (Figure 2). The median age, \( x_t \), and \( IP_m \) were 5.62, 1.32, and 4.30 years, respectively, for the non-Indian children and 8.10, 2.77, and 5.33 years, respectively, for the Indian children (Table 2).

The data was also fit to the four-parameter log-normal distribution to compare our results with Hall.\(^{21}\) The log normal distribution demonstrated slightly poorer but still very good fits (\( r^2 = 0.941 \) and 0.967 for the Indian groups respectively) (Figure 2). The median age, \( x_t \), and \( IP_m \) were 5.62, 1.32, and 4.30 years, respectively, for the non-Indian children and 8.10, 2.77, and 5.33 years, respectively, for the Indian children (Table 2).

#### TABLE 1.

<table>
<thead>
<tr>
<th>Source</th>
<th>Year</th>
<th>Location</th>
<th>n</th>
<th>Mean Age ± 1 sd (years)</th>
<th>Age at Diagnosis of Child with Legg-Calvé-Perthes Disease (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1     2     3     4     5     6     7     8     9     10    11    12    13    14    15</td>
</tr>
<tr>
<td>Not From India</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barker</td>
<td>1978</td>
<td>England</td>
<td>144</td>
<td>5.7 ± 2.1</td>
<td>0     11    11    20    28    25    24    9     8     6     2     0     0     0     0     0</td>
</tr>
<tr>
<td>Cosgrove</td>
<td>1991</td>
<td>Ireland</td>
<td>391</td>
<td>5.1 + 2.2</td>
<td>3     31    65    69    70    68    33    25    10    4     10    3     3     31    65</td>
</tr>
<tr>
<td>Fisher</td>
<td>1972</td>
<td>USA</td>
<td>188</td>
<td>6.1 + 2.0</td>
<td>0     0     14    25    38    36    34    18    13    7     2     3     0     0     0     0</td>
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<tr>
<td>Gray</td>
<td>1972</td>
<td>Canada</td>
<td>379</td>
<td>5.7 + 2.2</td>
<td>0     15    43    72    67    53    49    34    25    9     8     4     0     0     0     0</td>
</tr>
<tr>
<td>Harrison</td>
<td>1976</td>
<td>England</td>
<td>182</td>
<td>5.9 + 1.9</td>
<td>0     1     16    30    39    37    19    19    14    5     1     1     0     0     0     0</td>
</tr>
<tr>
<td>Kim</td>
<td>2006</td>
<td>Japan</td>
<td>589</td>
<td>6.6 + 2.2</td>
<td>1     10    35    48    90    104   120   72    38    40    19    5     5     2     0     0</td>
</tr>
<tr>
<td>Moberg</td>
<td>1990</td>
<td>Taiwan</td>
<td>57</td>
<td>6.3 + 2.0</td>
<td>0     1     5     13    7     14    13    9     9     1     1     0     0     0     0     0</td>
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<tr>
<td>Wiig</td>
<td>2006</td>
<td>Norway</td>
<td>425</td>
<td>5.4 + 2.2</td>
<td>4     25    60    63    78    81    50    29    22    6     2     2     2     0     1     0</td>
</tr>
<tr>
<td>All Combined</td>
<td>2406</td>
<td></td>
<td></td>
<td>5.8 + 2.2</td>
<td>8     110   298   397   521   530   439   394   193   77    37    34    15    7     1     0</td>
</tr>
<tr>
<td>From India</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shah</td>
<td></td>
<td>Manipal, India</td>
<td>505</td>
<td>8.1 + 2.3</td>
<td>0     0     8     16    49    58    84    78    73    55    22    8     0     2     0     0</td>
</tr>
</tbody>
</table>

\(^{a}\)Data from a center having a long continuing work in Ireland.\(^{b,36-38}\).

\(^{b}\)Data supplied from a multicenter Japanese study.

\(^{c}\)Data supplied from a center having a long continuing work in Norway.

\(^{d}\)Data from a center having a long continuing work in Manipal, India (Kasturba Medical College) 1, 2, 40.

FIGURE 2: Frequency distributions for children with LCPD by age at diagnosis. The 2406 non-Indian children are represented by the solid squares and the Indian children by the open triangles. The simple excellent fitting distribution \( \ln(y) = a + bx + c\ln(x) \) is represented by the thick line, and the log-normal distribution by the thin line. For the non-Indian children the excellent fit distribution is \( \ln(y) = -2.623 + 2.779x - 1.04\ln(x) \), \( r^2 = 0.994 \) and for the 505 Indian children is \( \ln(y) = -5.847 + 3.384x - 1.1.9\ln(x) \), \( r^2 = 0.959 \). The \( \ln(y) = a + bx + c\ln(x) \) better fits the data compared to the log normal distribution.
TABLE 2. Distribution Fits for 2911 Children with Legg-Calvé-Perthes’ Disease

<table>
<thead>
<tr>
<th>Function</th>
<th>Unadjusted Age at Diagnosis</th>
<th>Age at Diagnosis Decreased by 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median Age</td>
<td>x&lt;sub&gt;t&lt;/sub&gt;</td>
</tr>
<tr>
<td>Non Indian</td>
<td>ln(y) = a + bx + cln(x)</td>
<td>5.62</td>
</tr>
<tr>
<td></td>
<td>Log Normal</td>
<td>5.74</td>
</tr>
<tr>
<td>Indian</td>
<td>ln(y) = a + bx + cln(x)</td>
<td>8.10</td>
</tr>
<tr>
<td></td>
<td>Log Normal</td>
<td>8.18</td>
</tr>
</tbody>
</table>

Abbreviations: x<sub>t</sub> = age of the triggering event, IP<sub>m</sub> = median incubation period.
All ages in years.
Unadjusted age uses the age at diagnosis for modeling; the age decreased by 6 months models the distribution fits if the child had symptoms for 6 months before diagnosis.

TABLE 3. Distribution Fits for Each Individual Center Contributing Children with Legg-Calvé-Perthes’ Disease

<table>
<thead>
<tr>
<th>Center</th>
<th>n</th>
<th>r&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Median Age (years)</th>
<th>x&lt;sub&gt;t&lt;/sub&gt;</th>
<th>IP&lt;sub&gt;m&lt;/sub&gt;</th>
<th>r&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Median Age (years)</th>
<th>x&lt;sub&gt;t&lt;/sub&gt;</th>
<th>IP&lt;sub&gt;m&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barker</td>
<td>144</td>
<td>0.93</td>
<td>5.83</td>
<td>1.40</td>
<td>4.43</td>
<td>0.90</td>
<td>5.83</td>
<td>1.40</td>
<td>4.43</td>
</tr>
<tr>
<td>Cosgrove</td>
<td>391</td>
<td>0.96</td>
<td>4.66</td>
<td>0.74</td>
<td>3.92</td>
<td>0.96</td>
<td>4.90</td>
<td>1.34</td>
<td>3.56</td>
</tr>
<tr>
<td>Fisher</td>
<td>188</td>
<td>0.98</td>
<td>5.82</td>
<td>1.85</td>
<td>3.97</td>
<td>0.98</td>
<td>6.02</td>
<td>2.97</td>
<td>3.06</td>
</tr>
<tr>
<td>Gray</td>
<td>379</td>
<td>0.96</td>
<td>5.16</td>
<td>0.99</td>
<td>4.20</td>
<td>0.98</td>
<td>5.48</td>
<td>2.27</td>
<td>3.21</td>
</tr>
<tr>
<td>Harrison</td>
<td>182</td>
<td>0.95</td>
<td>5.45</td>
<td>0.65</td>
<td>4.80</td>
<td>0.97</td>
<td>5.68</td>
<td>2.70</td>
<td>2.98</td>
</tr>
<tr>
<td>Kim</td>
<td>589</td>
<td>0.96</td>
<td>6.48</td>
<td>2.15</td>
<td>4.33</td>
<td>0.94</td>
<td>6.64</td>
<td>1.39</td>
<td>5.25</td>
</tr>
<tr>
<td>Moberg</td>
<td>51</td>
<td>0.93</td>
<td>4.87</td>
<td>1.01</td>
<td>3.86</td>
<td>0.93</td>
<td>5.80</td>
<td>2.20</td>
<td>3.60</td>
</tr>
<tr>
<td>Wang</td>
<td>57</td>
<td>0.51</td>
<td>5.68</td>
<td>1.56</td>
<td>4.12</td>
<td>0.67</td>
<td>6.47</td>
<td>2.77</td>
<td>3.70</td>
</tr>
<tr>
<td>Wiig</td>
<td>425</td>
<td>0.97</td>
<td>5.11</td>
<td>1.09</td>
<td>4.02</td>
<td>0.94</td>
<td>5.34</td>
<td>2.16</td>
<td>3.18</td>
</tr>
<tr>
<td>All Combined</td>
<td>2406</td>
<td>0.99</td>
<td>5.65</td>
<td>1.79</td>
<td>3.86</td>
<td>0.97</td>
<td>8.30</td>
<td>4.61</td>
<td>3.69</td>
</tr>
</tbody>
</table>

Abbreviations: x<sub>t</sub> = age of triggering event, IP<sub>m</sub> = incubation period.

and non-Indian groups respectively) (Figure 1). For the log-normal distribution, the median age, x<sub>t</sub> and IP<sub>m</sub> were 5.74, 1.82, and 3.94 years, respectively, for the non-Indian children and 8.18, 3.89, and 4.29 years, respectively, for the Indian children.

We finally individually modeled each data set from the non-Indian group (Table 3). Aside from one study 15, all had good fits (all r<sup>2</sup> ≥ 0.93) considering the smaller n in each set. Most importantly, the conclusions remain similar: the triggering event in LCPD occurs in early childhood with x<sub>t</sub> 1-2 years and IP<sub>m</sub> ~4 years.

DISCUSSION

Hall 21 used the log-normal distribution and incubation period modeling in LCPD and noted a good fit, consistent with a single cause acting before two years of age. We studied other distributions, compared them to the log-normal distribution, and discovered a simpler, better fit (Figure 1). This fit was ln(y) = a + bx + cln(x), and places x<sub>t</sub> in LCPD at approximately 1.3 years of age in non-Indian children and 2.8 years in children from India, with an IP<sub>m</sub> of 4.3 and 5.3 years respectively. The log-normal distribution resulted in a slightly older x<sub>t</sub> of 1.8 years for the non-Indian children and 3.9 years for Indian children, and a slightly shorter IP<sub>m</sub> (3.9 to 4.3 years, respectively). The log-normal distribution does not fit the lower age frequencies as well, and it is this portion of the frequency distribution from which x<sub>t</sub> is calculated (Figure 1). This explains the differences between the results for these two distributions. This study suggests x<sub>t</sub> in LCPD occurs early in life but not in utero 18, 19.

Because LCPD is a chronic condition, the child will experience symptoms for a period of time before diagnosis. If the time of first symptoms is used as the age for modeling rather than the age at diagnosis, then the median age and x<sub>t</sub> will decrease and may result in IP<sub>m</sub> changes. However, no reliable data exists for the time span between first symptoms and diagnosis in LCPD; a general estimate from our clinical experience is 3 to 6 months. We analyzed this potential effect by adjusting the age at diagnosis downwards by 6 months and then modeling that data (Table 2). We found that the median age dropped by 0.5 years (as expected), x<sub>t</sub> by 0.35 years, with IP<sub>m</sub> dropping 0.07 to 0.13 years, a relatively trivial change even with the earlier ages. Therefore the conclusions still hold: x<sub>t</sub> in children with LCPD is early childhood with an IP<sub>m</sub> of ~ 4 to 5 years.

It might be suggested that Indian children with LCPD are diagnosed at later Waldenström stages of disease 42 compared to non-Indian children as an explanation of...
the age differences at diagnosis. However, previous literature has shown that Indian children are diagnosed at similar Waldenström stages as non-Indian children 45, refuting such an argument. One potential explanation between the Indian and non-Indian children is the delay in skeletal maturation in Indian children. This delay is often 1 to 2 years compared to Caucasian or African children 45-46, although Indian children of higher socioeconomic class do not demonstrate such a delay 46. Perhaps there is a critical time in the development of the vascularity to the proximal femoral epiphysis which corresponds to a certain physiological skeletal maturation (bone age). If an insult at that critical time is the cause of LCPD, then that critical time for Indian children would be delayed by 1 to 2 years, similar to the years noted in this study between \( x \) for the non-Indian (1.3 years) and Indian (2.8 years) children.

Similar \( IP_{m} \) with different \( x \), as found in this study can be explained by: 1) a common etiologic event with different host susceptibilities due to environmental/racial/social factors resulting in different \( x \), 2) different etiologic events that occur at different ages due to environmental/social/racial/factors, or 3) differing abilities in the individual hip to respond to the initial insult from vertical loading due to standing and/or running. This study most strongly supports 1) a common insult that occurs at different \( x \) in different populations dependent upon local factors such as geographic location or ethnicity. The other plausible option is 3) that Indian children, compared to non Indian children, require a greater exposure in length of time to the vertical loading forces from standing or running before the proximal femoral epiphysis is “fractured” which then begins the cascade of LCPD. The different etiologic events, theory 2), is not as plausible an explanation since a single disease is more likely to have the same rather than different etiologies.

The insult or etiologic agent in LCPD has long been debated. One proposed agent is passive smoke exposure (both post natal and prenatal) 18, 19, 47-49. This study does not support prenatal smoke exposure as an etiology of LCPD 18, 19, since \( x \) was a positive value, even when allowing for distributions with negative \( x \). Another proposed etiology is a coagulopathy 50-58. Although congenital in nature, coagulopathies might not affect the proximal femoral epiphysis with its loading forces until a particular postnatal time which then begins the cascade of LCPD. Finally, with similar \( IP_{m} \) for the Indian and non-Indian cohorts, the etiology is likely the same for these two groups; different etiologies would be more consistent with different \( IP_{m} \).

Criticisms to the use of incubation period modeling in chronic diseases 22 are 1) the very nature of chronic diseases and population dynamics may result in a log-normal distribution of age at onset, 2) such modeling is only appropriate where the population is stable and the incubation period is brief, and 3) it can be used to erroneously conclude that a prenatal exposure is involved indicating that there may be a genetic etiology. The etiology of LCPD is likely multifactorial as are many other chronic diseases, and incubation period modeling is appropriately applied to chronic diseases 22, 26-31, 59 especially to differentiate between etiologic factors acting before or after birth 27. Breast cancer data demonstrates an excellent log-normal fit, even though the predominant etiology is thought to be neither genetic nor a simultaneous common-source exposure to an agent 22. Truncated and/or absent/missing data can also adversely affect such modeling 22. In this study only series with consecutive patients with LCPD without age exclusions were included, eliminating the effect of truncated or absent data.

With these caveats in mind, this study demonstrated that the age at diagnosis of LCPD can be well modeled using a relatively simple frequency distribution \( \ln(y) = a + bx + c \ln(x) \), and which is better fitting than the log-normal distribution previously suggested. The \( IP_{m} \) for children with LCPD is ~ 4.3-5.3 years and the age of the triggering event/insult in LCPD is ~ 1.3 years in non-Indian children and ~2.8 years in Indian children. This will hopefully guide future investigations into the etiologic event/mecanisms of LCPD and reduce the number of such potential events/mechanisms.

**ADDENDUM I**

The normal distribution is mathematically expressed as

\[
y = \frac{1}{\sigma \sqrt{2\pi}} e^{-\left(\frac{x-\mu}{2\sigma}\right)^2}
\]

where \( e \) is the base of the natural logarithm.

The lognormal distribution is mathematically expressed as

\[
y = \frac{e^\left(-1/2\left(\frac{\ln x - \mu}{\sigma}\right)^2\right)}{x \sigma \sqrt{2\pi}}
\]

where \( e \) is the base of the natural logarithm.
REFERENCES


APPLICATION OF SURGICAL SKILL SIMULATION TRAINING AND ASSESSMENT IN ORTHOPAEDIC TRAUMA

Matthew D. Karam, MD1, Jenniefer Y. Kho, MD1, Tameem M. Yehyawi, MD1, Gary T. Ohrt, BSE1,2, Geb W. Thomas, PhD3, Brandon Jonard, BSME1, Donald D. Anderson, PhD1,2, J. Lawrence Marsh, MD1

INTRODUCTION

Importance of simulation

The surgical restoration of a severely fractured extremity is a complex procedure requiring skills that a surgeon trainee must acquire during their education. Traditional surgical education has consisted of a mixture of didactic lessons with periodic clinical and surgical apprenticeship-based experience. These experiences, although beneficial, are not uniform and do little to assure technical competence. The apprenticeship model is challenged not only by a lack of opportunities to expose trainees to the necessary variety of procedures,1 and the expense of such training,2,3 but also by the need to ensure patient safety while exposing trainees to new experiences.4

There is strong evidence that the current training approach may not be optimally safe. In a review of surgical errors, 63.5% of cases involved technical error and 29% included an error in judgment.5 Both of these types of errors can be ascribed to a lack of experience. These and similar findings have led to the call for greater transparency in the training and assessment of surgical residents. The American Board of Surgery has mandated that, rather than just documenting the surgeries a resident participated in, proficiency in basic laparoscopic skills must be documented prior to allowing graduates to be tested for certification.6

Surgical simulation can help address shortcomings in the traditional apprenticeship training model by providing residents with opportunities to (1) practice important procedures that they may not otherwise encounter and (2) practice procedures efficiently until competency is achieved, (3) without exposing live patients to undue risk. Simulation can provide immediate and detailed feedback that can improve learning efficiency. With newly imposed restrictions on resident work hours, financial pressures, and increased public scrutiny, simulation-based technical training and assessment tools are receiving renewed attention. Before a surgical simulator construct can be used to assess competency, however, the scientific validity of the simulator and of the performance assessment must be established.7 A well-designed and rigorously validated simulator can provide quantitative, repeatable assessment of specific surgical skills and can predict performance in the operating room.

The benefits of training using surgical simulation are already being realized in general surgery, particularly for laparoscopic surgery. Medical students and residents trained on simulators demonstrate improved performance in actual surgeries. For example, in one study, training on a laparoscopic simulator was shown to lead to reliably fewer errors during actual surgery on an anesthetized animal.8 In another study, residents were trained to a certified level in the laparoscopic simulator and then performed their first actual surgery with fewer errors and caused fewer injuries than did a control group of non-simulation-trained residents.9

Deficiencies in fracture simulation

Orthopaedic surgery in general, and orthopaedic trauma surgery specifically, has lagged behind other surgical disciplines in developing and incorporating simulation of surgical skills into education and assessment paradigms. What little simulation there has been has mostly consisted of learning anatomy and surgical approaches on cadavers and placing products often supplied by medical device companies on surrogate bone specimens. At the present time there are no validated methods to assess surgical skill in orthopaedic trauma surgery. Currently, only self-reported web based case logs (as mandated by the ACGME) are utilized to document surgical experience, which does little to assess actual involvement, skill, or competency. This is particularly unfortunate, since orthopaedic trauma is a subspecialty where patients do not have the luxury of choosing their surgeon. They must depend upon on-
call surgeons to have the skills required to safely and successfully care for their injuries. This is troubling, because currently the ability to competently perform orthopaedic trauma surgery is learned by trainees in residency programs and practiced everywhere around the country without public assurance of even minimal procedural competence.

Rationale for articular fracture as a good target for simulation

The surgical restoration of a joint surface following a comminuted articular fracture is a complex skill that poses technical challenges for the surgeon and potential limb-threatening risks for the patient. Yet, the first time a surgeon faces these distinct challenges will most likely be in the operating room. Precise anatomical restoration of the joint is critical to avoid debilitating post-traumatic arthritis. Treatment risks and complications, including wound breakdown and infection, osteomyelitis, non-union, and hardware failure, can lead to poor patient outcomes, even amputation. Limited percutaneous surgical approaches utilizing fluoroscopy have decreased the complication risk for the patient, but present even greater challenges to the surgeon than do traditional open approaches, due to visualization and soft tissue constraints.

Introduction to these advanced psychomotor and visual-spatial skills in a controlled, simulated environment would be advantageous to both the surgeon and patient. It allows for deconstruction of a complex procedure such as articular fracture repair into discrete tasks such as fracture reduction, temporary stabilization, hardware placement, and fluoroscopic assessment. Critical analysis of simulator performance also provides valuable information about which specific tasks young surgeons are struggling with, and a surgical skills training program could be tailored to address these deficiencies.

We have developed a new fracture simulation training program targeted for junior residents that is designed to improve cognitive and technical skills required to reduce an articular fracture. The purpose of this study is to describe the development and content of the fracture simulation training program and to report resident experience.

ARTICULAR FRACTURE REDUCTION SIMULATION TRAINING PROGRAM

The simulation model

The main objective of the study was to develop a comprehensive training and assessment program focused on improving articular reduction skills in a tibial plafond fracture model (Figure 1). The simulation environment utilizes various multi-segment, radio-dense polyurethane foam (bone surrogate) fracture constellations inside a synthetic soft tissue housing. The simulation task is to temporarily stabilize a three-segment fracture with Kirschner wires (Figure 2). Using fluoroscopic guidance, trainees reduce the fragments of the simulated fracture through a limited anterior window in the housing. The hand motions of the participant are tracked with sub-mm accuracy during the simulation using a four-camera optoelectronic Qualisys motion capture system (Qualisys AB, Gothenburg, Sweden).

Subject performance is also captured on multiple video channels, including video from a head-mounted

FIGURE 1. The image to the left shows a percutaneous articular fracture reduction surgery. The middle image shows the current simulator, in which a cast polyurethane surrogate of a fractured bone is contained inside an anatomic rubber housing. The fiducials attached to the back of the surgeon’s hand enable motion capture. The illustration on the right shows the fiducials as the Qualisys camera detects them (blue for the left hand, green for the right), from which hand motion is measured.
camera that allows determination of when and where attention is being focused (Figure 3). The video streams are consolidated into a single composite split-screen video, coupled with audio capture, for later one-on-one feedback by a traumatologist.

Trainees are assessed on time-to-completion and objective quality of the obtained fracture reduction (from post hoc 3D laser scans that quantify the re-apposition inaccuracy of each fragment, again with sub-mm resolution). Economy of subject hand movement, including the number of deliberate actions, and cumulative hand motion, are extracted from the motion capture data. [Analysis of the hand motion data is the subject of ongoing work and those data are not presented in this paper.] Radiation dose and fluoroscopy time are also recorded. An orthopaedic traumatologist scores each performance using a modified objective structured assessment of technical skill (OSATS) checklist, which was initially described and validated by Faulkner et al. In pilot studies with this simulator, we found that senior orthopaedic residents had more deliberate hand motions (less cumulative hand distance, a surrogate for less iatrogenic wound bed trauma) and more accurate fragment reductions than did junior residents.

The broader educational program consisted of two modules, cognitive and motor. The cognitive module was implemented through an online course that included a pretest, general knowledge about plafond fractures and fluoroscopy, and online video performance reviews. The second half of the program focused on acquiring motor skills by direct instruction and dedicated practice on the simulated model with real-time feedback from an orthopaedic traumatologist.

Cognitive Knowledge-Online Instruction

Online instruction was provided by participant enrollment in an online course on the surgical management of articular fractures (Figure 4). The course was implemented in ICON (Iowa Courses Online), the University of Iowa’s online course management system, supported by the University’s information technology services. ICON incorporates capabilities that support video content and interaction between trainee and instructor, and it makes the content available through a number of portable devices (computer, iPad, iPod, iPhone etc.).

A requisite pre-test was performed for baseline knowledge assessment regarding plafond fractures and articular fracture management. Participants were encouraged to review/study available online content. Course content (Figure 5) included learning objectives,
background of plafond fractures, relevant fracture and surgical anatomy, principles of surgical technique and principles of fluoroscopic evaluation. In addition, other available resources including video links to both expert and novice surgical simulations, and baseline video self-performances were available for independent review.

For the skills training module, two separate two-hour evening sessions were held during which participants received a brief didactic introduction into the objectives of the training program and surgical simulation exercise. Surgical instruments (Figure 6), reduction strategies, and fixation techniques were discussed in a small group setting.

Video review with each participant was conducted during a one-on-one coaching session, led by an orthopaedic traumatologist who had previously reviewed and documented particular strengths/weaknesses of the performance. These coaching sessions were held in private, and in a non-adversarial manner.

Subjects

Six PGY 1 and six PGY 2 orthopaedic residents at the University of Iowa enrolled in this study. Three participants in each of the PGY1 and PGY2 years were randomized for participation in the comprehensive training program while the other half were not, for a total of six in the intervention group and six in the control group.
ASSessment

All 12 PGY 1 and PGY 2 residents performed baseline and final surgical simulation exercises separated by a 4-week interval. The participants filled out questionnaires assessing the usefulness of the simulation training program and their overall experience. General comments were elicited as well. These responses were then compared between the two groups.

Resident Experience

The feedback received from the residents about the simulation exercise and the training program was overall very positive (Table 1). All six residents in the intervention group rated each aspect of the training program as “extremely helpful” (Table 2).

When asked to compare their overall experience between the two sessions on a five-point scale, the control group responded that the second session was the same in difficulty (median score 3/5) compared to the first session, while the intervention group thought that it was easier (median score 1.5/5) (Table 3). Subjectively, the control group thought that they performed the same or slightly worse (3.5/5) during the second session, while the intervention group believed that they were much better (1/5). The overall median scores combined were 2/5 for both questions.

Discussion

To our knowledge, there are no current validated methods to assess surgical skill competency in orthopaedic trauma. Mabrey et al.12 in a 2010 review of virtual reality simulators in orthopaedic surgery identified 16 described simulators. Further review revealed that nine papers involved knee arthroscopy simulators (1995–2006), four involved shoulder simulators (1999–2008), and only three involved the management of fractures (2007–2008.) This stands in contrast to the 246 citations identified for laparoscopic virtual reality simulation. In the area of fracture surgery, Blyth and coworkers have developed an entirely PC based virtual reality training system for basic hip fracture fixation, including a surgical simulator and an assessment component.13,14 Results from the recent report by Froelich et al.15 suggest that a computer-based simulator with haptic feedback could identify measurable differences in surgical proficiency between junior and senior orthopaedic surgery residents and may play an expanding role in resident education.

In this paper, we describe in detail the content of a comprehensive articular fracture reduction simulation-training program in PGY 1 and PGY 2 orthopaedic surgery residents. The simulation training program was felt to be extremely useful to the participants. We received great enthusiasm and positive feedback from participants. When the participants were asked to reflect on their performance between the two sessions, the intervention group believed that they performed much better during the second exercise while the control group thought they did the same or slightly worse. Our work strongly encourages the need to develop and implement surgical simulation programs in orthopaedics.

This simulation-training program was comprised of both a cognitive and skills module. The cognitive module was a web-based course that provided general background knowledge about plafond fractures and use of fluoroscopy, and technical tips on how to reduce an articular fracture. These core principles were then reinforced in a brief didactic session led by a fellowship-trained traumatologist, and then executed during the guided skills session. One-on-one video analysis was another instructional tool that allowed for direct expert
feedback. Each element of the intervention program was rated as extremely helpful.

The program reported in this paper consisted of only one session of dedicated practice; a longer follow-up study with multiple practice sessions will be needed to detect meaningful objective improvement. A randomized-controlled trial that examined the effect of deliberate simulator practice on the performance of a vascular anastomosis in an in vivo model suggests that residents exposed to an expert-guided tutorial with dedicated practice (10 anastomosis) performed much better than those who received only a tutorial.10

The number of practice sessions needed, and the timing of these sessions in order to maximize learning potential is difficult to determine. A recent study by Alvand et al.17 compared a group of medical students exposed to arthroscopy training versus no training to evaluate whether both groups were able to achieve a level of competency as characterized by stabilization of their learning curve after twenty episodes. Their results indicated that there were a group of medical students who could not be trained despite repetition. However, twenty episodes may not have been enough to capture all skill levels. Along these lines, we have not yet established a “pass” or “fail” score for our simulation model, but it would be interesting to investigate whether there is a cohort of residents who are unable to demonstrate a certain level of proficiency in the articular fracture simulation model, and whether this correlates to in vivo surgical skills.

A final remark is that in addition to expert-guided dedicated practice, we incorporated video feedback as a teaching tool. There are mixed reviews regarding video feedback as an effective teaching tool in orthopaedic surgery,18 although it has shown to be effective in other disciplines such as sports.19 It was rated highly by the residents in our study, but further work needs to be done to better define its role in skills training. Future planned studies include assessment of hand motion as an objective metric of technical skill, optimizing the training program, working towards a fluoroscopy free simulation and assessing the effect of other training aids to optimize performance.

CONCLUSION

In summary, the articular fracture reduction surgical simulation training program consisting of a cognitive and skills module represents a step forward in the development of a comprehensive orthopaedic surgical skills educational curriculum. This program presents a strong model for future surgical skill training programs, and more studies are needed to establish its reproducibility on a nationwide-level.

ACKNOWLEDGEMENTS

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ABSTRACT

Background: Peripheral nerve blocks (PNB) are a common adjuvant for anesthesia. There is little orthopedic literature regarding the incidence of neurogenic complaints and quality of pain control.

Methods: We instituted a questionnaire to postoperative patients who would have potentially received a PNB at a single institution between 2008 and 2009 and asked them to rate their pain on a standardized pain scale at several points in the post-operative period. The survey queried whether patients experienced severe pain, went to the ER, or experienced neurogenic complaints. Comparative data was also collected on patients who did not receive a PNB.

We instituted a follow up survey several months later to investigate the persistence of these complaints.

Results: 268 patients completed the survey, 215 patients with PNB and 53 control patients. There was a 38.14% incidence of neurogenic complaints in patients who received PNB as compared to 9.43% incidence in patients who did not receive a PNB, p <0.001. There was 27.9% (PNB) versus 15.1% (control) incidence of severe pain (p = 0.05). 24 patients that received PNB versus five control patients visited the ER or called the house officer (p = 0.71). Patients who received PNB had significantly better pain control immediately after surgery (p = 0.02) and improved pain control the same night (p = 0.04), but there was no difference in pain control the morning after surgery, 24 hours after surgery and at the one week post-operative period (p values 0.77, 0.28 and 0.69). At the several month follow-up, we found that 41 of the 80 (51%) patients had persistent complaints.

Conclusions: Patients who receive PNBs have more neurogenic complaints and severe pain. They have improved initial pain control, but the profile shows no difference after less than 24 hours. If patients experience initial neurogenic complaints, a significant percentage of these patients have persistent complaints several months after surgery. The relative benefit of PNBs must be weighed against the possibility of persistent neurogenic complaints.

Level of Evidence: Cohort study type III

INTRODUCTION

Peripheral nerve blocks are a common adjuvant for peri-operative analgesia. It has become a standard of the peri-operative pain protocol. It is also an important component in the pain management strategy in an era where adequate pain coverage is considered a priority and often felt to be inadequate 1.

BACKGROUND AND SIGNIFICANCE

There is much interest and literature regarding regional anesthesia efficacy and use in the orthopedic and anesthesia literature 2-4. A review of the literature and complications associated with regional anesthesia yields the following complications: neuroaxial hematoma, neurologic injuries, Horner's syndrome, laryngeal nerve paralysis, transient carotid bruits 5-8; pneumothorax, local plexus irritation, phrenic nerve injury and paralysis 5,9-12. There is also reported rare incidence of hematoma formation, total spinal anesthesia, cardiovascular depression, dyspnea, seizure and cardiovascular arrest 10,11,13-17.

Much of the literature supporting the use of regional anesthetic describes decreased hospital stay, reduced
intraoperative blood loss \(^{18}\), quicker short term gains in ROM and rehabilitation, decreased mortality and improved outcome in vascular surgery \(^{19}\), reduced post-operative narcotic consumption and related side-effects \(^{20}\) and decreased risk of myocardial ischemia \(^{21}\).

A myriad of peripheral nerve blocks are performed in most orthopedic practices. The orthopedic surgeon frequently encounters patients who complain of severe pain as the block wears off. The patients describe a sensation similar to the affected limb “falling asleep and then waking up”. More descriptive terms include: numbness, tingling, burning, stabbing and severe discomfort. These symptoms are frequently encountered in the setting of concurrent use of narcotics. This pain seems to be different than the pain described as incisional and surgical in nature. These dysesthetic symptoms do not appear to be present in patients who do not receive peripheral nerve blocks.

A review of the literature yields the possibility of peripheral nerve injury caused by needles used for regional anesthesia. It is reportedly associated with severe and persistent paraesthesia \(^{22-24}\).

In our clinical experience, the onset of the paraesthesias and dysesthesias seems to coincide with the expected duration of the block. To our knowledge, there are no published reports indicating whether these symptoms are due to injury to the nerve or just normalization of nerve function after a successful anesthetic. While these symptoms are likely present in most people who receive a block, there appears to be a sub-group of people who do not tolerate these dysesthesias and rather experience what they would describe as severe pain.

In this study, we compare the incidence of paraesthesia, neurogenic pain, severe pain, and pain scores in patients who received PNB to those who did not receive PNB at a single institution. The hypothesis of this study is there is a significant incidence of paraesthesia, neurogenic pain, severe pain and difference in pain scores in patients who receive PNB as compared to patients who do not receive a PNB.

**FIGURE 1.**

<table>
<thead>
<tr>
<th>Survey Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Type of orthopedic surgery they received. Shoulder, elbow, forearm, wrist, hand, hip, knee, ankle, foot, etc.</td>
</tr>
<tr>
<td>2. Whether the patient received a PNB.</td>
</tr>
<tr>
<td>3. Was there a point after surgery where the pain was “out of control”.</td>
</tr>
<tr>
<td>4. Did the patient have to call the on call doctor or go to the ER.</td>
</tr>
<tr>
<td>5. Did pain pills provide relief as the PNB wore off.</td>
</tr>
<tr>
<td>6. If the patient received a PNB, would they choose to have a PNB in the future. If the patient did not receive a PNB, would they elect to have one in the future.</td>
</tr>
<tr>
<td>7. Did the patient experience any persistent numbness, tingling, burning, increased sensitivity or inability to move toes, hand, fingers, ankle or wrist.</td>
</tr>
</tbody>
</table>

**RESEARCH DESIGN AND METHODS**

This cohort study was conducted with a set of standardized questions incorporated into the orthopedic clinic check-in kiosk. All adult post-operative patients were presented with the opportunity to provide data regarding their experience. The National Institute of Health sponsored Numeric Rating Scale (NRS) was used as a pain assessment tool. This tool is a standardized method for measuring patient’s pain levels\(^ {25}\).

Prior to instituting the protocol, the study received IRB approval. In order to validate the quality of the data collected in an anonymous nature, we performed a pilot study in which we prospectively consented the first 50 patients for a chart review in which responses to the survey were compared to data in their chart. In other words, the data provided by the patients including: site of surgery and whether or not they received a PNB, was validated by comparing it to the information in their medical record. This pilot study data correlated with the medical record with 100% accuracy.

Patients were screened and selected in the clinic according to the type of surgery they were having and the likelihood that they would receive a regional anesthetic. Children, and prisoners were excluded from participation in the study. The patients in this study had surgery performed in an ambulatory surgery center. We also excluded patients with a neurologic injury prior to the surgical procedure. At the time of surgery, the anesthesiologist discussed the anesthetic options including PNBs. Patients were allowed to make an informed decision with the advice of their anesthesiologist as to whether they would receive a PNB or anesthetic that did not include a PNB. These patients were invited to participate regardless of whether they received a PNB. No randomization was performed; rather the information gathered is a “snap shot” of our typical clinical practice.

The patients were asked to rate their pain at several points through the post-operative period, including: immediately post-operative, the evening of surgery, if they woke up during the night due to pain, the next morn-
Peripheral Nerve Blocks and Incidence of Post-operative Neurogenic Complaints and Pain Scores

**TABLE 1.**

<table>
<thead>
<tr>
<th>Region</th>
<th>Number Surveys</th>
<th>Number Complaints</th>
<th>Percent Complaints</th>
<th>Visit to ER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip/knee</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PNB</td>
<td>37</td>
<td>14</td>
<td>38%</td>
<td>0.0323</td>
</tr>
<tr>
<td>No PNB</td>
<td>20</td>
<td>2</td>
<td>10%</td>
<td>5</td>
</tr>
<tr>
<td>PNB</td>
<td>2</td>
<td>1</td>
<td>55%</td>
<td>1</td>
</tr>
<tr>
<td>No PNB</td>
<td>2</td>
<td>1</td>
<td>11%</td>
<td>5</td>
</tr>
<tr>
<td>P Value</td>
<td>0.0017</td>
<td>0.002</td>
<td></td>
<td>0.6579</td>
</tr>
<tr>
<td>Foot/ankle</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PNB</td>
<td>42</td>
<td>23</td>
<td>55%</td>
<td>0.0517</td>
</tr>
<tr>
<td>No PNB</td>
<td>18</td>
<td>2</td>
<td>35%</td>
<td>10</td>
</tr>
<tr>
<td>PNB</td>
<td>2</td>
<td>1</td>
<td>30%</td>
<td>0</td>
</tr>
<tr>
<td>No PNB</td>
<td>2</td>
<td>1</td>
<td>14%</td>
<td>1</td>
</tr>
<tr>
<td>P Value</td>
<td>0.6599</td>
<td>1.0000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand/wrist/forearm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PNB</td>
<td>86</td>
<td>30</td>
<td>35%</td>
<td>0.6599</td>
</tr>
<tr>
<td>No PNB</td>
<td>8</td>
<td>0</td>
<td>0%</td>
<td>6</td>
</tr>
<tr>
<td>PNB</td>
<td>0</td>
<td>1</td>
<td>14%</td>
<td>0</td>
</tr>
<tr>
<td>No PNB</td>
<td>0</td>
<td>0</td>
<td>0%</td>
<td>0</td>
</tr>
<tr>
<td>P Value</td>
<td>1.0000</td>
<td>1.0000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shoulder/elbow</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PNB</td>
<td>50</td>
<td>15</td>
<td>30%</td>
<td>6</td>
</tr>
<tr>
<td>No PNB</td>
<td>7</td>
<td>1</td>
<td>14%</td>
<td>0</td>
</tr>
<tr>
<td>PNB</td>
<td>1</td>
<td>0</td>
<td>14%</td>
<td>1</td>
</tr>
<tr>
<td>No PNB</td>
<td>0</td>
<td>0</td>
<td>0%</td>
<td>0</td>
</tr>
<tr>
<td>P Value</td>
<td>1.0000</td>
<td>1.0000</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**FIGURE 2.**

TABLE 1.

<table>
<thead>
<tr>
<th>Point in time</th>
<th>Pain Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No PNB</td>
</tr>
<tr>
<td>Initial pain</td>
<td>2</td>
</tr>
<tr>
<td>Bedtime pain</td>
<td>4</td>
</tr>
<tr>
<td>Pain upon awaking</td>
<td>5</td>
</tr>
<tr>
<td>Morning after pain</td>
<td>6</td>
</tr>
<tr>
<td>24 hour pain</td>
<td>7</td>
</tr>
<tr>
<td>One week later</td>
<td>8</td>
</tr>
</tbody>
</table>

**SOURC OF FUINDING**

No funding was received for this investigation

**RESULTS**

The initial surveys were all completed within 14 days of surgery. The patient data that was collected pertained to both upper and lower extremity surgical procedures. We collected 268 patient completed surveys: 215 patients received a PNB and 53 patients received traditional post-operative analgesia. Please see Table 1 for a summary of the surgical locations. There was a 38.14% (82/215) incidence of neurogenic complaints in patients who received PNBs as compared to a 9.43% (5/53) incidence in patients who did not receive a PNB (p< 0.0001). There were 60 patients who received PNBs and 8 patients with traditional analgesia that experienced severe pain in the post-operative period. The incidence of severe pain after surgery was 27.9% (60/215) in the PNB group versus 15.1% (8/53) in the control group (p<0.05). Twenty-four patients that received PNBs versus five control patients visited the emergency room (p= 0.72).

Notably, the hip/knee and foot/ankle regions had significantly increased complaints with PNBs (p= 0.03 and p=0.002, respectively), while the hand/wrist/elbow region displayed a trend toward significance (p=0.052). There was no difference in complaints for the shoulder/elbow region (p=0.64).

Patients who received PNBs had significantly better pain control immediately after surgery (p= 0.02), im-
proved pain control the same night (p=0.04), but there was no difference in pain control the morning after surgery, 24 hours after surgery and at the one week post-operative period (p=0.77, p=0.28 and p=0.69, respectively). Notably, amongst the patients who awoke in the night due to pain, patients that did not receive PNBs had significantly lower pain scores (p=0.01) (Figure 2).

With regard to patients taking oral narcotics in anticipation of the PNB wearing off, 37/215 (17%) patients indicated they did not take oral pain medications and 178/215 (83%) patients did take oral medications. Out of the patients with PNBs who had severe pain, 14/60 (23%) patients did not take oral pain medications in anticipation of the PNB wearing off while 46/60 (77%) did. Amongst these 46 patients who took oral pain medications, 14 (30%) patients indicated the medication did not help, 24 (52%) felt the medications helped with the pain, 8 (17%) did not respond. Fourteen patients who received PNBs indicated that they would not get a PNB again.

The late follow up surveys were collected within seven to thirteen months from the time of surgery. We were able to contact 80 of 82 patients who received a PNB and indicated neurogenic complaints. We found that 41 of the 80 (51%) patients complained of persistent neurogenic complaints. Sub-group analysis demonstrated 36 patients complaining of continued numbness/tingling, four patients had loss of strength and one patient complained of hypersensitivity. Amongst those patients, 24 claimed improving symptoms, 13 stable symptoms and four worsening symptoms. Fourteen patients continued to take medications to treat their complaints and seven patients had been to the pain clinic.

**DISCUSSION**

The majority of the literature related to regional anesthesia outcomes and complications comes from the anesthesia literature. This study provides some preliminary insight to the incidence of neurologic complaints and pain scores as seen from the orthopedic clinician’s perspective.

The several month follow up survey provided an opportunity to interview patients and determine with more accuracy the nature of their complaints. While 41 of the 80 patients indicated persistent dysfunction, we were interested to infer with greater accuracy whether the complaints were likely related to their original injury, surgery or regional anesthetic. A few of the specific complaints could be related to the original injury or surgery, while most of the complaints were likely related to the regional anesthetic. Obviously, attempting to differentiate the etiology of patients’ complaints over the telephone is inaccurate and difficult. This may suggest the high incidence of neurologic complaints in the setting of PNB may be artificially elevated. This may be due to inadequacy of the questionnaire and its ability to differentiate definitive cause of complaint and injury. Despite a high incidence of neurologic complaints in our data, most patients did not regret the decision to receive a PNB and would make the same decision if they were to choose again. Nonetheless, the majority of the comments collected from patients seemed to indicate persistence of paraesthesia, dysesthesias, weakness and dysfunction in an isolated neurologic distribution.

Review of the literature reveals several studies evaluating the efficacy and associated side effects of regional anesthesia. Barrington completed a phone survey on 6,069 patients with a total of 7,156 blocks and found thirty patients (0.5%) had clinical features requiring referral for neurologic assessment. He felt that 4/30 of the referred patients had a block-related injury, and noted a 0.98 per 1000 blocks incidence of systemic local anesthetic toxicity. Orebaugh found 8 adverse events including 5 seizures and 3 nerve injuries out of 5,436 patients who received blocks. He found a significantly higher incidence of complications when anesthesiologists did not use ultrasound for PNB localization. Fanelli prospectively studied 3,996 patients undergoing PNBs and found 69 patients (1.7%) developed neurologic dysfunction on the operated limb in the first post-operative month. Complete recovery required 4-12 weeks in all patients but one, who required 25 weeks. Liu looked at 230 patients and found the incidence of postoperative symptoms 8-11% at one week and 6-7% 4-6 weeks after surgery. Fredrickson evaluated 1,010 consecutive blocks and found the incidence of symptomatic patients to be 8.2% at day 10, 3.7% at one month and 0.6% at 6 months. Wiegel commented on a 0.6% incidence of local inflammation at the catheter insertion site, 0.2% local infection rate and one patient who suffered a compression injury to the femoral nerve due to a retroperitoneal hematoma.

Therefore, the range of reported neurologic complaints after a PNB procedure in the literature reviewed is 0.5% to 11%. Some variation can be attributed to technique, method of follow up for detection of complaints (telephone survey vs. clinic evaluation), and operator skill level. Regardless of technique and incidence of neurologic injury, the unfortunate patient who is injured can be devastated.

Regarding the quality of pain control after a PNB or traditional analgesia, Frost studied the efficacy of femoral nerve blocks (FNB) in the reduction of post-operative pain following anterior cruciate ligament reconstruction (ACLR). The patients were randomized to FNB to receive 0.25% bupivicaine or placebo of normal saline injected into the femoral nerve sheath. Both groups received a pre-operative intra-articular injection of bupiv-
icaine prior to the procedure. Overall, the data showed no difference between the FNB group and placebo group for pain reduction. However on the night of surgery, the FNB group did have a significant reduction in pain. They indicated that while FNB may reduce pain in the night of surgery, their ultimate conclusion was this may not be clinically significant and FNB was not recommended in the setting of outpatient ACLR surgery 34.

In a similar model, Mulroy et al compared post-operative analgesia in a FNB group and sham block group. In the sham block group they had 6/12 patients report inadequate analgesia. They found that patients who received sham blocks reported higher pain scores and requested intravenous analgesia more often 35.

Williams compared verbal pain scores in patients who had undergone ACLR. They found that patients who received a FNB had consistently lower pain scores on days one and two. They also concluded that FNB catheters reliably keep numeric pain scores below the moderate to severe pain threshold 36.

Mehdi randomized fifty patients to receive either a femoral nerve block or an intra-articular bupivacaine injection in ACLR surgery. He found that visual analog scores were not significantly different in the two groups and pain levels can be sufficiently controlled by intra-articular infiltration of bupivacaine coupled with oral analgesia 37. This is also notable given our finding of an increased incidence of neurogenic complaints with lower extremity PNBs.

One potential criticism of this study is its dependence on subject recall of pain. Hunter et al demonstrated that the recall of intensity and quality of pain was surprisingly accurate several days after the sentinel event 38. Babul and Darke indicated that memory for pain is both accurate and reliable and its use may be particularly suited to clinical trials where hourly pain assessments can be costly or impractical 39. Singer showed that pain severity assessments of acute painful events one and seven days later were similar and highly correlated with initial assessments 40. Lembo demonstrated that acute pain experiences are accurately recalled during a period of weeks 41.

A possible point of criticism of this study is speculation that patients who underwent more invasive procedures were more likely to receive a PNB. Physician bias was avoided by providing anonymous surveys that were distributed by non-physician clinic staff. Another criticism is the majority of the patients who completed surveys received PNBs. This reflects the nature of our practice, in that the majority of patients receive regional anesthesia. These study design weaknesses may be improved with further randomized controlled prospective studies.

**CONCLUSION**

Patients who receive PNBs are at an increased risk for developing post-operative neurologic complaints as compared to control groups. Patients who receive PNBs have improved initial pain control, but the pain control profile shows no difference after less than 24 hours. Patients who received PNBs and awoke due to pain had more severe pain than patient who did not receive PNBs. This data demonstrates a significant incidence of unexpected neurologic complaints. In fact, many of these patients continue to experience neurogenic complaints several months after surgery. The relative benefit of regional anesthesia, with an improved pain profile in the initial hours after surgery, must be weighed against the risk of neurogenic complaints. Surgeons should counsel their patients about the potential risk of PNBs. Additional studies are recommended to further describe the long-term consequences of PNBs and the quality of pain control provided.

**REFERENCES**


35. Mulroy MF, Battaglia MS, Hodgson PS, Owens BD. Femoral nerve block with 0.25% or 0.5% bupivacaine improves postoperative analgesia following outpatient arthroscopic anterior cruciate ligament repair. *Reg Anesth Pain Med* 2001;26-1:24-9.
Peripheral Nerve Blocks and Incidence of Post-operative Neurogenic Complaints and Pain Scores


ABSTRACT

Objectives: Vascular endothelial growth factor (VEGF) is a potent angiogenic factor that plays an important role during skeletal development and fracture healing. Previous experimental studies have shown that VEGF applied immediately after injury can stimulate bone repair in animal fracture nonunion models. However, the effectiveness of VEGF on an established fracture non-union has not been determined. The goal of this work was to test the ability of VEGF applied at a later stage on the healing of fracture nonunions.

Methods: In this study, a murine non-union model was induced by rapid distraction of a tibia osteotomy. This model exhibits radiological and histological evidence of impaired fracture healing at 7 days after the completion of distraction. VEGF (10 µg in 20 µl PBS/day, n=10) or control (20 µl PBS/day, n=10) was injected directly into the distraction gap through the posterior musculature on three consecutive days (7, 8, and 9 days after completing distraction). A third group of animals (n=10) with rapid distraction, but no injections, served as non-treated controls. Fracture healing was analyzed by x-ray, histology, and histomorphometry at 27 days after the last round of distraction. Results: Radiographs showed that half of the VEGF treated animals (5/10) achieved bony healing whereas the majority of PBS treated (7/10) and non-treated animals (8/10) did not exhibit bone bridging. Histological and histomorphometric analyses demonstrated that VEGF increased, but not significantly, the amount of bone formed in the distraction gap (1.35 ± 0.35 mm³), compared to the saline treated (0.77 ± 0.25 mm³, p=0.19) and non-treated animals (0.79 ± 0.23 mm³, p=0.12).

Conclusions: Results from this study demonstrate that VEGF potentially promotes bone repair, warranting further research in this direction.

Keywords: Vascular Endothelial Growth Factor, VEGF, fracture, delayed union, non-union, distraction osteogenesis.

INTRODUCTION

In the United States, there are over six million cases of fractures occurring each year, with about 5-10% of them do not heal on a timely manner 1. Blood supply is crucial for fracture healing and lack of perfusion is one of the most important factors that cause delayed fracture healing or non-union. In a mouse model, femoral artery resection prior to the creation of tibia fractures leads to a large amount of cell death and delayed bone repair 2.

During fracture healing, recovery of blood supply to the fracture site relies on angiogenesis, whereby new blood vessels form from preexisting ones. Inhibiting angiogenesis decreases bone formation, resulting in fracture non-union 3. Thus, improving angiogenesis and increasing blood supply are promising targets to treat delayed fracture healing or non-unions.

The process of angiogenesis is regulated by many growth factors. Among them, vascular endothelial growth factor (VEGF) is one of the most potent angiogenic factors. In fracture calluses, VEGF is expressed by hypertrophic chondrocytes and may be released from cartilage matrix by MMP9-mediated matrix degradation, which induces vascular invasion of the hypertrophic cartilage 4. The ability of VEGF to enhance bone regeneration has been established in several animal models 5,6. VEGF delivered as a protein or through transgenic approaches can promote healing of femoral fractures in mice 5, radius segmental defects in rabbits 5,6, and bone drilling defects in rats 7. While these studies have established the effects of VEGF on bone repair, the timing of VEGF administration in the treatment of fracture non-unions needs to be further determined for at least two reasons. First, in previous studies, VEGF protein...
Vascular Endothelial Growth Factor Improves Bone Repair in a Murine Nonunion Model

or genes were delivered at the time that bone injuries were created. Clinically, fractures that eventually develop into delayed healing or non-union frequently cannot be identified at the time of injury, and are recognized by radiography weeks or months later. Therefore, results from studies that administer VEGF immediately after bone injury are not directly applicable to those conditions where impaired healing presents at a later stage. Second, the development of fracture non-union is a complex process in which cellular and molecular environments are constantly evolving, and VEGF administered at different stages could have different effects. In the current study, we hypothesized that VEGF delivered to the site of an established bone non-union can improve bone repair. To address this question, we used a murine non-union model induced by rapid distraction. In this model, radiological and histological signs of impaired fracture healing, such as fibrosis which is commonly seen in human non-unions, are evident at as early as seven days after the completion of rapid distraction. We tested whether VEGF delivered at this time can stimulate bone formation in the distraction gaps.

MATERIALS AND METHODS

Animals and surgical procedures

All protocols have been approved by the Institutional Animal Care and Use Committee (IACUC) at our university. Male 129J/B6 mice (10-12 weeks old) were used in this study. Animals were anesthetized with an intraperitoneal injection of 0.02 ml/g of 2% Avertin (2-2-2-Tribromoethanol, Fluka, Buchs, Switzerland). One dose of Ancef (Cefazolin, 25mg/kg) was provided before surgery for prophylaxis. The left hind leg was shaved and prepared in a sterile manner. Two insect pins (0.25mm in diameter, Fine Science Tools, Foster City, CA) were placed perpendicularly to each other in the proximal and distal metaphyses. The tibia was centered within custom-made aluminum rings both proximally and distally, and bolts were tightened to secure the pins to the frame. The two rings were connected with three threaded rods (2/56 x 3/4 inch). An anterior longitudinal incision was then made over the mid-shaft of the tibia and an osteotomy was created. Incisions were closed with a running 5-0 nylon suture. Rapid distraction (0.36 mm/12 hrs) was performed immediately after surgery and then every 12 hours during the first 4 days by turning the nuts on the threaded rods. There were 9 rounds of distraction and the total distraction gap created was about 3.2mm. After recovery, animals were allowed to ambulate ad libitum. Buprenorphine (Sigma, St. Louis, MO) was given subcutaneously as needed for analgesia.

Delivery of VEGF

Our previous work demonstrated that by 7 days after completing rapid distraction, signs of non-union, including lack of new bone formation on radiological and histological examinations and presence of abundant fibrous tissue in the distraction gap on histology, can be observed in this model. Hence, this time was chosen to perform VEGF treatment and x-ray was used to confirm the possibility of nonunion. Animals were anesthetized by breathing isofluorene, human recombinant VEGF (Genentech, South San Francisco, CA. 10 µg in 20 µl PBS) or control (20 µl PBS) was directly injected into the distraction gap through the posterior musculature with a 30 gauge needle (Fig. 1). The position of the needle was confirmed by radiographs. Another group of mice receiving rapid distraction without injection were also used as controls.

TISSUE PREPARATION

Animals were sacrificed on day 27 after completing rapid distraction (i.e. 31.5 days after bone osteotomy and 20 days after first injection). Fractured legs were collected, fixed in 4% paraformaldehyde (PFA) at 4°C overnight, and decalcified in 19% EDTA for 10-12 days at 4°C. Decalcification was confirmed radiographically, and then the pins were removed. Tissues were dehydrated with graded ethanol solutions and embedded in paraffin. Sagittal sections (10 µm) through the tibia were collected throughout the cortex of the distal osteotomy site.

Histological and histomorphometric analyses

Every fifth slide was dewaxed, rehydrated, and stained with modified Trichrome staining to visualize bone in the fracture calluses. The distraction gap on
every 15th section was digitized under a Leica microscope. For each sample, 5-7 sections 300mm apart were analyzed. The area of new bone was measured if it fell between the osteotomized bone ends using Photoshop. Bone tissue was selected based on the blue staining and morphology and the pixels of selected bone were converted into area. The total volume of bone (BV) was calculated using the equation for a conical frustum: BV = 1/3h ∑ (Ai+Ai+1+ √AiAi+1). Ai and Ai+1 are the area of bone in the sequential sections; h is distance between sections (300mm), and n is total number of sections analyzed for each specimen10. Histomorphometric data were analyzed in SAS (version 6.12, SAS Institute, Inc, Cary, NC) using one-way Analysis of Variance (ANOVA).

RESULTS

Rapid distraction induces non-union

In this mouse model of tibia distraction osteogenesis, distraction at a rate of 0.36 mm/12 hours significantly impaired bone formation in the distraction gap, and this agrees with our previous data8. By 27 days of maturation, bridging calluses were absent from radiographs in 8 out of 10 animals. Some radiographic signs of bony union were observed in the other 2 animals. In the 8 animals exhibiting radiographic non-union, histological analysis demonstrated a small amount of new bone present at the fracture ends but not in the gap (Fig. 2A). Instead, the distraction gap was occupied by muscle, fibrous tissue, and fatty tissue (Fig. 2A), which are common histological findings in other models of delayed fracture healing or non-union2,3.

VEGF decreases the rate of non-union induced by rapid distraction

By 27 days of maturation, most (7 out of 10) of the saline injected control animals failed to heal their distraction gaps, as evidenced by the lack of bony bridging callus on radiographs and stained histologic sections. Similar to the non-injected controls described above, distraction gaps in the saline injected animals were mostly occupied by fibrous and adipose tissues (Fig. 2B).

In comparison, VEGF treatment decreased the rate of non-union. By 27 days, half (5 out of 10) of the animals in this group exhibited bridging bony calluses on radiographs. Histological analysis on these 5 animals demonstrated that a large amount of new bone formed in the distraction gap connecting the two fracture ends (Fig. 2C). A small amount of fibrous tissue and cartilage was also observed in the gap (Fig. 2C).

VEGF mildly increases the amount of bone in the distraction gap

Histomorphometric analysis quantifying new bone formation in the distraction gaps (Fig. 3) showed that similar amount of new bone was present in the non-injected controls (0.77 ± 0.25 mm3) and saline injected animals (0.79 ± 0.23mm3). In comparison, VEGF treated animals exhibited more bone formation in the distraction gaps (1.35 ± 0.35 mm3), however, the differences are not statistically significant (p = 0.12 for VEGF injected vs. non-injected, and p = 0.19 for VEGF vs. saline injected).

DISCUSSION

In this study we found that exogenous VEGF, applied at a time when radiological and histological signs of non-union are evident, potentially enhances bone formation. The mouse model of fracture non-union, resulting from osteotomy and rapid distraction, exhibits some histological signs of an atrophic non-union, including absence of a callus and the presence of fibrous and adipose tissues in fracture gaps. Results from the current study suggest that VEGF could be used to treat delayed fracture healing and non-union.

The molecular and cellular environments are constantly changing as bone repair progresses through its various stages. Many genes regulating osteogenesis, chondrogenesis, angiogenesis, and renervation are temporally expressed during fracture healing11-13. In distraction osteogenesis, the strongest expression of VEGF is found during the first several days after the completion of distraction14. Expression of VEGF transcripts is up-
regulated after injury and remains prevalent throughout
distraction osteogenesis, while expression of MMP (i.e.
MMP2, MMP9, and MMP13) transcripts are increased
during the phase of distraction, but to a lesser extent
during the phase of consolidation \(^{15}\). In fracture non-
unions, osteoblasts exhibit abnormal expression profiles
of genes that are related to mineralization \(^{16}\). Therefore,
the timing of VEGF treatment may significantly affect
the outcome of healing bone. It is well established that
VEGF delivered at the time of injury can improve bone
repair. In the current study, VEGF (10 µg) was deliv-
ered to the distraction gaps at 7 days after completing
delayed fracture healing were evident. VEGF treatment
at this stage appeared to stimulate bone formation and
decrease the rate of non-union. These results suggest
that VEGF treatment can be considered for problematic
fracture healing diagnosed weeks or months after injury.

Multiple mechanisms may underlie the stimulating
effect of VEGF on bone repair. VEGF is a potent an-
angiogenic factor and it may improve fracture healing by
promoting angiogenesis. Street et al. \(^{5}\) treated mouse
femur fractures with VEGF and found VEGF treated
fractures had 26% more vascularity than carrier treated
ones. In the model of fracture non-
unions-used in the current study, avascular fibrous tissue was present in
the distraction gap at 7-8 days after completion of rapid
distraction \(^{8}\), which was also the time point we chose to
administer VEGF. The presence of avascular fibrous
tissue in the distraction gap denotes the benefits of the
pro-angiogenic properties of VEGF. However, there is
literature suggesting that pro-angiogenesis might not
be the only mechanism through which VEGF enhances
bone formation. VEGF may have direct effects on
osteoblasts and osteoclasts. VEGF or its receptors are
expressed by osteoblasts \(^{5,17,18}\), and VEGF can enhance
the activity of cultured osteoblasts by increasing the
formation of bone nodules and alkaline phosphatase
expression \(^{5}\). VEGF also plays a role in osteoclastogen-
esis by upregulating RANK expression in osteoclast
precursors \(^{19}\). VEGF, by binding to its receptors present
on osteoclasts \(^{20}\), can increase the resorption activity of
mature osteoclasts \(^{21,22}\). Therefore, the effect of VEGF
on osteogenesis in our current study could result from
synergistic effects that include angiogenesis, osteoblas-
togenesis, and osteoclastogenesis.

We observed only a mild pro-osteogenic effect of
VEGF, which could be due to our delivery method. In
our study, VEGF was suspended in phosphate saline
buffer and directly injected into the bone defect. It is
possible that administered VEGF might have diffused
from the injection site too quickly, compromising the
outcome. Techniques that retain the exogenous VEGF
at the site, such as using the appropriate scaffolds or con-
trolled release techniques, could significantly improve its
function. As an example, Eckardt et al. applied VEGF
locally to a rabbit model of distraction osteogenesis using
osmotic pumps but failed to enhance bone formation \(^{23}\).

In another study, the same group of researchers found
that an equal amount of VEGF delivered with a carrier
was able to enhance bone repair in an experimental
rabbit non-union model \(^{6}\). Recently, other researchers
have tried to combine VEGF with osteogenic factors or
mesenchymal stem cells to achieve even better outcome.
In a rat cranial critical size defect model, dual delivery
of VEGF and bone morphogenetic protein-2 (BMP-2)
showed synergistic effects on bone formation at 4 weeks
after treatment. However, this effect was not detected by
12 weeks \(^{24}\). In another study, Kumar et al. transplanted
mesenchymal stem cells that co-express VEGF and
BMP-2 to a segmental bone defect in mice and found that
the combination improved the biomechanical properties
of newly formed bone \(^{25}\).

In conclusion, results from the current study demon-
strate that VEGF may have a role in stimulating bone
repair. While the current study shows a trend towards
the positive effects of VEGF on bone healing in this
murine rapid distraction non-union model, the results are
not statistically significant. From the results, however,
it is clear that many of the animals administered VEGF
showed a robust response to the factor. Larger numbers
of animals per group are required to further evaluate the
significance of this response. Further research is also
required to optimize the dosage and delivery method to
maximize the effects of VEGF.
ACKNOWLEDGEMENT

This work was funded by National Institutes of Health-\textregistered\textsuperscript{TM}, Orthopaedic Trauma Association (a research grant to CL), Orthopaedic Research and Education Foundation (a grant to CMO), and Zimmer Inc. We would like to thank Dr. Zena Werb for her helpful comments on the manuscript. Drs. Stuart Gansky and Sara Shain provided statistical analysis.

REFERENCES:


ABSTRACT
Introduction: Clopidogrel, an inhibitor of ADP-induced platelet aggregation, is indicated for the reduction of atherosclerotic events in patients with atherosclerosis documented by recent stroke, myocardial infarction, acute coronary syndrome, and established peripheral arterial disease. In cardiovascular studies, clopidogrel has been associated with increased chest tube output, transfusion rates, and re-exploration rates. Few studies have addressed the possible complications of clopidogrel in hip fractures. Our study aims to assess the perioperative blood loss and transfusion rates in geriatric patients with hip fractures on clopidogrel. We hypothesize that patients on clopidogrel will have higher perioperative blood loss and transfusion rates.

Materials and Methods: A retrospective, case control study chart review over a five year span was conducted. Of the 2,766 geriatric hip fracture patients surgically treated, 52 patients taking clopidogrel upon admission to the hospital were compared to patients not on the drug. All of the patients in the study were taken to the operating room within two calendar days of admission. Statistical analysis was performed using Wilcoxon’s, Fisher exact, chi square, and logistic regression methods.

Results: A total of 110 patients were included in the analysis, 52 (47%) were taking clopidogrel at the time of admission. These patients were compared to 58 (53%) patients not on the drug. No significant difference was found with respect to documented perioperative blood loss. Transfusion rates however, did vary. Patients who had been taking clopidogrel, prior to admission and subsequent surgery, had a transfusion rate of 56%, while those patients not on the drug had a transfusion rate of 31%. Logistic regression analysis showed taking clopidogrel up to admission was significantly associated (p = .0121) with receiving a blood transfusion following surgical treatment of a hip fracture.

Conclusion: A growing body of evidence supports early (within 48 hrs) surgery for elderly patients with hip fractures. The pharmacokinetics of clopidogrel do not allow for bleeding time to return to normal until the drug has been discontinued for five days. Our study shows that patients taking clopidogrel upon admission for hip fracture are at increased risk of blood transfusions when surgery is performed within two calendar days of admission. This risk must be balanced by the potential benefits of early surgery.

INTRODUCTION
Clopidogrel is an irreversible inhibitor of platelet aggregation and thereby increases bleeding time. Clopidogrel blocks adenosine diphosphate (ADP) from binding to the platelet receptor (P2Y12) and the subsequent ADP-mediated activation of the glycoprotein GPIIb/IIIa complex. Clopidogrel has a half life of eight hours and renders platelets inactive for approximately five to seven days, the average life span of a platelet. Platelet aggregation and bleeding time gradually return to baseline values five days after treatment is discontinued. Clopidogrel is indicated for the reduction of atherosclerotic events in patients with atherosclerosis documented by recent stroke, myocardial infarction, acute coronary syndrome, and established peripheral arterial disease. Furthermore, clopidogrel is now widely used postoperatively in patients undergoing cardiac and carotid stenting. A search of our institution’s database revealed that the number of patients taking clopidogrel has more than doubled in the past five years.

Clopidogrel and its effects on surgical patients have been widely studied in the cardiac literature. Yende and Wunderink concluded that clopidogrel in combination with aspirin is associated with an increased need for surgical re-exploration as well as risk of red blood cell and cryoprecipitate transfusions following coronary artery bypass surgery. Furthermore, Von Heymann
et al reported that aspirin and clopidogrel taken until two days prior to coronary artery bypass grafting is associated with significantly higher chest tube outputs. Their study also confirmed previous reports regarding higher rates of re-exploration secondary to bleeding in patients on aspirin and clopidogrel. With the increasing number of patients taking clopidogrel, studies continue to examine the implications of the irreversible platelet inhibitor in the surgical setting.

In orthopaedics, hip fracture patients comprise a particular group that may be impacted by the use of clopidogrel. The number of patients with hip fractures is increasing. The World Health Organization estimates that by 2050, a total of 6 million fractures of the hip will occur worldwide every year. The combination of increasing population age and longer life spans, the increasing use of clopidogrel, and the increasing number of hip fractures creates a unique issue and potential concern for orthopaedic surgeons. Furthermore, hip fractures are a major source of morbidity and mortality in the elderly population. Mortality in the Medicare population for those who sustain a hip fracture is estimated to be 13% at three months and 24% at one year. Multiple studies have shown the benefit of early surgery (within 48 hours). Reported benefits include decreased mortality and shorter hospital stays. With the goal of early surgical intervention to reduce mortality, hip fracture patients on clopidogrel have dysfunctional platelets and potentially increased bleeding times secondary to the pharmacokinetics of clopidogrel when surgery is performed. Simple bleeding time and platelet function have not returned to baseline within two days of stopping the drug.

The aim of this study is to compare blood loss and transfusion rates in elderly hip fracture patients on clopidogrel who were treated operatively within two calendar days of admission versus those who were not on the irreversible platelet aggregation inhibitor. By doing so we hoped to potentially provide additional insight in the complex management of geriatric hip fracture patients.

**MATERIALS AND METHODS**

An institutional review board approval was obtained prior to our study. All patients were treated at an academic level one trauma center. A retrospective case control study was performed in order to investigate blood loss and transfusion requirements of patients who underwent open treatment of a hip fracture, including femoral neck and intertrochanteric fractures over a five year time frame from 2000 - 2005. Exclusion criteria included 1) use of another anticoagulant or blood thinner except aspirin in combination with clopidogrel at the time of admission; 2) presence of any blood dyscrasia or hemoglobinopathy; and 3) delay of surgical intervention greater than two days. All patients were evaluated by an inpatient internal or family medicine team prior to operative treatment. All patients were medically optimized prior to surgical intervention. Clopidogrel was held prior to surgery in all cases and in a majority not resumed until two weeks post operative.

Patients taking clopidogrel upon admission/fracture were compared to a control group with no clopidogrel use. Using our electronic medical record, medical record numbers were obtained meeting the criteria of hip fracture. The search provided 2,766 patients who underwent surgical management of a hip fracture. Eighty-five of these patients were taking clopidogrel at the time of admission. Fifty-two patients met inclusion and exclusion criteria. Data collected for each patient included age, sex, time to surgery; method of surgical treatment, comorbidities, amount of intraoperative fluids, post operative transfusion, quantity of units transfused, intraoperative blood loss, and preoperative and postoperative hemoglobin levels. A total of 58 control subjects were matched to cases with regard to sex, age, comorbidities and surgical procedure performed. All members of the case group were taking clopidogrel at 75 mg per day at the time of admission. Patients in the control group had either not been on clopidogrel or had discontinued the drug at least one week prior to admission.

The amount of blood loss was recorded from the dictated operative report and anesthesia records from surgery. Transfusion requirements were noted in the medical record and dictated discharge summary. The decision to transfuse was at the discretion of the surgeon with consideration of the patient’s vital signs, medical history, laboratory values and recommendations from our medicine colleagues. The Biostatistics department helped with data analysis. A p-value of 0.05 or less with a confidence interval of 95% was considered significant. Wilcoxon’s, Fisher exact, chi square, and logistic regression methods were utilized. We hypothesized that patients on clopidogrel upon admission for a hip fracture would have both increased blood loss and transfusion rates.

**RESULTS**

A total of 110 patients were included in the study. The clopidogrel group consisted of 52 patients (14 males and 38 females). The control group consisted of 58 patients (16 males and 42 females). There was no statistical significance in gender between the two groups. The average age was 82.4 for the clopidogrel group and 77.6 in the control group. This was a statistical difference (p value = 0.009). Table 1 summarizes preoperative
Operative Treatment of Hip Fractures in Patients on Clopidogrel: A Case-Control Study

Only age was statistically significant between the two groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Clopidogrel Group (N=52)</th>
<th>Control Group (N=58)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>14</td>
<td>16</td>
<td>0.937</td>
</tr>
<tr>
<td>Female</td>
<td>38</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>82.4 +/- 8.9</td>
<td>77.6 +/- 8.7</td>
<td>0.009^2</td>
</tr>
<tr>
<td>Pre-operative Transfusion</td>
<td>9</td>
<td>7</td>
<td>0.559^2</td>
</tr>
<tr>
<td></td>
<td>43</td>
<td>46</td>
<td></td>
</tr>
</tbody>
</table>

Chi-Square test was used unless otherwise stated.
1 Wilcoxon’s test was used
2 Fisher’s exact test was used

Characteristics between the clopidogrel group and the control group (Table 1). With regards to comorbidities, the only statistical difference was found in history of stroke and transient ischemic attack between the clopidogrel and control groups (25 vs 11 respectively). Table 2 summarizes the medical comorbidities documented upon admission. No significant difference existed in the incidence of preoperative transfusion between the two groups (Table 2). The preoperative hemoglobin was 11.8 gm/dl +/- 1.5 in the group taking clopidogrel versus 12 gm/dl +/- 2 in the control group

Table 3 details the procedures performed on the 110 patients included in the study. No significant difference was found between the two groups among method of surgical treatment (Table 3). Selection of the procedure was at the discretion of the treating surgeon based on the patient’s fracture pattern and location. Table 3 also shows the recorded blood loss during surgery. Blood loss was averaged among the two groups as a whole and not studied specific to each of the four procedures performed. No significant difference was found between the two groups in regards to the procedure performed or intraoperative blood loss. There was also no significant difference in surgery time between the two groups with the study group averaging 65 +/- 40 minutes versus the control group averaging 59 +/- 38 minutes.

The lowest documented hemoglobin was 9 mg/dl +/- 1.9 in the clopidogrel group versus 9.5 mg/dl +/- 1.7 in

![Figure 1: Transfusion rate between patients on clopidogrel and patients not on clopidogrel.](image-url)
the control group, which was not significant (p = 0.41). There was, however, a significant difference in the transfusion rate between the two groups of patients (see figure 1). Twenty-nine of 52 (56%) patients taking clopidogrel were transfused postoperatively versus 18 of 58 (31%) patients in the control group (p = 0.008). Since age and transfusion rates were significantly different among the two groups, a logistic regression analysis was performed. The results, (Table 4) demonstrate that the clopidogrel group had a statistically higher risk of transfusion when compared to patients not on clopidogrel (p = 0.012). In our patients, age did not increase the probability of a postoperative transfusion.

**DISCUSSION AND CONCLUSION**

Multiple studies support early operative intervention for patients with hip fractures. Several studies have demonstrated increased mortality rate associated with surgical delay. Several studies have demonstrated increased mortality rate associated with surgical delay. Length of hospital stay has also been shown to be dependent on surgical delay. Siegmuth et al. found a significant increase in length of stay in patients operated on after 48 hours. Furthermore, there are economic consequences associated with operative delay in the treatment of hip fractures. Shabat recommended surgery within the first 48 hours, with early surgery being more cost effective with shorter hospital stays. Therefore, with goal of early intervention, delaying treatment until platelet function has returned is not ideal.

Recently, there have been two studies that examined the impact of clopidogrel in orthopaedic patients. Nydick demonstrated no increase in complications or transfusion requirements in patients undergoing non-elective orthopaedic surgery with clopidogrel. The clopidogrel group was taken to surgery within five days whereas our study looked at surgical intervention within two days. At two days the platelet function is still quite inhibited and our study demonstrates the effect of clopidogrel in early surgical treatment for hip fractures. Christy demonstrated no difference in early (<24 hours) or late (>24 hours) transfusion rates in patients on clopidogrel with pelvic fractures.

Our study examined the impact clopidogrel had on blood loss and transfusion rates in early (less than two days) operative treatment of elderly hip fractures. There was no statistical difference in intra-operative blood loss or preoperative transfusion rates; however, there was a statistical difference in postoperative transfusion rates (p = 0.012), age (p = 0.009), and history of stroke/transient ischemic attack (TIA) (p = 0.001) in the clopidogrel group. On regression analysis, age did not appear to be a significant factor to transfusion rates.

There are several areas of improvement to our study. Our study is a retrospective analysis with a relatively small number of patients. Transfusion risk with respect to specific procedures was not analyzed; rather, all four procedures were studied as a whole. We were unable to control for bias with respect to transfusion rate. There was no set criterion for decision to transfuse; however, no publications to date have demonstrated transfusion guidelines in management of hip fracture patients. A majority of transfusions are individualized, multifactorial, and based on experience of the treating physician. A prospective study with uniform transfusion criteria may further clarify the impact of clopidogrel. Furthermore, a higher percentage of patients on clopidogrel had a positive past medical history for stroke or TIA. With lack of a uniformly applied transfusion protocol, physicians treating these patients may have had lower thresholds for transfusion compared to patients without a history of stroke or TIA. This is a significant weakness of the study. Lastly, the strength of the study would have been improved by expanding our analysis to include patients taking aspirin.

In this study hip fracture patients on clopidogrel at time of admission had an increased risk of receiving a blood transfusion after early operative intervention. No increase in perioperative morbidity could be otherwise linked to the use of clopidogrel. Counseling patients on clopidogrel regarding the risk of transfusion for operative treatment of hip fractures should be considered; however, the benefits of early surgical intervention likely outweigh the risks of transfusion in patients sustaining hip fractures while on clopidogrel.

<table>
<thead>
<tr>
<th>Variable</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel versus control group</td>
<td>0.012</td>
</tr>
<tr>
<td>Age</td>
<td>0.965</td>
</tr>
</tbody>
</table>

**Table 4: Risk Factors for Transfusion**

Analysis of variables for transfusion.

Logistic Regression Analysis: Categorical variable considered were are and consumption of clopidogrel. The response variable is transfusion postoperatively.
REFERENCES:


CEFAZOLIN USE IN PATIENTS WHO REPORT A NON-IGE MEDIATED PENICILLIN ALLERGY: A RETROSPECTIVE LOOK AT ADVERSE REACTIONS IN ARTHROPLASTY

S. Haslam, MD, * D. Yen, MD,* N. Dvirnik BSc,+ D. Engen, MD^

Abstract
Background: A large number of patients presenting for total hip and knee arthroplasty report an allergy to penicillin. The reported incidence of cross reactions with cephalosporins in patients with penicillin allergy ranges from 3% to 18%. Perioperative antibiotic prophylaxis practices range from using cephalosporins to substituting clindamycin or vancomycin. The purpose of this study was to determine whether cefazolin can be used safely in the perioperative setting in patients with reported non-IgE mediated reactions to penicillin.

Methods: We retrospectively reviewed all primary total hip and knee arthroplasty (2012) and revision (278) cases done at a Canadian university hospital from 2007 to 2010. We calculated the prevalence of reported penicillin allergy, the specific reaction reported, and the observed reaction rate in penicillin allergic patients given cefazolin.

Results: The prevalence of reported penicillin allergy was 9.9%. There was a wide range of reported reactions, with 25% IgE mediated and 75% non-IgE mediated. Only 27% of patients reporting penicillin allergies were given cefazolin. There were no adverse reactions when non-IgE mediated penicillin allergy patients received cefazolin.

Conclusion: Surgical patients with reported non-IgE allergic reactions to penicillin have a low chance of adverse reaction to perioperative administration of cefazolin. Only a fraction of surgical patients with reported non-IgE mediated reactions to penicillin receive cefazolin perioperatively.

Introduction
Prior to 1995 penicillins were the most utilized antibiotics, and had the highest prevalence of drug allergy. Cephalosporins, especially cefazolin, a first generation cephalosporin, is currently used as the antibiotic of choice for the prophylaxis of surgical infections due to its effectiveness against gram-positive bacteria and its action against most clinically important aerobic gram-negative bacilli and nonbacteroid anaerobes. On a chemical level, cephalosporins and penicillins share a beta-lactam ring as well as certain side-chains believed to be the antigenic determinants responsible for cross-reactivity between these drugs. However, recent research and clinical reviews, aided by a better understanding of the chemistry and purer drug preparation, support the notions that the allergy overlap between them is much more limited than previously thought and that cephalosporin use should not be as restricted in penicillin allergic patients.

The reported incidence of allergic reactions to first generation cephalosporin antibiotics ranges from 0.0001% to 0.1%. The reported incidence of cross reactions with these medications in patients with penicillin allergy ranges from 3% to 18%. Because of these wide variations, practice recommendations range from using these medications if the allergy is mild to automatically substituting clindamycin or vancomycin regardless of the nature of the adverse reaction to penicillin. This mirrors the current practice for all surgical cases at our center for cefazolin use in patients with a reported penicillin allergy.

Substitution of cefazolin raises several concerns. Vancomycin exposure increases the risk of vancomycin resistant Enterococcus (VRE) infections and its use should be restricted to centres where methicillin resistant Staphylococcus aureus is endemic. Clostridium difficile infections can occur with the use of any broad spectrum antibiotic but is particularly associated with the use of clindamycin. Finally, cefazolin is the most cost effective drug per dose at our center (cefazolin – $0.85, clindamycin – $1.41, vancomycin – $7.60). Therefore, we hoped to be able to maximize the future safe use of cefazolin by determining if there is a subgroup of penicillin allergy patients that can be given Cefazolin without cross-reaction.

*Department of Surgery,
+Faculty of Medicine,
^Department of Anaesthesiology and Perioperative Medicine, Queen’s University
Corresponding Author:
Dr. Sean Haslam
Kingston General Hospital
76 Stuart Street, Kingston
Ontario, Canada K7L 2V7
e-mail: sghaslam@gmail.com
Cefazolin Use in Patients who Report a Non-IgE Mediated Penicillin Allergy

METHODS AND MATERIALS

We retrospectively collected data from 1962 patients who underwent 2290 hip and knee arthroplasty procedures between 2007 and 2010 at our University Health Sciences Centre, Ontario, Canada. We noted the presence of a patient reported penicillin allergy. The patient’s reported reaction was recorded. Reactions were characterized as IgE and non-IgE mediated. Urticaria, immediate airway compromise, angioedema, and anaphylaxis were considered IgE mediated11, whereas all other reactions fell under the category of non-IgE mediated (Table 1). The prophylactic antibiotic administered was recorded, as well as any resultant adverse reactions. The patients’ paper charts and electronic charts were searched for a record of adverse reactions. This included the anesthetic record (recorded by the anesthetist), the operative note (recorded by the surgeon), the operative record (recorded by the nursing team in the operating room), the progress notes (recorded by the surgical team rounding on the ward post-operatively until discharge from hospital), and the inpatient nursing notes (recorded by the bedside nurse post-operatively until discharge from hospital).

Penicillin allergy prevalence was calculated, and a chi-square analysis was performed. Hospital appointed program directors, with the support of the Departments of Anesthesiology and Perioperative Medicine, Medicine (Infectious Diseases), Surgery, and the Ethics Review Board at our center approved this retrospective study.

RESULTS

From 2007 to 2010, 1962 patients underwent 2290 arthroplasty procedures. These procedures were 1093 primary total knee replacements, 919 primary total hip replacements, 131 revision total knee replacements, and 147 revision total hip replacements.

The prevalence of reported penicillin allergy was 9.9% (196 patients). There was a wide range of reported reactions with IgE mediated allergies such as anaphylaxis, urticaria, angioedema and airway compromise accounting for 25% (49) of those reported (Table 1). Non-IgE reactions comprised 75% (147) of patients. Rash and unknown reactions were among the highest reported non-IgE mediated reactions at 39% and 14%, respectively.

No patients reporting an IgE mediated allergy received cefazolin. Of the 54 non-IgE mediated penicillin allergic patients who received cefazolin, no adverse reactions were reported, which was significantly different from the reported literature rates of 3% to 18%8,9 by chi-square analysis (p<0.03). We also noted that fewer penicillin allergic patients received cefazolin (54 of 196, 27%) compared to those who reported no penicillin allergy (1691 of 1826, 93%, p= <0.001).

DISCUSSION

Despite finding a similar prevalence for penicillin allergy to that reported in the literature, we observed a significantly decreased reaction rate to cefazolin among patients who report a penicillin allergy compared to the literature1. Based on a reported cross–reactivity rate of 3% to 18%8,9 we would have expected between two and ten patients (out of 54) to experience an adverse reaction. Our study saw zero adverse reactions which was noted to be significant (p=0.03). This could potentially be explained by the fact that only non-IgE mediated allergies received cefazolin at our institution.

<table>
<thead>
<tr>
<th>Type of Reaction</th>
<th>Number of patients reporting the reaction</th>
<th>Proportion of all reactions</th>
<th>Number of patients who received cefazolin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urticaria*</td>
<td>20</td>
<td>10%</td>
<td>0</td>
</tr>
<tr>
<td>Immediate airway compromise*</td>
<td>14</td>
<td>7%</td>
<td>0</td>
</tr>
<tr>
<td>Anaphylaxis*</td>
<td>10</td>
<td>5%</td>
<td>0</td>
</tr>
<tr>
<td>Angioedema*</td>
<td>5</td>
<td>3%</td>
<td>0</td>
</tr>
<tr>
<td>Rash</td>
<td>77</td>
<td>39%</td>
<td>36</td>
</tr>
<tr>
<td>Unknown or &quot;Cannot Remember&quot;</td>
<td>27</td>
<td>14%</td>
<td>4</td>
</tr>
<tr>
<td>Swelling</td>
<td>11</td>
<td>6%</td>
<td>4</td>
</tr>
<tr>
<td>Itching</td>
<td>8</td>
<td>4%</td>
<td>3</td>
</tr>
<tr>
<td>GI upset</td>
<td>8</td>
<td>4%</td>
<td>4</td>
</tr>
<tr>
<td>Blisters and boils</td>
<td>3</td>
<td>2%</td>
<td>1</td>
</tr>
<tr>
<td>Mouth Sores</td>
<td>3</td>
<td>2%</td>
<td>0</td>
</tr>
<tr>
<td>Colitis</td>
<td>1</td>
<td>&lt;1%</td>
<td>0</td>
</tr>
<tr>
<td>Coma</td>
<td>1</td>
<td>&lt;1%</td>
<td>0</td>
</tr>
<tr>
<td>Convulsions</td>
<td>1</td>
<td>&lt;1%</td>
<td>0</td>
</tr>
<tr>
<td>Hiccups</td>
<td>1</td>
<td>&lt;1%</td>
<td>0</td>
</tr>
<tr>
<td>Fever</td>
<td>1</td>
<td>&lt;1%</td>
<td>0</td>
</tr>
<tr>
<td>Lumps on Feet</td>
<td>1</td>
<td>&lt;1%</td>
<td>1</td>
</tr>
<tr>
<td>Positive Penicillin Allergy test</td>
<td>1</td>
<td>&lt;1%</td>
<td>1</td>
</tr>
<tr>
<td>Racing heart</td>
<td>1</td>
<td>&lt;1%</td>
<td>0</td>
</tr>
<tr>
<td>Serum Sickness</td>
<td>1</td>
<td>&lt;1%</td>
<td>0</td>
</tr>
</tbody>
</table>

* indicates IgE mediated reactions

Table 1: Summary of reaction types and rates.
Another possible explanation is that older studies overestimated the cross-reactivity rate between penicillins and cephalosporins since early cephalosporin antibiotics contained trace amounts of penicillin which had led to a frequent avoidance of cephalosporins in penicillin allergic patients, even after developments in purification techniques eliminated the contamination problem in the 1970’s. This is supported by a study by Novolbos et al., which noted that of 41 patients with IgE mediated penicillin allergy who received a cefazolin intramuscularly, no patients experienced an adverse reaction.

We noted that merely reporting a penicillin allergy (regardless of the reaction type) significantly decreased a patient’s chances of receiving cefazolin prophylactically. Despite an established guideline at our institution that permits cefazolin administration in non-IgE mediated penicillin allergic patients, there was little adherence to this counsel. This practice is likely historical, based on previous manufacturing practices whereby cephalosporin antibiotics contained trace amounts of penicillin. This has given rise to the propensity to substitute for cefazolin in these cases. We believe this illustrates a need for education amongst surgeons, anesthesiologists, and the entire surgical team regarding cefazolin administration in penicillin allergic patients.

Vancomycin is often administered over a prolonged period to avoid “Red Man Syndrome”. If vancomycin were not started in a timely manner and the full dose was not administered prior to incision then the prophylactic benefit of the antibiotic would be compromised. Studies have emphasized the importance for full dosing of prophylactic antibiotics prior to skin incision. To date there is no literature to support whether cefazolin is inherently better at preventing infection than vancomycin or clindamycin, only that cefazolin has a lower drug risk profile. The increasing use of vancomycin and clindamycin comes with the associated risks of vancomycin resistant enterococcus infection, nephrotoxicity, and C. difficile infection. Number needed to harm (NNH) can be used to help assess negative reactions between drugs with a higher NNH indicating lower risk. Clindamycin harbors a NNH of eight for C. difficile infection, while vancomycin exhibits a NNH of 14 for nephrotoxicity. Cefazolin’s NNH for C. difficile infection is 28. Because of these risks the Healthcare Infection Control Practices Advisory Committee has previously stated in their guideline “the routine use of vancomycin in antimicrobial prophylaxis is not recommended for any kind of operation.”

Minimizing other adverse reactions is one reason why orthopaedic surgeons may opt for cefazolin pre-operatively.

Our study is limited by its retrospective nature and reliance on previously recorded data. Underreporting of adverse events is one limitation of collecting data retrospectively. Another limitation is that we draw conclusions about safety of cefazolin use for the non-IgE mediated allergy group as a whole. Though we provide convincing data demonstrating a lack of adverse-reaction of our 36 patients with penicillin rash allergies, many of the other allergy subgroups were small. However, because of the large number of potential reactions and the high unlikelihood that penicillin cross-reactivity for these rarer reactions would exist, combining these into a single non-IgE mediated reaction group ultimately improves the analysis.

We find the disparity in antibiotic choice based on reporting a penicillin allergy and the lack of adverse reactions in certain penicillin allergic patients to be worthy of note. It appears that many patients who could otherwise receive cefazolin perioperatively are being prescribed an alternative antibiotic despite evidence to support the contrary. We believe that we have identified a group of patients who can be screened to receive cefazolin based on a history of non-IgE mediated penicillin allergy. Based on our findings it appears that cefazolin is safe to administer to patients reporting a non-IgE mediated penicillin allergy. However further prospective studies are warranted to further examine our findings.

REFERENCES


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MECHANICAL PROPERTIES AND ELUTION CHARACTERISTICS OF POLYMETHYL METHACRYLATE BONE CEMENT IMPREGNATED WITH ANTIBIOTICS FOR VARIOUS SURFACE AREA AND VOLUME CONSTRUCTS

Richard E. Duey, MD¹; Alexander CM. Chong, MSAE, MSME¹;²; David A. McQueen, MD¹;²; James L. Womack, MD³; Zheng Song, MS²; Tristan A. Steinberger²; Paul H. Wooley, PhD¹;²

ABSTRACT

Background: Numerous studies have examined the elution characteristics and the effects of antibiotics from bone cement. This study seeks to determine the effect that surface area and volume have on the elution characteristics and bioavailability of tobramycin and vancomycin when mixed in polymethylmethacrylate (PMMA) bone cement in various combinations. It also investigates the mechanical properties of antibiotic-impregnated bone cement and its relationship to surface area and volume.

Methods: Three antibiotic-bone cement combinations were used, and these consisted of PMMA mixed with tobramycin and vancomycin or tobramycin alone. Four groups of specimens (different surface area and volume) were made. The elution characteristics of the different specimens were examined using the minimum inhibitory concentration (MIC) method at different time intervals. The bacteria used during testing were methicillin-sensitive staphylococcus aureus (MSSA). The ultimate compressive strength (UCS) of the specimens was also determined at various time intervals.

Results: The bactericidal activity of a tobramycin/vancomycin combination against MSSA was not significantly greater than tobramycin alone. Tobramycin was more effective than vancomycin against MSSA (average: 168%, p<0.05). The inhibitory capabilities of tobramycin and vancomycin individually were not found to be additive. Combination 2 (1.0g tobramycin/1.0g vancomycin) had a higher antibiotic elution mass and rate for all sample sizes compared to the other two combinations (average: 170%, p<0.05). Surface area and volume did not have a significant effect on the elution rate of the antibiotics. The UCS of all samples tested was greater than 70MPa at all three testing intervals.

Discussion: Mixing tobramycin and vancomycin did not have a synergistic effect against the bacteria as expected. Increasing the concentration of antibiotics in bone cement increases both elution mass and elution rate over time. Although the UCS of the antibiotic-impregnated bone cement was affected by antibiotic elution and sample geometry, all testing results fell within previously accepted standards.

Clinical Relevance: This study advanced our overall understanding of the elution characteristics and biomechanics of PMMA bone cement impregnated with tobramycin and vancomycin.

Keywords: antibiotic, bone-cement, elution, surface, volume

INTRODUCTION

Local delivery of antibiotics using antibiotic depots has become a major factor in the management of deep musculoskeletal infections¹, ². The use of antibiotic-impregnated bone cement to treat musculoskeletal infection has been reported in the literature for more than three decades¹, ³ and ⁴. The elution of antibiotics from polymethylmethacrylate (PMMA) beads has been studied extensively both in vitro and in vivo⁵-⁰. The elution characteristics of antibiotic-impregnated bone cement can be affected by certain factors including the type of cement used¹¹, preparation methods¹², surface characteristics¹³, porosity of the cement¹⁴, and the amount and/or type of antibiotics used¹⁵. Despite all of this data, the current literature still leaves to question the effect that surface area and volume have on the overall performance of antibiotic-loaded cement.

Minimum inhibitory concentration (MIC) is the lowest concentration of an antimicrobial substance that will inhibit the visible growth of a microorganism after overnight incubation. MICs are important in diagnostic laboratories to confirm resistance of microorganisms to an antimicrobial agent and also to monitor the activity of
new antimicrobial agents\textsuperscript{18}. MIC is generally regarded as the most basic laboratory measurement of the activity, or strength, of an antimicrobial substance against an organism\textsuperscript{19}.

The two most common antibiotics mixed with bone cement are tobramycin and vancomycin. Tobramycin sulfate is an aminoglycoside antibiotic used to treat various types of bacterial infections, particularly those caused by gram-negative organisms. Tobramycin is preferred over gentamicin for Pseudomonas aeruginosa pneumonia due to better lung penetration and bactericidal activity. Vancomycin is a glycopeptide antibiotic used in the treatment of gram-positive organisms and is best known for its effectiveness against methicillin-resistant \textit{Staphylococcus aureus} (MRSA).

Several questions, however, still remain. First, will both tobramycin and vancomycin mix well with PMMA bone cement? Second, will combining tobramycin and vancomycin increase their overall bioactivity against microorganisms? Third, what kind of elution characteristics will these antibiotics have once the cement has cured? Fourth, do the physical dimensions of the cement have an effect on the elution characteristics of the antibiotics? Finally, how will the elution of the antibiotics alter the mechanical properties of the PMMA bone cement? To our knowledge, no one has previously addressed all of these issues. This study seeks to evaluate the elution characteristics of antibiotic-impregnated PMMA bone cement with varying surface areas and volumes. Additionally, it also examines the mechanical properties of the bone cement over time as the antibiotics are eluted.

The specific objectives for this study were two-fold: 1) investigate the elution characteristics and the mechanical properties of PMMA bone cement impregnated either with tobramycin and vancomycin, or with tobramycin only; and 2) evaluate the relationship surface area and volume have with the elution characteristics and mechanical properties of antibiotic-impregnated bone cement. The null hypotheses for this study was: 1) the antibiotic profile of the PMMA bone cement will be favorable, 2) its mechanical properties will not significantly change as the antibiotics are eluted, and 3) the surface area and volume of the cement will affect both the antibiotic elution and its mechanical performance.

**MATERIALS AND METHODS**

**Antibiotic-Impregnated PMMA Specimen Preparation**

Three different antibiotic-impregnated bone cement mixtures were used based on the clinical practice at our institution. Combination 1 was a pre-mixed Simplex P bone cement with tobramycin, which contains 1.0g (2.5 wt.%) of tobramycin in 40g of polymer powder (Stryker Howmedica Osteonics, Mahwah, NJ). The next two antibiotic-impregnated bone cement mixtures used finely powdered tobramycin (X-Gen Pharmaceuticals, Inc., northport, NY) and vancomycin (Hospira, Inc., Lake Forest, IL) mixed with 40g of Simplex P bone cement powder (Stryker Howmedica Osteonics, Mahwah, NJ). Combination 2 contained 1.0g (2.5 wt.%) of tobramycin and 1.0g (2.5 wt.%) of vancomycin in 40g of polymer powder. Combination 3 contained 0.5g (1.25 wt.%) of tobramycin and 0.5g (1.25 wt.%) of vancomycin in 40g of polymer powder. A total antibiotics concentration of 5% by mass is considered to be the gold standard\textsuperscript{20, 21}.

Four groups (A, B, C, D) of eighteen specimens each were made from each of the three antibiotic-impregnated bone cement combinations. Figure 1 and Table 1 show the design and dimensions, respectively, for the four groups of specimens. The samples for each group had a unique volume and surface area that were carefully
predetermined (Table 1). Group A specimens consisted of a solid disk designed to serve as a baseline for later comparison. The samples in groups B, C, and D were made up of cylinders each with a particular inner diameter, outer diameter and thickness. The central core of the specimens consisted of a professionally machined stainless steel rod that mimicked a prosthetic implant. This rod was left in place for all of the samples through each arm of the testing. Figure 2 shows images of actual samples.

The cement was prepared using a manual mixer. Centrifuging and vacuum techniques were not used in this study. The cement was transferred to the appropriate polyethylene molds and allowed to cure for 24 hours. After 24 hours, each specimen was inspected for any voids or powder clots, and any flawed specimens were excluded. All of the approved specimens were fully immersed separately in sterile phosphate buffered saline (PBS) inside plastic containers with lids. The volume of the saline was measured for each group of specimens. The containers were then placed on a swirl shaker inside an incubator (95% humidity, 37°C, 6% CO₂).

**Elution Kinetics Testing**

The measurement of the bioactivity of tobramycin, vancomycin and a combination of the two antibiotics was assessed using the MIC method. For this study standard Petri dishes containing Mueller-Hinton agar were plated with methicillin-sensitive *Staphylococcus aureus* ATCC 25923 (MSSA, NCTC 12981). Four dishes were used for each type of antibiotic and the combination of the two. A series of 8 two-fold dilutions ranging from 2000mg/mL to 7.81mg/mL was prepared, and 10mL of each dilution was placed in individual wells of the Petri dish (Figure 3). After overnight incubation of the plates at 37°C, the wells were examined for presence or absence of growth. Digital pictures were taken of the dishes and used to measure the diameter of the zone inhibition. The area of the inhibitory zone was then calculated. These dishes served as a standard data set to determine antibiotic concentrations during the elution kinetics testing.

To test the antibiotic elution characteristics, sequential samples were assayed for the MIC similar to the antibiotic activity tests. Only 6 of the 18 specimens from each group were used for this portion of the investigation. Sample intervals representative of 1, 3, 5, and 7 days were tested for their antibiotic elution characteristics. For each sample interval, the solution was removed and stored in another container at 4°C until analyzed. Then the appropriate amount of fresh PBS was placed back into the plastic container with the specimen. A series of three-fold dilutions (1:1, 1:3, and 1:9) was prepared, and 10mL of each dilution was placed in individual wells of the Petri dish. Digital pictures were taken of the dishes and used to measure the diameter of the zone inhibition. The antibiotic concentration for each solution was extrapolated from the diameter of the zone of inhibition using the computer growth equation constructed from the standard curves.

**Mechanical Testing**

In terms of mechanical performance, all testing was performed with strict adherence to the American Society for Testing and Materials (ASTM) F451-99a standards - Standard Specification for Acrylic Bone Cement (ASTM Standard, 2006). The dimensions for each cylindrical-shaped specimen were measured using a digital caliper and recorded prior to each mechanical test. Surface area
Mechanical Properties and Elution Characteristics of Polymethylmethacrylate Bone Cement

and volume for the antibiotic-impregnated PMMA samples were determined. For each antibiotic combination, six specimens from each group were tested at intervals of 0, 5, and 7 days resulting in eighteen specimens per group. All the specimens were tested in compression using an MTS Bionix servohydraulic materials testing system (MTS Model 858, Eden Prairie, MN). The specimens were loaded from -50N to complete structural failure at the rate of 20mm/min. Load and deflection data were measured and collected every 0.1 seconds by the MTS system. The ultimate compressive strength (UCS) was then determined. The mean and standard deviation of the groups were calculated for each type of antibiotic-impregnated bone cement. All mechanical tests were performed in air at environmental temperature.

Statistical analysis
Data retrieved for bioactivity, antibiotic elution rate, and ultimate compressive strength were analyzed using one-way analysis of variance (ANOVA) of SPSS software (Version 16.0; SPSS, Chicago, IL) with p<0.05 denoting significance. Post hoc tests were conducted using the Least Significant Difference (LSD) multiple comparisons test method. These analyses were used to determine the statistical relevance of the difference in bioactivity of the antibiotics, mechanical properties and elution characteristics in each group.

RESULTS

Elution Kinetics Testing
The mean inhibitory zones for vancomycin, tobramycin, and a combination of the two antibiotics against the S. aureus used in this study are shown in Figure 4. The graph illustrates the activity of the antibiotics at different concentrations. Overall, the activity of the tobramycin and vancomycin combination was not significantly (p>0.05) higher than the activity of tobramycin alone. However, tobramycin alone was significantly more efficacious than vancomycin (average: 168%, range: 117% - 257%; p<0.05). Consequently, the inhibitory capabilities of tobramycin and vancomycin individually, were not found to be additive.

After seven days in the 37°C buffered solution, the antibiotic-impregnated PMMA specimens did not show any evidence of gross deterioration. Figure 5 shows the total concentration of antibiotics released at four separate intervals during this time period. Table 2 lists the amount of antibiotics released and the rate of their release for each of the bone cement combinations and their four sample groups. The specimens from Combination 2 (1.0g tobramycin/1.0g vancomycin) had a higher antibiotic elution rate for all sample sizes when compared to Combination 1 and Combination 3 (average: 170%, range: 66% – 236%, Table 2). This difference was statistically significant (Table 3). The specimens from Combination 3 (0.5g tobramycin/0.5g vancomycin) had...
a higher antibiotic elution rate (average: 52.6%, range: 28.7% – 69.5%, Table 2) than those from Combination 1 (1.0g tobramycin), however this was not statistically significant (Table 3).

On day one there was a large amount of total antibiotics released for all samples followed by an exponential decay (Figure 5). For those specimens impregnated with both tobramycin and vancomycin, there was no significant difference (p>0.05) in the amount of antibiotics eluted when comparing groups with the same antibiotic combination but different surface areas and volumes (Table 4). However, the larger volume samples did tend to elute a higher amount of antibiotics for each of the combinations. On day three, samples containing either the low-dose combination of tobramycin and vancomycin or tobramycin alone eluted less than 0.7mg of antibiotics, thereby making it difficult to determine the total elution mass of antibiotics as a function of surface area and volume. For the specimens containing the high-dose combination of the two antibiotics, the amount of antibiotics eluted was high enough to show there was no difference based on surface area when holding volume constant (Group B vs C) (Figure 5, Table 4).

The total elution mass of antibiotics as a function of volume could not be determined due to the limited number of data points collected and the variable performance pattern of the different antibiotic combinations. No consistent relationship was identified (Figure 6a).
As for the total elution mass of antibiotics as a function of surface area, a linear relationship was identified between increasing surface area and increasing amount of antibiotics released. However, this was dependent upon the initial concentration as well as the combination of antibiotics, with the specimens containing the high-dose combination of vancomycin and tobramycin exhibiting this relationship (Figure 6b).

### Mechanical Properties and Elution Characteristics of Polymethylmethacrylate Bone Cement

**Mechanical Testing**

Ultimate compressive strength (UCS) testing was carried out, and six samples from each group were tested at each interval day for a total of 18 test samples. Results are shown in Figure 7. The UCS of all specimens tested during the seven days of incubation in the 37°C buffer was above the ASTM F541 and ISO 5833 minimum of 70MPa. At Day 0, the mean UCS for Group A was found to be significantly different (p<0.05) between the antibiotic-impregnated specimens. The same held true for Groups B and C. When antibiotic-free specimens in Group A were compared to antibiotic-impregnated specimens, the differences were significant (p<0.05). The UCS for Groups B and C was also significantly different (p<0.05) between antibiotic-free specimens and antibiotic-impregnated specimens. The combination of antibiotics and concentration level also influenced the UCS, with the specimen containing the high-dose combination of vancomycin and tobramycin exhibiting the highest UCS (Figure 7).

### Statistical Analysis of Effect of Volume and Surface on Antibiotic Release (one-way ANOVA, SPSS)

<table>
<thead>
<tr>
<th>Day</th>
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<th>Overall P-value</th>
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*Note: BCT represents PMMA impregnated with 1.0g tobramycin; BCTV represents PMMA impregnated with 1.0g tobramycin and 1.0g vancomycin; BCTV 0.5 represents PMMA impregnated with 0.5g tobramycin and 0.5g vancomycin.*
FIGURE 6. Average mass of antibiotics eluted as a function of: (a) specimen volume and (b) specimen surface area. Error bars represent the uncertainties of the total eluted mass at the 95% confidence interval.

<table>
<thead>
<tr>
<th>Day</th>
<th>Group</th>
<th>Material</th>
<th>P-value</th>
<th>Overall P-value</th>
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*Note: BCT represents PMMA with tobramycin (1.0g); BCTV represents PMMA with tobramycin (1.0g) and vancomycin (1.0g); BCTV 0.5 represents PMMA with tobramycin (0.5g) and vancomycin (0.5g); BC represents PMMA without any antibiotics. P-value < 0.05 indicating a statistically significant difference.
specimens no significant difference was detected, except for those specimens containing a low-dose tobramycin/vancomycin combination (Table 5). For Group B the mean UCS for antibiotic-free specimens was found to be significantly different from specimens with a high-dose tobramycin/vancomycin combination (Table 5). For Group C a significant difference in UCS was found between antibiotic-free specimens and those impregnated with tobramycin alone. For Group D no significant difference in mean UCS was found when comparing all specimen groups (Table 5).

At day 7, a significant difference (p<0.05) was detected in the mean UCS for Group A, and when comparing antibiotic-impregnated specimens to antibiotic-free specimens (Table 5). For Group B no significant difference was detected between specimens. For Group C the mean UCS was found to be significantly different (p<0.05) when comparing antibiotic-free specimens to antibiotic-impregnated specimens, except for those specimens with a low-dose tobramycin/vancomycin combination (Table 5). For Group D the mean UCS was also significantly different when comparing antibiotic-free specimens to antibiotic-impregnated specimens except for those with tobramycin alone.

When comparing UCS among different specimens in relationship to their geometry (i.e. surface area and

**TABLE 6. Statistical Analysis of Effect of Different Antibiotics Combination on Ultimate Compressive Strength (one-way ANOVA, SPSS)**

<table>
<thead>
<tr>
<th>Day</th>
<th>Material</th>
<th>Group</th>
<th>P-value</th>
<th>Overall P-value</th>
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<tr>
<td></td>
<td></td>
<td>D</td>
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</table>

*Note: BCT represents PMMA with 1.0g tobramycin; BCTV represents PMMA with 1.0g tobramycin and 1.0g vancomycin; BCTV 0.5 represents PMMA with 0.5g tobramycin and 0.5g vancomycin; BC represent PMMA without any antibiotics; P-value < 0.05 indicating a statistically significant difference.
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volume) statistically significant differences (p<0.05) were detected (Table 6). At Day 0 there was a significant difference in UCS between groups without antibiotics and those with antibiotics except when comparing Groups A and B. At Day 7 the mean UCS of the original PMMA specimens without antibiotics was found to be significantly different (p<0.05). When looking at specimens with antibiotics, the mean UCS of group A was significantly different when compared to all other groups.

The UCS of the specimens containing tobramycin alone (BCT) was significantly different (p<0.05), except between Groups C and D for day 0 and day 7 (Table 6). A significant difference in UCS was also found between samples impregnated with a high-dose tobramycin/vancomycin combination (p<0.05), except between Groups A and B (Days 0, 5 and 7) and Groups C and D (Days 5 and 7). Those specimens with a low-dose tobramycin/vancomycin combination had significantly different measurements of UCS, except between Groups A and C (Days 0 and 7), Groups A and B (Day 5) and Groups C and D (Day 7) (Table 6).

When comparing the UCS of all specimens between day 0 and day 7, a significant difference (p<0.05) was detected in the groups with a high-dose tobramycin/vancomycin combination, and in Group C with specimens containing a low-dose tobramycin/vancomycin combination (Table 7).

**DISCUSSION**

Antibiotic-impregnated PMMA is used routinely in treatment of infected total joint arthroplasties and occasionally in the management of chronic osteomyelitis. Penner et al. demonstrated that combining tobramycin and vancomycin in bone cement may have clinical advantages by increasing the antimicrobial spectrum and providing a synergistic effect. Their study used the fluoroescence polarization immunoassay method to measure the concentrations of the eluted antibiotics, but had no way of showing whether the antibiotics were biologically active against bacteria. In 2001 González Della Valle et al. demonstrated that the presence of tobramycin has a synergistic-like effect on the bactericidal activity of vancomycin, and their study used 3 patients who underwent total hip reimplantation with cement after chronic infection caused by methicillin-resistant *Staphylococcus aureus* and *Staphylococcus epidermidis*.

Our current study found that tobramycin released from PMMA is more bioactive than vancomycin against methicillin-sensitive *Staphylococcus aureus* (MSSA). Another important observation was that mixing tobramycin and vancomycin with PMMA bone cement does not have a synergistic affect against MSSA. This is the first report that we know of in the literature to demonstrate this finding. The non-additive, non-synergistic properties of this antibiotic combination may be due to less elution of vancomycin secondary to its greater molecular weight.

<table>
<thead>
<tr>
<th>Table 7. Ultimate Compressive Strength (UCS) comparison between Day 0 and Day 7 for different sample sizes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UCS Comparison in Percent</strong></td>
</tr>
<tr>
<td><strong>(Day 0 vs Day 7)</strong></td>
</tr>
<tr>
<td>BCT</td>
</tr>
<tr>
<td>BCTV</td>
</tr>
<tr>
<td>BCTV 0.5</td>
</tr>
<tr>
<td>BC</td>
</tr>
</tbody>
</table>

*Note: BCT represents PMMA with 1.0g tobramycin; BCTV represents PMMA with 1.0g tobramycin and 1.0g vancomycin; BCTV 0.5 represents PMMA with 0.5g tobramycin and 0.5g vancomycin; BC represent PMMA without any antibiotics; P-value < 0.05 indicating a statistically significant difference*
Klekamp et al\(^8\) stated that the molecular weight of vancomycin is 1,468 atomic mass units and the molecular weight of tobramycin is almost one-third (485 atomic mass units). This factor may also explain the discrepancy in bioactivity of vancomycin and tobramycin when obtaining the standard data set using for MIC testing. The increased mass of vancomycin may inhibit its dissipation across the Petri dish in liquid form.

Penner et al\(^8\) used 1.0g of vancomycin and 2.4g of tobramycin added to each 40g pack of bone cement powder to study in vitro elution characteristics, and they concluded that the elution rate of tobramycin was increased by 68% and that of vancomycin by 103% simply by combining these two antibiotics in the same batch of cement. Klekamp et al\(^8\) also studied the elution characteristics of tobramycin and vancomycin combined with Simplex or Palacos cement, using enzyme-linked immunosorbent assay, and they observed that the elution of tobramycin was compromised by the presence of vancomycin. Greeme et al\(^8\) also reported that the tobramycin elutes at higher levels and for longer periods than vancomycin. However, their results only compare the elution of tobramycin and vancomycin individually from Palacos and Simplex cement. Our results agree with those of both Klekamp et al\(^8\) and Penner et al\(^8\) that the combining tobramycin and vancomycin in PMMA bone cement had an additive effect on the in vitro elution rate.

Based on previous studies\(^6, 8, 10, 17\), there is no doubt that elution of antibiotics is a surface phenomenon related to pores and cracks within the bone cement matrix created by the antibiotics themselves. A majority of impregnated antibiotics remain entrapped within the cement core, therefore, it is no surprise that elution is improved with increasing surface area. Our results demonstrate that mixing vancomycin with the tobramycin in bone cement helps to increase the elution rate.

Kelm et al\(^4\) noted the effective antibiotic elution in vivo may be different from that observed in vitro. And according to Masri et al\(^9\), it is apparent that clinical application of these in vitro results is not straightforward. Work suggests that high antibiotic doses and maximal elution efficiency are necessary to maintain tissue antibiotic levels above the breakpoint sensitivity limit for long-term therapy. Our results support the use of two antibiotics in situations in which the absolute maximal amount of antibiotic elution is desired.

Additionally, our current study disproves the null hypothesis that the mechanical properties of PMMA bone cement will not significantly change as the antibiotics are eluted. The percentage drop in UCS between Day 0 and Day 7 was much higher for specimens made with larger amounts of antibiotics. However, the loading results of all groups and specimens with different combination doses of antibiotics after the seven days of incubation in the 37°C buffer still had the mean UCS above the ASTM F541\(^3\) and ISO 5833 minimum of 70MPa.

The UCS of the specimens was affected by two factors: 1) increased time within the solution, and 2) the thickness of the specimens. The time-related change in mechanical properties has been reported previously. Pelletier et al\(^8\) showed that after 4 weeks the PMMA bone cement was stronger than then the PMMA at 24 hours, which concluded that the PMMA specimen has time-dependent properties. These may explain why our mechanical test results after Day 7 the UCS of the high dosage antibiotic-loaded PMMA bone cement still within the ASTM and the ISO standards. The other factor affecting the UCS of the specimen was the thickness of the specimens. Paradoxically, even though there is an increase both in volume and surface area, the thicker the specimens the more likely the specimen will fail.

Areas of future interest include testing of other mechanical properties of PMMA bone cement, such as diametral tensile strength and fatigue properties. Also, further research is needed to investigate the biological activity of these antibiotics against other strains of bacteria such as *Staphylococcus epidermidis* (BK 2), methicillin-resistant *Staphylococcus aureus* (MRSA) and *Staphylococcus capitis* (ED2D), all bacterial species that frequently cause orthopaedic implant infections\(^32\).

**ACKNOWLEDGEMENTS**

The authors wish to thank Teresa L. Jones, MPH, MT (ASCP) for her assistant, revision and critical comments on the papers. The authors also wish to thank Tom Aldag, Shin Mah, Dimuthu Tilakaratne, and Rita Rai from National Aviation Institute of Aviation for their technical help and for the use of the MTS system. No benefits of any form have been received directly or indirectly to the subject of this article.

**REFERENCES**


ABSTRACT

Background: Control of surgical site infections (SSI) is imperative for the safety of our patients. As orthopedic surgeons we strive to have the lowest infection rate possible for all our surgical procedures. This study evaluates the effects of a simple outpatient peri-operative patient cleaning protocol (The Steiros Algorithm® Outpatient Surgery Protocol) on SSI rates.

Methods: We retrospectively reviewed the hospital’s infection rate database for all procedures from July 2005 until February 2011 performed by one general orthopedic surgeon (PAW) within one hospital system. The Steiros Algorithm® Outpatient Surgery Protocol was instituted on January 1st, 2009. We calculated and compared the deep and superficial SSI rate for orthopedic surgeries performed before and after the Outpatient Protocol was instituted. All patients had a minimum of one-year follow-up data. Lowest previously published estimated costs for SSI were used for a cost analysis ($17,708).

Results: The July 1st, 2005 through December 31st, 2008 SSI rate was 1.0% (13/1292). From January 1st, 2009 through February 28th, 2011 the SSI rate was zero (0/875). The SSI rates decreased 100%. Due to the reduction in SSI, the hospital saved a minimum of $154,059 over a two year period.

Conclusions: In this retrospective review, the Steiros Algorithm® Outpatient Surgery Protocol dramatically reduced the overall SSI rate to zero and saved money. We believe this is a simple, effective protocol that can be used for all orthopedic surgical procedures.

INTRODUCTION

Surgical site infections (SSI) are a serious complication of orthopedic surgeries, with total joint arthroplasty surgical infection rates ranging from 0.2% for primary total hip arthroplasty to 1.5% for total knee arthroplasty. Orthopedic SSI increase patient morbidity by lengthening hospital stays and increasing re-hospitalization and revision surgery rates. Identifying risk factors for infection and taking appropriate steps to remove the cause can reduce infection rates. It has been demonstrated that carriers of Staphylococcus Aureus are more likely to acquire Staphylococcus Aureus SSIs than non-carriers. As well, most nasal carriers also culture positive at more than one extra-nasal site. In addition, patient screening followed by preoperative decolonization with five days of nasal muciprin and chlorhexidine showers has been shown to improve methicillin resistant Staphylococcus aureus (MRSA) infection rates. We therefore hypothesized use of a peri-operative patient cleaning methodology (Steiros Algorithm® Outpatient Surgery Protocol) would lower the overall infection rate in patients undergoing orthopedic surgery.

METHODS

To test this hypothesis, we retrospectively studied all patients who had orthopedic surgery performed by one surgeon (PAW) in a single hospital system (Alegent Health, Omaha, Nebraska). The 1292 consecutive patients who underwent orthopedic surgery between July 1st, 2005 and December 31st, 2008 were the control group. The 875 consecutive patients who underwent procedures from January 1st, 2009 to February 31st, 2011 were the study group. The Steiros Algorithm® Outpatient Surgery Protocol was instituted on January 1st, 2009. The algorithm is an add-on preoperative and postoperative patient decontamination protocol which reduces bacterial bioburden from the surgical patient (unpublished data). The surgeon (PAW) asked all patients to buy the skin sanitizer/antiseptic (0.13% benzalkonium chloride with preservatives, Steirolotion®, Germcure, Houma, Louisiana) preoperatively during the preoperative risk
Methicillin-resistant *Staphylococcus aureus* (MRSA) is a type of bacteria that is resistant to certain antibiotics. These antibiotics include methicillin and other more common antibiotics such as oxacillin, penicillin and amoxicillin. Staph infections, including MRSA, occur most frequently among persons in hospitals and healthcare facilities (such as nursing homes and dialysis centers) who have weakened immune systems. Because of this, I like my patients to use the following perioperative protocol to reduce the risk of infection following surgery.

1) **Use Steirolotion® to decontaminate your body and skin the night before and morning of surgery.**

Steirolotion® is a Steiros® approved and tested medical grade skin sanitizer and kills the most common bacteria that cause disease. Specifically, it kills MRSA. Steirolotion® should be applied to your whole body including skin, nostrils, face, hands, scalp, and especially under your fingernails after you clean them. Anything that could harbor MRSA should be removed and cleaned, including false fingernails and piercings. I recommend application after a regular shower before bedtime and a second application on the morning of surgery. You apply this product to your skin and leave it on to dry which takes about 30-60 seconds. No need to rub or scrub it in and **do not wipe it off**. It forms a protective layer on your skin but once dry, you will not know it is on.

2) **We apply Steirolotion® while you are in the hospital.**

In the hospital and before surgery, the nurse will reapply Steirolotion® as described above. Please bring your bottle to surgery. You will receive your normal antibiotics and preoperative scrub in the operating room. These also help prevent infection.

3) **Continue to use Steirolotion® to decontaminate your body and skin for 5 days after surgery or until wounds are completely healed.**

While your incision is healing, bacteria can still enter into the wound and cause infection. Therefore, I recommend that you continue to apply Steirolotion® as described above for the 5 days after surgery, once your dressing is removed.

4) **Getting started.**

You will need only one bottle of Steirolotion® for surgery. This can be obtained at [www.germcure.com](http://www.germcure.com) or your local hospital pharmacy.

All these precautions will lower your risk of postoperative infection as much as possible. **If you have a previous history of MRSA infections**, please follow the above applications starting one week prior to surgery.
discussion and apply the product the night before and the morning of surgery. A patient handout (Figure 1) was given and reviewed by the surgery scheduler as well. She told the patients how to obtain the product from the local pharmacies or online and reviewed the one page protocol with the patients. The patient was told to bring the Steirolotion® to the surgery to help verify compliance by the surgeon. However, no specific tracking or documentation of compliance was performed. Preoperatively, after patient positioning, the surgeon applied the Steirolotion® to the operative site and surrounding skin and allowed it to dry. Routine operative prep and drape was then performed. Patients who had a cast or splint on applied to the operative site and allowed Steirolotion® to the surgery to help verify compliance by the surgeon. The patient was told to bring the product everywhere possible, and the surgeon made a single application once the splint or cast was removed before surgery.

Post-operatively, patients were told to apply the Steirolotion® daily to the wound from the time the dressing was removed until the wound was healed (about 1-2 weeks). The surgeon (PAW) assessed all patients at the time of surgery and during follow-up appointments to identify any allergic reactions.

During the study period, all standard hospital infection control protocols, preoperative antibiotic protocols and skin preparations were otherwise unchanged. Standard hospital protocol was a 4% chlorhexidine wipe in the preop surgical area prior to surgery. As well, chlorhexidine gluconate 2% with 70% ethyl alcohol (Chloraprep) was used for all preoperative skin preparation unless patients were allergic. All data was collected via the hospital infection control database using the standard hospital infection surveillance system. The hospital infection control practitioners review and investigate culture laboratory data, return to surgery data and monthly physician questionnaires during the postoperative period for one year in patients with implants and for 3 months in patients without implants. This includes data from all eleven regional hospitals in the system. The number of total joint arthroplasties performed was included in the infection data. All superficial and deep infections were included as based on the Centers for Disease Control and Prevention/National Healthcare Safety Network definitions for these conditions. All patients were followed for a minimum of one year. We did not collect demographic or any other patient specific data. For this reason, the study did not require approval by the Institutional Review Board.

All patients received peri-operative antibiotic prophylaxis according to the hospital protocol. The standard regimen was cefazolin 1 gram administered within 60 minutes before surgery followed by 1 gram every 8 hours for 24 hours if an inpatient. Alternatively, vancomycin 1 gram or clindamycin 600 miligrams was administered to patients with a type I allergy to penicillin. We calculated and compared the SSI rate for orthopedic surgeries performed before and after the algorithm was instituted. The Pearson chi square with a two tailed fisher exact test was used to determine the p value.

The lowest previously published estimated direct costs for orthopedic SSI were used for analysis of potential cost savings ($17,708 per average orthopedic infection).4,14

RESULTS

From July 1st, 2005 through December 31st, 2008, the SSI rates were 1.0% (13/1292). From January 1st, 2009 through February 31st, 2011, the SSI rates were zero (0/875).

The SSI rates decreased 100% (P=0.0026). Overall, 35% of the surgeries were inpatient and 65% were outpatient surgeries. 10% were total knee or total hip arthroplasties. During the study period (2009-2011) the number of total hip and knee arthroplasties (137) were greater than during the control period (80). No allergic reactions were noted at the time of surgery or during the postoperative application period. Due to the reduction in SSI, our cost estimate indicates the hospital saved $154,059 over a 26 month period.

DISCUSSION

The Steiros Algorithm® is a global environmental cleaning protocol for hospitals which reduces all forms of hospital acquired infections. Watson et al (unpublished data) found that the Sterios Algorithm®, an inpatient hospital cleaning protocol, dramatically reduced hospital acquired methicillin resistant Staphylococcus aureus (MRSA) rates to almost zero (0.11/1000 discharges) and saved the hospital almost $5,000 dollars per bed per year.15

As well, Watson et al (unpublished data) found that the Sterios Algorithm® significantly reduced total joint arthroplasty and spinal fusion SSI by over 60%.16 The data from this study shows that the Steiros Algorithm® Outpatient Surgery Protocol is a very safe, effective and simple way to reduce orthopedic SSI by reducing the bioburden on the skin of surgical patients.

Previous preoperative protocols have been used to reduce SSI. Bode et al17 preoperatively did a nasal rapid screening MRSA test and treated MRSA carriers with five days of twice daily nasal mupirocin and chlorhexidine 4% baths prior to surgery and lowered the general surgical infection rate from 7.7% to 3.4%. Rao et al18 also screened total joint arthroplasty patients preoperatively for S. aureus by nasal swab cultures. S. aureus carriers were decolonized with mupirocin ointment to the nares twice daily and chlorhexidine baths once daily for 5 days before surgery. He reduced the infection rate from 2.6% to 1.5%. The Steiros Algorithm® compares very favor-
ably with these studies with a zero overall (deep and superficial) infection rate. Our study had several limitations. First, the study was not randomized and we did not collect demographic or other patient-specific data, so selection bias is possible. Using patients whose surgeries were performed by a single surgeon from a stable population mitigates this bias. Furthermore, the large numbers of patients should help reduce the risk of selection bias. Second, we did not track and verify compliance other than the surgeon asking the patient if they used the product and brought it to surgery. The surgeon (PAW) applied the antiseptic in the immediate preoperative period 100% of the time. Third, we did not culture patients after the decolonization protocol to verify decolonization of specific bacteria types preoperatively. However, the dramatic reduction in infection rates suggests the decolonization was effective.

The algorithm uses a simple patient cleaning protocol that any surgeon can institute in their practice without hospital dependence or involvement. A low cost ($11.99 on line price), alcohol free preoperative biocide is applied, avoiding antibiotics that promote resistant organisms. As well the significant costs involved with MRSA screening, mupirocin prescription and chlorhexidine baths are avoided (up to $300). This allows for much easier application and compliance for patients undergoing all orthopedic inpatient and outpatient surgeries.

In summary, institution of the Steiros Algorithm® Outpatient Surgery Protocol dramatically reduced the orthopedic SSI rate and saved money.

REFERENCES
12. Unpublished Data Steiros® LLC.
ABSTRACT
The prevalence of congenital talipes equinovarus (clubfoot) in Vietnam is estimated to be approximately one in 1000 births. To date, no epidemiological studies have been conducted in this country to assess risk factors associated with this deformity. The purpose of this study was to evaluate specific environmental and socioeconomic factors that may increase the risk of an infant being born with clubfoot. A descriptive clinic-based study was conducted using structured questionnaires given to biological mothers of clinically confirmed clubfoot subjects (n=99) and biological mothers of children between ages 0-18 with no first or second degree family history of clubfoot as controls (n=97). Phenotypic data from clubfoot subjects was also collected. We found that males were twice as likely to have clubfoot and half of clubfoot subjects were affected bilaterally. There was no significant difference in the rate of left versus right clubfoot. Infant and maternal characteristics showing a strong association with clubfoot included breech presentation at birth (p=0.026) and young maternal age (p=0.033). Although there were no strong correlations with any sociodemographic paternal characteristics, a higher percentage of case fathers were younger at the age of conception compared to control fathers. The information from this preliminary study provides a framework for future epidemiologic studies in this population. An understanding of the risk factors associated with clubfoot will play an important role in understanding the pathophysiology of this disabling deformity.

INTRODUCTION
Congenital talipes equinovarus (clubfoot) is a birth defect characterized by atrophy of the calf muscles and equinus of the ankle, varus of the hindfoot, cavus and adductus of the forefoot. The defect can be associated with a neuromuscular disorder or a generalized syndrome such as spina bifida, arthrogryposis, or dystrophic dwarfism, but most clubfeet are isolated and idiopathic. The severity of the deformity is variable, ranging from mild to extremely rigid foot, and correction usually requires serial manipulation and castings followed by surgical procedures for the rare resistant cases. The prevalence of congenital clubfoot is approximately one in every 1000 live births. Numerous studies have reported different birth prevalences between racial and ethnic groups with 0.39 cases per 1000 live births among Chinese populations, 0.76 per 1000 live births in Hispanic populations, 1.12 per 1000 live births among white populations, and 6.8 per 1000 live births among Polynesian populations. In Vietnam, the prevalence of clubfoot is estimated to be one per 1000 births.

Despite extensive epidemiological, clinical, and basic science research, the etiology and pathogenesis of clubfoot remains unknown. Multiple studies have proposed certain risk factors to be associated with clubfoot, including male gender, maternal smoking, maternal age, maternal marital status, parity, maternal education and maternal diabetes. As of today, no epidemiological studies regarding congenital clubfoot have been conducted in the Asian population.

This study attempts to describe any specific factors that may be associated with increased risk of an infant being born with idiopathic clubfoot in Vietnam. Understanding interactions of specific factors will allow educational approaches to avoid them and provide a better understanding of the etiology and pathophysiology of this deformity.

MATERIALS AND METHODS
The proposal for this study was approved through the University of Iowa Institutional Review Board. After the study was explained in detail, interviewee consent was given verbally before questionnaires were collected. Structured questionnaires were used in this study to evaluate the rate of specific risk factors possibly associated with idiopathic clubfoot.
Questionnaires were given to cases and controls. Cases were biological mothers of live, singleton births with physician confirmed diagnosis of idiopathic clubfoot. Controls included a cluster sample of biological mothers of children between the ages of 0-18 who do not have a first or second-degree family history of congenital clubfoot and no other congenital abnormalities. The questionnaire asked for specific infant information including gestational age, birth weight, and birth month. Maternal and pregnancy information collected included age at conception, mode of delivery, presence of breech presentation, smoking history, education, and diabetes. Information collected about the biological father included age at the time of conception and smoking history. Clubfoot phenotype including laterality of the defect and infant sex was collected as well.

Because a strict birth-registry is not currently in place in Vietnam, the cohort for this case-control study was hospital-based. Collaborations with Dr. Huynh Manh Nhi and Dr. Vo Quang Nam, orthopaedic surgeons in Ho Chi Minh City (Vietnam’s largest metropolis), specializing in the care of clubfoot patients, provided us with access to their clubfoot patient lists. Additional clubfoot patient lists were compiled through extensive networking with other orthopaedic surgeons throughout major cities in Southern Vietnam. The biological mothers of these patients were informed about this study by their physician and were asked to bring their child back to the clinic for a follow-up visit at which time questionnaires were collected by a medical student fluent in Vietnamese and English. Questionnaires for controls were collected in pediatric departments of two major hospitals in Ho Chi Minh City. Recruitment of subjects and collection of questionnaires occurred within a 10-week period.

**Statistical Analysis**

Cochran-Mantel-Haenszel Statistics was used to determine association between particular risk factors and clubfoot. $P$-values <0.05 indicate statistical significant associations.

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Descriptive Statistics of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenotypic Characteristics</td>
<td>Cases (n=99)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>62 (63%)</td>
</tr>
<tr>
<td>Female</td>
<td>33 (33%)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Laterality</td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td>51 (52%)</td>
</tr>
<tr>
<td>Unilateral</td>
<td>45 (45%)</td>
</tr>
<tr>
<td>Left</td>
<td>20 (44%)</td>
</tr>
<tr>
<td>Right</td>
<td>22 (49%)</td>
</tr>
<tr>
<td>Missing</td>
<td>3 (7%)</td>
</tr>
</tbody>
</table>

**RESULTS**

Ninety-nine biological mothers of clubfoot and 97 mothers of non-clubfoot children were enrolled and phenotypic data was collected from 99 clubfoot cases.

Phenotypic data of all the clubfoot cases is shown in Table 1. Sixty-three percent of all clubfoot cases were males and 33% were females. There was no significant difference in the proportion of bilateral vs. unilateral clubfoot (53% bilateral and 47% unilateral) within all cases. No significant difference was seen in the proportion of bilateral vs. unilateral clubfoot within male cases (52% bilateral, 49% unilateral) or within female cases (58% bilateral, 42% unilateral) (data not shown). Of the 45 unilateral clubfoot cases, 20 (44%) had left clubfoot and 22 (49%) had right clubfoot (missing data for 3 cases).

Descriptive statistics describing possible risk factors associated with clubfoot are presented in Table 2. There was no association with infant characteristics (gestational age and birth weight) and clubfoot. Eleven percent of clubfoot cases did not have full-term births (<37 weeks gestational age) compared to 7% of controls. Nine percent of clubfoot cases were born less than 2500 grams compared to 4% of controls. However, breech presentation did show a strong association with clubfoot: 9% of clubfoot cases were born breech compared to only 2% of controls, corresponding to a $p$ value of 0.026. We found no seasonal variation associated with increasing risk for clubfoot. Forty-seven percent of both cases and controls were born between November-April and 48% of cases were born between May-October vs. 49% of controls.

The socio-demographic maternal characteristic that showed significant association with clubfoot was maternal age at conception: 35% of case mothers were < 25 years old compared to only 18% of control mothers. 46% of case mothers were between the ages of 25-34, and 8% were 35 or older when they conceived a baby with clubfoot compared to 58% and 15% of control mothers, respectively ($p=0.033$). The percentages of maternal smoking, diabetes, and education were similar between cases and controls. Socio-demographic paternal characteristics did not show strong associations with clubfoot, although a higher percentage of case fathers were younger than 25 years old at the time of conception compared to control fathers (9% and 3%, respectively). 55% of case fathers were between the ages of 25 and 34, and 23% were 35 years or older compared to 56% and 32% of control fathers, respectively. 62% of case fathers and control fathers reported a history of smoking.

**DISCUSSION**

Congenital idiopathic clubfoot is the most common musculoskeletal deformity affecting 1 to 7/1000 newborns. Although it is a well-recognized foot
deformity, the etiology and pathophysiology of congenital clubfoot remains unknown. Based on previously published data, there is likely etiologic heterogeneity involving both genetic and environmental influences. The results of our study confirm male sex as a strong risk factor for clubfoot (63% of males compared to 33% of females, n=96). The proportion of cases with bilateral clubfoot was similar to those previously reported. Prior studies have demonstrated a higher prevalence of right-sided clubfoot, however there was no significant difference in the percentage of right unilateral vs. left unilateral clubfoot in our study population (22% right, 20% left). No statistically significant differences for laterality were identified between males and females (data not shown). We did not find associations between low birth weight and preterm birth with clubfoot, contradicting previous reports. We did find, however, a strong association between breech presentation and congenital clubfoot, confirming findings in a previous study.

A seasonal variation for the incidence of clubfoot has been reported. Pryor et al. reported an increase in the prevalence of clubfoot babies born in the winter quarter, from December to February. Robertson and Corbett reported a significant seasonal variation in clubfoot, with the peak month of conception determined to be in June. Barker and Macnicol reported a seasonal

### Table 2

<table>
<thead>
<tr>
<th>Demographic Characteristics</th>
<th>Cases (n=99)</th>
<th>Controls (n=97)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gestational Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;37 weeks</td>
<td>11 (11%)</td>
<td>7 (7%)</td>
</tr>
<tr>
<td>37+ weeks</td>
<td>84 (85%)</td>
<td>90 (93%)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (4%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Birth Weight (grams)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2500</td>
<td>9 (9%)</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>2500-3500+</td>
<td>86 (87%)</td>
<td>92 (95%)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (4%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td><strong>Birth Month</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nov-Apr</td>
<td>47 (47%)</td>
<td>47 (47%)</td>
</tr>
<tr>
<td>May-Oct</td>
<td>48 (48%)</td>
<td>49 (49%)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (4%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td><strong>Breech Presentation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>9 (9%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>No</td>
<td>84 (85%)</td>
<td>94 (97%)</td>
</tr>
<tr>
<td>Missing</td>
<td>6 (6%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td><strong>Maternal Age at Conception</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>33 (35%)</td>
<td>17 (18%)</td>
</tr>
<tr>
<td>25-34</td>
<td>46 (46%)</td>
<td>56 (58%)</td>
</tr>
<tr>
<td>35+</td>
<td>8 (8%)</td>
<td>15 (15%)</td>
</tr>
<tr>
<td>Missing</td>
<td>12(12%)</td>
<td>9 (9%)</td>
</tr>
<tr>
<td><strong>Maternal smoking during pregnancy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1 (1%)</td>
<td>0</td>
</tr>
<tr>
<td>No</td>
<td>96 (97%)</td>
<td>97 (100%)</td>
</tr>
<tr>
<td>Missing</td>
<td>2 (2%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Maternal diabetes</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>No</td>
<td>95 (96%)</td>
<td>64 (66%)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (4%)</td>
<td>32 (33%)</td>
</tr>
<tr>
<td><strong>Maternal Education (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;12</td>
<td>64 (65%)</td>
<td>60 (62%)</td>
</tr>
<tr>
<td>&gt;12</td>
<td>32 (32%)</td>
<td>36 (37%)</td>
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<tr>
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<td>1 (1%)</td>
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<tr>
<td><strong>Maternal Marital Status</strong></td>
<td></td>
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<tr>
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<td>96 (97%)</td>
<td>97 (100%)</td>
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<tr>
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<tr>
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<td><strong>Paternal age at conception</strong></td>
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<tr>
<td>&lt;25</td>
<td>9 (9%)</td>
<td>3 (3%)</td>
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<td>25-34</td>
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<tr>
<td>35+</td>
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<tr>
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<td>9 (9%)</td>
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<tr>
<td><strong>Paternal smoking</strong></td>
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<tr>
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<td>61 (62%)</td>
<td>60 (62%)</td>
</tr>
<tr>
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<td>28 (28%)</td>
<td>36 (37%)</td>
</tr>
<tr>
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<td>10 (10%)</td>
<td>1 (1%)</td>
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The absence of the association of the risk of congenital clubfoot with certain socio-demographic characteristics to be associated with increased risk of an infant being born with clubfoot. However, findings among these studies have varied due to differences in methodology or study population. One of the most consistently reported associations with clubfoot cases and controls.

Many descriptive studies have reported specific socio-demographic characteristics to be associated with an increase in the risk of an infant being born with clubfoot. However, findings among these studies have varied due to differences in methodology or study population. One of the most consistently reported associations with clubfoot is maternal smoking. Smoking in Vietnam is strongly sex-linked. A 1997 national prevalence survey found about half of males but just 3.4% of females used tobacco smoke regularly. A study in 2002 by Morrow et al. confirmed that this low prevalence of female smokers is strongly enduring and mainly attributed to its “inappropriateness.” This finding holds true in our study population; of 196 women questioned in our study, only 1 woman reported having a smoking history. Therefore, our results do not confirm the linkage of maternal smoking and congenital clubfoot. However, 62% of fathers with clubfoot children reported a history of smoking thus complicating the interpretation of our results by the addition of likely second hand smoke exposure to these mothers.

Our study also shows young maternal age to be significantly associated with increased risk of clubfoot (35% of case mothers younger than 25 years old compared to 18% of control mothers, p=0.033), confirming findings from several studies including a multistate epidemiologic study of clubfoot cases and controls. Maternal diabetes, marital status, and education did not show associations with clubfoot within our study population.

CONCLUSIONS

This study supports previously reported findings that males are more commonly affected by clubfoot by a 2:1 ratio and that 50% are affected bilaterally. These findings are virtually unanimous across every study, suggesting a strong genetic association with clubfoot. Our findings also confirm previous research reporting strong associations with breeched presentation and young maternal age. The absence of the association between maternal smoking and clubfoot in our cohort contradicts numerous findings that have shown a strong association. Differences in culture may have led to this disagreement. However, paternal smoking and second hand smoking should be considered in future investigations. These preliminary findings provide a foundation for more sophisticated epidemiologic studies in the Vietnamese population as well as in the general Asian population in the future.

ACKNOWLEDGEMENTS

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REFERENCES

EVALUATION OF THE PROGRESS AND CHALLENGES FACING THE PONSETI METHOD PROGRAM IN VIETNAM

Vincent Wu; Michelle Nguyen; Huynh Manh Nhi MD; Do Van Thanh MD; Florin Oprescu MD, JD, MBA, MPH; Thomas Cook PhD; Jose A. Morcuende MD, PhD

ABSTRACT

Introduction: In 2003, an ICRC-SFD Ponseti program was introduced in southern Vietnam. Additional programs were introduced by the Prosthetics Outreach Foundation and independently by physicians trained at our center. The purpose of this study was to evaluate the impact, progress and challenges facing Ponseti practitioners and patients’ family members in Vietnam. In addition, web-conferencing (Ponseti Virtual Forum) for continued medical education in the method was also assessed.

Methods: Multiple questionnaires were developed to conduct face-to-face practitioner interviews, focus group interviews, and parental interviews. Observation was done at multiple site clinics to determine or confirm additional challenges faced by practitioners. Web conferencing was introduced to sites in Ho Chi Minh City and Da Nang City.

Results: The number of clubfoot patients treated with the Ponseti method has increased over time with approximately 1,252 infants treated between 2003 and 2010. Specific challenges were identified relating to communication, networking, distance and transportation, and finances for both practitioners and parents. The PVF was not only found to facilitate rapid, relevant dissemination of medical knowledge – thus increasing physician and patient satisfaction – but it may also be found to act as an interface in which medical culture, insight, and compassion are shared benefiting all virtual forum participants.

Conclusion: The identified progress and challenges mirrored that of similar studies done in other countries with several factors affecting progress. Focusing on improving communication channels and networking while working with the ministry of health may improve the facilitation of the Ponseti method in Vietnam. Further implementation and evaluation of the PVF may act as a guide for current and future programs in Vietnam or other countries.

INTRODUCTION

Congenital clubfoot is considered to be the most common congenital birth defect of the musculoskeletal system. Eighty percent of children living with clubfoot reside in developing countries where the limitations of medical knowledge and scarcity of resources prevent the adequate care of these individuals. Left untreated it leads to long-term physical, psychological, emotional, and economical adversity for affected individuals and families. In addition, because up to 50% of these individuals are affected bilaterally, it becomes even more evident how neglected clubfoot is one of the most common physical disabilities in the world (1,2). In Vietnam—where the prevalence of clubfoot is estimated to be 1/1000 births—affected individuals face diminished prospects for education and employment, leading to a dependency on family or external aid (e.g., begging) for survival (3).

With a 95% success rate, the non-invasive and resource-efficient Ponseti method is especially well suited for use in developing countries, such as Vietnam, due to its low cost and high impact results (1). The method is safer, more economical, more comfortable, and more feasible than traditional surgery (8, 9, 10). Economically, in respect to Vietnam, the Ponseti method is two to three times more cost effective than surgery: Surgery costs VND 4,300,000; Ponseti method costs VND 1,400,000 (3). The simplicity of the method also lends itself as a potentially crucial piece in countries with a shortage of physicians and in countries where physicians are over burdened: in addition to orthopedic surgeons, the Ponseti method can be done by physical therapists, nurses, or other health care professionals (2, 3).

With recent initiatives by organizations such as the International Community of the Red Cross and
the Prosthetics Outreach Foundation to establish the Ponseti method in Vietnam, a current evaluation of the method in Vietnam allows for the identification of factors aiding and challenging the method’s dissemination. Interestingly, principles from Everett Roger’s *Diffusion of Innovation* (4) and their application to a healthcare setting by Donald Berwick (11) indicate a complex interplay between the dissemination of an innovation, e.g., the Ponseti method, the viability of an innovation, the individuals implementing an innovation, and the social or organizational context and structure in which an innovation is introduced. The purpose of this study was to identify these factors through interviews with individual health care practitioners and patient’s family members. In addition, the introduction of the Ponseti Virtual Forum was done to provide additional resources and continued medical education to health care practitioners in this country.

The Ponseti Virtual Forum (PVF) is a web-conference-based collaborative forum for Ponseti practitioners to converse in real time and exchange information regarding experiences with difficult cases, developments in the realm of the Ponseti method, or even other medical knowledge as the use of the virtual forum evolves. The PVF portal on the Global Campus is powered by *Elluminate Live!* software program (https://globalcampus.uiowa.edu/index.html and http://www.continuetolearn.uiowa.edu/ccp/tech-support/elluminate.htm) which functions in low band-width settings (specially suited for developing countries) while allowing for videoconferencing, text messages, multimedia display and real-time document sharing.

**METHODS**

Multiple methods were used to gather information in order to increase the validity of the study through triangulation (5, 6). To evaluate impact, the number of health care providers trained in the Ponseti method, where they practice, and the number of children with clubfoot treated with the Ponseti method were determined over the phone or in personal interviews. Candidates for interviews were from participants of the International Committee of the Red Cross training held in Ho Chi Minh City in 2007 and 2008 (3, 12), participants of the Prosthetic Outreach Foundation (POF) training sessions, and various other individuals referred by Dr. Nhi Manh Huynh from the Hospital of Traumatology and Orthopedics in Ho Chi Minh City. In addition, POF provided a count for the number of clubfoot treated in POF sponsored hospitals.

For the evaluation of factors influencing its diffusion, the methods included:

**Semi-structured interviews (face-to-face or phone based)**

Interview questions involved both open-ended and closed-ended questions. A total of 106 individuals were contacted with 47 returning questionnaires. Focus groups, Two focus groups were organized in Ho Chi Minh City and Da Nang City with a cumulative total of 12 Ponseti participants.

**Interviews with parents**

A total of 99 parents were interviewed to compliment the health practitioner interviews. Interviews most often included perspectives from the mother, father, and/or extended family (grandparents, uncles, and aunts).

**Direct observation of clubfoot clinics**

Data collected from interviews and focus groups were recorded in Vietnamese, translated into English, encoded, and stored securely. In correlation with research done by Lu et al, (5), categories included topics related to: physician education, caregiver compliance, cultural aspects, public awareness, poverty, financial constraints on physicians/hospitals, and challenges of the treatment process.

The Ponseti Virtual Forum was introduced to the Da Nang Orthopedic and Rehabilitation hospital and to the Hospital of Traumatology and Orthopedics (HTO) in Ho Chi Minh City. A live session with an expert on clubfoot treatment (JAM) with physicians and patients at HTO was held with a total of 10 participants.

**RESULTS**

Of the 49 practitioners (physicians, nurses, physical therapists, and cast technicians) responding to questionnaire requests, 10 individuals indicated they no longer practiced the Ponseti method. These individuals were from Southern, Central, and Northern Vietnam and represented 21 different hospitals throughout these regions. The reasons stated included not having seen clubfoot patients from the time of initial training or having switched medical specialties or departments. Questionnaires from 2 physical therapists were also removed due to the inability to complete visitation documents before the end of the research period. As a result, the following findings reflect the response of 37 practitioners.

**Impact of the Program: Number of Practitioners Trained and Patients Treated**

The exact number of practitioners trained was not found due to the lack of a central database or directory and loose networking between practitioners trained in the Ponseti method. However, from the total contacts
that patients took home their records. A few physicians did, however, keep a personal record of clubfoot patients they treated. With these records and in conjunction with question 15 on the practitioner questionnaire (Appendix 1), it was possible to estimate the number of patients treated by the interviewed practitioners: roughly 1,252 infants between 2003 and 2010 (Figure 2). In regards to practitioner site, 653 patients were treated in Southern Vietnam beginning in 2003 with the majority being treated in 2007 and 2008; 466 patients were treated in Central Vietnam beginning in 2003 with the majority treated in 2006 onwards. In Northern Vietnam, a total of 129 clubfoot cases were treated by POF sponsored hospitals with the number of cases per year doubled in 2010.

CHALLENGES TO THE DIFFUSION OF THE PONSETI METHOD

As with the introduction of many novel ideas, models, or methods in the US and abroad, the rapid development, progression, and implementation of the Ponseti method in Vietnam has not been without both unique and common (among other countries) challenges to both health care practitioners and patients’ families.

Health Care Providers

The practitioner questionnaire included questions regarding the perceived advantages of the Ponseti method, ideas on how to better spread the method, and additional comments that individuals wished to share (Appendix 1). The most commonly identified advantage of the Ponseti

provided in Vietnam, there are at least 120 individuals who have been trained in the Ponseti method. Considering all practitioners who responded, the 49 individuals practiced in various provinces of Southern (37 practitioners from 15 hospitals), Central (6 participants from 3 hospitals), and Northern (4 participants from 3 hospitals) Vietnam (Figure 1).

Determining the exact number of patients treated with the Ponseti method vs. surgical methods was not possible. The medical system in Vietnam generally preferred...
method in Vietnam was its high success rates and low recurrences. It was regarded has its highly effective treatment for clubfoot. In addition, practitioners were appreciative of its non-invasive and low risk procedures. Other identified advantages were: ease of learning, ease of practicing, and versatility of who can learn the method.

Additional ideas on facilitation of the Ponseti method in Vietnam involved education and communication. In promoting the method to parents, many thought that more careful explanations about the treatment, treatment course and length, and importance of bracing could help increase treatment compliance. It was suggested by multiple individuals to present pictures, brochures, or posters to help parents better visualize and internalize the treatment process. It was also suggested that practitioners keep pictures of past cases, before and after treatment, to show to new families and to help the parents gain confidence in the Ponseti method and its practitioner. In the realm of education, most practitioners identified the need for educating the general public and also raising awareness in healthcare related schools or programs. Many suggested targeting obstetricians and midwives to better identify clubfeet and to be aware of the resources available for treatment. A community-based rehabilitation structure was also proposed.

Other comments included increasing availability of long-term training sessions, improving networking between providers within Vietnam and in other countries, requests for a way to be updated with new developments with the Ponseti method, having training sessions for the obstetrics department, and pondering on the availability of lighter casts to aid in improving patient comfort and parental concern.

**Technique and Protocols**

The use of long-leg casts is crucial to the treatment of clubfeet, and the vast majority of interviewees indicated the use of long-leg casts while 2 utilized non-protocol short-leg casts. Less homogeneity was seen with the Achilles tenotomy and anesthesia use (local vs. general). 7 practitioners “always” performed the Achilles tenotomy, whereas 25 “sometimes” did and 2 “never” did. 17 practitioners indicated the use of local anesthetics, 3 used general anesthesia, and 1 used both. Like cast specificity, the use of braces plays a significant role in preventing the recurrence of clubfoot once casting has corrected the position and form of the affected foot. 27 individuals used the “shoe with foot-abduction bar” as the brace of choice, 5 used AFOs, 2 indicated the use of Denis-Browne, and 1 did not use any bracing. Finally, half the practitioners utilized massage or physical therapy along with casting and bracing.

In assessing for various criteria that practitioners referenced in determining when the Ponseti method should or should not be used, four broad categories surfaced: age, severity, Pirani scale, and none. The age cutoff for the Ponseti use ranged from 2-7 years old; however, most of the practitioners indicated that they would always try the Ponseti method first before surgery regardless of age. Although the Ponseti method was accepted by most as the first option for clubfoot treatment, a few practitioners continued to utilize the Turco surgical method (5 individuals) and 3 utilized the elastic taping, Denis-Browne method.

Particular challenges arose with the procedural skill aspect of the Ponseti method. As with many procedure-based skills, practice and continual constructive feedback are necessary for both improving technique and maintaining confidence, especially when faced with cases involving nuances and complications. The vast majority of individuals who no longer practiced the Ponseti method – despite receiving training – indicated the lack of confidence as the underlying reason. These individuals, provincial practitioners, were trained but would not see clubfoot patients until a month or more after the initial training session. By this time, practical knowledge had been forgotten, and the individuals were predisposed to refer patients to cities for treatment. One way this challenge has been approached was through increasing one-on-one interaction time and increasing directed hands-on experience with casting clubfoot within the hospital environment. Dr. Nhi of the Hospital of Traumatology and Orthopaedics has been providing weekly and recurring training sessions with cast technicians and physiotherapists within HTO and other hospitals. This may help to address the issues of developing technique, confidence, and ensuring higher quality and consistent results.

**Provider and Medical Culture**

Challenges for providers in implementing the Ponseti method within a clinical setting were interwoven with time constraints, casting environment, operation system of the hospital or clinic, and medical culture. In contacting and scheduling appointments with patients, the practitioner did so independently without ancillary staff. For orthopedic surgeons, clubfoot patients were often scheduled between obligate surgeries during “free” time when surgeons could either rest or schedule a higher paying procedure to be done (opportunity cost). Significant amount of time was needed to be spent on educating parents and family members to ensure the best treatment outcome; however, this was identified as challenging when considering high volumes of patients, when the medical culture does not include patient education during a standard visit, and when most patient visits
are completed within 5 minutes. Under this context, an unpleasant time burden was associated with the Ponseti method.

Practitioner burden was also impacted by the casting environment. A broad range of hospital environments was observed; however, a typical urban hospital was often crowded and non-air-conditioned – quite significant considering Vietnam’s geographic location. The tropical heat, within casting areas consisting of 5-6 tables serving both children and adults, was augmented by the heat produced from overcrowding. With overcrowding also comes noise from waiting patients, from the gentleman in an adjacent casting table getting his broken arm reset, and from the baby crying during the Ponseti method casting procedure – an uncomfortable situation for all involved, patient and provider.

A unique challenge to providers was identified by a few of the high volume physicians. A newborn with untreated clubfoot was easier to treat with the Ponseti method; however, these practitioners often received infants who were previously treated incorrectly resulting in new challenges in the application of the Ponseti method. Often the foot was found to be stiffer and less malleable, parents were more skeptical of any type of casting procedure, and infants were conditioned into fearing physicians and casting – leading to more disruptive casting sessions.

No financial barriers were suggested by any of the practitioners. Practitioners do not necessarily lose income from practicing the Ponseti method. Conversely, many practitioners indicated that practicing the Ponseti method was essentially volunteer work due the minimal reimbursement gained by using the Ponseti method as opposed to performing surgical procedures. One practitioner questioned: if the outlook of physicians was only to do procedures to make money, what would happen to the patients who were equally needy but not as lucrative for physicians. The practitioner challenged that there were many more rewards to look for, not just monetary compensation. To say that there were only opportunity costs and only psychological satisfaction gained from altruism would be inaccurate. Where the health care system provides minimal rewards in treating clubfoot with the Ponseti method, cultural customs provided opportunities for families to express their gratitude towards their practitioner. As one physician stated: “[...] During the last Tet celebration, I have received many rewards from the families. The Vietnamese people considers Tet as an occasion to give gifts/money to whom they love/want to compensate (for) what they received. The money sum varies from 100.000 VND to 500.000 VND. One gave me 20 kg of rice, the mother kept the rice in one hand, and the baby in the other hand! All of these things made me rewarded!”

Health Care System and Communications Network

Specific challenges were identified stemming from having no specific protocol or integration of clubfeet treatment within the health care system and medical education institutions. Interviewees in both individual and focus group sessions identified the need to improve clubfoot education of obstetricians, midwives, and general public to ensure early identification and proper treatment.

Challenges in patient referral were augmented by the lack of a central directory of Ponseti practitioners – whether phone or website. Many practitioners, even within the same city, were not aware of others who utilized the Ponseti method; one positive outcome of conducting interviews and group sessions was providing the opportunity for networking to occur. Providers noted the need to strengthen communication and familiarity between Ponseti practitioners to improve referrals to better serve and minimize the burden on traveling families, to provide opportunities in exchanging experiences and consultation for complex cases, and to develop social support of practitioners who volunteer time and effort to do the Ponseti method.

PATIENTS’, PARENTS AND FAMILY NETWORK

Casting and Bracing

Unlike to the challenges facing providers, the obstacles parents faced were interdependent on education level, transportation, and personal financial ability. Bracing adherence and follow-up difficulties were the most mentioned challenges by both practitioners and parents. Parents sited feelings of pity and sympathy for their child’s discomfort as bracing caused chaffing of the infant’s skin and unbearable crying. Less commonly, concerns for comfort with casts and casting were voiced. Blisters and rashes from the humid weather were concerning to parents. The affordability of braces was an issue for some patients, and some physicians often purchased braces for their patients.

Following casting, follow-up visits were necessary to maintain brace fitting, to ensure bracing adherence, and to monitor for recurrence. However, due to the intricate interplay between parental education level, financial status, and burdens associated with distance and transportation, many parents ceased complying with follow-up schedules. In the most extreme cases of severe poverty, parents cut casting periods short as soon as their child’s foot appeared “normal” or adequate for walking. In addition to educating parents regarding the importance and consequences of deviating from protocol, the financial ability of the parents needs to be considered as an additional complication in completing treatment.
Finance and Transportation/Distance

Financial instability and poverty colored the challenges that were associated with transportation and distance. For patients living in cities, this was usually not a major deterrent from completing treatment and adhering to follow-up visits. Many parents from provincial towns, however, lost as much as 5-10 hours for a one-way trip to urban hospitals for treatment. Parents identified that trips to the hospitals resulted in the loss of the day’s wages, which was doubled due to needing 2 people to travel. If arriving early, parents often spent the night or early morning in a hospital common area. In the context of weekly visits and follow-up visits, this was seen to be a significant challenge to overcome. Many parents also identified the need to pool money or donation from neighbors in order to pay for bus fare, lodging, and food.

Cultural Aspects

For the vast majority of parents interviewed, the cultural norm was to seek treatment for their child’s clubfoot in hopes of providing a better future. A few mothers identified having felt some degree of shame, as often husbands or in-laws attributed their child’s deformity to something the mother or the mother’s family had done. However, the mothers understood the necessity of obtaining treatment for the child rather than hiding the child. Practitioners also expressed similar views during the interviews.

A unique and uncommon case was found to have cultural traditions preventing the completion of the Achilles tenotomy. Despite the tenotomy being a minor surgery, grandparents of this specific child were highly protective and refused the procedure even after pleading done by the physician. In Vietnamese culture, the grandparents have great weight in decision-making, and parents show respect by following their wishes. In this specific tradition, the child with clubfeet was the first-born male of the eldest son of the grandfather. As such, the child was seen as the sole carrier the grandfather’s bloodline, and any danger – tenotomy included – leading to the death of the child would effectively end the bloodline.

Another rare and unique cultural barrier to the Ponseti method was explained by a physician in Ho Chi Minh City. There was a belief that what others saw as a deformity, the family, with the affected child, saw as a “gift” or talent. By removing the deformity, the child would no longer be gifted and special.

Health Care System

Without specific guidelines for clubfeet treatment in the health care system and without a clear central database of Ponseti practitioners, parents and infants with clubfeet were the most adversely affected. 68% of parents were directly directed to Ponseti providers shortly after the birth of their child; however, roughly 30% of parents were sent home without further instruction or were told to seek treatment when the child was older. These parents independently sought for care and indicated being referred multiple times before eventually meeting a practitioner could perform the Ponseti method. As discussed earlier, these challenges caused delay in treatment and unnecessary conditioning of the child. Health care is free for all children under 6 in Vietnam; however, differences among hospital policies caused variations in what was covered under the insurance. In some hospitals, cotton used in casting was covered, whereas in other hospitals parents were required to purchase extra cotton.

PONSETI VIRTUAL FORUM

The virtual forum was introduced to two physicians – one in Ho Chi Minh City and the other in Da Nang. Preceding one of the focus group sessions, a virtual clinic session was held with my site mentor, ten of his colleagues, and the senior co-author (JAM) in Iowa City. Barriers and benefits of the virtual forums were assessed by post-survey questionnaires and observation.

Barriers

Technological and economical barriers were the most prevalent and were primarily related to resource limitations. To utilize the virtual forums, most of the physicians would need to obtain their own hardware (laptops) in addition to webcams or speakers to maximize the experience. During preparation setup, software compatibility with Java caused slight delays. Trouble-shooting this issue may also present as a barrier depending on the laptop used by the practitioner. Limited internet access also challenged the ability to access the virtual forum easily: select rooms had consistent wifi or LAN access; these rooms were often administration conference rooms rather than patient areas. Room availability and scheduling conflicts with patients would hamper room availability. The general use of computers among practitioners in Vietnam should also be considered. Although an increasing population of physicians were beginning to utilize computer technology, such as email, many physicians have not found efficiency in using these modes of communication to facilitate patient care (e.g., phone calls are faster in reaching an individual, hospital records are paper based, and limited internet connectivity). This predisposition may cause slight reluctance in utilizing the virtual clinics. Other issues that arose were more related to the actual virtual clinic session that was held in HTO. In regards to improvements to the session, the following was suggested: 1) more time for participants
to discuss, 2) allowing audience access to the microphone (only 1 available), 3) participant timeliness, and 4) language barriers.

**Benefits**

Despite these challenges, benefits were readily identified. Post-survey questionnaires confirmed that the session with Iowa City was helpful and interesting, and participants stated they would use the program in the future. Participants indicated the potential to use the virtual forums for exchanging experiences with other physicians, for presenting clinical information, for communicating and sharing data with foreign physicians and national physicians. The ability to communicate via video and document sharing was also found as strength of the virtual forum. This may prove beneficial to rural practitioners who may have internet connectivity, as was the case with a hospital in Tra Vinh (4-5 hrs bus from Ho Chi Minh City) which received a Bill and Melinda Gates foundation grant for improving computer and internet access to practitioners and patients at that hospital.

From the virtual forum session, physicians specifically identified gaining knowledge regarding complications with the Achilles tenotomy in minor surgery rooms and clubfoot recurrence. Practitioners identified the strength of being able to readily ask questions and receive answers live by using the virtual forum. The benefits were found to extend to family members of the case study, as they were able to learn information immediately about their child’s complication. Personal and professional development was identified by post-survey questionnaires. Individuals enhanced their knowledge in the area of recurrent clubfoot cases, improved interaction with patients, and strengthened communication and networking between those who attended the session. In attending the session, practitioners were able to meet others in the same field with similar interests in treating clubfeet and practicing the Ponseti method. Just as striking, the virtual forum session allowed one physician to better understand the importance of incorporating family member’s comments in treating clubfoot. The virtual forum was not only found to facilitate rapid, relevant dissemination of medical knowledge – thus increasing physician and patient satisfaction – but it may also be found to act as an interface in which medical culture, insight, and compassion are shared benefiting all virtual forum participants.

**DISCUSSION**

The ability to walk is crucial in navigating the societal structures of Vietnam. Therefore, complete, successful correction of clubfeet is necessary for both broadening the life paths available to an individual and preventing misconceptions of the Ponseti method from forming and deterring from the many strides that have occurred with the introduction of the technique to Vietnam in 2003. No evaluation of the entirety of the Ponseti programs (ICRC, POF, others) had been done, and the aim of the study was to identify the impact and challenges among these constituencies. Comparing the findings from Vietnam to other Ponseti sites in the world allows for the identification of common themes to aid in developing solutions applicable in all countries, while contrasting the unique challenges specific to Vietnam.

When considering other Ponseti sites with published results– the United States (New Mexico), Uganda, Malawi, and China – similar challenges were seen facing both practitioners and patients despite the difference in population, culture, and geography.

Barriers practitioners faced were also similar among the different countries. In all countries, transportation and distance proved to be consistent challenges for parents. Specifically, the issue of building confidence and the difficulty of gaining practical experience in new trainees was a challenge identified by the studies done in China and Uganda (5, 6). Like the Vietnamese practitioners, some of the Chinese physicians believed the need for a higher level of experience before treatment efficacy could be attained. With this specific issue of continuing education, the virtual clinics would be able to facilitate exchange of knowledge and expertise with physicians within the country and outside the country.

Patient and their families in all countries found difficulties in obtaining treatment and adhering to bracing. Like Vietnam, poverty contributed to these challenges. In New Mexico, Avilucea et al. found a 12.5 fold increase in recurrence due to bracing non-adherence in those who made less than 20,000 USD/year. Interestingly, the reported causes for brace non-adherence were similar between Vietnam and New Mexico. Parents in both regions identified concern for infant comfort, appearance of a “normal” of foot, or not understanding the importance of bracing to prevent relapses (13). Similar to findings in China, parents in Vietnam also identified disruption in daily activities by bracing as an additional factor leading to non-adherence.

A preliminary study done by Evans et al. evaluating the ICRC-SFD training program in Vietnam found similar progress and challenges that were present in POF and other programs. Similarly, the study found variable Achilles tenotomy completion; however, in that study it was additionally found that the inability to perform the procedure contributed to the incompletion of the Achilles tenotomy. This study also raised bracing availability and parent adherence as other challenges facing the ICRC-SFD practitioners (12).
Limitations of the study included the inability to obtain concrete documentation to confirm patient count estimations made by interviewees. The demographics of those interviewed heavily favored those practicing in Southern Vietnam. In addition, the setting in which these interviews took place occurred primarily with physicians employed at least half time by public hospitals. These hospitals were also primary hospitals within cities and provinces rather than small clinics. Some limitations with interviews may have resulted from conducting the interviews with physicians present in some cases. Often, regardless of the presence of a physician, parents or other family members were hesitant to answer questions regarding difficulties they may have faced in obtaining treatment. This may have stemmed from cultural politeness. Limitation in to the virtual clinic implementation was present as only 2 sites were introduced to the PVF. However, the web conferencing was highly rewarded and future work will need to be done to fully evaluate its implementation.

Though an array of challenges was identified by practitioners and patients, the diffusion of innovation model provides a basis for formulating solutions in conjunction to the current social context in Vietnam. As identified by the multiple surveys, potential areas that can aid in facilitating the Ponseti method include improving communication channels between practitioners and between practitioners and patients, working with the national ministry of health, and continuing partnerships with foreign NGOs.

Potential methods to improve communication channels include: 1) Creating a directory or website to consolidate patient referral systems by identifying Ponseti practitioners. This would also allow for parents to easily find practitioners if they have internet access. 2) Practitioner use of virtual clinics for exchanging ideas and experiences within Vietnam and with providers worldwide. 3) Conferences to strengthen social channels and networking – a crucial interface in spreading innovation. 4) The use of text messaging has been found to improve communication between patients and healthcare providers leading to improved treatment follow up and adherence (14).

Because organizational systems contribute to the relative of adopting new innovations, working with the Vietnamese National Ministry of Health may aid in ensuring widespread education of clubfoot treatment both to the general public and to various healthcare fields. In addition, partnership with the VNMH may catalyze a system wide solution for improving communication between practitioners and patients in different hospitals and provinces.

Much of the progress the Ponseti method has encountered in Vietnam is due to the tireless dedication of practitioners essentially volunteering their time to face the challenges of treating clubfoot. At the same time, partnership with foreign NGOs have helped continue to build interest in the Ponseti method and also provide much needed support for Ponseti providers, whether in training sessions or finding ways to improve diffusion of the Ponseti method in Vietnam. Continued partnerships with NGOs will doubtlessly be necessary to enable the children of Vietnam access to life changing Ponseti method.

In conclusion, the identified progress and challenges mirrored that of similar studies done in other countries with several factors affecting progress. Focusing on improving communication channels and networking while working with the ministry of health may improve the facilitation of the Ponseti method in Vietnam. Further implementation and evaluation of the PVF may act as a guide for current and future programs in Vietnam or other countries.

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APPENDIX 1

Clubfoot Questionnaire (For Healthcare Providers)
1. Confirm name of provider:
2. Confirm contact information:
3. Where is your practice located (City/Province)?
4. What type of physician are you?
5. Where are your patients primarily from?
6. How many clubfoot patients do you treat annually (per month)?
7. What methods did you use last year to treat clubfoot?
8. Who follows up on patients? (Nurse? Physician? Other? None?)
9. Have you been trained in the Ponseti method?
10. When did this training occur?
11. Where did this training occur?
12. What type of training? (theory/practice/both)
13. How much did training cost?
14. How many clubfoot patients have you treated since the training?
15. How many clubfoot patients have you treated using the Ponseti method?
   a. Short or long leg casts?
   b. Achilles tenotomy? (Always/Sometimes/Never)
   c. What kind of braces? (shoes, AFOs, foot abduction-bar, others?)
   d. Do you anesthetize patients? (Yes/No) How often?
   e. Do you combine with massage? (Yes/No)
   f. Do you combine with physical therapy? (Yes/No)
   g. What criteria do you use to select the treatment to use for clubfoot patients? (Age/Complexity/Other)
16. Since your Ponseti training, how many patients have you treated using other methods? How many using surgery? What other methods have you used?
17. What do you feel are barriers for the Ponseti method?
   a. The method itself? (Yes/No, Explain)
   b. For providers? (Yes/No, Explain)
   c. For the healthcare system in China? (Yes/No, Explain)
   d. For patients/culture/parents (e.g. patient doesn’t want to wear braces; parents don’t force patients to wear braces; stigma of brace;)? (Yes/No, Explain)
   e. Physical barriers/distance/transportation? (Yes/No, Explain)
   f. Financial barriers for patients? (Yes/No, Explain)
   g. Financial barriers for providers/hospitals? (Yes/No, Explain) (for example, if using the Ponseti method causes physicians/hospitals to receive lower income when compared with other methods.
18. How do you think neglected clubfoot can be prevented? How do you think we can reduce the time before patients with clubfoot are identified and treated?
19. Do you have an electronic file of clubfoot data you would be willing to share?
20. If the information we discussed is published, there will be no identifiers. Thank you for your time. Your answers are very helpful for this study. Do you have any questions?
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Qualitative Assessment of the Challenges to the Treatment of Idiopathic Clubfoot by the Ponseti Method in Urban India

Karan Gadhok BSE³, Mohan V Belthur MS, MD, FRCS (Tr&Orth)¹, Alaric J Aroojis, M.S. (Orthopaedics), D’Ortho, DNB (Ortho)², Thomas Cook PhD³, Florin Oprescu MD, PhD³, Ashish S. Ranade MS (ortho)⁴, and Jose A. Morcuende MD, PhD⁴

Abstract

The Ponseti method of clubfoot treatment has been shown to be a very safe, effective and minimally invasive technique when performed in medical centers in Europe and North America. However, only a limited number of studies have helped identify the challenges for effective treatment with the Ponseti method in India. In this study a qualitative approach was used through distribution of questionnaires, personal interviews and focus groups with orthopedic surgeons (in urban centers) and parents of patients with clubfoot. The following factors were evaluated: (i) physician education, (ii) alternative methods of treatment/modification of the Ponseti technique, (iii) compliance by parents, (iv) treatment in underserved areas, (v) culture, (vi) community knowledge of clubfoot, and (vii) the health care system in India. The results showed that all of the factors evaluated hindered outcomes for patients; however, parent’s compliance with bracing, lack of proper rural clubfoot treatment clinics, poverty and physician education were the most prominent challenges. The results of this study can be used to implement specific strategies to improve the diffusion and implementation of the Ponseti method for treating clubfoot throughout India.

Introduction

Congenital clubfoot is a common disabling condition that is prevalent across all populations. Clubfoot is a complex three-dimensional deformity of the foot characterized by adductus, cavus, varus, and equinus. Clubfoot can be idiopathic or part of a syndrome (such as myelomeningocele and arthrogryposis), and tends to affect males more often than females. If congenital clubfoot is left untreated, it can prevent normal gait development and result in a crippling lifelong physical disability.

There are a number of treatment options for infants born with clubfoot. Until recent times, the standard treatment was months of casting followed by surgery. There have been many surgical approaches described over the last century; however, long-term follow-up demonstrates poor outcomes from these procedures and a high rate of complication. In addition, surgical procedures are very expensive and require highly trained professionals. Especially in developing countries, this has been a challenge for children receiving treatment for clubfoot.

In recent years, the non-invasive treatment of clubfoot, developed by Dr. Ignacio Ponseti, has been shown to have a success rate above 95% and the best long-term outcomes. Therefore, the Ponseti method is fast becoming the gold standard for clubfoot treatment and is currently being implemented all over the world. Importantly, several medical centers in India have implemented the method in the past few years. India has a population of approximately 1.157 billion people and an annual birth rate of 21.72 births per 1,000 people. Assuming a conservative rate of one clubfoot per 1,000 live births, the number of infants born with clubfoot is estimated to be approximately 25,000 per year in India. The gross domestic product at purchasing power parity per capita (GDP – PPP) is $3,400 according to a 2010 estimate. With such a large population in poverty, an educational program for the treatment of clubfoot based on the Ponseti method has the potential to make a large impact in India. However, there is a lack of information on the challenges to its diffusion and implementation. Therefore the purpose of this study was to evaluate those challenges in urban medical centers in India.
MATERIALS AND METHODS

Questionnaires were given to, and face-to-face interviews were conducted with physicians practicing the Ponseti method to qualitatively evaluate the challenges to the Ponseti method in urban centers in India. These providers were chosen from lists of attendees at Ponseti training workshops and from referrals made by Ponseti providers already practicing the method. In addition, health care practices in both hospital and clinical settings were recorded which provided an in-depth look at the health care system and the initial impact of and challenges faced by diffusion of the Ponseti method.

Interviews were also conducted with parents of children with clubfoot by a medical student fluent in Hindi and English. Responses were collected over 12 weeks, and the results were translated into English and sorted into themes. Participant’s names were removed from the data and the data was stored in a secure location. Informed consent was obtained by having participant’s parents review a consent letter. This study was approved by the University of Iowa Institutional Review Board.

RESULTS

A total of 100 physician questionnaires were distributed and 38 were returned from physicians in Delhi (35), Bangalore (2) and Pune (1). All physician questionnaires were completed by orthopedic surgeons and residents. Fifteen face-to-face interviews were conducted with orthopedic surgeons and residents in Delhi (4), Pune (3), Mumbai (3), Bangalore (3), Vellore (1) and Chennai (1). A total of 19 patient questionnaires were completed by parents of clubfoot patients in Pune (4), Mumbai (7) and Bangalore (8). The following paragraphs describe the major challenges to clubfoot treatment identified by the results of this study.

Physician Education

Physicians who graduate with Bachelor of Medicine or Bachelor of Surgery (MBBS) degrees in India are generally regarded by their peers as well-educated medical practitioners. However, a common theme among many physicians interviewed was that many patients were referred to them after failure of treatment in other hospitals. In the physician questionnaires, the percentage of patients who were referred to them after failure of previous treatment averaged 11% (n = 24, range: 0.5% - 40%, SD: 10.7%). Physicians often cited lack of knowledge of clubfoot and treatment options among doctors in rural areas.

During interviews, an orthopedic resident stated that their curriculum in medical school had introduced them to the Ponseti method. In the questionnaires, physicians were asked if and at what point in their medical education they received training in the Ponseti method. Physicians were allowed to choose more than one answer with results as follows: 6% in medical school, 70% in residency, 24% in fellowship training and 9% as extracurricular. One of the physicians stated that he had not received any formal training in the Ponseti method and had learned the method through self study, including reading literature and using online resources. Another physician mentioned that he had come to the University of Iowa to be trained in the Ponseti method. Lastly, one physician stated that he had learned the Ponseti method at the Western India Regional Orthopaedic Conference (WIROC) under the guidance of orthopedic surgeons who were formally trained in the Ponseti method.

An interesting story which highlights physician knowledge as a challenge is of a neglected patient in Delhi. Both of the girl’s parents were physicians but weren’t aware of the Ponseti method of treatment. Their child’s clubfoot received treatment via the Ponseti method at an older age.

Alternative Methods of Treatment/Modification of the Ponseti Method

A number of physicians stated that they have, at least at times, departed from the Ponseti method principles and protocols. Approximately 24% of physicians stated that they used ankle foot orthoses (AFOs) instead of the recommended foot abduction brace (FAB), and 18% stated they used short casts instead of long-leg casts.

All physicians (37/37) had used the Ponseti method in the last year and 38% had used surgery in the treatment of clubfoot within the last year. A minority, 12% of physicians, considered the Ponseti method a challenge to proper treatment due to its being time and/or labor intensive. Approximately 28% and 33% respectively, replied that they combined massage and physical therapy with the Ponseti method to treat clubfoot. When physicians were asked what other methods they use to treat clubfoot, 5% reported the JESS (Joshi external skeletal stabilization) method of clubfoot treatment.

Because of parental compliance issues and difficulty accessing health care, surgery and longer gaps between castings have become alternative forms of treatment to fit patient and family needs. One physician reported that if he believed the patient would likely not return within a week of casting, he would request the parents bring the patient back in two weeks. Another interview revealed that if it seemed unlikely that the patient would return, then the idea of surgery seemed more appealing. In a different interview, a physician mentioned that he used general anesthesia for casting patients older than six months of age. Some physicians also apply additional casts to decrease rigidity in the Achilles tendon to avoid Achilles tenotomy.
Qualitative Assessment of the Challenges to the Treatment of Idiopathic Clubfoot by the Ponseti Method in Urban India

Compliance of Parents
Approximately 78% of physicians considered lack of follow-up to be a major challenge to proper treatment of clubfoot. Physician interviews revealed that parents were often very compliant during the initial casting. However, problems with compliance often occurred after initial correction was completed and the foot was no longer deformed. Many parents come great distances but decide to return to their villages after correction, and not return for follow-up. Since Ponseti treatment requires regimented follow-up and compliance with bracing, parents often return when their child’s foot has relapsed. During interviews, a number of common concerns about parental post-correction compliance were noted. A common concern was with parents who returned to their villages; the children subsequently outgrew their foot-abduction braces in a few months. Treatment with the Ponseti method involves long-term use of the FAB and parents often don’t have access to larger-size bracing in their local area. This was often the reason mentioned for relapse. Other concerns included the child’s crying during the first nights of bracing. Some parents give in to the child’s cries and remove the brace. It has also been reported that parents may continue bracing, but not for the appropriate amount of time required each day. In an attempt to change this trend, a physician in Vellore explained in an interview that he is currently creating a brace that will be able to monitor the amount of time a patient wears the brace each day.

Poverty
Approximately 64% of physicians considered financial limitations of the patient’s parents to be a challenge for proper use of the Ponseti method. The average costs for the Ponseti method, the surgical method and for post corrective braces are shown in Table 1. The average cost of the Ponseti method of treatment is lower than the average cost of the surgical method according to the physician questionnaires. The average costs for bracing, 785 INR (Indian rupees) as assessed by physician questionnaire, and 1017 INR per patient interview, are consistent with the costs of 800-1000 INR typically stated during physician interviews. During an interview with one doctor, it was learned that some children with clubfoot are not brought in for treatment because their parents believe the child could earn more money as a crippled beggar than they could without the clubfoot.

Hospitals in urban centers are often completely full and cannot admit new patients. Families that come from long distances then sleep overnight at the train station. The cost of transportation, a missed day’s wages and the cost of medical treatment are additional financial burdens on parents in the process of clubfoot treatment.

Treatment in Underserved Areas
Many physicians stated that the only way for patients to receive proper clubfoot treatment was to have their parents bring them to medical centers in urban areas. Doctors in rural areas often used massage as a sole treatment and some used incorrect casting methods. One parent stated that their child had been given 100 casts before coming for treatment at a medical center in Mumbai. Upon observation and subsequent interview with a physician in Pune, the family was extremely hesitant to proceed with the Ponseti method as casting had previously failed for their child.

Eighty-one percent of doctors considered distance and transportation to be a challenge for the proper treatment of children with clubfoot. Parent questionnaires revealed travel of an average 2.2 hours for treatment (n = 17, range = 5 minutes to 8 hours, SD = 1.95 hours). Some parents came from several states away and as far as 800 miles according to one physician’s questionnaire. When questioned about why parents choose to travel such distances when they often had the same-quality government and charity hospitals closer to their village, a physician stated that parents often go to hospitals that have received positive reviews from other community members.

Culture
During interviews, it seemed a common belief among physicians that girls were often treated for club foot much later in life than boys. One physician gave the example of many girls coming in for first treatment when they were of marrying age - since the deformity would hurt their chances of finding a husband. Of interest

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| TABLE 1. Cost related to clubfoot treatment from physician and patient questionnaires. |
|---------------------------------|-------------|-----------|-------------|-------------|-----------|-----------|-----------|
| **Category** | **Source** | **n** | **Average Cost (INR)** | **Average Cost (USD)** | **St Dev** | **Min** | **Max** |
| Ponseti | Physicians | 25 | 5900 | 1250 | 22500 |
| Surgery | Physicians | 18 | 9833 | 2200 | 30000 |
| Braces | Physicians | 24 | 785 | 17 | 50 | 1500 |
| Braces | Parents | 9 | 1017 | 22 | 425 | 850 | 1600 |
was that in some locations, the mother and the maternal uncle were responsible for care of the child’s deformity. The father’s role in treatment was unclear in these cases. One physician believed that patient compliance with treatment, bracing and follow-up would likely increase if the fathers could become involved in the process.

**Community Knowledge of Clubfoot**
Approximately 17% of cases (n = 26, range = 0-55%, SD = 16.7) of clubfoot were considered neglected according to physician questionnaires. Neglected clubfoot was defined as incomplete or absence of correction by the time the patient was expected to walk. Many of the neglected cases were away from urban cities with well-established medical centers. This was largely due to a lack of public knowledge about clubfoot. Some villagers believed that clubfoot was a polio deformity, according to one physician. People from villages were often unaware of possible treatments available to their children for completely deformity correction.

**Healthcare System in India**
Approximately 27% of physicians considered the healthcare system in India a challenge to the treatment of clubfoot. Physician and hospital financial constrains were considered a challenge to proper treatment in approximately 36% of physician questionnaires. The response included an example of orthopedists or hospitals receiving less income because the Ponseti method of clubfoot treatment was less expensive. One physician commented that orthopedists were reluctant to use or spread the Ponseti method as a treatment when surgery was more lucrative.

Approximately 88% of physicians considered parent compliance with bracing to be a challenge in the treatment of clubfoot using the Ponseti method. This is largely an infrastructure problem since the healthcare system in India is not as stratified with different levels of healthcare practitioners as in the US. Often, the only two well-defined roles of healthcare workers are nurses and physicians, for most communities. Social workers, nurse practitioners and other health care personnel could help fill a lot of gaps in India’s healthcare. For example, 95% of physicians stated that they follow up with parents after their child’s clubfoot treatment. Most of the physicians in this study work in very busy public hospitals and have little time to educate parents about bracing or to call them to ensure follow-up. One physician wrote that with appropriate education, parents could be persuaded to be compliant with their child’s bracing and that compliance may increase if nurse practitioners were available.

**DISCUSSION**
India is the second most-populous country in the world with 25% of its people (about 375 million) living below the poverty line. Approximately 25,000 children are estimated to be born with idiopathic clubfoot every year in India. With such a large population living in poverty, the non-invasive and inexpensive treatment of clubfoot with the Ponseti method has the potential to make a large impact on health outcomes for children who would otherwise be crippled by clubfoot. Table 2 shows the challenges to clubfoot treatment in India, and proposed solutions.

Studies on the development of sustainable Ponseti programs, and the challenges to Ponseti clubfoot treatment have been published from China, Malawi and Uganda. These countries have very different populations when compared to India. For example, Malawi and Uganda have relatively small populations (16 million and 35 million respectively) when compared to the world’s...
two most populous countries of China and India (1.34 billion and 1.19 billion respectively). The medical staff available to treat these populations is also quite different. Malawi and Uganda have < 1 and 1 physician per 10000 people, respectively. India and China have 6 and 14 physicians per 10000 people, respectively, which should allow for more access to treatment. Although these countries have very different populations, resources and cultures, the challenges that all countries face in treatment of clubfoot are very similar.

Poverty has been perceived as challenge to proper treatment of clubfoot in all four countries. A large proportion of the population in all these countries is the working poor. Since a large part of the population of these countries lives in rural areas, it can be very difficult for parents to take time off from work and travel to seek treatment for their children.

Compliance is one of the major challenges with clubfoot treatment, whether in developed countries or developing countries\textsuperscript{16-17}. Compliance with follow-up and bracing are considered challenges among physicians in India, similar to that found in China, Uganda and Malawi. However, as pointed out in a publication from Uganda\textsuperscript{15}, patient compliance should not be used as an excuse to remove responsibility for treatment failure from clubfoot programs. Parents in India would typically complete initial clubfoot correction but would often not return for follow-up. This suggests that the parents might not fully understand the implications of non-compliance after correction. Educating parents that bracing and subsequent follow-ups are essential to prevent relapse would likely help increase compliance significantly.

In India, Malawi and Uganda, the primary person responsible for the health of the child is the mother. However, in China, it was often the responsibility of both parents to take care of the child during clubfoot treatment. As stated by one physician during an interview, if fathers were more involved in their child’s care and understood the importance of follow-up and bracing, the rate of compliance would likely improve.

As shown from the model of clubfoot treatment in Uganda, it is important to create clubfoot-specific clinics for one to two days per week, with high quality standards, in an established hospital or clinic. This is essential to guarantee a high quality of treatment by physicians who are fully trained and who treat clubfoot patients on a regular basis. Physicians who only see clubfoot patients a few times a year often lose skill in performing the technique correctly, which can lead to a bad reputation for casting in the community. This was demonstrated by the physician in Pune who was trying to convince the parents that the Ponseti method would successfully treat their child after previous casting had failed.

Specialized clinics also allow for other staff, such as nurses, physical therapists and trained counselors, to share responsibility in treating the patient\textsuperscript{18-19}. For example, non-circular medical staff can educate the child’s family on the importance of bracing and follow-ups after correction. Physical therapists, nurses and other medical staff could be trained to follow up with patients. This would free physicians to treat more patients. Another advantage of having specialized clinics is that parents and patients at all stage of treatment can speak with each other about their children living without disability. When parents see previously treated children walking and running at the clinic, it can give them hope that their child will be able to do the same, with treatment.

Currently, major medical centers in urban India have very well trained medical professionals to treat clubfoot patients. Establishing high quality clinics in each of the 28 states should be the next logical step for the Ponseti method in India. Ideally, this would be followed by establishing clinics at District and Taluk headquarters (close to most villages) in each state of India, so that the Ponseti method of treatment is accessible to the majority of the population. To achieve this, the central and state governments of India must be persuaded to recognize the Ponseti method as the gold standard to provide safe, effective, economical and efficient treatment for idiopathic clubfoot. This would require a collaborative effort involving the World Health Organization, the Ponseti International Association, international and national NGOs, public and private industry, physicians and government agencies in India.

The authors are aware of the limitations of this study, as it is a qualitative assessment. The physicians interviewed were limited to those practicing in large urban cities, and the parents of clubfoot children who were being treated in those centers. However, the data collected was valid, arising directly from the experiences of the participants. In addition, triangulation of the data was possible as a number of different sources were interviewed; this showed differences in perspectives, but no major differences in reporting what challenges were encountered. Interestingly, interviews with practitioners and parents both showed remarkably similar findings. The main source of possible bias was that almost all participants were beneficiaries of the project in some way, either as employees or patients. Despite these limitations, the challenges that have been identified could help NGOs and local governments in India to focus their time and resources, and tailor future interventions to those specific challenges.

In conclusion, there are a number of challenges in India to the diffusion and implementation of the Ponseti method, many of which are similar to those encountered...
in other countries. The specific challenges found to be most important were lack of physician education, parent compliance with bracing, lack of proper rural clubfoot clinics and limited financial resources. The results of this study can be used to implement specific strategies to improve the diffusion and implementation of the Ponseti method for treating clubfoot throughout India.

REFERENCES
INITIAL PROGRAM EVALUATION OF THE PONSETI METHOD IN NIGERIA

Oluwole A. Akintayo, BS1, Olayinka Adegbehingbe, FWACS, FICS2, Thomas Cook, MD, PhD3, Jose A. Morcuende MD, PhD1

ABSTRACT
The Ponseti method for correcting clubfoot is a safe, effective, and low-cost treatment that has recently been implemented in Nigeria. This study evaluates the initial impact of the Ponseti method and the unique challenges to its diffusion among practitioners and patients. Information was obtained by traveling to Ponseti clinics to interview or give questionnaires to the Ponseti method practitioners and the parents of children with clubfoot. The challenges identified among the practitioners were: 1) an inadequate amount of information; 2) inadequate resources; 3) insufficient training programs; and 4) a lack of funding. The challenges among parents were: 1) a deficit in knowledge about clubfoot and its treatment; 2) financial constraints; 3) culture and religious practices, and 4) difficulties with treatment compliance. Information from this study can be used to implement specific strategies to improve the dissemination and implementation of the Ponseti method for treating clubfoot in Nigeria and throughout West African nations that share cultural and socioeconomic commonalities.

INTRODUCTION
Idiopathic clubfoot is the most common musculoskeletal congenital birth defect with a worldwide incidence of 1-6.8 per 1000 live births1. The effects of this deformity are magnified in developing countries like Nigeria by compounding older and untreated cases each year. Although Nigeria has half the population of the United States (140 million people), it is estimated that the prevalence of clubfoot is at least three to five times higher than in the United States4. Untreated clubfoot persists as a rigid deformity. Children and adults alike may experience pain, disability, discrimination, and hardship in their lives.

Since the 1980s, clubfoot in Nigeria has traditionally been treated using surgical methods. However, little progress has been made to resolve the clubfoot public health issue2,3. Some Nigerian orthopedic surgeons believe that early surgery does not have a real advantage, and extensive surgery may even be harmful4. In addition, in a country where 70% of the population lives in poverty5, finding money for surgery, especially when the deformity is not life threatening, seems a luxury that many cannot afford. A treatment method that is safe, quick, effective, economical, and easy to teach could have an enormous impact in the lives of thousands of children born with clubfoot in Nigeria.

In recent years, the Ponseti method for correcting clubfoot, created in the 1940s by Dr. Ignacio Ponseti, has become the worldwide gold standard for treating this deformity. The Ponseti method uses a combination of manipulations and casting to correct the deformity, and often involves a minimal, office-based procedure—an Achilles tenotomy. After the casting period, the child wears a foot abduction brace at night until the age of four to prevent relapse. The Ponseti method has been shown to achieve complete correction in as little as 16 days in >95% of patients. Additional surgical release is required in as few as 1% of patients6.

The results of the Ponseti method have encouraged efforts to make this method the gold standard in the treatment of congenital idiopathic clubfoot. The Ponseti International Association initiated a program for the diffusion of the method worldwide, and this method was introduced in Nigeria in December of 20097. The purpose of this study was to perform an initial evaluation of the Ponseti method in Nigeria, assessing the impact of the method and identifying the challenges to its diffusion and implementation. With timely evaluations, specific strategies can be employed to improve the diffusion and implementation of the program with awareness of attitudes about the Ponseti method that will allow culturally appropriate implementation.

1Carver College of Medicine, University of Iowa, Iowa City, Iowa, USA
2College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria
3College of Public Health, University of Iowa, Iowa City, Iowa, USA

Address correspondence to:
Jose A. Morcuende, MD, PhD
Department of Orthopedic Surgery and Rehabilitation
200 Hawkins Drive, 01023 JPP
Iowa City, IA 52242
Tel. (319) 384-8041
E-mail: jose-morcuende@uiowa.edu
MATERIALS & METHOD

This research project is a qualitative study conducted using semi-structured interviews, focus groups, observations, questionnaires to Ponseti practitioners and parents of clubfoot patients, and raw data gathered from patient records. Multiple methods were used in order to verify the data and validity of the study.

In December of 2009, a 2-day Ponseti clubfoot workshop was held in Ile-Ife, Osun state, Nigeria. Thirty-five physicians attended this educational program from 23 different hospitals located in 16 states, 20 cities, and another 15 participants attended the concurrent workshop on fabrication of foot abduction braces. Ponseti practitioners in 19 hospitals across 13 states and 17 cities were visited in order to observe their Ponseti clinics, perform one-on-one interview with the physicians or questionnaires, and to gather information about patient treatment (Appendix 1 & 2). Twenty-five physicians from 16 hospitals across 12 states were interviewed one-on-one or filled out questionnaires. Six residents that were trained after the workshop also filled out questionnaires. Finally, 42 parents of clubfoot children across these hospitals were either interviewed one-on-one or participated in focused groups.

Interviews were conducted in English and questionnaires were also written in English because English language is the official language in Nigeria. The data from these interviews, questionnaires, patient profiles, and observations made were collected and sorted into themes. The data was stored in a secure location. A team approach was used to draw conclusions about the organized data. The proposal was passed through the University of Iowa Institutional Review Board.

RESULTS

This 6-month evaluation of the Ponseti method adoption in Nigeria has three components: a) to create a profile of all the cases of clubfoot that have been treated with Ponseti method within the first 6 months of the Ponseti method inception in Nigeria; b) to identify the challenges to the implementation of Ponseti method among physicians; c) to identify the challenges to the diffusion and adherence to treatment protocol among the patients and/or their parents.

Patient Demographics

We generated a profile of clubfoot patients from data collected from 15 hospitals in order to explicate the impacts of the Ponseti method since its inception in December of 2009. We attempted to gather information from 19 hospitals, but only 15 hospitals had sufficient record on the patients seen in their Ponseti clinics. The information collected included patients’ age at the time of first visit, patients’ sex, laterality of deformity, and compliance with clinic visit. The total number of patients included in this study was 395. The results are in Table 1, Figure 1 and Figure 2.
Ponseti Method Among Care Providers

Twenty-five physicians and six residents from 16 hospitals in 12 states agreed to either one-on-one interviews or to filling out questionnaires. These include: 7 physicians and 5 residents from Osun state, 3 physicians from Oyo state, 1 from Ogun state, 1 from Rivers state, 4 from Lagos state, 1 from Ondo state, 2 physicians and 1 resident from Kwara state, 2 from Kaduna state, 2 from Edo state, 1 from Benue state, 1 from Enugu state and 1 from Ekiti state. All of the doctors that participated in this study are orthopedic surgeons.

The participants were asked to identify some of the barriers to the adoption, diffusion and the success of Ponseti method among Ponseti practitioners. The following is a synopsis of the challenges to the implementation of the Ponseti method among healthcare providers.

Inadequate flow of information:

Twenty out of the 31 orthopedic surgeons that were interviewed identified inadequate dissemination of information within the health system as a major barrier to the diffusion of Ponseti method. The interviewees expressed that there are difficulties in sharing information within departments inside a hospital and across different hospitals. All Ponseti practitioners were orthopedic surgeons and were practicing in tertiary hospitals. The implication, as explicated by our interviewees, is that the bulk of their patients were referrals, and a crucial aspect of a successful referral system is an adequate flow of information from referees to recipients. The Ponseti practitioners reported that the lack of a good network has slowed down the dissemination of information about the Ponseti method and its effectiveness to other surgeons and even to patients.

Of the 44 mothers of clubfoot children that were interviewed, 56% (24) were referrals from within the hospitals, 30% (15) were referrals from families and friends, and 14% (7) were referrals from outside hospitals and community clinics. From another perspective, 59% of the mothers said their babies were diagnosed at birth. However not all were initially referred to a Ponseti treatment center due to lack of proper information dissemination among physicians. Responders noted that referrals are crucial to their practices, and for Ponseti method of clubfoot management to be widespread, the information about the method has to reach different community clinics and many local hospitals. The midwives, pediatricians and family practitioners are in the front line of the fight against clubfoot, and thus there is a need for adequate flow of information between these primary level physicians and tertiary level surgeons that use the Ponseti method.

Inadequate resources:

The Ponseti practitioners indicated a lack of necessary resources to adequately equip Ponseti clinics as another major barrier to the success and dissemination of Ponseti method among health providers. Two important resources that were identified as lacking were adequate workforce and abduction braces.

The interviewees reported that sprouting Ponseti clinics were constricted by poor patient-to-doctor ratios, limited assistance, limited time, and limited space. In almost all of the 16 hospitals that participated in this study, orthopedic departments only had one 7-8-hour clinic day within a week for all orthopedic-related injuries, post-op patients, and clubfoot patients. The responders explained that attending to a single Ponseti patient requires time and space to remove previous casts, perform manipulations, and apply new casts. Our responders said it was a burden to accommodate a number of clubfoot patients with other kinds of orthopaedic patients within a short time window, within a confined space, and without an adequate number of staff. A few of the responders said they had made the efforts to secure a separate clinic day for their Ponseti patients but were unsuccessful because of lack of funding and support from their departments. Some providers said they would like to delegate more responsibilities of casting and manipulation to their nurses and lab technicians, but these would require training and funding, which were not available.

Limited availability of abduction braces was another impediment. Abduction braces are an essential part of the Ponseti method of clubfoot treatment. After a series of manipulation and casting, patients wear Steenbeck abduction braces for maintaining correction and to avoid relapse of the deformity. The Ponseti practitioners in our study commented that the physiotherapists trained during the Ponseti workshop to fabricate these abduction braces were not producing them due to interdepartmental disagreements between orthopedic surgeons and physiotherapists. As of the time of this study, there was only one hospital out of the 19 hospitals studied with a functioning Steenbeck abduction-brace production unit. The lack of Steenbeck abduction braces had discouraged many providers from using Ponseti method. Some of the interviewees reported their efforts to circumvent this problem by collaborating with local cobblers; however, the qualities of these braces were of inferior quality.

Insufficient training programs:

The participants in our study identified insufficient training programs as a barrier to adoption of Ponseti method. As of the time of this study, the only training ever held in Nigeria was the 2-day Ponseti workshop held in December of 2009 in Ile-Ife, Osun state. The
consensus among our interviewees was that more orthopaedics surgeons and healthcare providers at a primary level, including family practitioners, pediatricians and nurses, needed to be trained in the Ponseti method of or trained in identifying early stages of the deformity. Many providers believed that a high percentage of patients with clubfoot were not receiving appropriate treatment because their primary health providers were not aware of the treatment options and the superiority of Ponseti method over surgical interventions. Though 59% of parents that were interviewed reported that their babies were diagnosed at birth, Ponseti practitioners believed that this number should be higher. These practitioners advocated for another Ponseti method training section for more surgeons, family practitioners, pediatricians, and health officers overseeing rural clinics.

Along the same line, responders also identified the need for training nurses, lab technicians, and cobbler in specific areas of Ponseti treatment protocol. They explained that orthopedic surgeons have crowded out-patient clinics and clubfoot patients from states without Ponseti practitioners would flock to the nearest providers, further crowding already crowded clinics. Our interviewees commented that having staff that are competent in manipulation and casting and local cobbler that can produce quality braces on time will greatly improve Ponseti clinics and it the method’s diffusion.

**Lack of funding:**

The last factor identified from our interviews with Ponseti providers is the lack of funding and support from their respective departments, hospitals, and the government. The government had invested sparingly into the healthcare system in general, and the downstream effect was that clubfoot clinics had received minimal, if any, support from their respective hospitals and orthopedic departments, said our interviewees. This lack of support was evident in the infrequent training programs, insufficient workforce, lack of clinic, space, and the nonexistence of funding to fully equip Ponseti clinics. All the participants that attended the last Ponseti workshop paid for their own training fee; however, they were using the knowledge acquired to benefit their departments and hospitals. The interviewees mentioned that many healthcare providers would like to be trained in the Ponseti method of treating clubfoot but were discouraged when they realized they would have to pay for their training. The contact surgeon for the Nigeria Ponseti program and the organizer of the 2-day Ponseti workshop in 2009 reported that the reason they had not held another workshop was because they were still paying off debt from the previous workshop.

**PONSETI METHOD AMONG PATIENTS**

Parents of clubfoot patients, in addition physicians acclaimed the affordability, safeness, avoidance of surgery, and success of the Ponseti method. However, despite these benefits, many patients reported difficulties with the treatment protocol. In addition to asking healthcare providers about the hindrances to implementation of Ponseti method in their practices, they were also asked to identify some of the challenges to the diffusion and adherence to treatment protocol among patients and/or their parents. Also, 44 parents were interviewed about their experiences with Ponseti method and the difficulties they had encountered with the treatment protocol. The following is a synopsis of the hindrances to the Ponseti method among patients and/or their parents as reported by providers and patients.

**Deficit in the understanding of clubfoot and its treatment:**

59% of the parents that were interviewed reported that their babies were diagnosed with clubfoot at birth. These early diagnoses were attributed to hospital births where health professionals were present at birth to examine newborns and properly refer patients to the appropriate treatment centers. However, Ponseti providers reported that majority of births were at home, at maternity centers, or in community hospitals where the health officers in-charge most likely were not versed in musculoskeletal deformities and their treatment options. Consequently, the majority of clubfoot cases had gone undiagnosed. Interviewees explained that new mothers would receive advice from friends, family members, or neighbors to seek treatment at faith healers and traditional bonesetters or to try home remedies. Among the 44 parents that were interviewed, 12 parents (27%) tried different unsuccessful treatment methods for months before being directed to a clubfoot clinic. A mother told how she spent a significant amount of money at a local clinic where cast and splints were applied for months without any improvements. There was a mother who went to a faith healer who told her to bathe her baby in a stream a number of times; another mother was told to daily massage her child’s leg, which she did for up to a year before seeking proper treatment at a Ponseti clinic. Some parents admitted that they thought their babies’ deformed foot/feet would be amputated if they went to a hospital for treatment; some were afraid their babies would have to undergo surgery. Responders said parents were ignorant, and so were many health providers about clubfoot deformity and the treatment options available.

Two Ponseti providers interviewed in Ogun state reported that the first inclination for many of their patients was to seek treatment with bonesetters—traditional
healers that use animal rituals and splinting as their healing method. One of the surgeons said, “For every fracture that presents in the clinic, there are hundreds at traditional bonesetters.”

Financial Constraints:
Both physicians parents identified financial difficulties as another major hindrance for parents seeking treatment for their children’s clubfoot deformity. One of the Ponseti practitioners said: “Though Ponseti method is the cheapest method [of clubfoot treatment], many patient cannot afford it still.” Among the 44 parents that were interviewed, those that presented their children to Ponseti clinics months after receiving the diagnosis of clubfoot testified that they deferred treatment because they could not withstand the expenses at the time their children were diagnosed.

Physicians explained that the custom of treatment in Nigeria is for patients to pay upfront and purchase all the materials needed for their treatments or procedures. Consequently, parents have to purchase their own plaster of Paris and other materials before or at every clinic visit, and prepay for tenotomy and abduction braces. The cost of transportation and the cost of treatment for each clinic seemed to be very burdensome for many of the parents after the first few visits, said the providers. Consequently many patients defaulted with treatment.

In their testimonies, parents elaborated on the cost of transportation since many of them had to travel a long distance due to a lack of local Ponseti providers. This included transportation and lodging, but also the opportunity cost of a day’s worth of income lost due to the clinic visit. Parents explained how losing a day’s worth of income multiple times during the course of treatment could be difficult for a struggling family with multiple children.

Culture and Religious practices:
Responders explained that culture and religious practices were crucial factors in Nigerians’ health-seeking behaviors. A few of the parents recounted attributing their baby’s malformation to God’s will, punishment from God, or to a witchcraft. Ponseti providers commented that these mindsets and beliefs resulted in poor health-seeking behaviors among parents because they would conclude that western medicine could not confront spiritual matters. Thus some would turn to faith healers, herbalists and bonesetters.

Large family sizes was another cultural factor that influenced parental health-seeking behaviors. Physicians reported that age of presentation to Ponseti clinics and the compliance of parents to treatment protocols and follow-up appointments were influenced by the number of children present in their households or the number of children desired by the parents. In a survey conducted by the National Population Commission, 42.9% of men and 39.8% of women who already had 3 children planned to have another child sometimes in the future. According to this survey, the mean ideal number of children desired by Nigerian men was 7.2 and 6.1 by women. Ponseti practitioners responded that if parents desired more children, they were likely to postpone treatment of the diagnosed child or default during treatment because of their plans. As our responders explained, this could be attributed to the prolonged nature of Ponseti treatment and the cost of treatment.

The last identified cultural and religious influence on parents’ attitudes towards treatment is polygamy practices. One of the interviewees explained that because men can have multiple wives, especially among Muslim population where polygamy is most commonly practiced, many wives would not want to burden their husbands due to competition with other wives. Many husbands in this situation would not want to be bothered due to overwhelming demands on them from other wives and multiple other children. This adds another barrier to care for children with clubfoot.

Treatment Compliance:
Compliance rate among 206 patients in 7 hospitals was 65 percent (Figure 2). All of the factors from the results of our interviews discussed above—financial constraint, ignorance, culture and religious practices—were reported as influencing patients’ compliance. One other factor that influenced patients’ compliance was their understanding of the Ponseti method treatment progression and expectation. The 44 mothers that were interviewed admitted not understanding how Ponseti method works. Many of the parents interviewed said they did not have an understanding of the treatment phases; all they knew was the time of next appointment and what to bring or buy. Providers commented that many of the patients that defaulted mid-treatment felt that the treatment was completed after seeing the clubfoot visually corrected, not knowing there were additional steps of tenotomy and bracing or the importance of these steps. Ponseti practitioners also mentioned that parents were not compliant because they felt that their babies were uncomfortable in abduction braces. They also explained that because Nigerian mothers strap their babies on their back, the abduction braces interfered with this method of childcare.

Moving Forward into the Future
Participating parents and providers were also asked to identify ways to overcome the challenges that are facing the treatment of clubfoot in Nigeria and ways to improve the diffusion of the Ponseti method. The following is a synopsis of their suggestions:
1) Training of health professionals
Parents would like to have Ponseti practitioners in their own states, and complimenting that, Ponseti practitioners would like more of their colleagues trained in the Ponseti method. Physician participants suggested training on three fronts: a) training more surgeons to use the Ponseti method; b) refresher courses for those that were already trained; and c) training midwives, nurses and family practitioners to identify clubfoot deformity and to timely refer parents to appropriate treatment centers.

2) Increasing public awareness
Responders identified a need to increase public awareness of the Ponseti method. Ponseti practitioners said that while parents that gave birth in tertiary hospitals could depend on expertise of the faculties and newborn screening protocol in place for early identification of deformities and timely referrals, the concerning population, however, are parents that had home-births or at a local hospital without much resources, and those patients with neglected cases. Responders explained that there are many patients that were far from the corridor of health information, and there were many patients that still thought surgery was the only treatment option; there should be a massive effort to take Ponseti method to these patients and their health providers.

3) Improving patient education
One of the challenges discussed was the deficit in the knowledge of treatment progression by parents. Ponseti providers explained that patients stopped showing up for their appointments when they saw initial straightening of foot, thinking the treatment was completed. Proper patient education at initial consultation will help to reduce default and improve adherence to treatment, said the interviewees. It was suggested that a simple way to educate parents would be to providing pamphlets explaining clubfoot deformity, treatment phases, expectations, and success rates. Educating parents and family members would improve compliance to abduction brace usage and adherence to follow-up visits.

4) Training cobblers to make abduction braces
Because of difficulties obtaining abduction braces, Ponseti practitioners suggested holding another foot abduction brace fabrication workshop for local cobblers agreeing to work with Ponseti providers. Interviewees explained that this would expedite production rate, improve qualities, and reduce price.

5) Soliciting funding from non-governmental organizations
Financial constraint was a major limiting factor for Ponseti practitioners and parents, which was why responders suggested the possibility of soliciting funds from non-governmental organizations. Interviewees explained that funding would fuel everything from supporting parents that could not afford to buy materials, to organizing another Ponseti training workshop, to spreading the Ponseti method to rural communities.

DISCUSSION
With a population of more than 140 million residents, Nigeria is the most populous country in Africa; however, 70% of the population lives in poverty. In the setting of high population, poverty, and other more devastating diseases, a deformity such as clubfoot is often obscured by the challenges of daily living. With clubfoot cases compounding every year over the past several years, however, clubfoot is now a serious public health issue.

The fight against clubfoot in a developing country such as Nigeria has to be on three fronts: 1) early identification; 2) timely and affordable intervention; and 3) dissemination of the Ponseti method to patients and recruitment of more providers. What our results have shown is that the Ponseti method has made headway on these fronts within 6 months.

This study shows that within six months, the Ponseti method was used to treat 397 clubfoot patients, with over half of these patients between ages 0-11 months (Figure 1). Close to half of the patient population had neglected clubfoot, either untreated or unsuccessfully treated. This represents a vast improvement over prior practices in the hospitals involved in our study. The program has helped to identify clubfoot cases early and offered the timely and affordable intervention.

When a new innovation is introduced into an environment, there is a need for deliberate effort to propagate and sustain that innovation until it becomes self-propelling. The progress of the Ponseti method in its first 6 months in Nigeria can be attributed to the efforts of those that can be called “innovators” and “early adopters.” These “innovators” and “early adopters” are surgeons that have sacrificed their time and money to organize training and followed-up with those that were trained. However, there are still many challenges to attend to. A movement toward establishing an organized body of Ponseti practitioners should be the next step. This organized body can follow up on the challenges that have been identified by parents and by healthcare providers.

Evaluation of the Ponseti method and barriers that are impeding its implementation has been done in countries like Uganda, Malawi, China, Latin Americas, India, and many others. Despite the differences between the countries, the challenges of clubfoot treatment and the challenges to the implementation of the Ponseti method of treatment in these countries are very similar to the
challenges found in Nigeria. The scarcity of providers and the financial burden of treatment and travel are barriers to adherence to the treatment protocol.

Studies performed in these other countries revealed that financial constraint among patients is a major barrier to seeking treatment and adhering to the treatment protocol. In Nigeria, the Ponseti practitioners are located in 16 of 36 states with most of the states only having one practitioner. Similarly in China and Uganda, most of the Ponseti practitioners are in the metropolitan areas. A common problem that arises from this sparse distribution of Ponseti practitioners is that most patients travel long distance for access to a Ponseti practitioner. The burden of treatment and transportation has deterred many patients from seeking help. It is critical to expand the coverage of Ponseti treatment by recruiting more providers.

Patient compliance is another ubiquitous, multifaceted theme. Decline in compliance as treatment progresses is a corollary to patients’ financial instability. Patients’ lack of understanding of the treatment requirements also contributes to a decrease in compliance. Patients do not understand why they need to continue with casting or need for abduction braces after seeing the initial correction of their clubfeet. Reason for not wearing abduction braces in all these countries is unanimously because of the perceived discomfort or pain of the babies.

Though the challenges to the Ponseti method’s implementation are similar in many countries, there are, however, some unique circumstances that contribute to these challenges in Nigeria. One of these unique circumstances is the incredible diversity in Nigeria. There are 374 identifiable ethnic groups in Nigeria, with different traditions, beliefs, and practices. The challenges that were identified play out in different ways in different regions, thus requiring different strategies at times.

Despite the differences in population and duration of the Ponseti method program between Nigeria and Uganda, Nigeria can benefit from the strategies used in Uganda. Ponseti method practitioners in Uganda gained the approval of the Ministry of Health to officially make the Ponseti method a preferred treatment of clubfoot and to incorporate clubfoot care into the curricula of healthcare professionals in training. If these strategies can be achieved in Nigeria, it would be a giant step forward. Approval and implementation of the Ponseti method by the Nigeria Ministry of Health will improve awareness among the physicians and patients. Also, incorporating the Ponseti treatment of clubfoot into the curricula for health professionals will produce new generations of physicians exposed to the method.

CONCLUSION
This project has identified the challenges facing the Ponseti method implementation and the challenges to diffusion and adherence to treatment protocols among parents of clubfoot patients. In addition, we have profiled the patients that were treated during the 6-month period between the adoption of the method and this study, and have identified ways to improve the Ponseti method’s effectiveness. This information will provide healthcare planners with unique insights into ways to approach the needs of the patients and healthcare providers, and ways to implement effective awareness and treatment programs.

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APPENDIX 1

PROJECT QUESTIONNAIRE

1. Name of provider/Contact information/City, State of practice
2. What type of physician are you?

THESE QUESTIONS ARE ABOUT YOUR TRAINING
3. Describe your Ponseti training (theory/practical/both).
4. Can you make some comments about your training?
5. What clubfoot treatments were you using before your training?
6. What method(s) have you used after your Ponseti training?
7. How many clubfoot patients have you treated since the training...

THESE QUESTIONS ARE ABOUT CLUBFOOT PATIENTS
8. Where are your patients primarily from?
9. How do you follow up with your Ponseti patients during and after treatment?

THESE QUESTIONS ARE ABOUT PONSETI METHOD
10. Do you personally think Ponseti method works for treating clubfoot?
11. Can Ponseti method totally replace surgical method?
12. In your view, what are some of Ponseti method’s benefits in Nigeria?
13. What are some barriers to the adoption, diffusion and success of the Ponseti method among physicians and patients?
14. What are some effects of these barriers from questions 13?
15. How do you currently circumvent these barriers?
16. What are some ways of overcoming these barriers?
17. Suggestions for improving Ponseti method and outcomes in Nigeria.
18. How do you think neglected clubfoot can be prevented?
19. How do you think we can reduce the time before patients with clubfoot are identified and treated?
20. How do you think Ponseti international can help?
APPENDIX 2

The blue stars indicate the number of hospitals that were visited.
EVALUATION OF THE EFFECTS OF PLATELET-RICH PLASMA (PRP) THERAPY INVOLVED IN THE HEALING OF SPORTS-RELATED SOFT TISSUE INJURIES

Kellie K. Middleton, MPH1, Victor Barro, MD2, Bart Muller, MD3, Satosha Terada, MD1, Freddie H. Fu, MD1

ABSTRACT

Musculoskeletal injuries are the most common cause of severe long-term pain and physical disability, and affect hundreds of millions of people around the world. One of the most popular methods used to biologically enhance healing in the fields of orthopaedic surgery and sports medicine includes the use of autologous blood products, namely, platelet rich plasma (PRP). PRP is an autologous concentration of human platelets to supra-physiologic levels. At baseline levels, platelets function as a natural reservoir for growth factors including platelet-derived growth factor (PDGF), epidermal growth factor (EGF), transforming growth factor-beta 1 (TGF-β1), vascular endothelial growth factor (VEGF), basic fibroblast growth factor (FGF), hepatocyte growth factor (HGF), and insulin-like growth factor (IGF-I). PRP is commonly used in orthopaedic practice to augment healing in sports-related injuries of skeletal muscle, tendons, and ligaments. Despite its pervasive use, the clinical efficacy of PRP therapy and varying mechanisms of action have yet to be established. Basic science research has revealed that PRP exerts effects through many downstream events secondary to release of growth factors and other bioactive factors from its alpha granules. These effects may vary depending on the location of injury and the concentration of important growth factors involved in various soft tissue healing responses. This review focuses on the effects of PRP and its associated bioactive factors as elucidated in basic science research. Current findings in PRP basic science research, which have shed light on its proposed mechanisms of action, have opened doors for future areas of PRP research.

INTRODUCTION

According to the World Health Organization (WHO), musculoskeletal injuries are the most common cause of severe long-term pain and physical disability, and affect hundreds of millions of people around the world. The impact such injuries have on everyday life is substantial. Thus, the primary aim of orthopaedic surgeons is a safe and full recovery for their patients with a return to pre-injury level of activity as quickly as possible. The traditional management of orthopaedic and sports related injuries includes everything from conservative “RICE” treatment and physical therapy to corticosteroid injections and surgical intervention. Recently, advances in biomedicine and biotechnology have enthused the use of cell therapy, tissue engineering, and autologous blood concentrates to enhance healing and stimulate growth in bone and soft tissue injuries.

One of the most popular methods used to biologically enhance healing in the fields of orthopaedic surgery and sports medicine includes the use of autologous blood products, particularly, platelet rich plasma (PRP). PRP is an autologous concentration of human platelets to supra-physiologic levels. It is produced from a patient’s peripheral vein and centrifuged to achieve a high concentration of platelets within a small volume of plasma. It is then re-injected at a site of injury or inserted as a gel or other biomaterials during surgery.

Historically, platelets have been used to treat patients with thrombocytopenia or hemorrhage. Other blood products such as fibrin (in the form of surgical glue) have been utilized for wound healing. In fact, fibrin (in the form of a clot) has been used in a few studies to augment healing in meniscal repairs and also to augment graft healing in ACL reconstruction. Because of its limited use only for surgical procedures and the inability to modify the platelet concentration, fibrin in its various forms is not as extensively used as PRP for sports related injuries.

PRP therapy has grown in popularity over the past few years. Not only has there been an increasing number of...
basic science and clinical studies, there has also been a rising level of public awareness secondary to the use of PRP to treat high-profile athletes. In fact, one of the most cited articles to date on PRP therapy was published in the New York Times showcasing its use in two professional athletes\(^\text{[10]}\).

Many clinicians feel that PRP therapy is safe given its autologous nature and long-term usage without any reported major complications. For this reason in addition to its easy availability, it is readily used in clinical and surgical settings. Despite its widespread unregulated use, the efficacy of PRP therapy has yet to be established\(^\text{[11-13]}\). There are many unanswered questions concerning the composition of PRP, individual blood product characteristics, different protocols of production, different methods of administration, and mechanisms of action exerted by PRP and its individual components on a cellular level.

The actual mechanisms of action of PRP are extensive because of the release of a myriad of bioactive factors. There is a general consensus in PRP research that the injection of concentrated platelets, once activated, results in an exponential increase in numerous growth factors (Table 1) at the sight of injection. However, the function of many growth factors, chemokines, cytokines, and inflammatory mediators has not been elucidated, nor have the interactions between factors and their influence on neighboring cells. As such, the primary purpose of this article is provide an overview of PRP-mediated effects by discussing current research on growth factors and proposed mechanisms by which PRP exerts its downstream effects on healing muscles, tendons, and ligaments. This review will first address the natural healing process for soft tissue injuries; followed by proposed mechanisms of action of PRP and associated growth in tendon and ligament injuries, and muscle contusion. Finally, current and future areas of research will be discussed to address common unanswered questions concerning the application of PRP for sports-related injuries.

### TABLE 1. Growth Factors and Cellular Effects.

<table>
<thead>
<tr>
<th>Growth Factor</th>
<th>Cellular Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDGF Platelet Derived Growth Factor</td>
<td>Macrophage activation and angiogenesis</td>
</tr>
<tr>
<td></td>
<td>Fibroblast chemotaxis and proliferative activity</td>
</tr>
<tr>
<td></td>
<td>Enhances collagen synthesis</td>
</tr>
<tr>
<td></td>
<td>Enhances the proliferation of bone cells</td>
</tr>
<tr>
<td>IGF-I Insulin-like Growth Factor-I</td>
<td>Chemotactic for myoblast and fibroblasts and stimulates protein synthesis</td>
</tr>
<tr>
<td></td>
<td>Mediator in growth ad repair of skeletal muscle</td>
</tr>
<tr>
<td></td>
<td>Enhances bone formation by proliferation and differentiation of osteoblasts</td>
</tr>
<tr>
<td>TGF-β Transforming Growth Factor-β</td>
<td>Enhances the proliferative activity of fibroblasts</td>
</tr>
<tr>
<td></td>
<td>Stimulates biosynthesis of type I collagen and fibronectin</td>
</tr>
<tr>
<td></td>
<td>Induces deposition of bone matrix</td>
</tr>
<tr>
<td></td>
<td>Inhibits osteoclast formation and bone resorption</td>
</tr>
<tr>
<td></td>
<td>Regulation in balance between fibrosis and myocyte regeneration</td>
</tr>
<tr>
<td>PDEGF Platelet Derived Endothelial Growth Factor</td>
<td>Promotes wound healing by stimulating the proliferation of keratinocytes and dermal fibroblasts</td>
</tr>
<tr>
<td>PDAF Platelet Derived Angiogenic Factor</td>
<td>Induces vascularization by stimulating vascular endothelial cells</td>
</tr>
<tr>
<td>EGF Endothelial Growth Factor</td>
<td>Cellular proliferation</td>
</tr>
<tr>
<td></td>
<td>Differentiation of epithelial cells</td>
</tr>
<tr>
<td>VEGF Vascular Endothelial Growth Factor</td>
<td>Angiogenesis</td>
</tr>
<tr>
<td></td>
<td>Migration and mitosis of endothelial cells</td>
</tr>
<tr>
<td></td>
<td>Creation of blood vessel lumen</td>
</tr>
<tr>
<td></td>
<td>Creation of fenestrations</td>
</tr>
<tr>
<td></td>
<td>Chemotactic for macrophages and granulocytes</td>
</tr>
<tr>
<td></td>
<td>Vasodilation (indirectly by release of nitrous oxide)</td>
</tr>
<tr>
<td>HGF Hepatocyte Growth Factor</td>
<td>Stimulates of hepatocyte proliferation and liver tissue regeneration</td>
</tr>
<tr>
<td></td>
<td>Angiogenesis</td>
</tr>
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<td></td>
<td>Mitogen for endothelial cells</td>
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<td>Antifibrotic</td>
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THE NATURAL HEALING PROCESS IN SOFT TISSUE INJURIES

Acute sports-related soft tissue injuries result from a single, traumatic event (macro-trauma) such as muscle contusion or ligament sprain/tear. Chronic soft tissue injuries often result from repetitive mechanical stress (micro-trauma) or overuse followed by inflammation and take time to develop such as in the case of tendinopathies (e.g., rotator cuff tendinopathy and Achilles tendinopathy). Regardless of the type of injury, the wound healing process is shared among all soft tissues, with differences in timing, duration of phases, and interactions between key mediators (14-16).

The general healing cascade involves four overlapping phases: (1) hemostasis; (2) inflammation; (3) cellular and matrix proliferation, which begins within days of an injury and comprises the most important phase of healing; and (4) wound remodelling, the longest phase, which may involve scar tissue formation (17, 18).

Immediately following injury, capillary leak allows for the recruitment of hemostatic factors and inflammatory mediators. The coagulation cascade is activated leading to platelet aggregation, clot formation, and development of a provisional extracellular matrix construct (19). Platelets adhere to exposed collagen and circulating extracellular matrix proteins, which triggers the release of bioactive factors from alpha granules (20). These bioactive actors include growth factors, chemokines, and cytokines, in addition to pro-inflammatory mediators such as serotonin, bradykinin, prostaglandins, prostacyclins, thromboxane, and histamine (21).

The inflammatory phase follows in a highly orchestrated fashion. Chemotactic agents begin to summon neutrophils to the injured site within 1-2 hours in the early inflammatory phase. Later (around 48 – 72 hours post-injury), macrophages appear in the wound and play the leading role in wound debridement and regulation of inflammation. They are also involved in recruiting fibroblasts and endothelial cells. The last cells to enter the wound during the late inflammatory phase are lymphocytes.

The cellular and matrix proliferation phase is arguably the most important phase of wound healing; in part, because the cells involved serve as a metabolic engine driving tissue repair (22). These cells originate from pluripotent progenitor cells in adjacent tissues including intraplatellar fat pad for anterior cruciate ligament, muscle derived stem cells (23) and satellite cells (22) for muscle. After 2-3 days of wound healing, macrophages and chemotactic, mitogenic, and angiogenic growth factors recruit fibroblasts and epithelial cells to infiltrate the site of injury (22). Once in the wound, fibroblasts synthesize collagen and change to their myofibroblast phenotype to facilitate wound contraction. Angiogenesis and the formation of granulation tissue are also important aspects during the proliferative phase of healing.

The final phase of the healing process involves wound maturation and remodelling. During this phase, growth factors such as PDGF and TGF-β, and fibronectin stimulate fibroblasts proliferation, migration, and synthesis of the components of extracellular matrix (24, 25). The remodelling phase is tightly regulated to maintain the balance between degradation and synthesis. Type I collagen replaces Type III collagen, proteoglycan, and fibronectin through a process referred to as “creeping substitution” to form a more robust matrix with increased tensile strength (26). The maturation phase varies in duration depending on the extent of the wound pathology, individual characteristics, as well as specific tissue healing capabilities of the tissue involved (27, 28). Additionally, pathophysiological and metabolic factors can affect wound healing. They include local causes such as ischemia, tissue hypoxia, infection, and growth factor imbalance, as well as systemic causes such as metabolic disease and nutritional status. In such unfavorable environments, PRP has been shown to be a viable therapeutic adjunct for soft tissue injuries (29).

PRP: DEFINITION, PROPERTIES, PREPARATION AND COMPOSITION

Platelet-rich plasma (PRP) is an autologous concentration of human platelet to supra-physiologic levels. Platelets are irregularly shaped, non-nucleated cytoplasmic bodies derived from fragmentation of megakaryocyte precursors. They circulate in the blood of mammals expressing glycoproteins on their cell membranes and play a pivotal role in hemostasis and wound healing via the formation of fibrin clots (30, 31). At baseline levels, platelets function as a natural reservoir for growth factors including platelet-derived growth factor (PDGF), epidermal growth factor (EGF), transforming growth factor-beta 1 (TGF-βI), vascular endothelial growth factor (VEGF), basic fibroblast growth factor (FGF), hepatocyte growth factor (HGF), and insulin-like growth factor (IGF-I), to name a few (32-36). Such growth factors are released from the alpha granules of activated platelets and are involved in important cellular processes including mitogenesis, chemotaxis, differentiation, and metabolism (37). Hence, the rationale for increasing platelet concentration in compromised (or injured) tissue lies in the belief that additional platelets will result in the exponential release of multiple bioactive factors, and subsequently, enhance the natural healing process.

Many clinical studies have demonstrated the beneficial effects of PRP therapy in oral-maxillofacial, plastics, and orthopaedic surgery. In fact, autologous blood...
Evaluation of the Cellular Effects of PRP Therapy Involved in the Healing of Sports-Related Soft Tissue Injuries

Products including platelets were first popularized in the 1990s in oral and plastic surgery\(^ {38-42} \). Despite the increasing evidence of PRP as an augmenter of natural healing, its clinical efficacy in the management of sports-related injuries is still a matter of debate\(^ {11-13} \).

Platelet-rich plasma is produced from blood obtained by phlebotomy, which is centrifuged to achieve a high concentration of platelets within a small volume of plasma. The platelet-rich product is then re-injected at a site of injury or prepared as a gel or other biomaterial and inserted during surgery. There are numerous protocols and commercial systems for producing PRP. Traditionally, two centrifugation steps are used to isolate the erythrocyte fraction from theuffy coat (plasma containing platelets, leukocytes, and clotting factors). The second step separates the platelet-poor plasma (PPP) from the platelet-rich fraction. Single-step systems are also available. Centrifugation itself is likely the most critical step during the PRP preparation process, as centrifugal forces in spins greater than 800x gravity (g) may result in significant loss of granular loads of platelets, which would subsequently dilute growth factor concentrations\(^ {43} \).

A major limitation in evaluating the clinical effects of PRP is variation in established preparation protocols. Many different commercial systems are available that utilize different centrifugation machines and protocols (Table 2). Platelet and growth factor concentrations can vary depending on the system used\(^ {44} \). Furthermore, the presence or absence of leukocytes, which produce VEGF\(^ {45} \) and possess antimicrobial properties\(^ {46} \), and activating factors such as calcium chloride or thrombin further influence the quality of PRP and resulting effects. Additional variation in PRP products results from patient differences in age, medical comorbidities (particularly hematologic disorders), and healing capabilities. In essence, the effects of PRP are influenced by substantial differences in the content of platelet concentrates as well as individual characteristics, which likely contributes to its variable findings in the literature.

**ORTHOPOEDIC APPLICATIONS OF PRP**

PRP is commonly used in orthopaedic practice for sports-related injuries of skeletal muscle, tendons, and ligaments. It is thought to exert its effects through many downstream events secondary to release of growth factors and other bioactive factors from its alpha granules. These effects may vary depending on the location of injury and the concentration of important growth factors involved in various soft tissue healing responses.

**Skeletal Muscle**

Skeletal muscle injuries are common causes of severe long-term pain and physical disability, accounting for up to 55% of all sports injuries\(^ {47} \). Contusions and strains are the most frequent muscular lesions, representing more than 90% of all sports related injuries\(^ {48} \). Muscle injury represents a challenging problem in traumatology, as injured muscles heal very slowly and often with incomplete functional recovery\(^ {23} \). Furthermore, barriers to complete muscle recovery following injury are scarring and fibrosis suggesting that scar formation may be at the expense of muscle regeneration\(^ {49,50} \). For this reason, regulation of fibrosis is one of the goals of PRP therapy in the management of muscle lesions.

One study evaluating the healing process in skeletal

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**TABLE 2. Commercially Available PRP Systems.** Vol, volume; CaCl\(_2\), Calcium chloride; NS, not specified.

<table>
<thead>
<tr>
<th>Commercial System</th>
<th>Blood Vol (ml)</th>
<th>Centrifugation (No. of Spins)</th>
<th>PRP Vol (ml)</th>
<th>Platelet Concentration</th>
<th>Activator (+ / -)</th>
<th>Leukocytes (+ / -)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cascade(^ {\circledast} )</td>
<td>9-18</td>
<td>1</td>
<td>4-9</td>
<td>1-1.5x</td>
<td>CaCl(_2)</td>
<td>-</td>
</tr>
<tr>
<td>GPS III</td>
<td>60</td>
<td>1</td>
<td>10</td>
<td>9.3x</td>
<td>Trombin</td>
<td>+</td>
</tr>
<tr>
<td>ACP(^ {\circledast} )</td>
<td>9</td>
<td>1</td>
<td>3</td>
<td>2-3x</td>
<td>None</td>
<td>-</td>
</tr>
<tr>
<td>Smart PRP2(^ {\circledast} )</td>
<td>20-120</td>
<td>2</td>
<td>3-20</td>
<td>4-6x</td>
<td>Trombin</td>
<td>+</td>
</tr>
<tr>
<td>PRGF(^ {\circledast} )</td>
<td>9-72</td>
<td>1</td>
<td>4-32</td>
<td>2-3x</td>
<td>CaCl(_2)</td>
<td>-</td>
</tr>
<tr>
<td>Magellan(^ {\circledast} )</td>
<td>30-60</td>
<td>2</td>
<td>6</td>
<td>3-7x</td>
<td>CaCl(_2)</td>
<td>+</td>
</tr>
<tr>
<td>Angel(^ {\circledast} )</td>
<td>40</td>
<td>2</td>
<td>4</td>
<td>1-18x</td>
<td>None</td>
<td>+/-</td>
</tr>
<tr>
<td>Genesis CS(^ {\circledast} )</td>
<td>30-60</td>
<td>1</td>
<td>4-10</td>
<td>9x</td>
<td>CaCl(_2)</td>
<td>NS</td>
</tr>
<tr>
<td>Sequire(^ {\circledast} )</td>
<td>50</td>
<td>2</td>
<td>5</td>
<td>1.6x</td>
<td>Trombin Bovine</td>
<td>NS</td>
</tr>
<tr>
<td>Platelex(^ {\circledast} )</td>
<td>50</td>
<td>2</td>
<td>4-6</td>
<td>NS</td>
<td>Batroxbin</td>
<td>+</td>
</tr>
<tr>
<td>Symphony II PCS(^ {\circledast} )</td>
<td>55-110</td>
<td>1</td>
<td>NS</td>
<td>3-6x</td>
<td>Thrombin Bovine + CaCl(_2)</td>
<td>NS</td>
</tr>
</tbody>
</table>
muscle injury and the impact of inflammation on injured mice gastrocnemius cells found that prostaglandin E2 (PGE2) can regulate the level of fibrosis by decreasing the expression of TGFβ1 (52). TGFβ1 is an inducer of extracellular matrix (ECM) protein synthesis and fibroblast proliferation (54, 55). As a particularly strong inducer (56), TGFβ1 has been implicated in the fibrogenesis of various tissues including kidney, lung, and skin (57). It also appears to play a role in muscle injury as an inflammatory modulator (53).

Abolishing the fibrotic effects of TGFβ1 appears to allow for full recovery of skeletal muscle function. In a currently unpublished study evaluating the effects of PRP on skeletal muscle healing, PPR injections in combination with Losartan, an angiotensin II receptor blocker (ARB), were found to decrease fibrogenesis and increase angiogenesis in a rat muscle-contusion model (58). When exposed to angiotensin II, fibroblasts increase their production of TGFβ1 (59). As such, the inhibition of angiotensin II with an ARB resulted in decreased formation of fibrosis following traumatic muscle injury (59). In combination with PRP, Losartan further inhibited fibrosis formation while also increasing angiogenesis and myofiber regeneration in a murine model (58). Additionally, combined PRP/Losartan injections resulted in improved muscle strength, as measured in peak twitch and tetanic forces. These findings suggest that combination treatment with PRP/Losartan can improve muscle healing by exerting anti-fibrosis, pro-angiogenesis, and pro-myogenesis effects through inhibition of TGFβ1.

In a controlled laboratory study, either PRP or PPP was injected into contraction-induced strained muscles in rats at 0, 3, 5 and 7 days post-injury (60). PPP, commonly used as a research control, is produced by high-speed centrifugation separating plasma from platelets and erythrocytes. Compared to the PPP control, the PRP treated group showed significant improvement at multiple time points in the small strain model (60). Such improvement was attributed to the effects of PRP on muscle regeneration. In a similar study, autologous conditioned serum (ACS, Arthrex, Florida, USA), a PRP equivalent containing high concentrations of TGFβ1 and FGF-2, was injected into gastrocnemius muscles in mice at 2, 24, and 48 hours post-injury (61). Compared to the saline injection control, histological examination of the ACS-treated mouse muscles resulted in an 84% increase in satellite cell activation at 30 and 48 hours post-injury (62). Additionally, there was a significant increase in centrally nucleated myofibers and in the proportion of large-diameter fibers, suggesting myofiber regeneration.

The aforementioned studies have shed light on the importance of specific growth factors involved in myogenesis including IGF-1, FGF-2, HGF, and TGFβ1 (63-65).

The premise for the improvement in muscle regeneration and satellite cell activation following PRP treatment appears to lie in the tight regulation of platelet-released growth factors.

Tendon

Tendon injuries are very common disabling conditions in athletes. Tendon injuries include acute or chronic degeneration as well as partial or complete tendon ruptures (66). Full recovery requires a long, complex healing process, particularly in the case of tendon rupture and retraction. Even so, healed tendons are comprised of scar tissue that is mechanically inferior to normal tendon tissue. This, in turn, impairs normal tendon function and joint kinematics, predisposing the patient to further tendon injury. Although biopsies in a case of chronic tendinopathy show an absence of inflammatory cell infiltration, conservative treatments include anti-inflammatory agents (non-steroidal anti-inflammatory drugs and corticosteroids) and local anesthetic injections (67). The efficacy of these treatment modalities remains in question (67). Thus, recent orthopaedic basic science and clinical research has focused on PRP as an alternative modality in the management of tendon injuries (11, 32, 72, 73).

Several laboratory studies have shown the beneficial effects or PRP on the tendon healing process. Previous in vitro studies using cultured human tenocytes have shown that PRP (in a clot releasates form; PRCR) stimulates cell proliferation and total collagen production compared to those cultures treated with PPP clot releasates (74, 75). An additional study evaluating PRP effects on tendon healing found that PRCR also promoted differentiation of human tendon stem cells into active tenocytes with high proliferation rates and collagen producing capabilities (32). Collagen gene expression levels were also increased in response to PRP in equine flexor digitorum superficialis tendons including enhanced type I collagen, type III collagen, and oligomeric matrix protein expression without concomitant increases in catabolic metalloprotease expression (76). In addition to stimulating tendon stem cell (TSC) differentiation, tenocyte proliferation, and increasing collagen expression, PRP was also found to induce VEGF and HGF production in human tendon cells.

VEGF contributes to angiogenesis or new blood vessel formation (77). In an animal study evaluating the safety of PRP injections, autologous PRP was injected into normal patellar tendons of New Zealand White rabbits (78). Histological analysis at 6 and 12 weeks post-injection revealed a robust angiogenic response. In another study, locally injected PRP into a wounded rat patellar tendon resulted in an increased number of circulation-derived
cells involved in the tendon healing. Circulation-derived cells (inflammatory cells responsible for secreting growth factors and cytokines) and fibroblast-like cells that synthesize extracellular matrix were significantly increased in response to PRP treatment at 3 and 7 days post-injection. Though chemotaxis was not directly observed in this study, the authors hypothesized that chemotaxis of circulation-derived cells was likely induced by PRP.

Though angiogenesis plays an important role for the initial phase of wound healing by facilitating cell and inflammatory mediator chemotaxis, it may also be detrimental to ligament and tendon healing via the upregulation of matrix metalloproteinases (MMPs). Angiogenesis has been shown to alter the material properties of the extracellular matrix. The injection of VEGF into rat Achilles tendons has been shown to reduce biomechanical strength assessed by tendon stiffness and ultimate load. In anterior cruciate ligament (ACL) reconstruction, angiogenesis contributes to remodeling of the autologous tendon graft, but has also been shown to induce proteolysis of the extracellular matrix, hindering the mechanical stability of the maturing graft. The above controversial findings suggest that tendon healing may either be impaired or facilitated by angiogenesis, which highlights the importance of tight VEGF regulation.

HGF, one of the major growth factors released from activated platelets, is primarily involved in hepatocyte regeneration and proliferation and fibroblasts proliferation (Hannafin, Atta, Warren, & Bhargava, 1999). Additionally, HGF has also been shown to exert anti-inflammatory effects in human abdominal aortic aneurysm (AAA) tissue via modulating the cytokine profile. HGF-mediated regulation of pro- and anti-inflammatory cytokines has also been reported in animal models of acute kidney injury, endotoxemia, cardiac allograft transplantation, and myocarditis.

Based on the findings of the aforementioned studies, PRP-mediated effects on tendon healing could be secondary to improved vascularity (with careful consideration of the potential degradative properties of angiogenesis) and/or the anti-inflammatory effects of growth factors known to increase with exogenous administration of platelets. For instance, PRP has been shown to suppress cyclooxygenase (COX)-1, COX-2, and membrane prostaglandin E synthase (mPGE) expression in vitro. All three enzymes are involved in the inflammatory pathway. In vivo injection of PRP into injured mouse tendons resulted in decreased PGE production at multiple time points post-treatments. Reduced COX-1, COX-2 and mPGE expression in conjunction with decreased production of PGE suggest that PRP exerts anti-inflammatory effects on healing tendons and may contribute to pain reduction following injection. Repeated exposure to PGE has previously been shown to disrupt collagen fiber uniformity and normal tissue architecture in rabbit tendons. In this case, it follows that hindering production of PGE would be beneficial in tendon healing. However, other studies have found that PGE inhibition has actually resulted in decreased collagen synthesis and delays in tendon healing. These contradictory findings, again suggest the importance of regulation. PGE production must be tightly controlled to achieve a favorable balance between pro- and anti-inflammatory effects during tendon healing.

**Ligaments**

Besides tendon injuries, acute ligament sprains rank among the most common orthopaedic injuries. Most ligamentous injuries can be treated conservatively; e.g. isolated medial collateral ligament (MCL) ruptures. Other injuries, such as the anterior cruciate ligament (ACL) need surgical reconstruction given its relatively low healing potential. Recently, autologous blood products including PRP and growth factors (isolated or in combination) have been used to treat ligamentous injuries with the goal of accelerated healing and an earlier return to activity. One characteristic of the MCL that substantiates its healing capacity is increased vascularization compared to low-healing capacity ligaments such as the ACL. Hence, the rationale behind the use of autologous blood products is to increase blood flow and the delivery of inflammatory mediators. As previously mentioned, VEGF plays an important role in healing as a potent growth factor of angiogenesis.

In a laboratory study evaluating the role of VEGF on MCL healing, murine muscle derived stems cells (MDSCs), which have been shown to promote healing via neoangiogenesis, were retrovirally transduced to express VEGF (MDSC-VEGF); a soluble fms-like tyrosine kinase-1 (sFLT1; a VEGF-specific antagonist) gene (MDSC-sFLT1); and nLacZ promoter gene to track the fate of the donor cells after transplantation (MDSC). The control group was injected with phosphate-buffer saline (PBS) only. Rat VEGF (rVEGF) expression was significantly higher in the MCL cells transduced with MDSC-VEGF. In MCL cells transduced MDSC-sFLT1, rVEGF was strongly suppressed. Additionally, biomechanical strength of the injured MCLs was significantly higher in the MDSC-VEGF group compared to both the MDSC-sFLT1 group and the PBS control group. There was no significant difference in failure load between the MDSC-VEGF, MDSC, and normal MCL groups. The authors conclude that though supplemental VEGF does not further improve healing, inhibiting VEGF...
interferes with the regeneration process by delaying ligament repair\(^{(116)}\).

PRP has been shown to instigate the aggregation of inflammatory cells via release of chemotactic, angiogenic, and mitogenic growth factors released from activated platelets\(^{(22)}\). In the case of an MCL injury, PRP is thought to function during the early phases of healing, thus assisting in the recruitment of pro-inflammatory cells such as macrophages. During the proliferative and remodeling phases of healing, macrophages accumulate in an injured site and express either a pro-inflammatory or anti-inflammatory phenotype. M1 macrophages are involved in phagocytizing cellular debris, recruiting additional reparative cells (e.g. myofibroblasts), and assisting in pro-inflammatory cytokine release. M2 macrophages promote angiogenesis, matrix remodeling, and ultimately assist in scar tissue formation by releasing anti-inflammatory cytokines\(^{(26, 117)}\). Both phenotypes play important roles in ligament healing, and in conjunction with platelet-released growth factors, macrophages help regulate angiogenesis, fibroblast differentiation, and collagen production. In MCLs, non-specific inhibition of macrophages using clondronate (a bisphosphonate) can help subdue excessive granulation tissue formation, but impairs early matrix formation and ligament strength\(^{(26)}\). In ACL reconstruction; however, inhibition of macrophages at the bone-tendon junction resulted in improved healing\(^{(118)}\). The reasons behind the opposing findings are multifactorial with innate differences in healing capacity likely playing a role.

With increasing attention being paid to ACL graft maturation, PRP has been used to augment healing in the case of animal ACL repair and reconstruction. In a porcine model of suture repair after ACL transection, ligaments treated with a collagen-PRP hydrogel showed significant improvement in biomechanical properties including load and linear stiffness at 4 weeks post-repair compared with untreated repairs\(^{(119)}\). Furthermore, a collagen-PRP hydrogel was shown to improve ACL wound site filling in a canine ACL injury model\(^{(120)}\). Both fibrinogen and fibronectin were restored in the wound site treated with collagen-PRP hydrogel. Additionally, procollagen I (a marker for collagen formation) and vWF (a marker for revascularization) were restored in the wound site. These findings support PRPs role in fibroblasts chemotaxis and adherence to extracellular matrix structures\(^{(122)}\) and also demonstrate that the collagen-PRP scaffold stimulates ingrowth of fibroblast and endothelial cell invasion, mimicking the natural function of the fibrin clot\(^{(9, 120)}\).

The effects of PRP on clinical outcomes of ACL reconstruction are also being evaluated. One study evaluated the ability of collagen-platelet composite (CPC), or blood platelets added to a collagen scaffold, to restore

<table>
<thead>
<tr>
<th>Unanswered Questions in PRP Research</th>
<th>Opportunities for Future Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recommendations for administration of PRP?</td>
<td>Assessment of timing, dosing, and frequency of doses.</td>
</tr>
<tr>
<td>What is the optimal concentration of platelets?</td>
<td>Evaluation of required platelet concentrations by injury site and wound characteristics.</td>
</tr>
<tr>
<td>Does this optimal concentration vary depending on the injury site?</td>
<td></td>
</tr>
<tr>
<td>Where should PRP be administered?</td>
<td>Evaluating histological, biomechanical, and clinical differences in outcomes based on site of administration. For instance, application over the bone, over the tendon; injection within the tendon, within the ligament, or intra-articular.</td>
</tr>
<tr>
<td>What technique for administrating yields the greatest results?</td>
<td></td>
</tr>
<tr>
<td>Are all PRPs created equally?</td>
<td>Evaluation of the influence of patient variation on autologous blood product composition and quality.</td>
</tr>
<tr>
<td>At what phase of the healing cascade does PRP exert the greatest effect?</td>
<td>Evaluation of histological, biomechanical, and clinical differences in outcomes based timing of injection from original injury.</td>
</tr>
<tr>
<td>How do different centrifugation speeds affect platelet behavior? Growth factor concentrations?</td>
<td>Assessment of platelet behavior under various conditions and at different stages of the healing cascade.</td>
</tr>
<tr>
<td>Do platelets and released growth factors stay localized at an injury site?</td>
<td>Assess localization of PRP using immunostaining techniques, isotopic labeling, and imaging modalities.</td>
</tr>
<tr>
<td>Side effects of PRP?</td>
<td>Evaluation of the potential adverse effects of PRP therapy</td>
</tr>
</tbody>
</table>

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TABLE 3. Opportunities for future research.
knee function following ACL reconstruction in a caprine model\textsuperscript{(122)}. The authors assessed the effect of platelet composition on post-operative knee laxity and graft structural properties. They found that anteroposterior (AP) laxity significantly decreased in the CPC group compared to the control, but no significant differences in failure load or linear stiffness were observed between groups. When evaluating both groups combined, a higher systemic platelet count positively correlated with improvements in anteroposterior (AP) knee laxity at 30° and 60° of knee flexion as well as linear stiffness and graft strength\textsuperscript{(122)}. This study finding had the greatest implications with respect to the use of PRP in ACL reconstruction. As previously mentioned, administration of PRP results in the localization of platelet-released growth factors including IGF-1, TGFβ-1, VEGF, PDGF, and FGF-2\textsuperscript{(123)}. Each of these growth factors – and likely many more – play a role in tissue healing. Pertaining to ACL reconstruction, TGFβ-1 (pro-inflammatory) has been shown to stimulate ACL cell migration in vitro\textsuperscript{(123)}, and PDGF-AB and FGF-2 can stimulate ACL proliferation in a 3D collagen scaffold\textsuperscript{(124)}.

**FUTURE DIRECTIONS OF RESEARCH**

Major strides have been made in PRP research with findings influencing the management of orthopaedic injuries. Despite the multitude of clinical and basic science studies published within the last year, many important questions remain unanswered including those concerning the dosing, timing, and frequency of PRP injections; different techniques for delivery and location of delivery (over the injured tissue, within the injured tissue, or intra-articularly); optimal physiologic conditions for injections; and the concomitant use of recombinant proteins, cytokines, additional growth factors, biological scaffolds, and stems cells (Table 3).

In a recent systematic review evaluating clinical outcomes of PRP use in orthopaedic injuries, the authors concluded that one of the most challenging barriers to critical evaluation is lack of standardization in preparation and dosage of autologous blood concentrates\textsuperscript{(125)}. Specific alterations in growth factor concentration, supplementation of platelet activators, leukocytes, and or other cellular components decrease the generalizability of clinical and basic science findings, rendering any results difficult to interpret.

Individual patient characteristics also contribute to the observed variation in PRP content and quality as well as the cellular responses to autologous blood products. Age or skeletal maturity has been shown to influence ACL cell metabolic activity, apoptotic rate, collagen production, and response to PRP in a porcine model\textsuperscript{(126)}. The diversity of the human population can affect physiologic responses to PRP. Thus, future research studies should account for individual differences in age, gender, healing capabilities and whole blood characteristics.

Another important topic for consideration in PRP research is defining the optimal dose or concentration of platelets and growth factors in PRP. Although a correlation was found between increased platelet count and increased ACL graft strength\textsuperscript{(122)} – “more” platelets and growth factors may not necessarily be more effective. In a study using a porcine model to assess optimal platelet concentration in PRP, increased concentration did not seem to have an effect on functional outcomes of primary ACL repair\textsuperscript{(127)}. PRP containing 5x the baseline systemic platelet count and PRP containing 3x the baseline systemic platelet count did not compromise ligament stiffness and resulted in similar biomechanical outcomes despite histological differences\textsuperscript{(127)}. The 5x group ACLs had increased cellularity, more organized collagen bundles, and more elongated fibroblasts. The finding of similar biomechanical outcomes despite differences in histology raises another important question in PRP research: is there a relationship between cellular findings following PRP treatment and actual clinical implications? Previous animal studies have demonstrated that increased cellularity during early wound healing may have a positive impact on ligament\textsuperscript{(128)} and tendon\textsuperscript{(126)}; however, others have found no such relationship\textsuperscript{(130, 131)}. From a basic science standpoint, elucidation of specific cellular responses to PRP involves the evaluation of the inflammatory cells involved, their interactions, and behavior in an altered cellular environment. This response will likely vary depending on the injury site and thus, provides another avenue for continued PRP research.

To our knowledge, there are no studies reporting the negative effects of PRP. The assumption that autologous products are intrinsically safe should be critically evaluated. When cells are in their natural environment, they behave “naturally” meaning many of their activities, interactions, and released bioactive factors can be predicted. However, when cells and cell fragments are exposed to unnatural environments, for instance, a high-speed centrifugation process, the resulting products and exerted effects may be less predictable. Furthermore, there is no guarantee that platelets (in the form of PRP) will remain localized at the site where they are injected. Dissemination may result in unexpected results in surrounding tissues or even systemically. As such, the safety of autologous blood products – especially in the presence of cell, growth factor, and platelet activator adjuncts – proves yet another aspect of PRP therapy warranting research.
CONCLUSION

There is not one overarching mechanism of action of PRP given the differences in platelet content, resulting growth factor concentrations, and varying downstream cellular responses. What is known is that PRP contains a high concentration of platelets and that these platelets, once activated, release numerous growth factors into the surrounding environment. The resulting cellular effects are both pro-inflammatory and anti-inflammatory in nature and appear to be dependent on many different factors including the stage of the natural healing process, the site of the injury, and cellular environment. The interplay between individual growth factors and their resulting effects are currently being evaluated through well-designed basic science studies. Despite the volumes of basic science research supporting the use of PRP for sports related injuries, clinical evidence for PRP therapy has not been well established due to many of the unanswered questions addressed above. Continued basic science research elucidating the downstream effects of PRP can help drive clinical research. Strong scientific and clinical findings can then be used in conjunction to help develop clinical recommendations for the use of PRP in the management of sports related injuries.

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Evaluation of the Cellular Effects of PRP Therapy Involved in the Healing of Sports-Related Soft Tissue Injuries


ABSTRACT

Purpose: There is no consensus in the literature regarding the optimal surgical treatment of symptomatic partial rotator cuff tears. We attempted to determine the optimal surgical treatment for partial articular-sided rotator cuff tears through a systematic review of appropriate studies.

Methods: Medline®, PubMed, Ovid, and the Cochrane Register of Controlled Trials were searched for all studies published between January 1991 to March 2010 that used the key words “shoulder”, “partial rotator cuff tear”, “PASTA”, “articular-sided rotator cuff tear”, “incomplete rotator cuff tear”, “arthroscopic” and “repair”. Inclusion criteria were studies (Level I to IV) that reported clinical outcomes in patients who had arthroscopic evaluation and arthroscopic or mini-open treatment of a symptomatic partial articular-sided rotator cuff tear. One of three surgical treatments was used: debridement with or without acromioplasty; transtendon arthroscopic repair; or tear completion with repair. Exclusion criteria included studies with over 50% overhead throwers or athletes, studies that involved an open approach to the rotator cuff without arthroscopy, and data presented in technical notes or review papers. Data abstracted from the studies included patient demographics, tear characteristics, surgical procedure(s), and clinical outcomes.

Results: Of 588 studies involving partial rotator cuff tears, 14 studies were identified which met our inclusion and exclusion criteria. All studies were Level IV retrospective case-series studies. Seven studies reported outcomes after rotator cuff debridement. Tear completion and repair was performed in three studies. Transtendon repair of a partial articular-sided rotator cuff tear was performed in three studies. Although different outcome measures were used, each study reported subjective and objective improvement postoperatively. One study compared outcomes in patients who underwent arthroscopic debridement versus another group where patients had tear completion and mini-open repair. Improved long-term results and decreased reoperation rates were reported in the tear completion and repair group.

Conclusion: On the basis of the available evidence, no single technique provides superior clinical outcomes. Level I and II comparison studies are needed to determine the optimal treatment of partial articular-sided rotator cuff tears.

INTRODUCTION

Although partial rotator cuff tears were first described by Codman in 1934, very little was known about their recognition and treatment until shoulder arthroscopy became popular in the 1990’s. With improved pre-operative MRI imaging, our understanding of partial rotator cuff tears is increasing. Partial rotator cuff tears can be articular-sided (Partial Articular Sided Rotator Cuff Tears or PASTA lesions), bursal side or intra-tendinous (seen only on imaging studies). These tears can be secondary to internal impingement in young throwing and overhead athletes, or be due to trauma, and most commonly represent the early stages of degenerative rotator cuff tendon tearing. While there are many studies in the literature that describe the treatment of these tears, there is no general consensus on the optimal surgical treatment of symptomatic partial rotator cuff tears. We elected to limit our review to articular- sided tears.

Several factors are felt to be important in determining the treatment of partial tears. Partial tears in overhead athletes are felt to be secondary to either occult instability or loss of humeral rotation and thus require their own separate analysis and treatment. In the 1980’s and early 1990’s, surgical treatment of all types of partial rotator cuff tears consisted primarily of rotator cuff debridement. In 1990, Ellman described a classification system that graded the partial-thickness tear by determining the amount of exposed articular footprint. Grade I tears were less than 3 mm deep, grade II tears were between

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1University of Iowa Dept of Orthopaedic Surgery
2University of Connecticut Health Center, Hartford Connecticut

Matthew Bollier, M.D.
Institute for Orthopaedics, Sports Medicine and Rehabilitation
Department of Orthopaedics and Rehabilitation
The University of Iowa
matthew-bollier@uiowa.edu
(319) 467-8254
than 50% of the tendon thickness. Several authors recommended debridement for tears less than 50% of the tendon thickness and repair for tears greater than 50% of the tendon thickness. Calvano studies have shown some variability in the medial-to-lateral distance of the supraspinatus footprint from 6.9 to 21 mm, and controversy exists regarding the amount of exposed footprint needed for a tear to be classified as a 50% partial-thickness tear.

Surgical treatment has evolved from simple arthroscopic debridement to transtendon arthroscopic repair and completion of the partial tear and repair of the newly created full-thickness tear. It is unclear which surgical treatment option provides the best clinical and functional outcome. Designed a systematic review of published studies examining clinical outcomes after surgical treatment (debridement, completion and repair, or transtendon repair) of partial articular-sided rotator cuff tears in an attempt to answer this question. Our hypothesis was that clinical studies would not show a difference in subjective and objective clinical outcomes when comparing among three different surgical techniques.

**METHODS**

**Literature Search**

We searched Medline®, PubMed, Ovid, and the Cochrane Register of Controlled Trials for all published literature from January 1991 to March 2010 using the following key words: “shoulder”, “partial rotator cuff tears”, “PASTA”, “articular-sided rotator cuff tear”, “incomplete rotator cuff tear”, “arthroscopic” and “repair”. General terms were used to avoid missing any potential studies. All studies were cross-referenced, and all abstracts and presentations were eliminated. Inclusion criteria included studies (Level I to IV) that reported clinical outcomes in patients who had arthroscopic evaluation and arthroscopic or mini-open treatment of a symptomatic partial articular-sided rotator cuff tear. In addition, studies needed to separate articular-sided tears from bursal-sided tears and use one of three surgical treatment options: debridement with or without acromioplasty, transtendon arthroscopic repair, or tear completion and repair. Exclusion criteria included bursal-sided partial tears, studies with over 50% overhead throwers or athletes, studies that involved an open approach to the rotator cuff without an arthroscopic component, and data presented in technical notes or review papers. Data abstracted from the studies included patient demographics, tear characteristics, surgical procedure, and clinical outcomes.

**Data Abstraction**

Data was abstracted from each of the 14 studies that met our inclusion and exclusion criteria. Demographic data included type of study, level of evidence, number of patients enrolled, mean age, number of shoulders, gender and arm dominance. The Ellman tear grade was collected for all studies using this classification system. Associated procedures were identified. Preoperative and postoperative clinical outcome scales used were the University of California, Los Angeles (UCLA), American Shoulder and Elbow Surgeons (ASES), Constant-Murley score, L’Insalata score, satisfactory Neer score, and/or a visual analog pain score. We did not include postoperative imaging as only two studies reported these outcomes. The data was collected in table format using Excel computer data basing program (Microsoft, Redmond, WA). No statistical analysis was performed.

**RESULTS**

**Literature Search**

Using the general search terms, 39,942 articles were found. When performing a search for keyword “partial rotator cuff”, 588 studies were identified and the abstracts of each of these articles were reviewed to identify those applicable to the study. Forty-eight studies were thought to be appropriate for analysis. After a full-text review of inclusion and exclusion criteria, ten studies were excluded because they were technique articles. Thirteen studies were excluded because they were review articles. Biomechanical studies (2) of partial rotator cuff tears were also excluded. Four studies involved over 50% athletes and were excluded. One study was excluded because it compared classification systems and one study was excluded because it did not separate articular-sided partial tears from bursal-sided partial tears. Four studies were excluded because they involved an open approach to the rotator cuff and didn’t involve arthroscopic or mini-open treatment of the partial rotator cuff tear. There were 14 studies that met the final inclusion and exclusion criteria and were included in the final data analysis.

**OUTCOMES**

Study design, level of evidence, total number of shoulders treated, mean age, tear grade, average follow-up time, and outcome measures used were included in our analysis (Tables 1-4). All studies were Level IV evidence and consisted of retrospective case series reviews. There were 497 partial articular-sided rotator cuff tears in the studies that met our inclusion criteria. Three-hundred and three (61%) shoulders had cuff debridement without repair. The average age of patients in the debridement group was 52 years and 94.5% of patients had a subacro-
TABLE 1.

<table>
<thead>
<tr>
<th>Surgical Debridement of Partial Rotator Cuff Tears</th>
<th>Assessment of Clinical Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>Study</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>--</td>
</tr>
<tr>
<td>Snyder et al.</td>
<td>Case Series</td>
</tr>
<tr>
<td>Gartsmann et al.</td>
<td>Case Series</td>
</tr>
<tr>
<td>Cordasco et al.</td>
<td>Case Series</td>
</tr>
<tr>
<td>Cordasco et al.</td>
<td>Case Series</td>
</tr>
<tr>
<td>Park et al.</td>
<td>Case Series</td>
</tr>
<tr>
<td>Kartus et al.</td>
<td>Case Series</td>
</tr>
<tr>
<td>Ozbaydar et al.</td>
<td>Case Series</td>
</tr>
<tr>
<td>Liem et al.</td>
<td>Case Series</td>
</tr>
</tbody>
</table>

mial decompression. Transtendinous repair was performed in 64 (13%) shoulders with an average age of 47.5 years. Thirty of these patients (47%) had a concomitant subacromial decompression. Completion of the partial tear and repair was performed in 102 patients (21%) with an average age of 54 years. Subacromial decompression was performed in 100 patients (98%).

Surgical Debridement of Partial Rotator Cuff Tears

There were seven studies that met our inclusion criteria in which the partial tear was treated with arthroscopic debridement of partial articular-sided rotator cuff tear (Table 1). All studies were case series and Level IV evidence. Five studies included only Ellman grade I or II tears (less than 50% rotator cuff insertion thickness). One study did not grade tears and one study included Ellman grade III tears.

In 1991, Snyder followed 31 partial articular-sided rotator cuff tears treated with debridement. Tear grade and depth were not recorded. Mean follow-up was 23 months (range, 10-43 months). Twenty-six patients (84%) had satisfactory outcomes (UCLA score greater than 28) and the average UCLA score was 33 (0-35). Twenty-nine patients (93%) had satisfactory results based on Neer’s criteria. Results were similar in patients who had a subacromial decompression compared to those without.

In 1995, Gartsman and Milne reported on 111 articular-sided partial rotator cuff tears with an average age of 42.5 years. They divided patients into three groups: impingement, instability, and trauma. The partial tear was thought to be secondary to impingement in 85 shoulders. Forty-four of these tears were Ellman grade I, 29 were grade II, and 12 were grade III. The tear was arthroscopically debrided and an acromioplasty was performed in every case. Average follow-up was 32.3 months (range, 26 to 84 months). Subjective pain scores improved in this group from 6.7 to 1.2, but no shoulder outcome scores were reported.

In 2002, Cordasco reported on 162 patients who had arthroscopic debridement and acromioplasty for a symptomatic partial rotator cuff tear. Included were 44 shoulders with Ellman grade II partial articular-sided tears and 19 articular-sided Ellman grade I tears. Mean follow-up was 4.5 years (range, 2-10 years). Failure of treatment was defined by a L’Insalata score of less than 70 at follow-up. No failures were noted in the grade I tears while 2 out of 44 (5%) of the grade II tears were considered failures.

In 2003, Park followed 24 shoulders with Ellman grade I and II tears. At the time of arthroscopy, the average articular-sided tear depth was 4.5 mm. All tears were treated with debridement and subacromial decompression. Average follow-up was 3.5 years (range, 2-6 years). ASES scores improved from an average of
What Surgical Technique Provides the Best Outcome for Symptomatic Partial Articular-Sided Rotator Cuff Tears?

**TABLE 2. Surgical Transstendon Repair of Partial Articular-Sided Rotator Cuff Tears**

<table>
<thead>
<tr>
<th>Source</th>
<th>Study</th>
<th>Level of Evidence</th>
<th>No. of Partial Tears</th>
<th>No. of Artic-Sided Tears</th>
<th>Mean Age</th>
<th>Tear Grade</th>
<th>Average Follow-up</th>
<th>Assessment of Clinical Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ide et al.</td>
<td>Case Series IV</td>
<td>IV</td>
<td>17</td>
<td>17</td>
<td>42</td>
<td>III</td>
<td>39 months</td>
<td>17.3/32.9 [p &lt; 0.01] NR NR NR NR NR</td>
</tr>
<tr>
<td>Tauber et al.</td>
<td>Case Series IV</td>
<td>IV</td>
<td>16</td>
<td>16</td>
<td>NR</td>
<td>II, III</td>
<td>NR (p &lt; 0.01)</td>
<td>15.8/32.8 [p &lt; 0.01] 7.9/1.2 NR NR NR NR</td>
</tr>
<tr>
<td>Castricini et al.</td>
<td>Case Series IV</td>
<td>IV</td>
<td>31</td>
<td>31</td>
<td>53</td>
<td>II, III</td>
<td>33 months</td>
<td>44.4/91.6 [p &lt; 0.01] NR NR NR</td>
</tr>
</tbody>
</table>

38 preoperatively to 88 postoperatively. Pain scores improved in all patients.

In 2006, Ozbaydar reported on 12 patients with partial articular-sided tears with less than 50% of the footprint, treated with arthroscopic debridement and bursectomy. Fourteen of 19 patients had a subacromial decompression (if a subacromial spur was present). Average follow-up was not recorded. Mean UCLA scores improved from 16.8 preoperatively to 29.0 postoperatively. They did not separate partial bursal-sided tears from partial articular-sided tears when reporting outcomes.

In 2006, Kartus examined 13 articular-sided rotator cuff tears. All patients underwent debridement and acromioplasty. The mean follow-up was 101 months (range, 60-128). The average Constant score at follow-up was 72 (range 35-97). No pre-op score was recorded. Abduction strength was similar on the operative side compared to the contralateral side.

In 2008, Liem evaluated 46 patients with Ellman grade I or II tears. Twenty-six Ellman grade I tears were managed with acromioplasty alone and 20 Ellman grade II tears were treated with debridement and acromioplasty. At an average follow-up of 50 months, the ASES score improved from 37.4 to 86.6. Mean postoperative Constant score was 87.6 points. No significant differences were found when comparing the outcomes of grade I and grade II tear treatment.

**Transtendon Repair of Partial Rotator Cuff Tears**

There were three studies that met our inclusion criteria and involved an arthroscopic transtendon repair of a partial articular-sided rotator cuff tear (Table 2). All studies were Level IV evidence. One study only included Ellman grade III tears and two studies included both Ellman grade II and III tears.

In 2005, Ide evaluated 17 patients who underwent arthroscopic transtendon repair of Ellman grade III partial articular-sided tears using suture anchors. Subacromial decompression was not reported. Mean follow-up was 39 months (range, 25-57 months). UCLA scores improved from 17.3 preoperatively to 32.9 postoperatively. Japanese Orthopaedic Association Shoulder Scores improved from 68.4 preoperatively to 94.8 postoperatively. No complications were reported and only one patient had a fair or poor result.

In 2008, Tauber reported on 16 patients who underwent arthroscopic transtendon repair of partial articular-sided tears using trans-osseous tunnels. Seven patients had an Ellman grade II tear and nine patients had a grade III tear. Average follow-up was not recorded, but all patients were evaluated at a minimum of 18 months. Mean UCLA scores improved from 15.8 preoperatively to 32.8 at follow-up. Pain scores decreased from 7.9 to 1.2. There were no differences in outcome when comparing grade II and grade III tears.

In 2009, Castricini examined 33 patients who underwent transtendon arthroscopic repair of a partial articular-sided rotator cuff tear. They included both Ellman grade II and III tears and used suture anchors for repair as described by Lo and Burkhart. Seven of 33 patients underwent subacromial decompression and 8 patients had either biceps tenodesis or tenotomy. Mean follow-up was 33 months (range, 26-45). The Constant score increased from 48.2 preoperatively to 91.6 postoperatively.

**Surgical Completion and Repair of Partial Rotator Cuff Tears**

There were three studies which met our inclusion criteria and involved arthroscopic completion and repair of a partial articular-sided rotator cuff tear (Table 3). All studies were Level IV evidence. All three studies included only partial tears greater than 50% of the insertion thickness.

In 2007, Deutsch evaluated the outcome of 41 Ellman grade III partial-thickness tears; 33 were articular-sided and eight were bursal-sided. Tear thickness was between...
60-90% of the tendon thickness with a mean tear depth of 75% or 9 mm. All patients underwent completion of the partial tear and suture anchor repair. Thirty-nine of 41 patients had a subacromial decompression. Mean follow-up was 38 months (range, 24-50). Average ASES scores improved from 42 preoperatively to 93 postoperatively. Pain level and satisfaction scores were significantly improved in all patients.

In 2008, Porat and colleagues49 examined 36 patients with partial articular-sided tears greater than 50% who were treated with arthroscopic completion and repair. They used 14 mm as the average footprint thickness and measured the exposed footprint intra-articularly. In these tears, a marking suture was placed and the tear was then evaluated in the subacromial space. Once the marking suture was discovered, a shaver was used to complete the tear. Single- or double-row suture anchor repair was then performed depending on how the tear reduced to the footprint. Thirty-four of 36 patients received a subacromial decompression. Patients were followed for a minimum of two years (range, 24-73 months). They reported 83% good to excellent outcomes. The UCLA score improved from 17.25 preoperatively to 31.47 postoperatively.

In 2009, Kamath et al47 reported on 42 cases which underwent arthroscopic completion of a symptomatic partial articular-sided partial-thickness tear greater than 50% (5-6 mm) to a full-thickness tear with subsequent repair. There were 33 articular-sided tears and nine bursal-sided tears. All patients had a subacromial decompression. Patients were followed for a minimum of two years (range, 24-73 months). They reported 83% good to excellent outcomes. The UCLA score improved from 17.25 preoperatively to 31.47 postoperatively.

Debridement vs. Mini-open Repair

In 1999, Weber56 compared 32 patients with Ellman grade III tears who had arthroscopic debridement and acromioplasty to 33 patients with Ellman grade III tears who had acromioplasty, tear completion and mini-open repair. Treatment groups were not randomized but were determined by preoperative doctor-patient discussion. There were 29 articular-sided tears and three bursal-sided tears in the debridement group, and 28 articular-sided tears and five bursal-sided tears in the repair group. All patients had a subacromial decompression. Follow-up averaged 47.7 months in the debridement group and 38.1 months in the repair group. The average postoperative UCLA scores in the debridement group were statistically less (22.7) when compared to the repair group (31.6). There were six re-operations in the debridement group because of post-operative pain, and none in the repair group. Weber concluded that debridement and acromioplasty are not adequate treatment of most grade III partial tears.

### DISCUSSION

When analyzing partial rotator cuff tears, there are wide ranges in patient age, tear pattern, tear depth, location, and grade. Younger overhead athletes often develop articular-sided partial rotator-cuff tears from internal impingement, and middle-aged patients are more likely to have partial tears secondary to external impingement or intrinsic tendon degeneration. In order to focus our review, we identified studies that reported clinical outcomes in patients who had arthroscopic evaluation and arthroscopic or mini-open treatment of a symptomatic partial articular-sided rotator cuff tear. We excluded studies that included overhead athletes or bursal-sided tears. The three primary surgical techniques for managing partial articular-sided rotator cuff tears are debridement, transtendon repair, or takedown and repair. This systematic review focused on compar-

### TABLE 3.

<table>
<thead>
<tr>
<th>Source</th>
<th>Study</th>
<th>Level of Evidence</th>
<th>No. of Partial Tears</th>
<th>No. of Articular Sided Tears</th>
<th>Mean Age</th>
<th>Tear Grade</th>
<th>Average Follow-up</th>
<th>UCLA Score Pre-op/Post-op</th>
<th>Analog Pain Scale Pre-op/Post-op</th>
<th>ASES Score Pre-op/Post-op</th>
<th>Constant Score Pre-op/Post-op</th>
<th>L’Insalata Score Pre-op/Post-op</th>
<th>Satisfactory Score Pre-op/Post-op</th>
<th>Satisfactory Score Pre-op/Post-op</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deutsch A</td>
<td>Case Series IV</td>
<td>41</td>
<td>33</td>
<td>60</td>
<td>&gt;50%</td>
<td>III</td>
<td>38 months</td>
<td>6.5/0.8</td>
<td>(p &lt; 0.001)</td>
<td>42/93</td>
<td>(p &lt; 0.001)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Porat et al</td>
<td>Case Series IV</td>
<td>36</td>
<td>36</td>
<td>60</td>
<td>&gt;50%</td>
<td>III</td>
<td>42 months</td>
<td>6.5/2.7</td>
<td>(p &lt; 0.001)</td>
<td>47/0/82.7</td>
<td>(p &lt; 0.001)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Kamath et al</td>
<td>Case Series IV</td>
<td>42</td>
<td>33</td>
<td>53</td>
<td>&gt;50%</td>
<td>III</td>
<td>36 months</td>
<td>17.2/31.5</td>
<td>(p &lt; 0.05)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
</tbody>
</table>
What Surgical Technique Provides the Best Outcome for Symptomatic Partial Articular-Sided Rotator Cuff Tears?

In comparing clinical outcomes among these groups. All studies were Level IV evidence and consisted of retrospective case series. However, we did identify one retrospective non-randomized comparison study.

Comparing clinical outcomes among the three groups was difficult because different outcome instruments were used. In the debridement group, two of seven studies used UCLA scores for outcome assessment, two studies used ASES scores, two studies reported Constant scores and two studies used visual analog pain scores. One study used the L’Insalata shoulder outcome questionnaire. In the transtendon repair group, two of three studies reported UCLA scores postoperatively and one of three studies used the Constant score. In the studies involving takedown and repair, one of the three studies reported UCLA scores and two of three studies used ASES and visual pain scores.

When comparing the three groups, UCLA, ASES, and Constant scores were similar (Tables 1-3). The average UCLA score was 27.9 (range, 22.7-32) in the debridement group, 32.85 (range, 32.8-32.9) in the transtendon repair group, and 31.5 in two studies of takedown and repair. The mean Constant score was 79.9 in the debridement group. Only one of seven studies reported Constant scores after either transtendon repair or rotator cuff takedown and repair. Average ASES score was 87.3 in the debridement group and 87.9 in the takedown and repair group. No study reported ASES scores in the transtendon repair group. No single surgical technique provided superior clinical outcomes. In Weber’s comparison study, he reported significantly higher UCLA scores in the repair group compared to the debridement group for Ellman grade III partial tears.56 However, patients were not randomized and the type of surgical treatment was determined preoperatively by the surgeon.

Current teaching on arthroscopic treatment of partial articular-sided rotator cuff tears suggests that takedown and repair or transtendon repair should be considered when the tear depth exceeds 50%, and debridement can be performed if the tear is less than 50%. Five of six studies in the rotator cuff debridement group included only Ellman grade I and II tears (less than 50% thickness). In contrast to the debridement group, the studies in the two repair groups almost exclusively consisted of grade III partial tears (greater than 50%).47, 49, 54, 55 Selection bias showed studies with rotator cuff repair were done on higher-grade partial tears and studies examining debridement were performed on lower-grade tears.

In addition, ten of the 14 studies used the classification system described by Ellman.5 Grade I tears were less than 3 mm deep, grade II were between 3 and 6 mm, while grade III were greater than 6 mm and involved more than half of the tendon. Most studies made the assumption that grade III tears involved over 50% of the tendon insertion. However, cadaveric studies have shown variability in the medial-to-lateral distance of the supraspinatus footprint from 6.9 to 21 mm.7-9 Equating a tear depth of 50% with 6 mm of exposed footprint may not be accurate in all cases.

**Recommendation for Partial Articular-Sided Tears <50%**

Despite the selection bias in the literature and lack of Level I, II, or III studies, arthroscopic debridement and subacromial decompression do appear to provide improved clinical outcomes and decreased pain for partial articular-sided tears of less than 50%.46, 50-53 Unfortunately, there are no studies comparing debridement versus repair in this group. Although some surgeons anecdotally report greater strength improvement with repair compared to debridement, there is no evidence at the current time to support this.

**Recommendations for Partial Articular-Sided Tears >50%**

In one study, improved clinical outcomes were achieved with repair compared to debridement for partial articular-sided tears greater than 50%.56 There were three studies involving transtendon repair and three studies involving takedown and repair of partial articular-sided tears greater than 50%.45-47, 49, 54, 55 Each case series

<table>
<thead>
<tr>
<th>TABLE 4. Comparison of Clinical Outcome of Debridement vs. Mini-Open Repair of Partial Rotator Cuff Tears</th>
<th>Assessment of Clinical Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>Comparison</td>
</tr>
<tr>
<td>-------</td>
<td>-------------</td>
</tr>
<tr>
<td>SC</td>
<td>Debridement of Partial Rotator Cuff Tear</td>
</tr>
<tr>
<td>Weber</td>
<td>Mini-open Repair of Partial Rotator Cuff Tear</td>
</tr>
</tbody>
</table>
reported satisfactory clinical outcomes postoperatively. There have been a considerable number of surgical technique articles describing various ways to perform a transtendon rotator cuff repair for a partial articular-sided tear.\textsuperscript{12, 25} Unfortunately, there are no prospective studies comparing transtendon repair versus takedown and repair. Although theoretical advantages exist in performing a transtendon repair, we are unable to make any conclusions that superior clinical outcomes are achieved when compared to takedown of the tear and repair.

**CONCLUSIONS**

On the basis of the available evidence, we were unable to conclude which of the three operative procedures for symptomatic partial articular sided rotator cuff tear results in the most favorable outcome. Every study that met our inclusion/exclusion criteria was a retrospective case series with differing outcome measures that did not allow making comparisons between the studies. Most studies reported satisfactory outcomes after debridement, transtendon repair, or tear takedown and repair. However, every study was a retrospective case series. In addition, different clinical outcome measures were used in each study making it difficult to draw conclusions. Future studies are recommended that prospectively evaluate repair versus debridement, or transtendon repair versus takedown and repair in a homogenous group of partial rotator cuff tears of the same depth and location.

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1. **Codman EA.** The Shoulder. Rupture of the Supraspinatus Tendon and Other Lesions in or About the Subacromial Bursa. privately printed 1934:478-80.


What Surgical Technique Provides the Best Outcome for Symptomatic Partial Articular-Sided Rotator Cuff Tears?


ABSTRACT
Injuries of the posteromedial corner of the knee are relatively common. These can be isolated or combined with other ligament lesions. In some cases the treatment of postero-medial corner injuries is controversial. After a brief description of the anatomy and biomechanics of the medial side of the knee, this paper reviews the indications for isolated and multiligamentous medial/posteromedial corner injuries both in the acute and in the chronic setting. In addition, the most common surgical techniques for repair and reconstruction are described in addition to outcomes based upon a review of the literature.

INTRODUCTION
Injuries to the medial collateral ligament (MCL) and posteromedial corner of the knee are very common and can be isolated or combined with other ligamentous lesions. A thorough understanding of the anatomy of the medial side of the knee is essential for a correct diagnosis and appropriate treatment. The high reparative potential of the MCL with conservative treatment and the complications (primarily knee stiffness) associated with surgical repair/reconstruction are at the base of the controversies regarding the treatment of medial/posteromedial ligamentous injuries. No decision algorithms are available and a wide variety of surgical techniques have been described regarding this topic. These include direct repair, capsular plication, and reconstruction procedures. The goal of this review is to discuss the indications, most common techniques, and outcomes of medial/posteromedial ligamentous injuries of the knee.

ANATOMY AND BIOMECHANICS
The anatomy of the medial side of the knee has been extensively described by LaPrade et al.1 The structures of the medial side of the knee include: 1) bony landmarks (medial epicondyle, adductor tubercle, gastrocnemius tubercle on the femur, medial tibial plateau, and the medial aspect of the patella), 2) ligaments (superficial medial collateral ligament, deep medial collateral ligament, posterior oblique ligament, medial patello-femoral ligament, and the postero-medial capsule), and 3) tendons (adductor magnus, medial head of the gastrocnemius, semimembranosus, and the pes anserinus). A thorough knowledge of the anatomy is essential in diagnosing and treating injuries to the medial side of the knee.

The superficial medial collateral ligament (sMCL) has one femoral and two tibial attachments (proximal and distal). The femoral attachment has an oval shape and is located 3.2 mm proximal and 4.8 mm posterior to the medial epicondyle. The proximal tibial attachment is primarily to soft tissues, mainly to the anterior arm of the semimembranosus tendon. The distal tibial attachment of the sMCL is just anterior to the posteromedial crest of the tibia (Fig 1). The average distance of the proximal tibial attachment is 12.2 mm from the tibial joint line. The average distance of the distal tibial attachment is 94.8 mm from the femoral attachment, and 61.2 mm from the tibial joint line. The average distance from the distal tibial attachment to proximal tibial attachment is 49.2 mm1.

The deep medial collateral ligament (dMCL) is a thickening of the medial joint capsule. The dMCL consists of the meniscofemoral (MF) and meniscotibial (MT) ligaments (Fig 2). The MF ligament is longer than the MT ligament and its attachment is located 15.1 mm posterior and distal to the medial epicondyle. The MT ligament is shorter, thicker and attaches just distal (3.2 mm average) to the cartilage of the medial tibial plateau1. The posterior oblique ligament (POL) consists of 3 fascial attachments: superficial, central (tibial), and capsular. The 3 attachments course off the distal aspect of the semimembranosus tendon mainly, but also off the medial meniscus, posteromedial tibia, and medial head of the gastrocnemius (Fig 3). On average, the POL attaches on the femur 7.7 mm distal and 6.4 mm posterior to the adductor tubercle and 1.4 mm distal and 2.9 mm anterior to the gastrocnemius tubercle1.
Biomechanically, the MCL represents the main restraint to valgus forces and a secondary restraint to external/internal rotation and posterior translation of the tibia. The sMCL provides the greatest stability to valgus forces over the entire range of motion. The contribution of the sMCL to internal rotation stability increases beyond 30° of knee flexion when the postero-medial capsule is slackened. Sectioning the dMCL, if the sMCL is intact, produces almost no changes in terms of medial stability. Conversely, the postero-medial capsule is in tension and provides some stability to valgus forces, posterior tibial translation, and internal rotation only with the knee extended. The POL is able to provide both secondary stability to tibial internal and external rotation at early knee flexion and posterior stability to the tibia in knee extension. The role of the POL becomes even more pronounced in the setting of MCL deficiency in both valgus and rotational stability.

**CLINICAL EXAMINATION AND IMAGING**

During the clinical evaluation, an accurate history will lead the practitioner to suspect a medial sided knee injury when the traumatic mechanism includes a valgus force. Abnormalities in the gait should be noticed and the knee is evaluated for hemarthrosis or malalignment. Palpation along the course of the MCL may demonstrate tenderness to palpation suggestive of an MCL injury. Tenderness over the adductor tubercle or proximal medial tibia may indicate injury at the origin or insertion sites of the MCL. Pain over the medial joint line may indicate an associated medial meniscus tear.

The stability of the knee is then tested in all planes in order to evaluate antero-posterior, lateral, and rotational instability. Anteromedial rotatory instability is detected by performing the anterior drawer test while holding the tibia in external rotation. Any evidence of anterior subluxation of the medial tibial plateau during a valgus stress test with the knee in 30 degrees of flexion might
also indicate the presence of anteromedial rotatory instability. Valgus stress should be performed at 0 and 30° of knee flexion. Although the American Medical Association classification is a valuable system, the authors prefer the Fetto & Marshall classification. The Fetto & Marshall classification divides medial sided knee injuries into: grade 1 (no valgus laxity), grade 2 (valgus laxity at 30° of flexion) and grade 3 (valgus laxity at 0° and 30°). As mentioned, valgus instability at 30° of flexion (when the postero-medial capsule is slackened) is suggestive of a tear of the sMCL. On the other hand, with valgus instability at full extension both sMCL and postero-medial capsule are likely to be torn.

Weight bearing radiographs of the knee are obtained in antero-posterior and lateral views. If valgus malalignment is present a weight bearing long leg radiograph is obtained.

MRI is helpful in diagnosing associated bone and soft tissue injuries (anterior and posterior cruciate ligaments, postero-lateral corner, and medial meniscus) as well as determining the location and extent of medial/postero-medial ligamentous injuries.

**Treatment Options**

Conservative treatment consists of a hinged knee brace with weight bearing as tolerated and crutches for initial pain relief. The patient can start isometric and range of motion exercises immediately. Crutches are discontinued when the patient can walk without limping.

The indications for the treatment of medial side injuries of the knee in the acute and chronic setting are summarized in Table 1 and 2 respectively. The tables describe the algorithm of treatment derived from the review of the literature, with the possible options for every specific scenario. Key points in the decision making are: 1) chronicity of the MCL rupture (acute is considered < 3 weeks, subacute 3-6 weeks, and chronic >6 weeks); 2) alignment; 3) the presence of bony avulsions; or 4) MCL entrapment. In the acute setting, a grade I or II MCL can be managed conservatively. Conservative treatment can also be indicated in grade III MCL tears with neutral or varus limb alignment. In there is severe valgus alignment, intraarticular MCL entrapment, or large bony avulsions an acute MCL repair is indicated. The treatment of combined anterior cruciate ligament and grade III MCL tears is controversial. The first option is to conservatively treat the MCL and after 3-4 weeks perform an ACL reconstruction. If the knee is still unstable medially after the ACL reconstruction, an MCL reconstruction or capsular procedure can be concurrently performed. Alternatively, an early ACL reconstruction can be performed with conservative management of the MCL, in order to allow MCL healing with a more stable knee. The third option is a combined early ACL reconstruction with an acute MCL repair. The treatment is controversial also in case of combined ACL, PCL, and grade III MCL injuries. The treatment options include: 1) conservative management of the MCL with...
delayed ACL/PCL reconstruction; 2) acute MCL repair combined with PCL reconstruction and delayed ACL reconstruction; or 3) acute MCL repair combined with ACL/PCL reconstruction.

In the chronic setting, a distal femoral varus osteotomy should be considered if isolated medial instability is associated with valgus limb alignment. In the case of combined valgus and anterior instability, ACL reconstruction is performed and the knee is evaluated intraoperatively for medial laxity. If the knee shows at full extension a medial opening greater than 4 mm compared to the contralateral side, capsular procedures with or without augmentation or MCL reconstruction are indicated. In the case of combined valgus and anterior instability, ACL reconstruction is performed and the knee is evaluated intraoperatively for medial laxity. If the knee shows at full extension a medial opening greater than 4 mm compared to the contralateral side, capsular procedures or MCL reconstruction can be considered.

**TABLE 1. Medial knee instability: indications in the acute setting.**

<table>
<thead>
<tr>
<th>GRADE</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-II</td>
<td>CONSERVATIVE TREATMENT</td>
</tr>
<tr>
<td>III</td>
<td>Normal or varus alignment</td>
</tr>
<tr>
<td></td>
<td>Severe valgus alignment or intraarticular MCL entrapment or large bony avulsions</td>
</tr>
<tr>
<td></td>
<td>ACUTE REPAIR</td>
</tr>
</tbody>
</table>

**TABLE 2. Medial knee instability: indications in the chronic setting.**

<table>
<thead>
<tr>
<th>Alignment</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>VALGUS</td>
<td>DISTAL FEMORAL VARUS OSTEOTOMY</td>
</tr>
<tr>
<td>NORMAL OR VARUS ALIGNMENT</td>
<td>CAPSULAR PROCEDURES +/- AUTO OR ALLOGRAFT AUGMENTATION</td>
</tr>
<tr>
<td>ACL RECONSTR + INTRAOP EVALUATION OF MEDIAL LAXITY AT FULL EXTENSION, COMPARED TO CONTRALATERAL SIDE</td>
<td>MCL RECONSTRUCTION</td>
</tr>
<tr>
<td>VALGUS + ANTERIOR INSTABILITY</td>
<td>MCL RECONSTR. OR CAPSULAR PROC. +/- AUGMENTATION (if &gt; 4 mm opening)</td>
</tr>
</tbody>
</table>
Many techniques have been described for the treatment of medial and posteromedial ligamentous injuries of the knee, including: 1) direct repair for selected acute cases, as described above; 2) capsular procedures, which consist in re-tensioning of the lax structures in the subacute/chronic scenarios; and 3) reconstruction procedures. Several different techniques described in the literature are reviewed below7-17. Currently there is no evidence regarding the surgical timing and treatment decision making with regards to which type of procedure or technique to use (i.e. capsular procedures versus reconstruction).

SURGICAL APPROACH

Examination under anesthesia is performed to completely assess the injury. Arthroscopy can be used to rule out any other associated lesions and to determine the site of the dMCL injury. In the acute setting, arthroscopy should be performed quickly and with gravity inflow, to minimize fluid extravasation. A hokey-stick (or longitudinal) incision is made from the medial proximal tibia to the medial femoral epicondyle, curving posteriorly in line with the intermuscular septum. For isolated repairs either distally or proximally, a more limited approach is used. In case of MCL reconstruction, some authors prefer a 2 incision approach to the femur and tibia. Attention should be paid to preserve the saphenous nerve. The crural and sartorial fascia is incised longitudinally. Hematoma is removed. The injured structures are then identified7.


The surgical approach and dissection are carried out as described for the repair. The meniscus and the posteromedial structures are visualized and probed for laxity. The goal of this technique is to remove the laxity from the injured posteromedial structures by creating increased distance between the origin and insertion. The posteromedial capsule needs to be released from the meniscus and re-sutured to it in a more advanced position (Fig 5A,B). Then the lax structures are attached to an adjacent intact structure in a pants-over-vest fashion. Occasionally, mid-substance and tibial-sided injuries require augmentation, due to the poor soft tissue quality. The sMCL is fixed at 30° of knee flexion7.

CAPSULAR PROCEDURES

Re-tensioning of the posteromedial structures

The surgical approach and dissection are carried out as described for the repair. The meniscus and the posteromedial structures are visualized and probed for laxity. The goal of this technique is to remove the laxity from the injured posteromedial structures by creating increased distance between the origin and insertion. The posteromedial capsule needs to be released from the meniscus and re-sutured to it in a more advanced position (Fig 5A,B). Then the lax structures are attached to an adjacent intact structure in a pants-over-vest fashion (i.e. lax POL is advanced forward and sutured to the intact sMCL)9,10(Fig 5C,D).
En masse elevation

This procedure is indicated when a generalized laxity of the postero-medial structures is present. The weakest point (femoral or tibial) should be identified. The structures at the weakest attachment must be released as an entire tendon/ligament unit (en masse) (Fig 6A,B). This unit must be armed with sutures, re-tensioned, and fixed back to an isometric point on the bone. The bone around the isometric point is “roughed-up” until good bleeding is achieved (Fig 6C). Fixation can be achieved with staples or suture anchors9. (Fig 6D)

RECONSTRUCTION TECHNIQUES

Kim’s technique

The semitendinosus is harvested, preserving the tibial attachment (Fig 7B). A K wire is inserted on the anterosuperior border of the medial femoral epicondyle. The semitendinosus tendon is looped around the wire and isometricity (<2 mm migration) is tested by pulling the suture at the tendon and moving the knee through a full ROM (Fig 7C). A 6.5 mm cancellous screw and an 18 mm washer are placed through a hole, drilled 9 mm (the radius of a washer) proximal to the isometric point (Fig 7D). Decortication is performed around the drill hole. After manual tensioning of the graft, the screw is tightened with the knee in 30° of flexion and varus stress. The free end of the graft is pulled under the direct
Treatment of medial and posteromedial knee instability: indications, techniques, and review of the results.

Lind’s technique

Incision, semitendinosus harvesting, and isometricity evaluation are as described by Kim. A tunnel (diameter of the double-looped tendon) is drilled in the isometric point. The tendon loop is then armed with a baseball suture, passed into the tunnel and fixed with an interference screw (same diameter as the tunnel) (Fig 9B). This is performed with the knee in 10° of flexion and neutral rotation. A tibial tunnel (same size of the graft) is then drilled in the posterior corner of the medial tibial condyle from anterior to posterior. The drill hole is aimed to exit 10 mm below the tibial plateau, posterior and lateral to the semimembranosus insertion. The free end of the graft is passed through the posterior tibial tunnel opening, and fixed here with an interference screw (same diameter as the tunnel) to reconstruct the posteromedial corner (Fig 9C,D). This is tightened with the knee in 60° of flexion and neutral rotation.13

Yoshiya’s technique.

Two skin incisions (6-7 cm) are made at the proximal and distal insertions of the sMCL. The semitendinosus and gracilis tendons are harvested, detached distally, and each of them made into a single- or double-stranded tendon graft. Two sutures with an extracortical fixation device are attached to 1 end of the graft, while stay sutures are placed at the other end. The center of the insertion of the sMCL is selected as the distal attachment of the neoligament, while the proximal attachment is the medial epicondyle. Isometricity is evaluated with adjustments mainly on the femoral side (Fig 10B). Two sutures with an extracortical fixation device are attached to 1 end of the graft, while stay sutures are placed at the other end. The center of the insertion of the sMCL is selected as the distal attachment of the neoligament, while the proximal attachment is the medial epicondyle. Isometricity is evaluated with adjustments mainly on the femoral side (Fig 10B). The distal end is fixed with the extracortical device, and the proximal end with an interference screw or soft tissue screw and washer with the knee in 30° of flexion and a varus stress) (Fig 10C).14

Stannard’s technique

In Stannard’s modification of Kim’s technique, the free end of the semitendinosus is sutured to the intact insertion of the semitendinosus itself on the tibia (Fig 8B,C). The graft is tensioned with the knee in approximately 40° of flexion and a slight varus stress.

head of the semimembranosus tendon and sutured to the tendon itself in 30° of knee flexion.11
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Coobs, Wijdicks et al. technique.

The technique consists of a reconstruction of the two main structures (sMCL and POL) of the medial side of the knee with use of two separate grafts with four reconstruction tunnels (Fig 11B,C,D).

Allografts or gracilis and semitendinosus autografts can be used. Isometricity is evaluated with K wires and sutures for both bundles. Correctly sized tunnels are drilled at the isometric points. The sMCL is tightened at 30° of knee flexion and the POL is tightened at 0°. Fixation is achieved with interference screws15,16.

Borden’s technique

With a 2-incision approach, a passing pin is drilled into the medial epicondyle. Next, the suture is looped over the passing pin in the femoral epicondyle. The suture is then passed along the MCL and pulled from the tibial incision.

Isometry is tested by holding the suture at the anterior aspect of the MCL tibial insertion and moving the knee through a full range of motion. A pin is placed into the tibia at the isometric point. The hamstring tendons are then retracted posteromedially. The isometric point for a posterior tibial tunnel is then determined in a similar fashion. A second Steinmann pin is placed.

A tibialis anterior tendon is prepared in a double-bundle loop (Fig 12B). The femoral tunnel is drilled to a depth of 30 mm, and the tibial tunnels to a depth of 25 mm (same size as the graft ends). The graft is then pulled into the femoral tunnel and fixed with an interference screw (Fig 12C). The free ends of the allograft are then passed down the soft-tissue plane and retrieved from the tibial incision (Fig 12D). The posterior bundle is fixed with an interference screw with the knee in internal rotation and 60° of flexion. The anterior bundle is fixed in the same way, but with the leg internally rotated and flexed to 30°17.

Tips to find the isometric point

Finding the isometric point on the tibia, but mostly on the femur is essential to achieve good stability and avoid stiffness after MCL reconstruction. Three different methods can be used to find the isometric points:

1) Two K wires can be positioned at the presumptive isometric points. A suture is then looped around the K wires and held with a Kelly clamp. In case of isometricity the suture should have the same tension throughout the full range of motion (Fig. 13A).
Treatment of medial and posteromedial knee instability: indications, techniques, and review of the results.

2) Alternatively, when a hamstring graft is left attached distally, a k wire is positioned at the isometric point on the femur, the graft is looped around it and marked with a surgical marker. The knee is then taken through a full range of motion. Displacement of the marks with respect to the K wire greater than 2 mm indicates a non isometric point on the femur (Fig. 13B).

3) Last, the graft can be looped around the K wire positioned at the presumptive isometric point on the femur and held with a Kelly clamp. If the graft is isometric, it will show uniform tension throughout a full range of motion (Fig. 13C).

Authors’ preferred technique and post-operative rehabilitation

The authors’ preferred technique is Kim’s procedure. This technique is favored because it is easy, reliable, inexpensive, and allows for both sMCL and POL reconstruction. Although controversies exist regarding the most reliable surgical technique for reconstruction, isometricity is essential to obtain favorable results.

Post-operatively, the patient is kept in a hinged knee brace with protected weight bearing. Passive range of motion from 0 to 90 degrees is begun immediately. Hyperextension and flexion over 90 degrees should be avoided during the first 2 weeks. Isometric and closed kinetic chain strengthening are allowed immediately. Full range of motion is allowed 2 weeks after surgery, and full weight bearing is allowed 6 weeks after surgery. Return to full activities is generally allowed 6 months after surgery.

OUTCOMES

The outcomes are summarized in Table 3. Derscheid et al18 described the results of conservative treatment for acute grade I and II MCL injuries in 51 football players. They reported excellent outcomes for both groups, with a slightly longer recovery for grade II injuries. Similar results were reported by Lundberg19. Indelicato et al20 showed good or excellent results with conservative treatment for acute grade III injuries. Reider22 described similar results between early functional rehabilitation and surgery or immobilization for acute grade III MCL injuries. On the other hand Kannus et al. 21 showed poor results of conservative treatment for grade III injuries, with subsequent medial instability, dysfunction of the ACL, muscle weakness, and arthritis. Hughston et al23,24 reported excellent results with acute surgical repair of the medial side of the knee for anteromedial instability 2+ or more. Good results were reported in the acute and

FIGURE 12. A) Borden’s technique (see text). B) A tibialis anterior tendon allograft is prepared in a double-bundle loop. C) The graft is pulled into the femoral tunnel and fixed with an interference screw. D) The free ends of the allograft are passed down the soft-tissue plane and retrieved from the tibial incision.

FIGURE 13. Techniques to find the isometric points (see text).
As shown in the outcomes table, the studies available in the literature are mostly case series, with heterogeneous study groups (with or without associated ligamentous injuries), and using different medial laxity grading systems or outcome scores. In light of these considerations, comparisons between the results reported between the studies are difficult to make.

CONCLUSION

Understanding of the anatomy of the medial side of the knee, correct indications, and precise surgical technique are essential to achieve good results in the treatment of medial/postero-medial knee instability. The majority of patients who sustain MCL injuries of varying severity can achieve pre-injury activity level with non-operative treatment alone. However, the treatment of grade III MCL injuries (with gross valgus instability at 0° of flexion) is still controversial. The most severe injuries (especially with severe valgus alignment, intra-articular MCL entrapment, large bony avulsions, or multiple ligament involvement) may require acute operative repair or augmentation. In addition, surgical reconstruction is indicated for isolated symptomatic chronic MCL laxity.

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Treatment of medial and posteromedial knee instability: indications, techniques, and review of the results.

ABSTRACT
The natural history and optimal treatment for idiopathic toe walking are unknown. The literature is full of poorly documented treatment regimens with few even medium term follow up studies. The senior author reports his nearly 30 year approach to this disorder and his failed attempt to perform a follow up study of his particular treatment regimen. We conclude with our considered interpretation of the present state of knowledge about idiopathic toe walking and our treatment opinions.

INTRODUCTION
What should one do when confronted by a 4 year old entirely normal child who attends clinic with his parents because he walks on his/her toes 90% of the time? Lovell and Winter’s Pediatric Orthopaedics, sixth edition states the following:

“The treatment of ITW [idiopathic toe walking] begins with instructions given to the parents regarding the importance of a long-term commitment to assisting the child with both heel cord stretching and dorsiflexion strengthening exercises…. If toe-walking persists, serial heel cord dorsiflexion casts should be considered….After casting, articulated AFOs with plantar-flexion stops are used fulltime…. If the use of serial stretching casts does not realize a satisfactory clinical improvement in the tendency to toe-walk, then heel cord lengthening procedures will be necessary to effect a change in gait. Persistent toe-walking secondary to a heel core contracture can potentiate both forefoot splay and a disproportionately wide foot compared to the heel. Standard footwear may not accommodate the wide forefoot and narrow heel. External tibial torsion frequently develops to compensate for the lack of foot flat contact. This external tibial torsion deformity becomes more obvious once the heel cord has been lengthened. It may be severe enough to warrant corrective osteotomy.”1

Cincinnati Children’s Hospital Medical Center expended great effort and developed an Evidence-Based Care Guideline for Management of Idiopathic Toe Walking. They recommended a similar sequence of PT, casts, AFO and TAL for failures.2 Treatment was determined largely by amount of passive dorsiflexion measurements and percentage of time spent toe-walking. A podiatric review recommended a similar program.3

On the other hand, a summary of the evidence for “What is the appropriate evaluation and treatment of children who are toe walkers?” in the Journal of Family Practice concluded simply that “There is no convincing evidence that any treatment is necessary for toe-walking.”4 Others have reached similar conclusions.5,6 Middle ground suggesting that treatment is rarely needed are common.7 The literature is unclear on the natural history of ITW, whether non-operative treatment is effective, and whether treatment is ever needed.

Since beginning Practice in 1984, the senior author has used the same treatment algorithm for ITW. Children who walked on their toes and were 3 years old (younger if there was a fixed equinus contracture) were treated with 6 weeks in walking plaster casts. If serial casts were necessary to gain neutral dorsiflexion, the 6 weeks began after the serial casts. If the casting failed, an AFO with neutral plantar-flexion stop was used until the child out-grew the device or the family abandoned it. If both these non-operative treatments failed, a tendon-Achilles lengthening was offered. We recently attempted to ascertain the effectiveness of this treatment protocol. Typically, after each treatment, the patient was given a PRN return and the parents were asked to call and make a new appointment if their child began toe walking again. Therefore, we identified 98 patients and sent questionnaires about the effectiveness of my treatment. We received only 14 responses to my questionnaire.
Idiopathic Toe Walking: To Treat or Not to Treat, That Is the Question

Therefore, we are unable to determine the effectiveness of my treatment. This prompted us to review the literature once again to try to determine what treatment, if any, is appropriate for ITW.

MATERIAL AND METHODS FOR STUDY OF SENIOR AUTHOR’S PATIENT COHORT

After obtaining IRB approval, a search of our electronic record for patients coded for “toe walking” was done. Many children with ITW were probably coded as “leg deformity” or some other code, but we did not attempt to find these as we had sufficient patients coded as “toe walking” for a reasonable case series study. We reviewed the charts to eliminate all neurological and traumatic causes of toe walking and identified 98 children with ITW. The treatment was abstracted from the medical record. A questionnaire (Table 1) was sent to the last address in the medical record along with consent forms. When a questionnaire was returned to a wrong address, the commercial address service Intelius was used to find a more recent address. We received 14 completed questionnaires.

RESULTS OF THE STUDY OF THE SENIOR AUTHOR’S PATIENT COHORT

Fourteen of ninety-eight patients responded. The mean age treatment was 4 years 8 months (range 2-9 years). Mean age at followup was 10 years 6 months (range 5-21) Of 10 patients treated by 6 weeks of short leg casts, 5 permanently stopped toe walking and 5 did not. Of 3 patients treated with 6 weeks of short leg cast and botox, all continued to toe walk. The one patient who presented with AFOs prescribed by a neurologist continued to toe walk. Of two patients treated with AFO after failed short leg cast, one quit toe walking and one did not. Of 3 patients treated with AFO after failed short leg cast and botox, 2 quit toe walking and one did not. Of two patients who underwent TAL after failed short leg cast and AFO, one quit toe walking and one did not.

Return to toe walking after treatment with a cast or AFO occurred immediately to 6 months after stopping treatment. One patient quit toe walking on his own 2 years after treatment with casts. No patient had treatment elsewhere.

At present eight children were not toe-walking at an average age of 12 years (range 7-21 years) and six children continued to toe walk at an average age of 8 years and 6 months (range 5-14 years). No present toe walkers reported pain or any other foot problem.

MATERIALS AND METHODS FOR ITW LITERATURE REVIEW

A Pub Med review of “idiopathic toe walking’ articles in English was performed. The bibliographies of these articles were perused for further references. Articles that reported outcomes of treatment were included.

RESULTS OF ITW LITERATURE REVIEW

Review of treatment literature is summarized in Tables 2-5.

Natural history (Table 2)

Of 103 subjects in three studies who were never treated (except some with physical therapy) 45 resolved and 53 did not. One study of 48 patients had 40 patients continuing to toe walk but the average age at presentation was 3.2 years and the average followup was only 2 years. A study with 20 year follow up had 8 subjects resolve and one continue to toe walk. The third study had 29 patients resolve with followup of 3-8 years and 12 continue to toe walk at a followup of 9-14 years.

<table>
<thead>
<tr>
<th>TABLE 1: Questionnaire</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How old is your child now? ________</td>
</tr>
<tr>
<td>2. Has your child walked with feet flat on the ground since treatment by Dr. Dietz?</td>
</tr>
<tr>
<td>□ Yes □ No</td>
</tr>
<tr>
<td>If NO:</td>
</tr>
<tr>
<td>a. How long after treatment did your child start toe-walking again?</td>
</tr>
<tr>
<td>□ Right after treatment stopped</td>
</tr>
<tr>
<td>□ Number of weeks after treatment stopped ________</td>
</tr>
<tr>
<td>□ Number of months after treatment stopped ________</td>
</tr>
<tr>
<td>□ Can’t remember</td>
</tr>
<tr>
<td>3. Did your child eventually stop toe-walking on his/her own?</td>
</tr>
<tr>
<td>□ Yes (at what age? ________) □ No</td>
</tr>
<tr>
<td>4. Did your child have other treatment AFTER treatment by Dr. Dietz?</td>
</tr>
<tr>
<td>□ Yes □ No</td>
</tr>
<tr>
<td>If yes, what treatment? __________________________</td>
</tr>
<tr>
<td>__________________________</td>
</tr>
<tr>
<td>Did this treatment work in eliminating toe-walking?</td>
</tr>
<tr>
<td>□ Yes □ No</td>
</tr>
<tr>
<td>5. Is your child presently toe-walking?</td>
</tr>
<tr>
<td>□ Yes □ No</td>
</tr>
<tr>
<td>If Yes, Does the toe-walking cause problems:</td>
</tr>
<tr>
<td>□ Yes □ No</td>
</tr>
<tr>
<td>What activities does it limit? __________________________</td>
</tr>
<tr>
<td>__________________________</td>
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<td>__________________________</td>
</tr>
</tbody>
</table>
Casting and/or AFO (Table 3)

Of 63 patients treated variably with casts and/or AFOs, 45 resolved and 16 continued to toe walk. Casting was 3-10 weeks. AFO treatment length was not clear. Followup was an average of 6 weeks in one study and 14 months in another. The other studies had followup averages of 23 years and 11 years but comprised a total of only 10 patients.
Triceps surae lengthening (Table 5)

Of 45 children treated surgically in 4 studies who reported whether the children quit toe walking or not, all were reported to have resolved with the caveat that 5 of 17 children in 2 studies occasionally toe walked and of 13 children in another study “some older children walked on their toes occasionally”. One study of 15 patients reported that 10 parents were “satisfied” and 5 were “neutral” or “dissatisfied”. A gait analysis outcome paper reported that all 14 had improved but not normal gait parameters. A final paper reported that 14 patients surgically treated had increased muscle lengths.

DISCUSSION

Idiopathic toe walking is not rare in a pediatric orthopaedic clinic and it often, but not always, engenders significant concern for parents. What do we know? The natural history is not known. It appears clear that adults who were toe walkers do not continue to walk in the sever equinus (“ballet position”) that causes much of the concern in childhood. Anecdotally, adult toe walkers have a “bouncing” or “mincing” gait with less than normal heel contact during stance phase. Whether this results in any problems is unknown. The adult foot and ankle surgeons at our institution do not see patients with forefoot or midfoot problems or Achilles tendonitis with ankle surgeons at our institution. It is quite possible that these treatments speed resolution of toe walking in some children who were destined to stop toe walking anyway. Since they are non or minimally invasive, an argument can be made to try any or all of them if the alternative is surgical lengthening. On the other hand, there are costs (time, direct expenses for casts/braces, doctor visits) that are not insubstantial in an aggressive non-operative approach that is not proven to be effective. Surgery seems to be effective in most patients in eliminating or improving toe walking. The gait is not always normalized and sub-clinical weakness is still apparent after a year. The risks of surgery are small and the expense is significant.

CONCLUSIONS

1. We believe idiopathic toe walking should be considered a cosmetic deformity and treated only if the gait troubles the family.
2. Non-surgical treatment can be used in surgery-averse families even though its effectiveness is uncertain.
3. Surgical treatment is a reasonable choice for families desiring rapid resolution of the toe walking.

BIBLIOGRAPHY


SAPHO SYNDROME – A PICTORIAL ASSAY

Lokesh Khanna M.D.; Georges Y. El-khoury, M.D.

ABSTRACT:
SAPHO (synovitis, acne, pustulosis, hyperostosis and osteitis) syndrome is a distinct clinical entity representing involvement of the musculoskeletal and dermatologic systems. It is well known to rheumatologists because of characteristic skin manifestations and polyarthropathy. However, few reports exist in the orthopaedic literature. It is important to be aware of SAPHO syndrome as it can mimic some of the more common disease entities such as infection, tumor, and other inflammatory arthropathies. Anterior chest wall pain centered at sternoclavicular and sternocostal joints is an important and characteristic clinical finding which can point to its diagnosis. A patient may undergo different diagnostic tests and invasive procedures such as biopsies before a diagnosis is made. Imaging can be helpful by offering a detailed evaluation of the abnormalities. More importantly it helps in revealing subclinical foci of involvement due to the polyostotic nature of the disease. The treatment is mostly nonsurgical. NSAIDS are the first line agents. However multiple new agents are being used for refractory cases. Surgery is reserved to treat complications.

INTRODUCTION
The association between musculoskeletal and skin lesions was first described by Windam et al in 1961 [1]. SAPHO stands for synovitis, acne, pustulosis, hyperostosis and osteitis. It is used to describe a combination of inflammatory conditions involving joints and characteristic skin lesions. The acronym was first coined by the French rheumatologist Chamot, in 1987, to describe a syndrome of acne, pustulosis and hyperostosis [2]. Since then it has been referred to by different names including sternoclavicular hyperostosis, non-bacterial osteitis, chronic recurrent multifocal osteomyelitis (CRMO), pustulotic arthro-ostitis, and spondylarthritis hyperostotica pustulo-psoriatica [3, 4, 5, 6, 7]. It is important to be aware of different manifestations of this syndrome as it can have clinical features identical to more common and more recognized diseases such as infections, seronegative spondyloarthropathies, and tumors. A patient may undergo multiple diagnostic tests including biopsies before a correct diagnosis is made. SAPHO syndrome is well known to dermatologists and rheumatologists, but there are only few reports in the orthopaedic literature [8].

CLINICAL FEATURES
SAPHO syndrome can affect all age groups from childhood to adulthood. There is a slightly higher incidence in the female population [3, 5, 6, 7]. Most of the reports have come from Japan and Europe. This may be due to increased awareness in these areas, rather than a higher incidence [8, 9]. Characteristic skin lesions include severe palmar and plantar pustulosis (PPP) along with severe acne (acne conglobata) which may represent a form of psoriasis. SAPHO has a variable clinical course with remissions and relapses. The skin manifestations and skeletal abnormalities may not coexist and may be separated by many years [14, 15].

The affected individuals usually present with pain, swelling, and limitations of movement in the affected joints. Although patients may present with a single site of involvement initially, a thorough search should be made to evaluate for the presence of subclinical foci due to the polyostotic nature of the disease. The characteristic and most common feature is anterior chest wall pain. Children can present with extremity pain due to involvement of long bones. Pain is usually subacute to chronic; however, it can be debilitating, can affect nighttime sleep, and can be accompanied by fever [7, 8, 9]. The lab tests can be normal or may show elevated inflammatory markers. Patients with spinal involvement can present with numbness and radicular pain. The spinal lesions in SAPHO syndrome generally have a good prognosis and rarely cause neurological deterioration [9]. However, vertebral destruction may result in a kyphotic deformity or quadriplegia in severe cases [9, 10]. There have been multiple reports of mandible and temporomandibular joint involvement presenting with recurrent pain, swelling and limitation of movement at the jaw progressing to ankylosis [11, 12, 13].

Corresponding Author: Georges Y. El-Khoury, M.D., F.A.C.R.
Professor of Radiology and Orthopaedics
Director, Musculoskeletal Radiology Section
Department of Radiology
The University of Iowa
200 Hawkins Drive
Iowa City, IA 52242, U.S.A.
Telephone: (319) 356-3654
Fax: (319) 356-2220
**IMAGING FINDINGS**

Imaging plays an important role due to the characteristic osteoarticular manifestations which can help in determining the diagnosis. Most patients show polyostotic involvement. The sternoclavicular junction is the most common site of involvement in adults, followed by the spine and sacroiliac joints. The sternoclavicular, costochondral and manubrioisternal joints are involved in decreasing order of frequency [20-24].

**Radiographs**

On radiographs, there is bone expansion and medullary canal stenosis, which results in diffuse thickening of the periosteum, cortex and endosteum. There may be accompanying osteolysis and osteosclerosis [16,17]. Ossification of the costoclavicular ligament and hyperostosis at the sternal end of the first ribs are important early findings (Figure 1). The joint involvement is characterized by arthritis with joint space narrowing. There can be associated bone erosions and periarticular osteopenia. Ankylosis may be present and brings pain.
50 year old man presented with trauma and back pain. (a) Radiograph of the lumbar spine showed sclerotic areas in multiple vertebral bodies. These were initially suspected to be sclerotic metastases. (b) A bone scan obtained showed high uptake in the sacroiliac joints and lumbar spine. (c) A sagittal reformatted image of the lumbar spine showed sclerotic lesions and erosions centered on the corners of vertebral bodies and adjacent end plates. No associated soft tissue mass was seen. Corner erosions are one of the characteristic features of SAPHO. (d) to (f) MRI of lumbar spine including sagittal T1, T2 and T1 fat-sat contrast images showed corner lesions to be hypointense on T1, hyperintense on T2 with contrast enhancement. There is no abnormal signal in disc or any associated fluid collection which rules out an infectious etiology. (g) MRI Pelvis axial T2 fat suppressed image centered at SI joints showed edema around the bilateral sacroiliac joints, more severe on right side.

Sacroiliitis is seen in up to 50% of patients and is usually unilateral with erosions and sclerosis along the iliac side of the joint [17, 26] (Figures 2, 3). Although all the abnormalities can be seen on plain radiographs, CT is the modality of choice to determine the extent of the lesions.

In children and adolescents, the metaphyses of long bones, followed by the clavicles, are the most commonly involved areas. The femur and tibia are the most common sites for long bone involvement (Figure 4). The clavicle is the most common site of anterior chest wall involvement, starting medially and extending laterally.

The spine is the second most common site of involvement in children and adults, with the thoracic spine most commonly affected [9, 10, 25]. The lesions may start at the vertebral body or end plates [17] (Figure 2, 3). Maugars et al. proposed that lesions begin with the enthesis and lead to osteolysis, erosion, synovitis, hyperostosis, and finally synostosis followed by ankylosis and reduction of hyperostosis [26]. Nonspecific spondylitis and diskitis are the most common imaging findings (Figures 2d to 2f).

**Magnetic Resonance Imaging**

MRI is helpful in revealing subclinical foci and to identify active lesions by the presence of bone marrow edema on water sensitive sequences such as T2 weighted and STIR. The bony changes may extend to involve adjacent soft tissues on MRI (Figures 1f and 1g).

In the spine, high T2 signal in the disc, vertebral sclerosis, hyperostosis, and paravertebral ossification can be seen. Vertebral body corner erosions may be seen which appear low on T1 and high on T2 weighted.
sequences and with gadolinium enhancement [27, 28]. Loss of vertebral body height may result in a kyphotic deformity. Lack of abscess formation, sequestra, or paravertebral soft tissue involvement helps differentiate SAPHO from pyogenic spondylodiskitis [27, 28].

Scintigraphy

Whole body scintigraphy can also be useful for identifying subclinical foci [18]. 18FDG PET/CT has been used to differentiate active and inactive lesions. It can also distinguish lesions in SAPHO from pyogenic spondylodiskitis [19]. Symmetric high radionuclide uptake in the sternocostoclavicular joints can be seen on bone scan termed as “bull’s head sign” [20].

Etiology and pathogenesis

Various hypotheses have been proposed to explain the cause of SAPHO syndrome. The foremost among them is an infectious etiology. Propionibacterium acnes, an anaerobic saprophyte found in human skin has been isolated from the biopsy specimens of bone and synovium [23, 24, 29]. Despite these few case reports, antibiotic trials have been found to be ineffective [18].

There have been suggestions in the literature of a possible link to seronegative spondyloarthropathies [9, 17, 24, 29]. Paravertebral ossification along with palmar plantar pustulosis point to an association with psoriasis [26, 27, 28]. HLA B27 may be positive in up to 30% of SAPHO patients [17].

Figure 3. Spondylodiskitis and sacroiliitis in SAPHO syndrome. 46 year old female presented to the emergency treatment center with acute chest pain and had a chest CT done to rule out pulmonary embolism. (a, b) There were multiple areas of hyperostosis and sclerosis in the manubrium, clavicle and first rib on the left side. (c) The sagittal reformatted image of the thoracic spine showed sclerotic lesions in the adjacent vertebral bodies. Disc spaces are well preserved. The spine is the second most common site of involvement in children and adults. These were earlier diagnosed as suspicious for metastatic disease. The patient had no history of cancer and further investigations revealed no focus of a primary tumor. (d) The Ferguson view of the sacroiliac joints and (e) a CT pelvis showed sclerosis and erosions in the bilateral sacroiliac joints, more severe on left side. Sacroiliac involvement in SAPHO is either unilateral or bilateral asymmetric, mainly involving the iliac side of the SI joint. This patient was also found to have palmar and plantar pustulosis.
Figure 4. Hyperostosis and osteitis involving the long bones in SAPHO syndrome. 21 year old female presenting with pain in both legs. (a) Radiograph of both knees showed bony expansion and new bone formation (hyperostosis) with sclerosis. Long bone involvement is more common in pediatric patients. (b) Bone Scan showed increased uptake in both the distal femur diaphysis. (c) and (d) MRI showed thick periosteal reaction along with marrow edema (osteitis) in both femora. (e) to (h) follow up imaging studies after an year including radiographs of both knees, a bone scan and MRI of both femora respectively; showed significantly decreased disease activity after anti-TNF factor treatment.
DIFFERENTIAL DIAGNOSIS

The clinical findings of SAPHO can resemble other diseases such as osteomyelitis, osteosarcoma, Ewing Sarcoma, Paget’s disease, metastases, osteitis conden- sants of the clavicle, and POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes) [30, 31]. However there are some characteristic features which can raise the suspicion and help in reaching a proper diagnosis. SAPHO should be strongly suspected in patients with multiple areas of bony abnormalities which may include joints, axial and appendicular skeleton along with anterior chest wall pain, with unremarkable lab tests and no history of inflammatory arthropathy or primary cancer. Imaging studies are the best next step to further evaluate the lesions and reveal subclinical foci.

TREATMENT

The treatment of SAPHO syndrome is empirical and is mainly symptomatic. NSAIDS are the mainstay of treatment [6,7,8,14]. Corticosteroids, colchicines, sulfasalazines, and methotrexate are used as second-line agents. Antibiotics, calcitonin, and anti-TNF agents are used for refractory cases including persistent bone lesions including osteitis. Oral and intravenous bisphosphonates have been tried successfully [32]. The spondylitis in SAPHO syndrome generally has a good prognosis treated conservatively. However, it may cause severe destruction rapidly, which may be best treated surgically [9]. Mandibular involvement has been treated with hyperbaric oxygen therapy and minor surgical procedures such as decortication and curettage. Wide resection is reserved for patients with deformity, loss of function, increasing pain, and failure of conservative treatments [33].

CONCLUSION

SAPHO is a distinct clinical entity with characteristic imaging features. It is crucial to be aware of its manifestations so as to diagnose it and differentiate it from other diseases. It is important to remember that the skin manifestations and bony involvement may not be present at the same time.

REFERENCES

SAPHO Syndrome – A Pictorial Assay


ABSTRACT
Trochlear dysplasia is a risk factor for patellofemoral instability. Trochleoplasty involves reshaping the trochlear groove to provide increased patellofemoral stability. We obtained post-operative radiographs, MRI, and outcome scores in 6 patients who underwent this procedure. All 6 of the patients were satisfied with their outcome following trochleoplasty with no recurrent instability events. Mean bony sulcus angles decreased from 148 degrees to 129 degrees. However, 4 of the 6 patients reported anterior knee pain. Similar to previously published studies, trochleoplasty can reliably improve patellofemoral stability in patients with severe trochlear dysplasia, but a high percentage of patients will have pain postoperatively.

INTRODUCTION
Trochlear dysplasia is characterized by a shallow, flattened trochlear groove. A study done by Brattstroem in the 1960s observed an association between trochlear dysplasia and patellofemoral instability. This relationship has been studied to a much greater extent in Europe than it has in the United States. One form of treatment for patellofemoral instability in patients with severe trochlear dysplasia is a surgical procedure called trochleoplasty, in which the trochlear groove is reshaped to improve patellar stability. Although the efficacy of trochleoplasty has been shown to be high, many patients who have undergone this procedure have reported residual pain and degenerative joint disease postoperatively. This study seeks to evaluate the long term outcomes for patients who have undergone trochleoplasty.

Patellofemoral Anatomy and Biomechanics
The patellofemoral joint consists of the articulation between the patella and the trochlea. The trochlea is a very complex osseus structure that varies in morphology from proximal to distal. Specifically, the lateral wall is highest proximally and decreases in height distally. In addition, there is extensive variability between individuals with regards to trochlear morphology. Bony and cartilage sulcus angles can be used to evaluate the anatomy of the trochlear groove. MRI has been advocated for visualization of the trochlea because chondral geometry allows for more accurate representation of trochlear anatomy. Stability of the patellofemoral joint is achieved by the coordinated action of static, dynamic, and osseous constraints. Static constraints include the medial retinacular structures, the MPFL and the medial patellotibial ligament, while the primary dynamic constraint is the vastus medialis obliquus muscle.
During full extension of the knee, the patella is proximal to the trochlear groove. In the first 20° to 30° of knee flexion, the MPFL guides the patella into the trochlear groove. When the knee has achieved 30° of flexion, the patella should be entirely constrained by the trochlear groove with less than 1 cm of lateral translation. At this point, the contribution of soft tissue constraints toward patellar stability becomes minimized, and the osseous constraint becomes the chief stabilizer of the joint. The height and angle of the trochlear groove provide the primary constraint against lateral patellar movement during continued knee flexion.

Patellofemoral Instability
Several anatomic phenomena can contribute to patellofemoral instability. Deficient proximal medial restraints, trochlea dysplasia, patella alta, and malalignment (TT-TG > 20 mm) are risk factors for patellofemoral instability. A deficiency in the static or dynamic constraints can lead to improper centering of the patella into the trochlear groove during early knee flexion. In one study, Cash and Hughston demonstrated that there was a 43% risk for recurrent patellofemoral instability following non-surgical treatment of patellar instability in patients with predisposing factors, such as VMO dysplasia or trochlear dysplasia. However, in patients who were treated non-surgically for patellar instability
who did not have predisposing factors to patellofemoral instability, this risk was reduced to 20%.11

**Trochlear Dysplasia**

Trochlear dysplasia has been shown to be present in < 2% of the population but in over 85% of people with recurrent patellofemoral instability.12 Dejour and Le Courture found that 96% of patients with patellofemoral instability had trochlea dysplasia on plain x-rays.13

Dejour et al13 have developed a classification system that classifies trochlear dysplasia into four grades, differing in the severity of dysplasia. This classification system is dependent on the evaluation of lateral and axial radiographs (Figure 1).

Type A trochlear dysplasia is characterized by a shallow groove when seen axially, the presence of a crossing sign on the lateral radiograph, and a bony sulcus angle of >145° (Figure 2). Type B trochlear dysplasia is characterized by the presence of a supratrochlear spur or prominence on the lateral radiograph as well as a flat trochlea when viewed axially. Type C trochlear dysplasia is characterized by a double contour when seen laterally and lateral convexity as well as medial hypoplasia when viewed axially (Figure 3). Type D trochlear dysplasia, the most severe grade, is characterized on lateral radiograph by a double contour and a supratrochlear spur, and it is seen axially as having asymmetric trochlear facets as well as a cliff between the medial and lateral facets.
Treatment of Patellofemoral Instability

Each of the risk factors must be considered individually when selecting appropriate surgical management for these patients. In the patient that is skeletally mature with a normal TT-TG distance and absent patella alta, MPFL reconstruction is recommended even when trochlea dysplasia is present. A study performed by Steiner et al14 evaluated 34 patients with recurrent patellar instability and trochlear dysplasia who underwent MPFL reconstruction, and post-operatively there were no episodes of patellar instability or subluxation. When there is a TT-TG distance of >20 mm, the malalignment should be addressed with a tibial tubercle transfer.

The term trochleoplasty refers to any procedure in which the trochlea is reshaped to provide stability to the patellofemoral joint. Indications for trochleoplasty include recurrent patellofemoral instability with radiographic evident of severe trochlear dysplasia and failed previous patellofemoral surgical stabilization. Contraindications include patellofemoral joint degenerative disease and arthritis.15,16 Most descriptions of this procedure include either the open or arthroscopic removal of subchondral bone in the trochlea and subsequent compression of the cartilage into the newly deepened groove (Figures 3-8). Recurrent patellofemoral instability is very rare post-operatively, although residual pain is a common finding in studies following patients after trochleoplasty.21-28

Figures 5-8 are photos that were taken during a trochleoplasty.

METHODS

IRB approval was obtained. Patients who had trochleoplasties performed in the past 10 years at the University of Iowa were located using CPT codes in the University of Iowa electronic medical record database. The patients were contacted and invited for followup. Lateral and Merchant x-ray views were obtained, from which bony sulcus angles and CD ratios were obtained. The presence of patella alta was also recorded. MRIs
Outcomes after Trochleoplasty

Excavation) trochlea, leaving the full thickness cartilage and a thin layer of bone intact. Once it was possible to ballot the cartilage surface over the excavation, the cartilage down the middle of the trochlea was incised with a 10 blade or a very sharp osteotome and the cartilage could be compressed, both medially and laterally, creating a deep groove. The cartilage was then fixed and placed using four suture anchors with #2 suture and suture bridge construct. After the trochleoplasty was complete, a MPFL reconstruction was performed.

The patient’s bony sulcus angle decreased from 142° to 109°, and the MRI demonstrated a cartilage sulcus angle of 114°. These sulcus angles demonstrate that Patient 1 had a deeper trochlear groove post-operatively which should provide resistance against lateral patella movement and patellar dislocations. In fact, this patient reported no cases of patellofemoral instability after her trochleoplasty. Her pre-operative WOMAC score was 66.5% while her post-operative WOMAC score improved to 27.1%. Post-operatively, her KOOS survey showed a score of 63%. The patient stated that she was satisfied with this procedure.

**TABLE 1. Case 1 Physical exam data**

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<td>J sign</td>
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**TABLE 2. Case 1 Radiographic and MRI data**

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</tr>
<tr>
<td>Pre-operative bony sulcus angle</td>
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<tr>
<td>Post-operative bony sulcus angle</td>
<td>109°</td>
</tr>
<tr>
<td>Post-operative cartilage sulcus angle</td>
<td>114°</td>
</tr>
</tbody>
</table>

**CASE 1**

15 year old female with history of recurrent patellar instability and chronic knee pain who underwent a trochleoplasty after recurrent patellofemoral instability status post tibia tubercle transfer. After tibial tubercle transfer, she still had recurrent patellar instability.

**Description of procedure**

The surgical approach was through the previous anterior and longitudinal incision. The extensor mechanism was exposed. Given her previous lateral release and medial imbrication, a lateral parapatellar arthrotomy was performed extending from the vastus lateralis down to the lateral aspect of the tibial tubercle. Two screws were then removed from the tibial tubercle without difficulty from her previous osteotomy of the tubercle. A lateral parapatellar arthrotomy was then completed. The patella was everted. The patellar articular surface appeared to be maintained. There was significant dysplasia and hypoplasia of her trochlea. A burr was used to remove the bone beneath the articular cartilage of the (subchondral excavation) trochlea, leaving the full thickness cartilage and a thin layer of bone intact. Once it was possible to ballot the cartilage surface over the excavation, the cartilage down the middle of the trochlea was incised with a 10 blade or a very sharp osteotome and the cartilage could be compressed, both medially and laterally, creating a deep groove. The cartilage was then fixed and placed using four suture anchors with #2 suture and suture bridge construct. After the trochleoplasty was complete, a MPFL reconstruction was performed with allograft.

The patient’s bony sulcus angle decreased from 142° to 109°, and the MRI demonstrated a cartilage sulcus angle of 114°. These sulcus angles demonstrate that Patient 1 had a deeper trochlear groove post-operatively which should provide resistance against lateral patella movement and patellar dislocations. In fact, this patient reported no cases of patellofemoral instability after her trochleoplasty. Her pre-operative WOMAC score was 66.5% while her post-operative WOMAC score improved to 27.1%. Post-operatively, her KOOS survey showed a score of 63%. The patient stated that she was satisfied with this procedure.
CASE 2

17 year old female with history of recurrent patellar instability and chronic knee pain. Previous surgery had included a distal realignment and medial imbrication which failed to provide patellar stability.

Description of procedure

The patient's previous anterior longitudinal incision was used. A lateral parapatellar arthrotomy was made next to the patella. This served also as a lateral release. Two 3.5 fully threaded screws were removed from the tibial tubercle at the patient's request.

The patient had a very dysplastic medial and lateral femoral condyle with virtually no groove. The same technique described in case #1 was used to create the trochleoplasty. This deepened the sulcus approximately 1 cm. A MPFL reconstruction was performed after completion of the trochleoplasty.

The patient in case 2 originally had a bony sulcus angle of 161°, which was reduced to 132° post-operatively. This signifies a deeper trochlear groove, thus providing joint stability. Her axial MRI displayed a cartilage sulcus angle post-operatively of 128°. Patient 2 had a pre-operative WOMAC score of 80%, indicating that she was dissatisfied with the state of her knee. Post-operatively, this was greatly improved to 22%, and in addition, her post-operative KOOS score was 65%. At follow-up, the patient reported mild pain but no instability whatsoever. She also stated that she was satisfied with her trochleoplasty procedure.
Outcomes after Trochleoplasty

CASE 3

16 year old female with a history of recurrent patellar instability. She reported an average of 2-3 patellar dislocations per week. Prior to her trochleoplasty, two other surgeries had been attempted, including an arthroscopic lateral release and an open VMO advancement.

Description of procedure

A midline incision was made over the patella and carried proximally for a distance of approximately 4.5 cm distally. A medial arthrotomy was done because of the previous approach. The trochlear groove was noted to be very small and shallow. The patella itself had minimal cartilage wear but was very small and easily mobile. Trochleoplasty was performed as described previously. Following the trochleoplasty, a tibial tubercle transfer was performed.

The patient in case 3 had a post-operative bony sulcus angle of 127°, and her post-operative cartilage sulcus angle was 119°. Although her pre-operative outcome scores were not available, her post-operative WOMAC score was 0%, and her post-operative KOOS score was 98.2%. These two scores indicate that patient 3 was extremely satisfied with the status of her knee. At the time of follow-up, she reported no pain and no episodes of patellofemoral instability. The patient stated she was fully satisfied with her operation.

<table>
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<table>
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<td>Post-operative crossing sign</td>
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<td>CD ratio</td>
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<td>Post-operative bony sulcus angle</td>
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<tr>
<td>Post-operative cartilage sulcus angle</td>
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FIGURE 13. Case 3 Post-operative Merchant x-ray

FIGURE 14. Case 3 Post-operative axial MRI
TABLE 7. Case 4 Physical exam data

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TABLE 8. Case 4 Radiographic and MRI data

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<td>130°</td>
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</table>

CASE 4

17 year old female with a history of recurrent patellar instability, reporting 2-3 episodes of patellofemoral instability per week. Prior to her trochleoplasty, an arthroscopic lateral release had been performed, but she stated that this procedure afforded her little to no relief.

Description of procedure

A longitudinal incision in line with the previous incision was made excising the previous scar. A medial arthrotomy was then made. The patella was everted and the trochlea was inspected. It was found to be significantly hypoplastic with virtually no groove present. Trochleoplasty was performed in the usual fashion. After the trochleoplasty was completed, a tibia tubercle transfer and medial imbrication were performed.

Patient 4 had a post-operative bony sulcus angle of 135° and a cartilage sulcus angle of 130°. Once again, because the procedure was performed several years ago, pre-operative imaging and outcome scores were unavailable. The patient’s post-operative WOMAC score was 0%, and her KOOS score was 98.2%, signifying great satisfaction with the procedure. She reported that she had no post-operative pain or instability, and she was thoroughly satisfied with the procedure.
Outcomes after Trochleoplasty

**CASE 5**

38 year old female with a history of recurrent patellar instability and knee pain. She is an amateur bodybuilder, and thus her patellofemoral instability severely limited her normal level of activity. Prior to her trochleoplasty, a Fulkerson osteotomy was performed, which provided her little relief from patellar instability.

**Description of procedure**

A midline incision was made. Following the medial arthrotomy, the patella was then retracted laterally. A #1 Vicryl was used to create double row suture fixation with overlap of the VMO and the medial retinacular structures. Approximately, 30-40% overlapped over the patella. The double row fixation was completed. Trochleoplasty was performed as previously described.

Patient 5 had a pre-operative bony sulcus angle of 143°, and this was reduced to 124° post-operatively. The post-operative cartilage sulcus angle was 138°. The patient’s pre-operative WOMAC score was 66%, which improved to 8% at the time of follow-up. Her KOOS score at this time was 82%. Her follow-up outcome scores indicate that she was satisfied with the procedure. The patient reported that post-operatively, she had mild, residual pain but no episodes of patellofemoral instability. She also stated that she was entirely satisfied with the procedure.

<table>
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<td><strong>Patella Tilt</strong></td>
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<th>TABLE 10. Case 5 Radiographic and MRI data</th>
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<td><strong>Post-operative crossing sign</strong></td>
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<td><strong>Post-operative bony sulcus angle</strong></td>
</tr>
<tr>
<td><strong>Post-operative cartilage sulcus angle</strong></td>
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</table>

**FIGURE 17. Case 5 Pre-operative Merchant x-ray**

**FIGURE 18. Case 5 Post-operative Merchant x-ray**
A total of 12 trochleoplasties had been performed in the past 10 years at the University of Iowa. Six of these knees were able to be evaluated in this study. The averages of many of the parameters in this study are summarized in Table 13.
Stability of the patellofemoral joint is achieved by the coordinated action of static, dynamic, and osseous constraints. Beyond 20° to 30° of knee flexion, osseous constraints become the predominant form of resistance against patellar subluxation. Trochlear dysplasia is characterized by a shallow trochlear groove with reduced resistance to lateral patellar movement. It is strongly associated with patellofemoral instability. Because of the myriad etiologies of patellofemoral instability, there are various options for surgical intervention, including extensor mechanism realignment, soft tissue balancing and ligament reconstruction. Trochleoplasty is a procedure defined as the surgical reshaping of the trochlear groove to provide resistance against lateral patellar translation, and it is uncommonly utilized. Although residual pain is often present, trochleoplasty is very effective at providing patellofemoral stability.[17-21]

Several studies have been performed evaluating the long-term outcomes of trochleoplasty; however, these are primarily European studies, as trochleoplasty has not been widely studied in the United States. The results from the studies are summarized in Table 14.

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<table>
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<th>TABLE 14. Data from other studies evaluating trochleoplasty outcomes</th>
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Our findings are similar to European outcomes following trochleoplasty.[17,18,19,20,21,22] The six knees evaluated at the University of Iowa were seen at an average follow-up time of 68 months, and the average bony sulcus angle decreased from 149° to 128°, indicating deepening of the trochlear groove. In this study, success rate was defined as both subjective patient satisfaction as well as the absence of post-operative patellofemoral instability. All of the patients in this study reported satisfaction with their procedure. Although one patient reported severe post-operative pain, he was happy with the patellofemoral stability. None of the patients in this study reported post-operative instability; however, 4/6 (66%) of the patients reported at least some residual pain. Although there was a high proportion of patients with residual anterior knee pain, this must be viewed closely at an individual basis. Two of the patients (three knees) reported having sustained trauma to the knee within one week prior to their follow-up, and this may have affected the presence of pain at the time of their clinical visit. One of these patients was also an amateur bodybuilder, and thus her heavy squatting may also have been one etiology for her pain.

In this study, 5 of the 6 patients had numerous previous surgeries prior to the trochleoplasty and continued to have patellar instability. With a dysplastic trochlea, the patella is not stable despite corrections in alignment and soft tissue stabilization. In severe trochlear dysplasia, there is convexity near the proximal edge of the trochlea. In these cases, soft tissue stabilization and a tubercle transfer are not enough to prevent recurrent patellofemoral instability.

Because of the rarity of this procedure, the sample size in this study was small (n=6), which reduced the statistical power of this study. A total of 10 patients (12 trochleoplasties) have been performed in the last 10 years at the University of Iowa. Although 6/12 of the knees were available to evaluation, 6 of the patients did not return for follow-up. Two of the patients were not able to reached, one patient died, and 2 others did not want to come back.
This is the first study performed in the United States evaluating long term outcomes following trochleoplasty. Based on this study, trochleoplasty should be viewed as a necessary procedure in cases of severe trochlea dysplasia when patellofemoral stability cannot be obtained by proximal or distal reconstruction. Although patients often report the presence of post-operative residual pain, there is a very high success rate in preventing future episodes of patellofemoral instability as well as a high subjective patient satisfaction rate.

REFERENCES

ABSTRACT

Background: Elite wrestlers place tremendous stress through their cervical spine. These athletes are at risk for cervical trauma and may develop radiculopathy from recurrent episodes of injury. Team physicians and athletic trainers are faced with the challenge of treating these injuries in such a way as to allow the athlete to safely and expeditiously return to competition. Epidural steroid injections can be a successful complement to a conservative treatment algorithm for these complex injuries.

Study Design: Case Series

Methods: Five upper-level NCAA collegiate wrestlers who experienced symptomatic cervical radiculopathy were identified from an archival review. The majority of the athletes had MRI evidence of cervical disc disease, with corresponding subjective complaints and physical examination findings including pain and weakness that precluded continued competition. All athletes were treated conservatively with initial activity modification, strengthening, rehabilitation, NSAIDs, and, ultimately, cervical epidural steroid injections.

Results: All five athletes successfully returned to competition without negative clinical sequelae or need for operative intervention. The athletes demonstrated subjective improvement in their symptoms and strength, and all were able to return to a high level of competition. The cervical epidural steroid injections were found to be safe, effective, and well tolerated in all of the athletes.

Conclusions: Elite wrestlers with cervical radiculopathy can be effectively and safely managed with a conservative regimen that includes cervical epidural steroid injections, which may allow them to continue to compete at a high level.

INTRODUCTION

Collegiate athletes frequently experience high-energy collisions, including blunt force and traction injuries to the cervical spine, cervical nerve roots, and/or brachial plexus. In some cases, this trauma can cause a pinch-stretch neuropraxia phenomenon known more colloquially as a “burner” or “stinger”. These injuries represent the more benign end of a spectrum that can include catastrophic fractures and permanent neurologic injury. Although “burners” and “stingers” are relatively common in this population, the true pathophysiology of these injuries remains poorly understood. These injuries are accompanied by transient shooting pains, numbness, weakness, and paresthesias in the neck and affected extremity. Repetitive injury or large-force single trauma can cause inflammation, vascular insufficiency, or bony or soft-tissue impingement on the cervical nerve roots, leading to persistence of these upper extremity symptoms beyond that expected with simple burners/stingers. This constellation of symptoms is broadly categorized as cervical radiculopathy. These injuries may precipitate severe complaints, but in many cases, respond well to conservative treatment.

These injuries pose a special clinical challenge for physicians and athletic trainers, who are charged with ensuring a safe and expeditious return to sport for the athlete. Accelerated rehabilitation protocols and targeted therapy can facilitate treatment and expedite recovery. This investigation outlines the use of epidural steroid injections (ESI) as an adjunctive therapy in the conservative treatment of collegiate wrestlers with cervical radiculopathy and persistent weakness and pain.

CASE PRESENTATION, WORKUP, AND MANAGEMENT

Case 1:

A 22-year old male collegiate wrestler presented with several weeks of right-sided neck pain and increasingly frequent “stingers” radiating down his right upper extremity. Symptoms were exacerbated with a Spurling maneuver and frequently occurred during wrestling. Manual motor testing demonstrated 4/5 strength in the right deltoid and triceps muscles. Due to concern for cervical radiculopathy, magnetic resonance imaging (MRI) was obtained which demonstrated disc protrusion and compression at C3-C4 and C4-C5 (FIGURE 1). As part of his conservative treatment regimen, he underwent an epidural steroid injection centered at C7-T1. He experienced a rapid return to function and was able to return to wrestling with no complaints of pain or dysfunction for the duration of the season. One year later he had a return of symptoms with recalcitrant right-sided neck pain and activity-related “stingers” radiating down the right upper extremity. He underwent a repeat cervical ESI with
relief of his symptoms. Four months later he had yet another recurrence of pain associated with new-onset 4/5 weakness in his right deltoid. A repeat MRI confirmed C3-4 bilateral neural foraminal narrowing and right-sided C4-5 neural foraminal narrowing. A third injection was performed and the patient once again returned to full activity.

Case 2:
A 19-year old male competitive wrestler presented with neck pain and left arm weakness associated with increasingly frequent “stingers” involving the left upper extremity. Manual motor testing revealed decreased grip strength and thumb extension strength of the left hand. Subsequent MRI demonstrated evidence of a left sided C6-7 disc extrusion (FIGURE 2). In addition to NSAIDs, the patient was given a short course of oral corticosteroids and referred for rehabilitation. Despite this treatment regimen, he remained symptomatic several weeks later. A repeat physical examination demonstrated 4/5 strength in his left wrist flexors and a positive Spurling test. The patient was then referred for a cervical ESI and he underwent an epidural steroid injection centered at C7-T1. Within a few weeks he experienced complete resolution of his pain and weakness. Three months after his ESI, the patient was cleared to return to full wres-
Epidural Steroid Injections for the Treatment of Cervical Radiculopathy in Elite Wrestlers

Case 1:
A 22-year old collegiate wrestler presented with neck pain, left arm weakness, and numbness, exacerbated by a recent match in which he attempted to turn out of a front headlock. Physical examination findings demonstrated a positive Spurling sign, and 4/5 left deltoid and triceps strength. Subsequent MRI demonstrated a disc osteophyte complex at the C6-7 level on the left side, resulting in moderate to severe narrowing of the neural foramen (FIGURE 3). An interlaminar cervical ESI was performed centered at C7-T1, with symptomatic relief beginning within one week of the injection. By six weeks, the patient had complete resolution of his pain and near-complete restoration of strength, with only a mild discrepancy in comparative strength in the left triceps and wrist flexors. By two months after the injection, his strength deficits had resolved and his activity restrictions were lifted. Several months later, the patient experienced new-onset contralateral radicular symptoms, with pain radiating into the right thumb. Physical examination findings demonstrated mild weakness with wrist extension and elbow flexion. Repeat MRI demonstrated a right-sided C5-6 disc herniation with concomitant impingement at the C5-6 neural foramen. Approximately eight months after his original ESI, the patient underwent a repeat ESI. Symptoms resolved for another four months, but with further competition, the left-sided complaints recurred. Further imaging with MRI showed progressive disc herniation involving the left C6-7 neural foramen. A third ESI was performed. The patient had marked improvement in his strength, with only occasional pain. He requested an additional injection prior to participation in the NCAA championships. Following this injection, the patient was able to successfully participate in competition, and his radiculopathy continues to respond to medical management for several years.

Case 2:
A 22-year old competitive wrestler presented with neck pain, right-sided radicular symptoms that were less severe than the left side. Repeat MRI demonstrated a stable left-sided C6-7 disk extrusion. The athlete underwent another ESI and was able to return to competition with full resolution of his complaints.

Case 3:
A 22-year old competitive wrestler presented with neck pain, left arm weakness, and numbness, exacerbated by a recent match in which he attempted to turn out of a front headlock. Physical examination findings demonstrated a positive Spurling sign, and 4/5 left deltoid and triceps strength. Subsequent MRI demonstrated a disc osteophyte complex at the C6-7 level on the left side, resulting in moderate to severe narrowing of the neural foramen (FIGURE 3). An interlaminar cervical ESI was performed centered at C7-T1, with symptomatic relief beginning within one week of the injection. By six weeks, the patient had complete resolution of his pain and near-complete restoration of strength, with only a mild discrepancy in comparative strength in the left triceps and wrist flexors. By two months after the injection, his strength deficits had resolved and his activity restrictions were lifted. Several months later, the patient experienced new-onset contralateral radicular symptoms, with pain radiating into the right thumb. Physical examination findings demonstrated mild weakness with wrist extension and elbow flexion. Repeat MRI demonstrated a right-sided C5-6 disc herniation with concomitant impingement at the C5-6 neural foramen. Approximately eight months after his original ESI, the patient underwent a repeat ESI. Symptoms resolved for another four months, but with further competition, the left-sided complaints recurred. Further imaging with MRI showed progressive disc herniation involving the left C6-7 neural foramen. A third ESI was performed. The patient had marked improvement in his strength, with only occasional pain. He requested an additional injection prior to participation in the NCAA championships. Following this injection, the patient was able to successfully participate in competition, and his radiculopathy continues to respond to medical management for several years.

Case 4:
A 22-year old collegiate wrestler sustained a traumatic hyperextension-rotation injury during competition when his opponent landed on his head and forced his neck back and to his left. Subsequent to this episode, he experienced increasingly frequent “stingers” when wrestling, describing weakness in his left arm and shoulder as well as pain and numbness that radiated down his left arm and into the hand. Symptoms were reproducible by performing a Spurling test. An MRI demonstrated a diffuse broad-based disk bulge at C7-T1 (FIGURE 4). He underwent an interlaminar ESI centered at C7-T1 with complete resolution of his symp-
Case 5:

A 19 year-old male collegiate wrestler presented with chronic neck and left shoulder pain of two years duration, associated with biceps and wrist extension weakness. He failed conservative and medical management with Gabapentin, NSAIDs and rehabilitative therapy, and continued to have exacerbations of his symptoms during wrestling practice. On exam he was found to have 4/5 strength in left elbow flexion and wrist extension, and left shoulder discomfort with a Spurling maneuver. The patient underwent an interlaminar cervical ESI centered at C7-T1 with complete resolution of his symptoms and was able to return to competition without any further dysfunction.

DISCUSSION

Cervical radiculopathy is a clinical diagnosis in which patients demonstrate sensory and/or motor changes in a distribution specific to an affected cervical nerve root. It is frequently caused by compression of an exiting cervical nerve root. There are a variety of pathological conditions that can result in cervical nerve compression including degenerative cervical spine changes, disc extrusion, and other soft tissue abnormalities. Diagnosis is established by detailed physical exam, and the cause of radiculopathy may be localized with radiographs and advanced imaging. Symptoms are colloquially referred to as “stingers”, and are frequently caused by traction injuries to the brachial plexus, compression of the cervical nerve roots, or a pincer mechanism in which there is some degree of spinal cord compression by the
posterior-inferior margin of the superior vertebral body and the anterior-superior portion of the lamina of the vertebra below. Physical exam findings usually consist of weakness in the deltoid, biceps, and shoulder external rotators.

True brachial plexus injuries are more commonly seen in younger patients who experience a traction injury involving lateral neck flexion away from the affected side and shoulder depression toward the affected side. Although neck pain can accompany the upper extremity symptoms, this is often less prominent. These traction injuries are felt to represent a reversible peripheral nerve neuropraxia, resulting from a temporary physiological block in nerve conduction.

Cervical root lesions are caused by compression of the nerve root or dorsal root ganglion in the intervertebral foramen. Radiographs frequently show evidence of cervical disk disease or stenosis. The injury mechanism is hyperextension with lateral neck flexion, and pathology can be attributed to a combination of factors including inflammatory mediators, angiogenic changes, and intraneural edema. In contrast to traction injuries of the brachial plexus, neck pain is a more prominent clinical finding in cervical root lesions. Furthermore, the presence of a positive Spurling sign and decreased cervical range of motion can assist in differentiating between cervical root lesions and brachial plexopathies.

These symptoms can be severe in athletes with underlying congenital cervical stenosis. Furthermore, wrestlers and other athletes are at risk for the development of disc disease and early degenerative spine changes due to soft tissue trauma and recurrent injury across the cervical spine. Decreased disc height space and degenerative changes at the uncovertebral and zygoapophyseal facet joints has been reported to be responsible for 70-75% of cases of cervical spondylosis, with the remainder attributed to herniated nucleus pulposus (20-25%) or tumors and infections. MRI is recommended for patients who experience severe or persistent neurologic symptoms. EMG studies can be done to further define injuries with persistent or recalcitrant symptoms.

The incidence of these injuries in wrestlers remains unknown. Evaluations of football players suggest that one or more stingers were experienced by at least 50% of football players at least once during their careers. Castro et al reported a 7.7% yearly incidence and a prevalence of 18% of stingers in collegiate football players. These injuries are most common in linemen, defensive ends, and linebackers. More generally, it is felt that slightly more than half of the adult population will experience neck and radicular symptoms at some time during their lifetime, although these symptoms rarely progress to fulminant myelopathy. Up to 66% of patients treated with long-term conservative management indicated the persistence of symptoms. Furthermore, 23% of patients who complained of persistent neck pain or radicular symptoms were unable to return to their previous employment.

Cervical radiculopathy can be diagnosed by obtaining a thorough patient history, physical examination, appropriate imaging studies and in some cases electrophysiologic testing that are all concordant. Nonetheless, cervical radiculopathy is a clinical diagnosis and there are no universally accepted criteria for diagnosis. Treatment is symptom-based, and clinicians must appropriately identify and classify the patient’s
problems, then select the appropriate combination of treatment options including the use of medication, therapeutic modalities, rest, immobilization, patient education, physical therapy, and manual therapies to treat their symptoms. Patients with cervical radiculopathy have a favorable prognosis in the long term, and several conservative treatments appear to be effective in resolving symptoms and improving function. While there is a paucity of high quality prospective research studies to support the use of individual treatment modalities, a multimodal approach can be beneficial in alleviating symptoms. Although the commonly recommended therapies such as immobilization, traction, physical therapy, and manipulation, have not been tested in high quality prospective studies, these therapies can also be beneficial. The approach used must distinguish the acuity of the symptoms and the anatomical sources.

Pharmacotherapy, such as the use of analgesics, corticosteroids, NSAIDS, muscle relaxants, antidepressants, and anticonvulsants can provide some symptomatic relief to athletes. Narcotics can be used in an acute and short-term setting, but prolonged use should be avoided due to addictive and depressive side effects. Antispasmodics and medications used for muscle relaxation also have a role in acute and short-term treatment. These medications can facilitate early rehabilitation and recovery.

Short-term immobilization with a soft collar may reduce symptoms in the acute stages but has not been shown to change the course of the disease process. Cervical traction may relieve nerve root compression and irritation by temporarily enlarging the neural foramen, but there is insufficient evidence to support the use of mechanical traction to treat chronic cases of neck pain with or without radicular symptoms. A gradual progression of gentle range of motion exercises and stretching may be supplemented by use of massage and therapeutic modalities such as heat, ice, and electrical stimulation to decrease symptoms and improve range of motion. As symptoms resolve, a gradual, progressive strengthening program to recondition the musculature may be added as tolerated. While many rehabilitation programs include exercise therapy and modality utilization, there is little clinical research supporting its use. Patient education may help some patients learn to manage their symptoms, though a systematic review did not show that it is of benefit in the treatment of neck pain and radicular arm pain.

As suggested by the present investigation, precise, fluoroscopically-guided transforaminal epidural steroid injections have been found to have a favorable role in nonoperative treatment of radiculopathy. A recent systematic review suggested that the evidence for cervical pain relief with transforaminal epidural steroid injections was moderate. These injections, however, have been associated with a reduction in surgical treatment for patients experiencing cervical radiculopathy. In an investigation of epidural steroid injections, patients had a reduction in radicular pain scores, experienced long lasting pain relief, and 5 of the 21 patients studied cancelled and avoided surgery. In a retrospective cohort study, Heckmann et al. evaluated the functional outcomes of patients with cervical radiculopathy by comparing patients treated with surgery or conservative care. At an average follow-up of 5.5 years brachalgia was completely or essentially improved in 97% of the conservative care group and 75% in the surgical group. Motor weakness improved in 94% of the conservatively treated patients and 50% of the surgically treated patients. With regard to return to daily activities, 90% of the conservative treatment group versus 67% of the patients in the surgical group did not feel disabled. The authors concluded that patients with radiculopathy can be treated conservatively with good results.

Although generally safe, cervical interlaminar epidural steroid injections are performed with some associated complications. Abbasi et al. reviewed the reported incidence of complications and found a rate of complications ranging from 0 to 16.8%. The authors concluded that interlaminar cervical epidural steroid injections are relatively safe procedures. The use of cervical transforaminal injections has largely been abandoned due to to complications related to intravascular injection that have produced spinal cord injury and paraplegia or quadriplegia. The adverse events associated with these procedures are usually minor and transient in nature, however, major adverse events that have been reported include epidural hematoma, subdural and intradural complications which lead to respiratory depression, moderate hypotension, and sudden apnea with acute cardiovascular collapse, dural puncture headache, neuropathic symptoms, intracranial hypotension, permanent spinal cord injury, intravascular injection, pneumocephalus, venous air embolism, cervical epidural abscess, Cushing’s syndrome, and death. No patients in the present investigation experienced any untoward effects of the injections.

The decision to return an athlete to competition remains complex and controversial. Conservative management of cervical radiculopathy can allow for successful rehabilitation of athletes and can facilitate their return to sport. In order for a patient to return to sport, they must demonstrate full cervical range of motion, normal upper extremity strength, and the athlete must appear healthy with full resolution of their “burner syndrome” symptoms. Contact athletes should not return to play until the risks of re-injury and permanent dysfunction are minimized. With appropriate diagnosis, treatment, and rehabilitation, athletes can safely return to sport. Players who experience residual weakness, cervical anomalies, or abnormal imaging or EMG studies should be excluded from contact sports.
CONCLUSION:
Collegiate wrestlers place tremendous stress across their cervical spine and are vulnerable to cervical trauma, which may result in radiculopathy from recurrent episodes of injury. These injuries can be chronic in nature and athletes with recalcitrant symptoms may be forced to end their athletic career. Treatment options for cervical radiculopathy in young competitive athletes include conservative measures such as temporary activity modification, immobilization, strengthening, rehabilitation, and gradual return to activity. Medical management may include NSAIDs, neuromodulators, short burst corticosteroids, and analgesic medications. For patients with focal disease and symptoms that are refractory to conservative and medical management, surgery may be necessary. Unfortunately, return to competition following cervical spine surgery may not be recommended.

Based on the present investigation, elite wrestlers with cervical radiculopathy can be effectively and safely managed with a conservative regimen that includes cervical epidural steroid injections. These injections can be beneficial for athletes with both clinical evidence of cervical radiculopathy and MRI-documented anatomic abnormalities. The duration and effectiveness of cervical ESIs can be variable, but may be definitive in some cases. Team physicians and athletic trainers are faced with the challenge of treating these injuries in such a way as to allow the athlete to safely and expeditiously return to competition. Cervical epidural steroid injections may facilitate a quicker return to competition for some athletes, and the present study suggests this treatment can be well tolerated, safe, and effective in a population of elite wrestlers.

REFERENCES
ABSTRACT
A 9-year-old boy sustained a previously unreported Salter-Harris III coronal plane fracture of the anterior capitellum after a 20-foot fall from a tree. The fracture was diagnosed on x-ray and an MRI confirmed the fracture pattern. During surgical treatment, an anterolateral approach to the elbow allowed direct visualization of the fracture fragment, anatomic reduction, and fixation with a bioabsorbable pin. At one year follow-up the patient's range of motion and function was symmetric to the contralateral extremity. This paper reviews the literature regarding the epidemiology, classification, and management of the rare pediatric capitellar fracture.

INTRODUCTION
Pediatric fractures of the capitellum are rare injuries. These fractures represent not only an injury to articular cartilage but also a potential insult to the physis. When present, pediatric capitellar fractures are often misdiagnosed and may go untreated\(^1\). The resultant malunion may compromise elbow function\(^1\). There is debate over the ideal surgical intervention, with historical opinion recommending excision of the fragment\(^2,3\) and more recent reports favoring open reduction and internal fixation\(^1,5,6,7,8\). Fixation methods include smooth Kirschner wires, headless compression screws, lag screws and bioabsorbable pins\(^8,9,10\). We present a case of an anterior capitellar Salter-Harris III fracture in a child that was treated using an anterolateral surgical approach. The parents of our patient consented to publishing the data regarding their son’s case.

CASE REPORT
A 9-year-old boy was using a rope to climb a tree when the rope broke at a height of 20 feet. He fell through branches onto a dirt surface landing on his outstretched right hand. He sustained an isolated injury to his right upper extremity. He was evaluated at his local hospital and diagnosed with a distal radial buckle fracture and placed in a splint. His neurovascular exam was normal. He subsequently saw a local Orthopaedic surgeon who noted abnormality of the capitellum on plain films (fig. 1a). His treatment was transferred to our institution 10 days following his injury. An MRI revealed a Salter-Harris III fracture through the capitellum with superior displacement of the anterior fractured fragment (fig. 1b). The remaining posterior portion of the capitellum was intact. The fracture did not extend into the trochlea or the lateral condyle. The patient was treated surgically 2 weeks after his injury with open reduction and internal fixation.

SURGICAL TECHNIQUE
General anesthesia was selected and the patient was placed in the supine position. To avoid the posterior blood supply to the humerus and allow direct visualization of the fracture for anatomic reduction, a standard anterolateral approach was performed.

The incision began proximally overlying the lateral aspect of the biceps muscle. It was then directed medially to cross the elbow joint obliquely and then directed back laterally over the proximal forearm (fig. 2). The surgical dissection continued between the biceps and brachioradialis origin. The lateral antebrachial nerve was protected. The radial nerve was identified on the deep surface of the brachioradialis and retracted laterally. Dissection continued distally to the biceps tendon. The brachialis muscle was reflected medially off the distal humeral metaphysis and elevated distally to expose the joint capsule. The capsule was opened longitudinally directly over the displaced fracture fragment. There was a large fracture fragment involving the anterior half of the capitellar ossification center. The fracture line did
not enter into the trochlea and the posterior portion of the capitellum was intact. The fragment was reduced under direct visualization and provisionally fixed with an anterior to posterior Kirshner wire. Image intensifier was used to ensure that the physis was not violated and the wire remained entirely within the capitellar ossification center (fig. 3). The wire was exchanged for a 1.5 mm bioabsorbable pin (Trim-It, Arthrex, Naples FL). The elbow was then found to have full passive range of motion with good stability. The skin and subcutaneous layers were closed with absorbable sutures and the elbow was immobilized in neutral rotation and 70 degrees of flexion for 6 weeks.

Serial post surgical radiographs demonstrated maintenance of reduction and the patient was released to full activities at 3 months (fig. 4). His range of motion at six months showed full pronation, supination and extension with 15 degrees less flexion as compared to the contralateral extremity. At one year, his motion was complete and symmetric to the other side (fig. 5). He had no complaints of pain and his radiographs showed no resorption around the pin or signs of avascular necrosis.

**DISCUSSION**

The orthopaedic literature on capitellar fractures reflects the infrequency of the injury. The prevalence of this fracture is unknown. Marion and Faysse reported on 2000 elbow fractures in children and described one capitellar fracture in their series13. Current classification is the same for adults and children(fig. 6). Type I is most common and is referred to as the Hahn-Stienthal type. This involves the capitellum and underlying cancellous bone. The Type II, or Kocher-Lorenz is rare in children and is a purely articular fracture with minimal underlying bone attached11. Type III is similar but involves impaction of the capitellar surface with comminution and Type IV is described as a coronal plane fracture which involves a portion of the adjacent trochlea. The described patient sustained a type I fracture.

This case report proposes the anterolateral approach for pediatric capitellar fractures. Imtani et. al. published the results of 6 adults with distal humeral coronal shear injuries who were treated with this same approach and internal fixation. They described that the approach allowed excellent visualization for reduction of the fracture.
and placement of the implants. They showed a good outcome with no neurovascular complications\textsuperscript{14}. The literature contains multiple reports of related fractures which have been addressed through the extensile lateral approach\textsuperscript{1,5,7,11,12,15,16,17}. For our patient, the decision to use the anterolateral approach was to permit fixation perpendicular to the plane of the fracture while avoiding the growth plate. In addition, the anterolateral approach does not require release of the common extensor origin, allows direct visualization of this type of fracture and avoids the posterior blood supply to the capitellum. Most papers on this topic are in the adult population where the physis and the blood supply may not represent the same concern.
Our nine year old patient is, to our knowledge, the youngest ever reported. His coronal plane Salter-Harris III fracture is previously undescribed and adds to the sparse data regarding this injury. The largest pediatric case series is by Letts et al. who reported on seven adolescent capitellar fractures in a seven year review of fractures at his institution. Five of the patients in his series were treated operatively and all had good results. All of his patients had full pronation and supination but only three of the five had full flexion and extension as did our patient. The youngest age in the series was 11 with an average of 14.7 years. Also, Sodl et al. described a type II injury in a twelve-year-old patient. Ruchelsman described a case series of 16 adults with fractures of the capitellum treated with operative fixation and reported average ulnohumeral motion arc of 123 degrees and overall 94% good and excellent results.

The infrequency of these injuries can be explained through an understanding of the mechanism and the maturation of the distal humerus. The proposed mechanism involves a sheering injury from the radial head during a fall on an outstretched hand with the elbow extended. The mainly cartilaginous nature of the capitellum prior to age 12 makes this fracture less likely and a lateral condyle fracture more likely. It is thought that increased valgus and hyperextensibility places the elbow at risk for these injuries. Accordingly, examination of our patient’s contralateral elbow revealed 5 degrees of hyperextension.

There have been differing opinions in the orthopaedic literature regarding management of capitellar fractures. Historically some authors have proposed excision of the fragment while others have favored open reduction and fixation. Percutaneous reduction with a Steinmann pin has also been proposed. The current literature reflects the opinion that the Type I and IV fractures are addressed with some form of reduction and fixation while type II and III fractures are treated usually by excision. There have been case reports of successful treatments of type II fractures as mentioned above. Historic and recent papers agree that malunion of the fracture fragment severely impacts elbow function.

The authors propose the anterolateral approach as an alternative exposure for capitellar fractures. The approach is limited in that it is not extensile and requires a plane of dissection much closer to the important neurovascular structures in the elbow. Further use of the anterolateral approach and comparison with the extensile lateral approach would be beneficial.

CONCLUSION

Although rare, capitellar fractures can be seen in children as young as 9 years old. In our case, the anterolateral approach allowed excellent visualization of the fracture facilitating anatomic reduction and internal fixation without violation of the physis. The authors recommend consideration of an anterolateral approach for selected pediatric capitellar fractures.

REFERENCES

DEFINITIVE TREATMENT OF BILATERAL ACETABULAR AND PELVIC RING INJURIES USING EXTERNAL FIXATION

Benjamin C. Taylor, M.D.1, Attila Poka, M.D.2

ABSTRACT
Bilateral pelvic ring and acetabular fractures are rare injuries. The optimal treatment of these patients and their outcomes remain largely unknown. We present a three year follow up of a case of bilateral posterior pelvic ring injuries and acetabular fractures treated successfully with limited internal fixation and external fixation.

INTRODUCTION
Bilateral pelvic ring injuries are infrequently encountered; the addition of bilateral acetabular fractures to such an unstable pelvis is exceedingly rare1,2. In one review of 1612 patients with pelvic and/or acetabular fractures, only one patient sustained bilateral pelvic ring and acetabular injuries6. Such injuries are typically the result of high-energy trauma and nearly always associated with other significant injuries3. However, although associated injuries have been well described for the isolated pelvic ring and acetabular fractures4,5, minimal depiction of associated findings with this combined injury pattern has been reported at this time6. Due to the high-energy nature of this injury pattern, a thorough multidisciplinary evaluation and treatment model at a trauma center is recommended, as other life-threatening injuries can be present. The optimal treatment of this type of injury is currently unknown. Similarly, outcomes for this type of bilateral injury are largely unknown at this time. Ertl et al. reported on outcomes with unilateral concomitant pelvic ring and acetabular fractures; he noted that treatment of this complex injury usually requires staged treatment and was associated with SF-36 Physical Functioning and Role Physical categories below normative values3. We present a case of bilateral pelvic ring and acetabular fractures treated with external fixation and limited internal fixation, with follow-up of three years.

PRESENTATION
The patient is a 24-year-old previously healthy female who was ejected from her vehicle during a multiple rollover accident. She sustained a loss of consciousness at the scene and underwent nasal intubation in the field by the first response team. Upon evaluation in the trauma bay, she was diagnosed with a right pneumothorax and associated flail chest with paradoxical respiration; a chest tube was promptly placed. Additionally, she was found to have a multiligamentously unstable right knee and weakly dopplerable bilateral pedal pulses. Ankle-brachial indexes were then obtained and both were measured as greater than 0.9. Initial pelvic radiographs revealed bilateral transverse acetabular fractures as well as a displaced left sacral fracture and right sacroiliac joint widening (Figure 1). A computed tomography (CT) scan was then obtained and confirmed her bilateral pelvic injuries.
Definitive Treatment of Bilateral Acetabular and Pelvic Ring Injuries Using External Fixation

ring and acetabular injury (Figure 2a-c). She remained hemodynamically stable after crystalloid and blood replacement, and was able to follow commands under light anesthesia the following day. A dense right peroneal nerve motor and sensory palsy was noted.

The patient was taken to the operating room approximately 22 hours after admission for reduction and stabilization of her unstable knee and pelvic injuries. A spanning external fixator was first used to stabilize her knee. Once her limb was stabilized, an anterior pelvic external fixator was placed, utilizing a single pin on each side through the anterior inferior iliac spine to access the dense supraacetabular bone7. External fixation bars were applied and secured as the lower extremities were held in internal rotation and manual compression applied to the bilateral iliac wings. After the pelvic ring and acetabular fractures were stabilized anteriorly, bilateral 8.0 mm partially threaded iliosacral screws were placed to stabilize the left sacral fracture and right sacroiliac joint widening. Postoperative images are shown in Figure 3.

Postoperatively, she developed a deep venous thrombosis of the right leg, which was treated with an inferior vena cava filter and warfarin. The remainder of her hospitalization was without issue and she was discharged to an extended care facility 26 days after her initial admission. She was readmitted for definitive treatment of her right knee injury; surgery was performed 42 days after injury, with removal of the spanning external fixation, knee manipulation, primary repair of a distal medial collateral ligament rupture, and reconstruction of her anterior and posterior cruciate ligaments using allografts.

Nine weeks after her injury, her anterior pelvic external fixator was removed, with no subsidence of her pelvic

FIGURE 2. Representative axial cut computed tomography images are shown in A and B, revealing a right sacroiliac joint dislocation and left sacral fracture (2A) as well as bilateral displaced transverse acetabular fractures (2B). A 3-D computed tomography image is shown in 2C, again revealing bilateral pelvic ring and acetabular fractures.

FIGURE 3. Postoperative anteroposterior radiograph showing reduction of the pelvic ring and acetabular fractures by means of bilateral posterior iliosacral screws and an anterior external fixator.
injuries. She was then lost to follow-up, but ultimately returned for evaluation of non-radiating lumbar pain at three years post-injury. She did not exhibit any gait abnormalities and denied pain with ambulation. She maintained full active range of motion of her bilateral hips and did not have pain with FABER testing. She did complain of right knee stiffness and had a passive range of motion of 5-100 degrees. Her right peroneal nerve palsy had partially resolved, with 2/5 ankle dorsiflexion strength and present but decreased light touch sensation in the peroneal nerve distributions. Radiographs and a CT scan were obtained to evaluate her pelvic ring and acetabuli (Figure 4a-e). She was diagnosed with a lumbar strain and was ultimately lost to follow-up a second time.
DISCUSSION

As shown by this patient case, concomitant bilateral acetabular and pelvic ring injuries can be associated with other significant injuries requiring multidisciplinary input and care. In addition, prolonged hospitalization is to be expected with such an injury; this patient resided in either the hospital or an extended care facility for nearly twelve weeks.

In this patient presentation, the posterior injuries were not altogether unusual, but the acetabular fractures were very atypical, as they can be better thought of as a continuation of the energy dissipation of the pelvic ring injury. The bilateral transverse acetabular fractures acted similarly to the more typical anterior pelvic ring injury (rami or symphysis), allowing the rotational displacement of the posterior structures. Clear understanding of the mechanism and fracture displacement allowed treatment of this injury utilizing a closed surgical reduction, minimizing surgical morbidity as compared to a traditional open approach for each of these injuries, which would be associated with potentially significant blood loss and a high risk of complications.

This particular patient fared well from the standpoint of her pelvis and acetabular fractures after a limited surgical insult. Percutaneous fixation has been well established for both pelvic ring and acetabular fractures, and in cases such as this, such a surgical tactic may prove to be advantageous, provided an acceptable reduction is able to be obtained and maintained.

REFERENCES

ABSTRACT

Pneumorachis or epidural emphysema is defined as free air in the spinal canal which is seen following trauma, head trauma, manipulations, epidural injections, and spinal surgery. We report on the case of a 62-year-old with cervical and thoracic pneumorachis following a traffic accident.

INTRODUCTION

Pneumorachis or epidural emphysema is defined as free air in the spinal canal. It has been described following chest trauma, head trauma, manipulations, epidural injections, spinal surgery, ERCP and/or which occurs iatrogenically. We report on a 62-year-old with isolated cervical and thoracic pneumorachis following a traffic accident.

CASE REPORT

A 62-year-old male driver was involved in a head-on collision with another car in a high-speed traffic accident. He was evacuated from the scene and transferred to the regional hospital. CT of the chest and abdomen, performed as a part of the trauma series due to the mechanism of injury, revealed pneumorachis in the cervical and thoracic spine without any spinal fractures. Air was noted in the epidural space and neural foraminae (Figures 1, 2). There was a large amount of subcutaneous emphysema in the paraspinal muscles (Figure 1). No neurological deficit could be elicited. He was examined by a spinal surgeon who clinically cleared his cervical spine. The pneumorachis was managed conservatively and the patient subsequently made an uneventful recovery.

There was no associated pneumothorax or free intra-abdominal air. The patient had a right hemothorax and a non-displaced sternal fracture with a small amount of pneumomediastinum (Figure 3). The hemothorax was treated with an intercostal chest drain. He had sustained a right femoral fracture as well which was managed with an intramedullary nail.

DISCUSSION

Pneumorachis is a rare and under-diagnosed condition. Air has been described in the literature in epidural, extradural and subarachnoid spaces. Newbold described pneumorachis following basilar skull fractures. Epidural emphysema is also described following epidural and spinal injections. Asthma is also one of the etiological factors. Other causes can include blunt trauma, tumor, abscess and vacuum disc. Kon et al. reported epidural air in all patients with spontaneous pneumomediastinum. These are usually asymptomatic. Radicular symptoms are a rare presentation of epidural emphysema, and are managed conservatively, though Krasoudakis and colleagues suggested percutaneous aspiration of air in patients with a neurological deficit. The presence of intrathecal air following trauma should be managed as an open injury due to the risk of meningitis.

In this case, a large amount of air was noted in the paravertebral soft tissues. Air was also noted in multiple neural foraminae and in the spinal canal. We hypothesize that air from the subcutaneous emphysema tracked along the meningeal covering of the nerves, and eventually tracked into the spinal canal. The patient was managed conservatively as he was asymptomatic. He made an uneventful and full recovery.

We feel that practitioners need to be aware of pneumorachis, especially in patients with blunt trauma, and that such patients should be managed with expectant treatment.
Epidural emphysema following blunt trauma: A case report and review of literature

FIGURE 1. Axial CT of the upper thoracic spine and sagittal reconstruction of the cervical spine demonstrating air in the epidural space (arrow) and within the paraspinal muscles.

FIGURE 2. Sagittal CT and coronal reconstruction of the cervicothoracic spine demonstrating epidural emphysema tracking into the neural foramina.

FIGURE 3. Axial contrast-enhanced CT (lung windows) showing large right hemothorax (+) with pneumomediastinum (arrow).
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ABSTRACT

The deltoid ligament is the primary ligamentous stabilizer of the ankle joint. Both superficial and deep components of the ligament can be disrupted with a rotational ankle fracture, chronic ankle instability, or in late stage adult acquired flatfoot deformity. The role of deltoid ligament repair in these conditions has been limited and its contribution to arthritis is largely unknown. Neglect of the deltoid ligament in the treatment of ankle injuries may be due to difficulties in diagnosis and lack of an effective method for repair. Most acute repair techniques address the superficial deltoid ligament with direct end-to-end repair, fixation through bone tunnels, or suture anchor repair of avulsion injuries. Deep deltoid ligament repair has been described using direct end-to-end repair with sutures, as well as by autograft and allograft tendon reconstruction utilizing various techniques. Newer tenodesis techniques have been described for late reconstruction of both deep and superficial components in patients with stage 4 adult acquired flatfoot deformity.

We describe a technique that provides anatomic ligament-to-bone repair of the superficial and deep bundles of the deltoid ligament while reducing the talus toward the medial malleolar facet of the tibiotalar joint with anchor-to-post reinforcement of the ligamentous repair. This technique may protect and allow the horizontally oriented fibers of the deep deltoid ligament to heal with the appropriate resting length while providing immediate stability of the construct.

INTRODUCTION

The deltoid ligament is the primary ligamentous stabilizer of the ankle joint. Both superficial and deep components of the ligament can be disrupted with a rotational ankle fracture, chronic ankle instability, or in late stage adult acquired flatfoot deformity. The role of deltoid ligament repair in these conditions has been limited and its contribution to arthritis is largely unknown. Neglect of the deltoid ligament in the treatment of ankle injuries may be due to difficulties in diagnosis and lack of an effective method for repair.

Operative management of deltoid ligament injuries may be indicated acutely in unstable bimalleolar equivalent ankle fractures, particularly when the mortise remains wide medially after anatomic fixation of the lateral side of the ankle. This has been associated with entrapment of the deltoid within the medial gutter of the ankle. Delayed repair may be indicated for medial ankle instability with or without hindfoot malalignment. Most acute repair techniques address the superficial deltoid ligament with direct end-to-end repair, fixation through bone tunnels, or suture anchor repair of avulsion injuries. Deep deltoid ligament repair has been described using direct end-to-end repair with sutures, as well as by autograft and allograft tendon reconstruction utilizing various techniques. Newer tenodesis techniques have been described for late reconstruction of both deep and superficial components in patients with stage 4 adult acquired flatfoot deformity.

We describe a technique that provides anatomic ligament-to-bone repair of the superficial and deep bundles of the deltoid ligament while reducing the talus toward the medial malleolar facet of the tibiotalar joint with anchor-to-post reinforcement of the ligamentous repair. This technique may protect and allow the horizontally oriented fibers of the deep deltoid ligament to heal with the appropriate resting length while providing immediate stability of the construct.

SURGICAL TECHNIQUE

An approximate 6cm longitudinal incision is centered over the posterior aspect of the medial malleolus oriented at a slight oblique angle from proximal-posterior to distal-anterior, ending distally over the mid talus. Dissection is carefully performed to identify and protect
the saphenous nerve and veins. The posterior tibial tendon sheath is incised longitudinally allowing posterior retraction of the tibialis posterior tendon and improved visualization of the deltoid ligament complex. Incising the tendon sheath posteriorly leaves a robust anterior sheath for later repair to prevent tendon subluxation. A small anteromedial capsulotomy is made along the anterior border of the superficial deltoid ligament. This capsulotomy allows evaluation of the deltoid ligament injury, the medial gutter for osteochondral injuries, loose bodies, entrapment of the ruptured deltoid ligament, and joint reduction. After identification of the anatomy of the deltoid ligament injury the deep surgical approach is performed. In cases of deltoid avulsion from the medial malleolus the avulsion can be completed and the flap reflected inferiorly. In less common cases of talar avulsion a reverse flap is created. If the superficial deltoid tibio-calcaneal bundle is avulsed from its calcaneal insertion this can also be repaired with a separate suture anchor into the sustentaculum. After the deep exposure is completed, debridement of the medial gutter of loose bodies and/or scar tissue is undertaken. Every attempt should be made to delineate the deltoid ligament before debridement of the medial gutter to avoid iatrogenic injury to the ligament which could hinder later repair.

A suture anchor double-loaded with heavy non-absorbable sutures is placed in the talus at the talar insertion of the deep deltoid ligament. The intercollicular groove can be used as an antero-posterior guide for anchor placement. This location is usually in the center of the talar body when observed from a true lateral fluoroscopic image with the ankle near neutral dorsiflexion. Through the proximal end of the incision or a separate stab incision, a 3.5mm post screw with or without a washer is placed medially in a central position of the medial malleolus just proximal to its flare to decrease the risk of hardware prominence. Alternatively a small plate may be placed in this position for the same purpose.

The ankle mortise is reduced with the ankle in neutral dorsiflexion. Should the deep deltoid injury be at the medial malleolar origin or in the mid-substance (Figure 1), all four suture limbs are passed through the intercollicular groove in an extra-osseous fashion and tied around the post with the ankle reduced. The screw is advanced until tight. A combination of fluoroscopic and direct visualization through the anteromedial capsulotomy should be performed to verify anatomic reduction of the ankle. Once this is verified, the four suture limbs that are now tied to the medial malleolar post are placed in the deltoid ligament in a fan-like fashion incorporating the superficial and deep components and approximating them to the medial malleolus. The initial tying of the suture limbs to the post prior to soft tissue repair accomplishes a direct anchor-to-post reinforcement of the repair while still allowing for anatomic repair of the deltoid itself.

Less commonly, the deltoid ligament is disrupted or attenuated near its talar insertion (Figure 2). In this case two suture limbs are initially used to repair the deep

FIGURE 1: In this case, the deltoid injury is near the medial malleolar attachment, which is most common. The star represents the talar insertion of the deep deltoid, the x demonstrates the superficial deltoid. The four suture limbs are first tied around the tibial post prior to repairing the deep and superficial deltoid ligaments.

FIGURE 2: In this case, the deltoid injury is near the talar insertion, which is less common. The star represents the talar insertion of the deep deltoid, the x demonstrates the superficial deltoid. The deep deltoid is first tied down to its talar insertion and then further repair proceeds as in Figure 1, parts C and D.
deltoid back to its insertion using horizontal mattress technique. The four suture limbs including the two from the tied knot are passed through the intercollicular groove and tied over the post. The four suture limbs are then managed in the same fashion as above.

Once the repair is completed, the tibialis posterior tendon is replaced within its tendon sheath and the tendon sheath is repaired with two simple interrupted 2-0 absorbable sutures to prevent tendon subluxation. The wound is thoroughly irrigated and closed. A dry sterile dressing is applied with an overlying well padded short leg splint. Preoperative and postoperative radiographs of an SER IV-equivalent ankle fracture treated with fibular ORIF and anatomic repair of the deltoid ligament with this technique are shown in Figure 3 and Figure 4.

Postoperative protocol: The patient remains non-weightbearing to the surgical extremity initially in the postoperative splint. They return to clinic for a wound check 2 weeks postoperatively. The patient is nonweightbearing in a CAM boot from 2 to 6 weeks postoperatively but begins to perform active range of motion of the ankle out of the boot when seated/lying. At the 6 week postoperative visit the patient begins to bear weight as tolerated and weans from the CAM boot based on their comfort.

DISCUSSION

There have been many descriptions of the anatomy of the deltoid ligament which often vary in their details.3,9,12 Despite these variations, the modern paradigm is based on a cadaveric study that described three superficial and two deep deltoid ligaments.13 The relationship between form and function is well demonstrated in regard to the layers of the deltoid ligament. The superficial deltoid ligament has been shown to resist talar abduction while the deep deltoid has been shown to be more closely related to rotational stability of the talus within the mortise.15,16

While the indications for deltoid ligament repair are evolving, the goal of surgery should involve anatomic restoration of both deep and superficial deltoid ligaments. The technique described in this article has become the standard method by which the senior authors address deltoid ligament repair. In contrast to previously described techniques, it allows for repair of the deep deltoid along its entire course including medial malleolar avulsion, intrasubstance, and medial talar avulsion injuries. In addition to anatomic repair of the deep and superficial deltoid ligament, the technique also provides protection of the repair through a direct anchor-to-post suture reinforcement.

REFERENCES


Orthopaedic surgeons deployed to Afghanistan are primarily responsible for the provision of care to injured US and coalition soldiers. A vast and well-coordinated system of echeloned care has evolved to rapidly treat and evacuate injured soldiers. Orthopaedic care of injured Afghan civilians represents a common secondary mission performed by deployed orthopaedic surgeons. In this article, I describe my experiences while deployed to Afghanistan in 2011 as part of the Special Operations Surgical Team.

ABSTRACT

Orthopaedic surgeons deployed to Afghanistan are primarily responsible for the provision of care to injured US and coalition soldiers. A vast and well-coordinated system of echeloned care has evolved to rapidly treat and evacuate injured soldiers. Orthopaedic care of injured Afghan civilians represents a common secondary mission performed by deployed orthopaedic surgeons. In this article, I describe my experiences while deployed to Afghanistan in 2011 as part of the Special Operations Surgical Team.

CARE OF THE WOUNDED COALITION SOLDIER IN AFGHANISTAN

The evacuation and care of wounded soldiers has evolved throughout the history of warfare. In the recent conflicts in Iraq and Afghanistan, an echeloned approach to trauma care has been instituted. There are five levels of care. The principles of damage control surgery are applied at each level, and an efficient system of air evacuation allows for rapid transfer of wounded warriors to US facilities for definitive care.

Level I care begins with immediate care on the battlefield. All soldiers are trained in basic battlefield first aid and carry equipment including tourniquets, angiocaths for needle decompression, and oral airways. In addition, each unit has combat medics who provide first-line medical care. Soldiers are trained to use tourniquets liberally on the battlefield for extremity wounds. Evacuation often proceeds from the battlefield to a battlefield aid station, which is manned by either a physician or a PA. ATLS and resuscitation are performed at this location. However, there is no surgical capability and holding capacity is limited. A wounded soldier who requires surgical treatment may bypass the aid station and be routed directly to a higher level of care.

Surgical capability begins at Level II facilities. Level II facilities are strategically located throughout the theater of operations. All facilities provide basic laboratory and imaging capability and are staffed by orthopaedic surgeons, general surgeons, nurse anesthetists, critical care nursing staff, and other personnel to provide laboratory, radiography, ward, and OR support. Level II resources allow provision of Damage Control Surgery in a timely fashion. With respect to orthopaedic care of extremity injuries, initial debridement and provisional external fixation are typically provided. Fluoroscopic imaging is generally available. Only coalition soldiers with relatively minor injuries are treated definitively at Level II facilities. Soldiers are rapidly transported from the Level II facility to a higher level of care, which typically occurs within a few hours of arrival at the Level II facility.

Level III facilities are larger, fixed facilities which have a capability similar to US civilian trauma centers. There are two Level III facilities in Afghanistan. Specialists assigned to Level III facilities often include vascular surgeons, thoracic surgeons, urologists, obstetrician/gynecologists, neurosurgeons, otolaryngologists, and ophthalmologists in addition to general and orthopaedic surgeons. Advanced imaging, laboratory, and critical care resources are available. With respect to injured coalition soldiers, Level III facilities allow for additional resuscitation and provisional surgical treatment en route to higher levels of care. Orthopaedic care typically involves repeat debridement, application or adjustment of external fixation, and Wound VAC application. Evacuation to higher levels of care often occurs within 24 hours or less of arrival to a Level III facility.

Level IV represents the first facility in which definitive surgical management can be provided outside the combat zone. With respect to Afghanistan and Iraq, soldiers are evacuated from the Level III facilities to Landstuhl Regional Medical Center in Germany. Injuries are further evaluated, debrided, and provisionally stabilized as needed. Definitive fixation is only performed for simple, closed injuries. Patients are usually held no longer than 72 hours prior to transport back to the United States for definitive care.

Level V care is provided by several military treatment facilities in the United States. Efforts are made to evacuate the patient as close to his home station as possible while still providing the necessary capabilities. Many of these complex extremity wounds require a high level of...
skill and experience to manage appropriately. Military facilities able to provide the full spectrum of care and rehabilitation for complex injuries are located in Washington D.C., San Antonio, and San Diego.

CARE OF LOCAL NATIONALS

While care of coalition soldiers in theater is generally limited to damage control surgery, definitive care is provided to Afghan soldiers, police, and civilians at Level II and Level III facilities throughout Afghanistan. In fact, at many locations the majority of care is provided to Afghans. This involves management of complex extremity injuries that challenge available material resources as well as the individual orthopaedic surgeon’s knowledge and technical skill.

SPECIAL OPERATIONS SURGICAL TEAM

I deployed to Afghanistan as part of the Air Force Special Operations Surgical Team (SOST). Team members included a general surgeon, an orthopaedic surgeon, an emergency physician, a nurse anesthetist and a surgical technician. SOST was developed in 2003 to enhance the speed, flexibility, and reach of surgical care in support of special operations missions. SOST provides scaled increments of capability depending on the mission and anticipated time at a given location. For shorter missions, the team travels with only backpacks and can set up resuscitative and surgical capability within 10 minutes of arrival at any location. In the most remote locations, orthopaedic care is limited to debridement, fasciotomies, and provisional stabilization via external fixation, usually without the aid of fluoroscopic guidance.

MY EXPERIENCES DEPLOYED TO AFGHANISTAN

From July to December of 2011 I was in Afghanistan with the Special Operations Surgical Team. Based upon the theater needs at the time, our unique capabilities were only required for a small percent of the time. Therefore, we had the opportunity to visit a number of different locations and augment other coalition facilities while waiting for missions specific to our capabilities. We also spent time mentoring at an Afghan Hospital, a very unique professional and cultural opportunity. (In the remainder of this article, I’ll describe some of my experiences.)

Level III Facility, Bagram Air Field

Bagram Air Field is located north of Kabul in Northeast Afghanistan and is one of the largest bases in Afghanistan. The base was actually a primary staging point for Soviet operations in the 80s, and a contentious strategic location in the subsequent Afghan Civil War. During the US’s ten-year involvement, Bagram Air Field has continued to play a central role. Many coalition troops in supporting roles remain in Bagram while deployed, and many others pass through en route to more forward locations. This large facility actually contains coffee shops, fast food and movie theaters.

Craig Joint Theater Hospital, located on Bagram Air Field, is a level III facility. As noted above, this type of facility rapidly accepts transfers from lower level facilities, provides additional resuscitation and stabilization, and facilitates transfer back to the United States via Germany. Imaging capability such as CT and angiography, as well as specialized surgical capability including vascular and neurological surgery can also be employed at this location.

Three Air Force orthopaedic surgeons are assigned primarily to Craig Joint Theater Hospital. This generally includes a fellowship-trained hand surgeon and orthopaedic traumatologist. A typical deployment here is six months. In addition to the assigned surgeons, many other surgeons will briefly pass through the facility on their way to more forward locations. I spent two weeks at this facility in August of 2011 and had the opportunity to assist with clinical duties. The orthopaedic resources and facilities are very much on par with what one would expect at a Level I facility in the United States. Multiple implants are available, including various nails and pre-contoured plates, as well as surgical microscopes and the full gamut of microvascular surgical equipment.

At Bagram, the orthopaedic surgeon has the opportunity to evaluate the majority of all orthopaedic injuries sustained by US and other coalition soldiers in Afghanistan as they pass through en route to Germany and the United States. Almost all injuries have already been provisionally stabilized and debrided at a Level II facility. Their second debridement is performed at Bagram. While I was at Bagram, I gained an appreciation for the remarkable volume and severity of extremity injuries sustained in this conflict. Many of the injuries are the result of blasts from improvised explosive devices (IEDs). The dismounted (walking) IED blast represents a particularly severe injury often associated with bilateral lower extremity traumatic amputations with associated abdominal, peroneal, and upper extremity injuries. With improved technology such as body armor, many previously fatal injuries are now survivable, making effective treatment and rehabilitation of severe extremity injuries more common.

A second role of the orthopaedic surgeon assigned to Bagram is the definitive care of local Afghan soldiers and civilians. Again, high-energy gunshot wounds and IED blasts are very prevalent. Some of the more difficult local-national cases from around Afghanistan can be
referred to Bagram on a space-available basis. General principles of managing war wounds are again employed to include provisional fixation and multiple debridements prior to attempts at definitive treatment. Often, there are questions of limb salvage versus amputation. Although the International Red Cross does provide fairly consistent, if primitive, prosthesis care throughout much of the country, the Afghans were generally very resistant to consent to elective amputation in almost any circumstance. I did participate in multiple procedures designed to preserve limbs, including rotational flaps as well as nerve repairs, tendon transfers, and complex hand reconstruction procedures. Unfortunately, postoperative complications such as infection seemed to be relatively common, and follow-up at this large, centralized facility was quite inconsistent, even after complex procedures. Interestingly, many patients with external fixators in place did not return to be seen after their operations.

Level II Facility, Southern Afghanistan

Approximately 10 weeks of my deployment were spent augmenting an existing Forward Surgical Team (FST) in southern Afghanistan, in a region which was a previous Taliban stronghold. During my deployment it was an area of contention and frequent violence. Many Afghans affiliate more with their ethnic group and local tribe than with the nation as a whole. These regional variations were obvious during my brief time in Afghanistan. Generally speaking, people in this region practiced more fundamental Islam, were less educated, and were less tolerant of western notions of women’s rights compared to other regions.

The facility included a four-bed trauma bay, a single OR with two tables, as well as plain radiography and fluoroscopic capability (Figure 1). Level II facilities typically are stocked with basic small- and large-fragment plate and screws as well as external fixators. We were also able to arrange for the incorporation of intramedullary nails for tibial and retrograde femoral nailings as well as flexible rods for pediatric femur fractures.

As an orthopaedic surgeon, I stayed busy here, performing over 150 cases over a ten-week period (Figure 2). Over 90% of the surgeries were provided to local Afghan soldiers and civilians, including many children. IED injuries were quite prevalent as were gunshot wounds. In addition, when resources were available, we also provided orthopaedic care for non-war related trauma including traffic accidents and simple falls.

In my first year of surgical practice at Eglin Air Force Base, Florida, I performed primarily arthroscopic procedures and occasional trauma cases – usually limited to simple, closed fractures. This certainly did not prepare me for the complex extremity trauma I saw in Afghanistan. Fortunately, I was very well trained at Iowa and could discuss and work together on difficult cases with Dr. Brannan, another orthopaedic surgeon assigned to the facility. Given our limited resources, we often had to be a bit creative in choosing implants and reconstruction options.

We performed the first tibial and femoral intramedullary nailing procedures in this region. This represented a significant improvement over definitive external fixation, which was the previous preferred treatment. I also performed a number of flexible nail cases for pediatric femur fractures, avoiding definitive external fixation or prolonged traction in children too large for immediate spica casting.

Soft tissue management represented the primary challenge in managing complex war wounds. Skin grafting was employed frequently, as were rotational gastroc and soleus flaps for open tibia wounds. These procedures were often performed in conjunction with iliac crest bone grafting. Free flaps were not attempted due to surgeon and resource limitations. Patients requiring free-flap coverage were often told that amputation was the only option available to them.

The opportunity to provide care to Afghans at this location was a very rewarding and valuable professional experience for me. For much of my time in Afghanistan, I felt much more like a humanitarian worker than a US military soldier. I was able to make decisions, perform surgery to the best of my ability, and document only what was needed to insure appropriate continuity of care. We were truly the only medical option for many people and had the opportunity to significantly improve their lives. It was a refreshing experience and increased my interest in future overseas volunteer activities.
By Afghan standards, the ANA hospital was very well equipped. The primary administrator of the hospital was a well-connected Afghan general. The hospital had an ICU with ventilators as well as two modern ORs. Orthopaedic equipment included basic plates and screws, external fixators, and SIGN nails. However, limitations to providing modern care did exist. For example, we could run no laboratory tests due to absent or tainted reagents. The purity and integrity of medications such as IV antibiotics were always in question. The largely well-meaning and dedicated medical staff at the hospital dealt with these challenges daily.

I worked with two Afghan surgeons who performed both general surgery and orthopaedic procedures. Standards for medical and surgical training are much different in Afghanistan compared to western nations. Both surgeons had largely been trained as apprentices. One received most of his training from Soviet surgeons when Afghanistan was under Soviet control. The other trained for a few years in a large hospital in Kabul. Years of constant war and conflict had honed their basic trauma skills. Both could perform amputations with great skill and speed. We performed several interesting surgeries...

**Forward deployment in support of Special Operations Teams**

Our Special Operations Surgical Team (SOST) spent several days at far forward locations in support of small-unit special operations missions. I cannot discuss specific locations, but we traveled by helicopter with only backpacks and could quickly set up provisional surgical and resuscitative capability in tents or even outdoors, as needed. I carried the “surgical table” in my backpack, which simply consisted of a litter and stanchions. By participating in these missions, I gained even more appreciation for the unique talents, dedication, and bravery of these elite special forces units.

**Mentoring at an Afghan National Army Hospital, Western Afghanistan**

Our team also spent seven weeks mentoring Afghan surgeons in an Afghan National Army Hospital (ANA) in western Afghanistan. The culture and people of this region sharply contrasted with those from other regions. Even the Dari language was distinct. People tended to be more educated, and women played a more prominent role in society.

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The Deployed Military Orthopaedic Surgeon: Experiences of a Recent Iowa Graduate in Afghanistan

Figure 3: Enjoying lunch with members of the SOST team and our Afghan colleagues at the Afghan National Army Hospital in western Afghanistan.

Together. Femoral nonunions were relatively common following definitive external fixator treatment, and we plated a number of these with iliac crest autograft.

Surgical mentoring at the Afghan hospital during a time of war certainly presented some unique challenges. Cultural and language differences were profound. I was younger than both of my Afghan colleagues and was a visitor in their hospital. Although there were some frustrating moments initially, I hope that our work ultimately provided benefit to the Afghan surgeons and the facility in general. I sincerely enjoyed having the opportunity to work in an Afghan hospital, learn about their culture, and develop friendships with my ANA colleagues (Figure 3).

CONCLUSIONS

Orthopaedic military surgeons in Afghanistan care for injured US soldiers and provide musculoskeletal care to the local populations. Although it is difficult to be away from family and assume an increased level of personal danger, deploying as an orthopaedic surgeon to Afghanistan clearly represented the most valuable and rewarding experience of my young professional career.

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TELLING: AN ORTHOPAEDIC RESIDENT’S REVIEW OF A NEW BOOK ABOUT PHYSICIAN-PATIENT COMMUNICATION

Michael Q. Potter, MD

ABSTRACT

Former Iowa Orthopaedics Residency graduate Kevin B. Jones has written a book about the challenges of uncertainty in medicine and their impact on every individual’s interaction with the healthcare system. In What Doctors Cannot Tell You, Jones seeks to open a new conversation between physicians and patients about the unknowns in delivering medical care.

BOOK REVIEW

Anyone acquainted with the practice of medicine knows that uncertainty is a part of the game. Most of the time, a certain constellation of symptoms suggests a certain diagnosis. But might it not be another, with a different set of expectations for evaluation, prognosis and treatment? These layers of ambiguity do not accord well with the public stereotype of the physician—confident, white-coated, a mere question or test away from the correct diagnosis and definitive treatment plan. Nor do most physicians routinely discuss with their patients their doubts or the gaps in their knowledge. In What Doctors Cannot Tell You: clarity, confidence and uncertainty in medicine, a book meant for physicians and patients alike, Dr. Kevin B. Jones addresses head on this issue of uncertainty in medicine.

Dr. Jones currently works at the University of Utah as a researcher and orthopaedic surgeon specializing in malignancies of bone and soft tissue. He is an alumnus of the Iowa orthopaedic residency program and holds an undergraduate degree in English from Harvard University. In his practice as a sarcoma surgeon, Jones confronts high stakes and unknowns on a daily basis, and he draws on these experiences in crafting his first full-length work.

Each chapter in What Doctors Cannot Tell You is structured as a series of patient stories from Dr. Jones’ experiences as a trainee and a physician. He uses these stories as a jumping off point to explore larger themes in the context of specific patients. Jones revisits each patient anecdote at chapter’s end and from it suggests a principle about medicine and a question for patients to consider with their physician. He states at the outset that his goal is to “break the code of silence within which too many physician-patient conversations take place,”—to encourage frank discussion of what is known and unknown, knowable and unknowable in the process of making medical decisions.

This is undoubtedly a noble goal in the abstract, but in practice it seems a bit quixotic, so much tilting at windmills to suggest a physician could really have a full and frank discussion with every patient. Open conversation with patients takes time, and time in medicine is usually in short supply. The role of the “old-school”, infallible doctor can be played with few lines, and if we know from the outset what’s best for the patient, why not cut to the chase? It seems we all should want an honest conversation with our patients, but do we really want them inviting us into it by asking questions and challenging assumptions? Jones makes a good case that an informed conversation is an admirable goal for each patient encounter, but given the time pressures and constraints of modern medicine, I am not fully convinced such a conversation is always practical or even possible.

Perhaps the bigger obstacle in physician-patient communication is bridging the gap in knowledge and language between the doctor and the public. Jones faces a similar dilemma in trying to address his book to both groups. Physician readers may criticize the book for oversimplifying the medical details, for painting in broad strokes issues that are actually more complex and nuanced. Conversely, the lay-public may be put off or intimidated by the statistics and technical elements woven through the text. Jones does his best to find the middle ground. His patient stories are meant to appeal to an audience less versed in the arcane of medicine, but he does not discount the value of specialized knowledge. As he states in the epilogue:

This book is about improving the process of medicine, not about the outcomes of specific medical decisions. You have read stories from
patients with many different conditions and at many different moments in that process. Stories help us understand the weaknesses of the process. Stories encourage me to be honest about those weaknesses. Stories cannot replace science when it comes to understanding the outcomes of specific medical decisions. Science is flawed, but it offers the best information we have to guide decisions.

(pp. 218-9)

In striving to bridge the gap between physician and public, Jones relies on anecdotes to make science understandable. More than time constraints that limit physician patient interactions, bridging the knowledge gap is perhaps the major challenge we as physicians face in communicating effectively with patients. It is certainly the challenge Jones faces writing for both audiences simultaneously.

In the prologue, Jones describes a conversation with the mother of a child diagnosed with sarcoma. Plunged into a chaotic and difficult situation, she clings to the details of her son’s chemotherapy protocol as a talisman against the unknown. “I will do anything for my Ewan,” she tells Jones. “He’s all I’ve got. I can follow this protocol to keep him safe.” (p. 3)

Jones’ reflections on this statement are instructive. As a physician, he recognizes that while Ewan’s chemotherapy regimen represents the best consensus of medical thinking and clinical experience, and while it has in the past resulted in favorable outcomes for other children in Ewan’s situation, adherence to the protocol alone cannot guarantee safety. As a human being, though, he responds to the mother’s anguish and holds his tongue. As he does, he notes, “my silence probably reinforced a promise she had heard in the unspoken words of the oncologist earlier in the day…yes, she and Ewan should stick to the protocol as closely as possible. But obedience alone wouldn’t save him.” (p. 4)

Jones also discusses the less than admirable track record medicine has of sharing its internal debates with the public. In a vignette called “Civics and Specifics,” Jones delves into the controversial utility of PSA testing. He describes how this debate raged among physicians for several of decades. Despite this, almost every major media outlet in the nation has had a lead article about PSA testing within the last 6 months. How has this old debate become news? Well, we never really talked about it with our patients; we only argued amongst ourselves.

Similar consideration is given to the history of mammography, hormone replacement therapy, and cardiac surgery’s pump head phenomenon, but Jones does not spare his own specialty. From NASCIS to Vioxx, pertrochanteric femur fracture fixation implants to arthroscopy indications, he hits the high (and low) points within orthopaedics. He does so not to criticize or condemn, but rather he seeks to understand why we in medicine often say the things we say with so much greater confidence than our evidence provides. Take the example of the VA arthroscopy study. Jones relates his personal disappointment that arthroscopic debridement of arthritic knees regained some popularity after an initial decline following the study’s publication, but he also notes that some practitioners have returned to it without clear financial incentive. Right or wrong, he makes no judgment—after all, he notes, how else can we achieve a surgery-sized placebo effect for arthritic patients?

Jones also writes at some length about the specific challenges of surgeons and our desire to appear confident. As I transition from junior resident to senior
As a physician in-training, *What Doctors Cannot Tell You* rings most true in its descriptions of the internal debates that face doctors to one degree or another in each patient interaction. This book deftly articulates the human struggle of what to tell and what to hold back. Jones may not give us clear answers, but he clearly wants to start the conversation. If lay readers find his writing as accessible as I think they will, he may just get his wish. In the best case, *What Doctors Cannot Tell You* will also provoke physicians to think critically about how to communicate with patients individually and how to open up the medical discussion to the public at large.

REFERENCES


