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PUBLICATION RATES VARY ACROSS ORTHOPAEDIC SUBSPECIALTIES: A LONGITUDINAL ANALYSIS OF AAOS ABSTRACTS

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ABSTRACT

Background: Presentation of research at national orthopaedic meetings and subsequent publication are important for both information exchange among surgeons and individual academic advancement. However, the academic landscape and pressures that researchers face may differ greatly across different subspecialties. This study attempts to explore and quantify differences in research presented at national conferences and its implication on ultimate likelihood of publication in peer-reviewed journals.

Methods: All abstracts from the Annual Meetings of the American Academy of Orthopaedic Surgeons (AAOS) from 2016 and 2017 were reviewed and categorized based on subspecialty focus. Resulting publications were identified using a systematic search of PubMed and Google Scholar databases. Multivariate binary logistic regression modelling was used to assess the predictive value of abstract characteristics on eventual publication.

Results: A total of 1805 abstracts from the 2016 and 2017 AAOS conferences were reviewed. The overall publication rate of abstracts following the AAOS meetings was 71.6%, with an average time to publication from abstract submission deadline and impact factor of 19.8 months and 2.878, respectively. Statistical differences were observed across subspecialties with respect to publication rate (p<0.001), time to publication (p<0.001), and impact factor (p<0.001). The subspecialty with the highest publication rate, largest impact factor, and shortest average time to publication was Sports Medicine with 83.2%, 3.98, and 17.6 months, respectively; despite lower average sample size (p<0.001) and frequency of multicenter design (p<0.001) compared with other subspecialties. The subspecialty with the lowest publication rate and impact factor was Hand and Wrist with 53.3% and 1.41, respectively. Multivariate logistic regression analysis demonstrates a lower likelihood for internationally authored abstracts (OR: 0.75, p=0.021) and higher likelihood for basic science abstracts (OR: 1.52, p-value=0.023) to reach publication.

Conclusion: Differences in publication rate across orthopaedic subspecialties were observed with articles in sports medicine more likely to be published, published quickly, and featured in a higher impact factor journals. Understanding these differences, and how they relate to the publication and promotion of novel research, is important for orthopaedic researchers.

Level of Evidence: IV

Keywords: AAOS, orthopaedic subspecialties, subspecialty, publication rate, research, orthopedics

INTRODUCTION

In the field of orthopaedic surgery, the American Academy of Orthopaedic Surgeons (AAOS) annual meeting provides a forum for the presentation of new ideas, stimulation of discussion, and encouragement of research development at all stages of training.[1] With a total attendance approaching 30,000 individuals including 13,000 pyhsicians,[2] the opportunity for the distribution of new practice changing ideas is high.

National conferences have an individual peer review process that approves abstracts for presentation. However, sufficient information to review is often lacking and individual reviewer bias has been noted to contaminate this process.[3,4] As a result, not all abstract presentations will go on to pass the rigorous journal submission review process. This and other author specific factors contribute to the barriers to publication faced by authors.[5] Publication rates of abstracts presented at AAOS have shown an increasing trajectory over recent years with most recent podium abstract publication rates reaching 68% from the 2010 conference.[6-10]

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The importance of accurate information being presented is demonstrated by a review of prominent orthopaedic textbooks indicating that between 53% to 63% of chapters referenced at least one abstract from a conference meeting.[7] Additionally, presentations are commonly referenced by physicians in lectures and during hospital rounds. These may influence clinical practice and the training of next generation physicians. As a result, it is important to understand the frequency at which research presented at academic conferences will pass the peer review process as well as what factors are predictive of eventual publication.

The objectives of this study were to determine (1) the overall publication rates and time to publication of podium presentations from the 2016 and 2017 AAOS national meetings; (2) whether publication rates differ based on subspecialty focus; and (3) abstract and author specific characteristics indicative of future publication.

METHODS

The final programs of the 83rd and 84th annual meetings of the American Academy of Orthopaedic Surgeons taking place in March of 2016 and 2017 were retrospectively reviewed. All abstracts of podium presentations were included in this observational study. Poster and scientific exhibit presentations were excluded from analysis. Abstracts were reviewed by three separate investigators to determine study characteristics including international status, total number of subjects, topic of investigation (basic science vs radiographic measurement study vs pain management vs medical education vs cost analysis vs other), and study design (multicenter vs single center vs randomized controlled trial vs use of national database vs meta-analysis vs survey based study). Level of evidence was assigned for each abstract according to the most recent JBJS guidelines.[11] Article subspecialty focus was classified according to designation within the AAOS meeting program (Adult Reconstruction vs Foot and Ankle vs Hand and Wrist vs Musculoskeletal Oncology vs Pediatrics vs Practice Management vs Shoulder and Elbow vs Spine vs Sports Medicine vs Trauma).

Studies conducted at institutions outside of the United States were classified as international. When author collaboration occurred between US and international authors, the country of the primary author was used to determine international status. An article was designated as basic science if the methodology involved the use of animal models, biomechanical analysis, or in vitro techniques. A studies sample size was defined as the number of patients included in the analysis. A studies sample size was excluded from calculations if a large nationwide database was used.

Subsequent publication was identified by a computerized search of PubMed and Google Scholar databases using abstract title keywords and combinations of first and senior author names. If a manuscript was identified, information recorded included date of publication, journal of publication, and the impact factor of the journal. If the first or second investigator could not identify an abstract with a corresponding publication, a third investigator repeated the search with similar methodology. Journal impact factors were determined from the Journal Citation Reports produced by Clarivate Analytics.[12] Time to publication was calculated as the difference between the date of publication and the abstract submission deadline for that years conference.

Chi-Squared and Fisher's Exact tests were used to compare binary and categorical variables between specialties. Kruskal-Wallis test was used to compare the number of patients per abstract, time to publication, and impact factor. Kaplan-Meier test plotted with inverse survival analysis was performed to evaluate differences between abstract focus using a log-rank test. Multivariate binary logistic regression modelling was used to assess the predictive value of abstract characteristics on eventual publication. All statistical analysis was performed using SPSS software for Macintosh, version 23. A significance threshold of $p<0.05$ was used for all analyses.

RESULTS

1805 of 1836 podium presentation abstracts were identified from 2016-2017 and evaluated with 31 withdrawn or not available. A total of 485 (26.9%) abstracts were classified as international across both conferences. There was a higher proportion of multicenter studies in the 2017 abstracts compared to 2016 (15.6% vs 11.0, $p=0.003$). There was no difference between conference years in terms of international abstracts ($p=0.506$), topic of presentation ($p=0.831$), specialty focus ($p=0.966$), level of evidence split ($p=0.058$), proportion of survey based studies ($p=0.067$), database studies ($p=0.289$), meta-analyses ($p=0.336$), randomized controlled trials ($p=0.480$), or publication rate ($p=0.088$). The overall publication rate of all abstracts was 71.6% at final follow up.

The largest subspecialty represented was adult reconstruction with 494 (27.4%) abstracts. The smallest was musculoskeletal oncology with 60 (3.3%) abstracts. The subspecialty with the highest proportion of international authored abstracts was Musculoskeletal Oncology (45.0%, $p<0.001$). The highest proportion of basic science articles was in Sports Medicine (20.3%, $p<0.001$). Differences were observed across subspecialties for both time to publication ($p<0.001$) and impact factor ($p<0.001$). The subspecialty with the largest impact factor and shortest average time to publication was Sports

Table 1. Publication Characteristics by Orthopaedic Subspecialty

Subspecialty	Total Number of Abstracts	% International	% Basic Science/ Anatomy/ Biomechanics	% Published Abstracts	Time to Publication in Months (IQR)	Impact Factor (IQR)
Adult Reconstruction	494	28.9%	8.5%	68.6 %	19.5 (13.0-24.0)	3.36 (3.0-3.52)
Foot and Ankle	105	28.6%	6.7%	65.7 %	18.6 (7.5-28)	1.66 (0.22-2.34)
Hand and Wrist	90	23.3%	13.3%	53.3 %	20.7 (9.25-31.75)	1.41 (0.19-2.09)
Musculoskeletal Oncology	60	45.0%	15.0%	61.7 %	20.9 (11.5-30.5)	2.88 (1.93-4.15)
Pediatrics	116	8.6%	19.0%	66.4 %	26.9 (16.5-36.5)	2.56 (1.73-4.15)
Practice Management	89	9.0%	0%	58.4 %	15.0 (5.0-20.0)	2.42 (0.92-3.52)
Shoulder Elbow	206	37.9%	17.0%	76.2 %	19.3 (11.0-25.0)	3.01 (2.09-4.43)
Spine	205	20.5%	9.3%	79.5 %	19.2 (10.0-28.0)	2.39 (1.73-3.20)
Sports Medicine	232	30.6%	20.3%	83.2 %	17.6 (9.0-23.0)	3.98 (2.59-6.09)
Trauma	208	26.4%	8.2%	73.1 %	22.5 (13.0-30.0)	2.19 (0.92-2.87)
Total	1805	26.9%	11.6%	71.6%	19.8 (11.0-26.0)	2.88 (1.76-4.13)

Table 2. Abstract Characteristics for Each Orthopaedic Subspecialty

Subspecialty	Average Sample Size*	Multicenter (%)	Level of Evidence 1 or 2 (%)	Randomized Controlled Trials (%)
Adult Reconstruction	589.7	67 (13.6)	145 (29.4)	55 (11.1)
Foot and Ankle	116.1	10 (9.5)	29 (27.6)	8 (7.6)
Hand and Wrist	135.4	8 (8.9)	31 (34.4)	5 (5.6)
Musculoskeletal Oncology	117.8	13 (21.7)	9 (15.0)	0
Pediatrics	233.1	24 (20.7)	18 (15.5)	2 (1.7)
Practice Management	722.2	19 (21.3)	16 (18.0)	5 (5.6)
Shoulder and Elbow	297.4	9 (4.4)	54 (26.2)	23 (11.2)
Spine	294.6	27 (13.2)	40 (19.5)	12 (5.9)
Sports Medicine	192.5	15 (6.5)	52 (22.4)	13 (5.6)
Trauma	308.9	47 (22.6)	39 (18.8)	16 (7.7)
Total	333.7	239 (13.2)	433 (24.0)	139 (7.7)

Values expressed as mean or number (%).
*Excluding large national databases.

Medicine with 3.98 and 17.6 months, respectively (Table 1). This was in spite of having a lower average sample size (297.4, $p<0.001$), frequency of multicenter design (4.4%, $p<0.001$), and proportion of level one or two studies (22.4%, $p<0.001$) compared to other subspecialties. The subspecialty with the highest proportion of randomized controlled trials was Shoulder and Elbow (11.2%, $p=0.002$) (Table 2).

Differences in publication rate were significant, with the highest and lowest rates occurring in Sports Medicine (83.2%) and Hand and Wrist (53.3%), respectively ($p<0.001$) (Figure 1). The subspecialty with the largest percentage of articles published in a single journal was adult reconstruction with 47.8% of articles leading to publication in the Journal of Arthroplasty. This was also the most common journal when considering all published abstracts (14.2%) (Table 3).

Multivariate regression demonstrated that international classification was identified as a detriment to publication (OR, 0.75; CI, 0.59 – 0.96). Basic science methodology (OR, 1.52; CI, 1.06 – 2.18) and multicenter collaboration (OR, 1.68; CI, 1.21 – 2.35) were both noted as significant predictors of future publication. When comparing likelihood of publication to the hand and wrist subspecialty, Spine (OR, 3.43; CI, 1.99 – 5.88) and Sports Medicine (OR, 4.45; CI, 2.58 – 7.66) were both significantly more likely to predict future publication, among other subspecialties (Table 4).

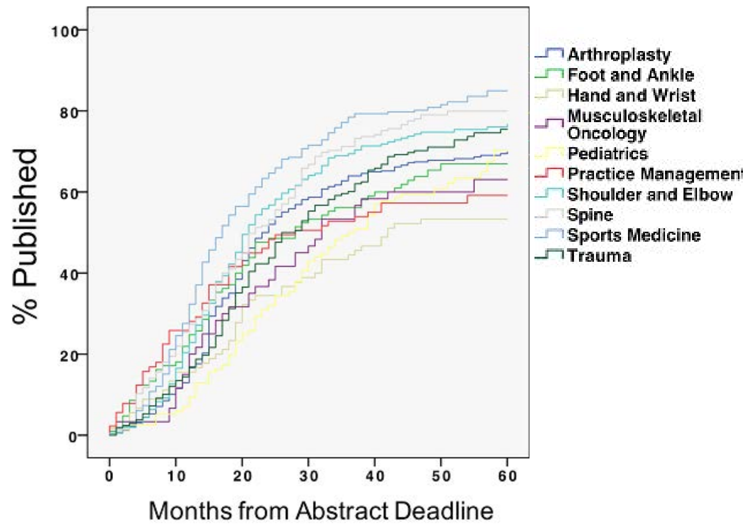

Figure 1. Kaplan Meier Curve indicating time to publication by sub-specialty.

Table 3. Most Common Journal of Publication for Each Orthopaedic Subspecialty

Specialty	Top Journal Name	Number (%)	Impact Factor
Adult Reconstruction	The Journal of Arthroplasty	160 (47.8)	3.524
Foot and Ankle	Foot and Ankle International	19 (27.9)	2.341
Hand and Wrist	Journal of Hand Surgery	14 (29.8)	2.09
Musculoskeletal Oncology	Clinical Orthopaedics and Related Research	7 (18.9)	4.154
Pediatrics	Journal of Pediatric Orthopaedics	25 (32.5)	2.046
Practice Management	The Journal of Arthroplasty	12 (23.1)	3.524
Shoulder and Elbow	Journal of Shoulder and Elbow Surgery	55 (35.0)	2.865
Spine	The Spine Journal	38 (23.3)	3.196
Sports Medicine	The American Journal of Sports Medicine	52 (26.9)	6.093
Trauma	Journal of Orthopaedic Trauma	45 (29.6)	1.826
Total	The Journal of Arthroplasty	184 (14.2)	3.524

Table 4. Analysis of Potential Predictive Factors for Publication

Factor	% Published	OR	CI	p-value
International vs Local				
International	68.2	0.75	0.59 – 0.96	0.021
Local	72.4			
Basic Science vs Clinical				
Basic Science	79.0	1.52	1.06 – 2.18	0.023
Clinical	70.3			
Multicenter vs Single Center				
Multicenter	77.8	1.68	1.21 – 2.35	0.002
Single Center	70.3			
Level of Evidence				
1 or 2	70.7	1.06	0.82 – 1.36	0.668
3, 4, N/A	71.5			
Specialty				
Adult Reconstruction	68.6	1.96	1.24 – 3.10	0.004
Foot and Ankle	65.7	1.76	0.98 – 3.15	0.057
Musculoskeletal Oncology	61.7	1.42	0.72 – 2.79	0.313
Pediatrics	66.4	1.56	0.88 – 2.76	0.130
Practice Management	58.4	1.18	0.65 – 2.16	0.582
Shoulder and Elbow	76.2	2.99	1.76 – 5.07	<0.001
Spine	79.5	3.43	1.99 – 5.88	<0.001
Sports Medicine	83.2	4.45	2.58 – 7.66	<0.001
Trauma	73.1	2.33	1.38 – 3.93	0.001
Hand and Wrist	53.3	-		

DISCUSSION

Presentation of research at academic conferences is a common method for conveying methodologies and results of current research. However, the publication of projects in a peer-reviewed journal represents a permanent and validated method for research distribution. At the AAOS national meeting, abstract publication rate has been shown to be between 34% and 66%.[6-8] The purpose of this study was to determine if differences in publication rate exist based on subspecialty focus and to assess paper and author characteristics that may contribute to eventual publication. The current study demonstrated an overall publication rate of 71.6%, which is consistent with published results and likely reflective of increasing publication trends in recent years.[6-10] Sports Medicine abstracts had the highest rate of publication, the shortest time to publication, and the highest average impact factor among subspecialties despite comparable quality characteristics to other subspecialties.

Since research is selected for conference presentation based solely on the submitted abstract with no opportunity for revisions following peer review, knowing when to use presentations at scientific meetings to guide clinical practice can be challenging. It has been shown that 1.7% of podium abstracts presented led to a publication with a different conclusion between presentation and publication[6] and that up to 30% had changes in study population size.[6,7] Given publication rates below 100% and evidence of important inconsistencies between the abstract and final publication,[13] it remains important to use caution in interpreting research presentations.

Similar to studies of the 2001 and 2010 AAOS conferences,[6,8] the current study shows higher rates of publication in Sports Medicine (83.2%) and Spine (79.5%) abstracts relative to other subspecialties. For Sports Medicine in particular, this difference was accompanied by the fastest time to publication and the highest average journal impact factor of publication. This is consistent with a previously reported rate of publication of presentations following the American Orthopaedic Society for Sports Medicine annual meeting from 2006-2010 being 73.3%.[14] This rate is significantly higher than rates of publication following arthroplasty,[15] trauma,[13] musculoskeletal oncology,[16] and spine[17] specific conferences. By also observing these trends within the AAOS conference abstracts, it lends credence to the idea that field specific factors likely drive these differences in publication. Additional reasons for these differences include the potential audiences of the research being published. For instance, topics published regarding sports medicine topics may be of interest to not just orthopaedic surgeons, but also nonoperative sports medicine physicians, athletic trainers, or physical therapists. This represents a larger potential audience and higher demand for research in these fields. Given the importance of publication frequency and number of citations towards academic progression and promotion in orthopaedic surgery,[18-21] further study is needed to understand how these factors affect individual surgeon academic advancement across different subspecialties.

The average time to publication from abstract submission deadline was 19.8 months. This represented the time between the abstract submission deadline and the ultimate date of publication. This is in concordance with the most recent published study assessing time to publication from the trauma and adult reconstruction subspecialties at AAOS.[22] Various barriers to publication following orthopaedic conference presentation have been reported including time limitations, continuation of data collection, difficulty with co-authors, low prioritization, and potential gender bias.[5,23,24] How these barriers may differ based on subspecialty warrant further study.

The proportion of international presentations was 26.9% of all abstracts presented at AAOS, with the lowest rates of international research being presented in the Practice Management and Pediatric subspecialty categories. Research performed outside the United States was found to be less likely to lead to future publication. Previous studies have demonstrated the association between a journals' nationality and the nation of the articles that they publish.[25-27] Studies in Gastroenterology and JAMA, both US journals, demonstrated that studies with US authors and those enrolling patients in the US had a higher likelihood of publication in their respective journals.[28,29] However, our finding here is the first time this phenomenon has been reported in the orthopaedic surgery literature.[22,30,31] Given the upward trend in international publications, from countries including China and Korea,[32] studies using different patient populations or orthopaedic treatments are important to guide practice of orthopaedic surgery in the United States.

This study has several limitations. The authors note that while similar approaches to tracking publications following abstract presentation have been used in previous studies,[7,8,14] our searches were limited to PubMed and Google Scholar databases. Thus, we failed to identify articles not indexed in these specific databases potentially underestimating the true rate of publication. This may be especially relevant for international authors and may be a contributor to the lower publication rate in this group. Additionally, we worked under the assumption that authors worked to publish their research as soon as possible. However, this may not always be the case, particularly when more data collection is indicated prior to publication. Additionally, our follow up was limited to a minimum of 48 months and maximum of 60 months after abstract submission deadline. However, it has been noted that the vast majority of publications occur within the first several years following conference presentation.[11,22,33,34] Finally, the impact of the COVID-19 pandemic and its effect on publication rates was unable to be included here.

This study provides useful guidance for physicians attending the AAOS conference to understand the likelihood of information presented ultimately passing the peer review process. Further work is needed to explore barriers to publication following abstract presentation and the influence of publication pressures on orthopaedic surgeons practicing in different subspecialties.

CONCLUSION

Abstracts presented at the AAOS conference tended to have different publication rates depending on subspecialty, with Hand and Wrist articles being almost 30% less likely to be published when compared to those in Sports Medicine. Articles in Sports Medicine were more likely to be published, published quickly, and featured in a higher impact factor journal despite having a lower average sample size and being less likely to report multicenter investigations. These differences are most likely the result of number and quality of subspecialty-specific journals. Understanding these differences and how they relate to the availability of scientific information and individual academic advancement merits further exploration.

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DEFORMITIES INFLUENCING DIFFERENT CLASSES IN PROGRESSIVE COLLAPSING FOOT

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ABSTRACT

Background: The current classification system of progressive collapsing foot deformity (PCFD) is comprised of 5 possible classes. PCFD is understood to be a complex, three-dimensional deformity occurring in many regions along the foot and ankle. The question remains whether a deformity in one area impacts other areas. The objective of this study is to assess how each one of the classes is influenced by other classes by evaluating each associated angular measurement. We hypothesized that positive and linear correlations would occur for each class with at least one other class and that this influence would be high.

Methods: We retrospectively assessed weight bearing CT (WBCT) measurements of 32 feet with PCFD diagnosis. The classes and their associated radiographic measurements were defined as follows: class A (hindfoot valgus) measured by the hindfoot moment arm (HMA), class B (midfoot abduction) measured by the talonavicular coverage angle (TNCA), class C (medial column instability) measured by Meary's angle, class D (peritalar subluxation) measured by the medial facet uncoverage (MFU), and class E (ankle valgus) measured using the talar tilt angle (TTA). Multivariate analyses were completed comparing each class measurement to the other classes. A p-value <0.05 was considered significant.

Results: Class A showed substantial positive correlation with class C (ρ=0.71; R^2=0.576; p=0.001). Class B was substantially correlated with class D (ρ=0.74; R^2=0.613; p=0.001). Class C showed a substantial positive correlation with class A (ρ=0.71; R^2=0.576; p=0.001) and class D (ρ=0.75; R^2=0.559; p=0.001). Class D showed substantial positive correlation with class B and class C (ρ=0.74; R^2=0.613; p=0.001), (ρ=0.75; R^2=0.559; p=0.001) respectively. Class E did not show correlation with class B, C or D (ρ=0.24; R^2=0.074; p=0.059), (ρ=0.17; R^2=0.071; p=0.179), and (ρ=0.22; R^2=0.022; p=0.082) respectively.

Conclusion: This study was able to find relations between components of PCFD deformity with exception of ankle valgus (Class E). Measurements associated with each class were influenced by others, and in some instances with pronounced strength. The presented data may support the notion that PCFD is a three-dimensional complex deformity and suggests a possible relation among its ostensibly independent features.

Level of Evidence: III

Keywords: PCFD, flatfoot, hindfoot moment arm, meary's angle, talonavicular coverage angle, talar tilt angle, middle facet subluxation, middle facet uncoverage, peritalar subluxation, weight bearing CT, WBCT, AAFD

INTRODUCTION

A group of experts recently came to a consensus agreement on a new classification system of PCFD.[1] The proposed changes were supported by the idea that PCFD is a multi-faceted 3D deformity that can show up in many different case scenarios. The new classification included 5 different classes that could occur simultaneously. Each class could further be subdivided into stage I (flexible) and stage II (rigid). Class A indicates hindfoot valgus deformity, class B indicates midfoot/forefoot abduction deformity, class C evaluates forefoot varus deformity and medial column instability, class D

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is specific for peri-talar subluxation and finally class E evaluates ankle joint instability and valgus talus tilting in the ankle mortise.[1]

According to the new classification system, patient could have one or more item of the deformity at the same time. However, to our knowledge, the relationship between each component of PCFD deformities was not studied so far.

The main aim of this project is to evaluate how each component of PCFD is influenced by other deformities using the proposed angular measurements.

We hypothesized that all classes would be affected by at least one component of the deformity, determined by a high coefficient correlation.

METHODS

This research was approved by our institution's institutional review board and followed the Declaration of Helsinki and the Health Insurance Portability and Accountability Act (HIPAA). The study was IRB approved (approval number 202012422) In this single center, retrospective cohort study, we reviewed our weightbearing computed tomography (WBCT) database from 01/01/2018 to 12/31/2020. The database includes all patients who underwent WBCT imaging for different foot and ankle conditions. Patients with rigid deformities, advanced ankle or foot joints arthritis, previous foot or ankle surgery, prisoners, tarsal coalition, inflammatory diseases, infection, neuropathy, and patients younger than 18 years old were excluded. We included 32 patients with PCFD; 22 (68.75%) patients were females 17 (53.13%) were left sided. The average age of the cohort was 47.06 (SD ± 8.21) with BMI of 33.03 (SD ± 8.21).

Weight bearing CT imaging

All WBCT (pedCAT; Curvebeam, Warrington, PA) data were acquired using a standardized procedure with patients in an upright weightbearing posture. Three-dimensional (3D) data were transformed to axial, sagittal, and coronal images and uploaded digitally to the appropriate software (CubeVue; CurveBeam).

Two fellowship-trained orthopaedic foot and ankle surgeons independently evaluated WBCT studies. Five different WBCT parameters were evaluated to assess each component of the deformity. Hindfoot moment arm (HMA) was evaluated in the coronal plane, the anatomical axis of the tibia was extended distally to the floor level. The coronal images are scrolled until the most plantar weight bearing point of the calcaneus was identified. HMA was measured as the distance between this point and the extension of the anatomical axis of the tibia at the floor level. HMA quantify the amount of valgus deformity of the hindfoot (Class A).[2-4] (Figure 1). Talo-navicular coverage angle (TNCA) was measured in the coronal plane, the articular surface of the navicular was identified with care to avoid including the navicular tuberosity or osteophytes. Another line represents the talar articular surface at the talonavicular joint was established. The TNCA was measured as the angle between the perpendicular lines to both articular surfaces lines. It represents the amount of forefoot/midfoot abduction (Class B).[5,6] (Figure 1). In the sagittal plane, Meary's angle was measured between the longitudinal axis of the talus and longitudinal axis of the first metatarsal. This angle evaluates medial column instability (Class C).[7] (Figure 1) Class D was evaluated by the way of middle facet uncoverage (MFU); On the sagittal images of the hindfoot was scrutinized to get the perfect capture of the middle facet, then same captured area was evaluated in coronal cuts. The length of the middle facet of the talus is measured then uncovered distance of the calcaneus was measured (from the medial aspect of the calcaneus to the most medial aspect of the middle facet of talus). The percentage of MFU is calculated by dividing the measured uncovered calcaneal distance to the total length of talus middle facet.[8] (Figure 1). Talat tilt angle (TTA) was measured on the sagittal images at the center of the talus dome in coronal image. A line was drawn tangential to the distal tibial articular surface and another line was measured along the superior talar surface then the angle between the two lines represented the talar tilt angle. TTA represents class E deformity.[4](Figure 1).

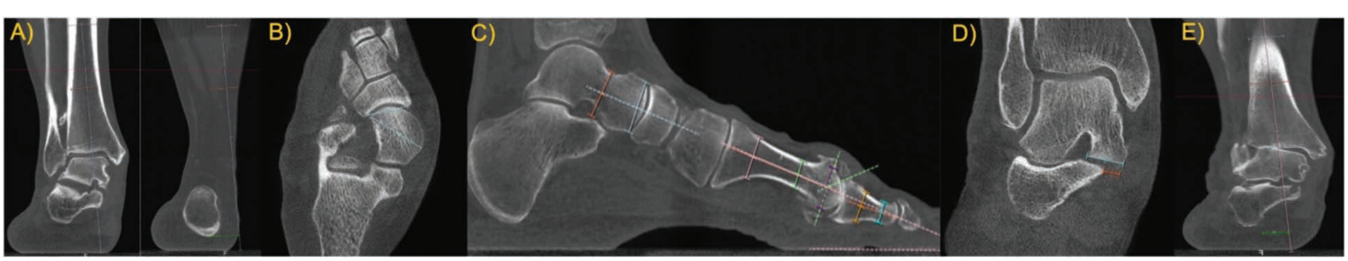

Figure 1A to 1E. The five WBCT parameters evaluated in the present research; (1A) Hindfoot moment arm (Class A); (1B) Talo-navicular uncoverage angle (Class B); (1C) Meary's angle (Class C); (1D) Middle facet uncoverage (Class D); (1E) Talar tilt angle (Class E).

Statistical analysis

SPSS was used to do all the analysis (IBM Corp, Armonk, NY). For continuous variables, the mean and standard deviation were given. For discrete variables, the frequency and percentage were reported. Cohen kappa with 95% confidence intervals (CIs) was used to find the reliability between observers.[9] Fleiss kappa analysis with 95% confidence intervals (CIs) was used to report the reliability between readers.[9] Landis and Koch used kappa values to show the level of agreement: 0.00-0.20 for poor, 0.21-0.40 for fair, 0.41-0.60 for moderate, 0.61-0.80 for substantial, and 0.81-1.00 for almost perfect agreement.[10] Multi-variate analyses were done assessing each class of measurement in relation to other classes' metrics. Additionally, Belsley-Kuh-Welsch technique was used to assess data multi-collinearity.[11] Heteroskedasticity and normality of residuals were assessed respectively by the Breusch-Pegan test and the Shaprio-Wilk test respectively. A p-value <0.05 was considered significant for all the used statistical tests.[12]

RESULTS

The average HMA was (8.19 mm SD ± 8.58), TNCA was (29.34° SD ± 14.01), Meary's angle was (23.83° SD ± 10.95), MFU was (41.84% SD ± 15.72) and TTA was (2.46° SD ± 0.27). (Table 1)

After removing confounding variables, each class was separately evaluated. Class A which represents hindfoot valgus deformity was evaluated using HMA and was found to have a moderate positive correlation with TNCA (Class B) (ρ=0.59; R^2=0.386; p=0.001). Class A also showed moderate positive correlation with class D (MFU) (ρ=0.7; R^2=0.489; p=0.001). A substantial positive correlation was found between class A (HMA) and Meary's angle (Class C) (ρ=0.71; R^2=0.576; p=0.001). No correlation was found between HMA and TTA (ρ=0.17; R^2=0.14; p=0.204). (Figure 2 and 3)

On evaluation of class B (forefoot/midfoot abduction) which was evaluated by measuring the TNCA, a moderate positive correlation was found between class B (TNCA) and class A (HMA) and Meary's angle (Class C) (ρ=0.59; R^2=0.386; p=0.001) and (ρ=0.66; R^2=0.413; p=0.001) respectively. A substantial positive correlation was found between class B (TNCA) and class D (MFU) (ρ=0.74; R^2=0.613; p=0.001). No correlation was found between TNCA and TTA (ρ=0.16; R^2=0.137; p=0.221). (Figure 2 and 3)

Medial column instability (represents class C deformity) was assessed by Meary's angle and showed a substantial positive correlation with class A (HMA) (ρ=0.71; R^2=0.576; p=0.001) and class D (MFU) (ρ=0.75; R^2=0.559; p=0.001). A moderate positive correlation was found as well with class B (TNCA) (ρ=0.66; R^2=0.413; p=0.001). No correlation was found between Meary's and Talar Tilt (ρ=0.08; R^2=0.03; p=0.541). (Figure 2 and 3)

Class D which evaluates peri-talar subluxation (PTS), represented by middle facet uncoverage percentage (MFU),was moderately correlated with class A (HMA) (ρ=0.7; R^2=0.489; p=0.001). A substantial positive correlation was present between class D (MFU) and Class B (TNCA) as well as with class C (Meary's angle) (ρ=0.74; R^2=0.613; p=0.001), (ρ=0.75; R^2=0.559; p=0.001) respectively. No correlation was found between MFU and TTA (ρ=0.18; R^2=0.109; p=0.176). (Figure 2 and 3)

Finally, class E evaluation which represents ankle valgus deformity was evaluated using talar tilt angle (TTA), it showed poor positive correlation with class A (HMA) (ρ=0.26; R^2=0.246; p=0.036). No correlation was found between class E and class B (TNCA), or Class C (Meary's angle) or class D (MFU) (ρ=0.24; R^2=0.074; p=0.059), (ρ=0.17; R^2=0.071; p=0.179), and (ρ=0.22; R^2=0.022; p=0.082) respectively. (Figure 2 and 3)

Table 1. Values of Measurements of Different PCFD Classes

Measurements	Mean (Standard deviation)	ICC value
HMA (Class A)	18.19 mm (± 8.58)	0.88 (0.73-0.94)
TNCA (Class B)	29.34° (± 14.01)	0.80 (0.57-0.90)
Meary's angle (Class C)	23.83° (± 10.95)	0.77 (0.61-0.85)
MFU (Class D)	41.84 (± 15.72)	0.89 (0.71-0.92)
TTA (Class E)	2.46° (± 0.27)	0.91 (0.74-0.95)

HMA: Hindfoot moment arm. TNCA: Talonavicular coverage angle. MFU: Middle facet uncoverage. TTA: Talar tilt angle. ICC: Interclass coefficient.

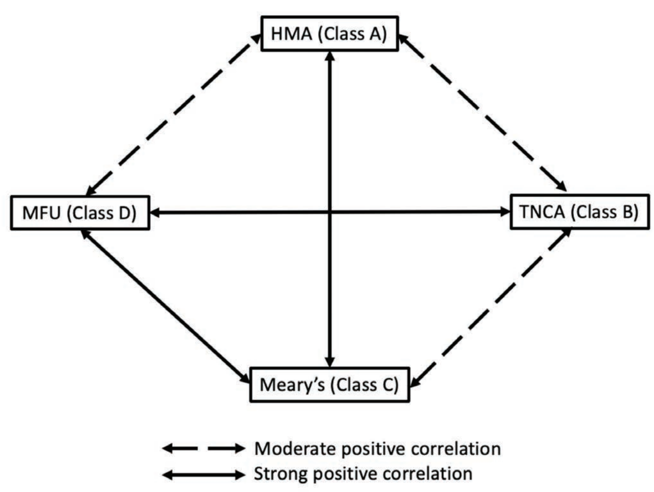

Figure 2. Correlations between different PCFD classes.

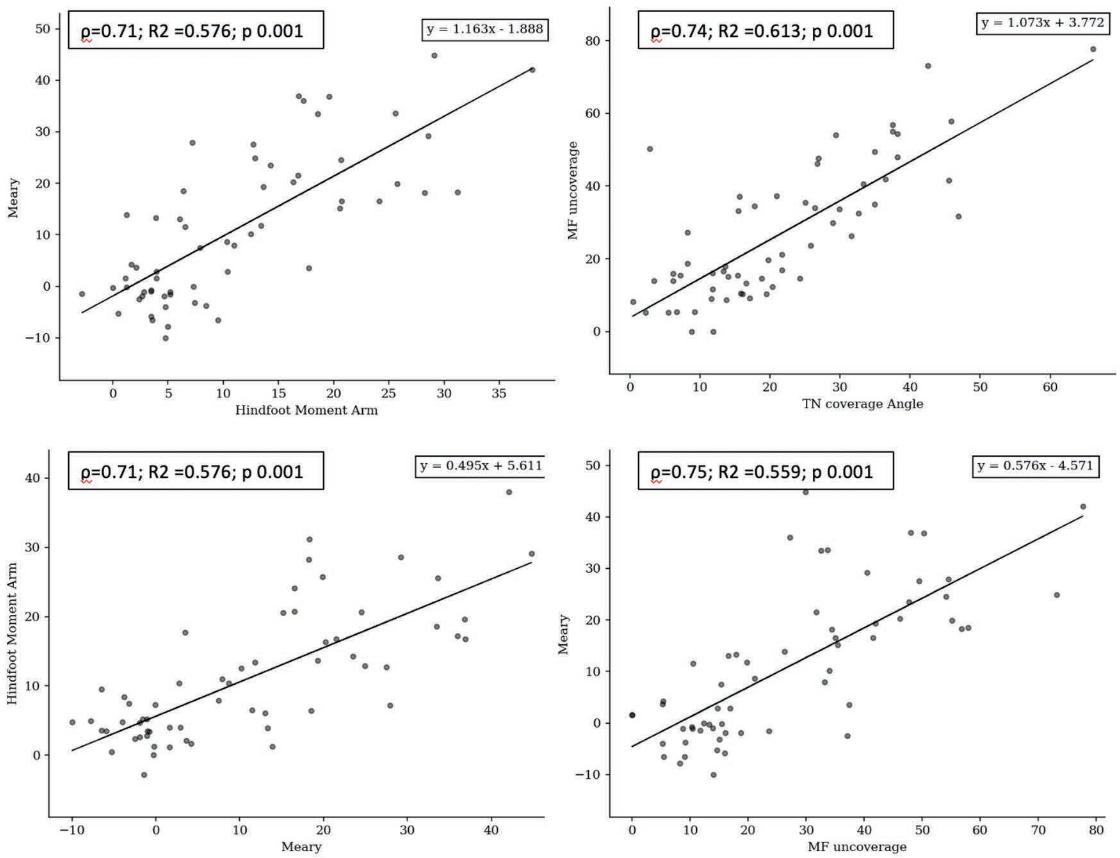

Figure 3. Strong correlations between different classes.

DISCUSSION

The most important finding of this study that it shows all of PCFD classes are correlated to each other except for class E (ankle valgus deformity) which prove out proposed hypothesis to be true. class A (HMA) showed strong positive correlation with class C (Meary's angle) (ρ=0.71; R^2=0.576; p 0.001). class B (TNCA) showed substantial positive correlation with class D (MFS) ρ=0.74; R^2=0.613; p 0.001). class C and D showed strong positive correlation as well (ρ=0.75; R^2=0.559; p 0.001).

Since almost all of classes (except class E) showed at least one or more strong correlation with at least one other deformity class, it substantiates the notion of PCFD deformities are inter-related and they didn't follow a clear pattern of occurrence.[13,14]

Only MFU (Class D) and Meary's angle (Class C) were found to be strongly correlated with two other classes (Class B and C) and classes (A and D) respectively, which supports the proposal of MFU as a sensitive marker of peri-talar subluxation (PTS) in PCFD patients.[8,15] Actually, results of the current study is indirectly supported with the work by Kim et al. when they found substantial correlation between TNCA (Class B) and the narrowing at sinus tarsi between talus and calcaneus (which is a late step after MFU in PCFD patients) (r = 0.64, P 0.001).[16] In a previous study, MFU was found to be correlated as well with foot and ankle offset (FAO); MFS > 27.5% was found to be a threshold for higher FAO and thus greater mal-alignment.[15,17] Additionally, we found that Meary's angle (which represents the medial arch of the foot) is correlated with HMA (indicator of hindfoot mal-alignment) and MFU. Hindfoot mal-alignment due to failure of dynamic structures or static stabilizers like spring or deltoid ligament could potentially lead to collapse of medial arch of the foot medial arch. Conversely, medial arch collapse due to mid-foot arthritis, mal-united fractures or dislocations could potentially leads to hindfoot mal-alignment.[18,19]

Lee et al. and Mansur et al. studied the inter and intra-observer reliability of PCFD classification, they found only 5.8% and 1.4% of the patients have isolated deformity which supports our finding of the current study that different PCFD classes are influencing each other and rarely occur in isolation.[20,21]

In addition to correlation between angular measurements of different PCFD classes, there is correlation between angular measurements and the Foot and ankle offset (FAO) which is an optimized tool that assess foot alignment and evaluate the relation between the center of the tripod of the foot and the center of ankle joint.[17] De Netto et al. found that FAO (3D measurement) is significantly influenced by class A (HMA) ($P < 0.00001$) and class B (TNCA) ($P = 0.00004$).[17,22]

Talus instability or incongruency inside the ankle mortise was not influenced by all other components of PCFD deformities, so careful assessment of PCFD patient is important to detect class E deformities. That could be an indirect sign valgus ankle deformity could happen in chronic PCFD deformity with attenuation of static and dynamic supporting ankle structures, however it also could occur somehow independently of foot deformities i.e., with only mild and initial degrees of deformities. We think it's important to always evaluate the ankle both physically and radiologically in the setting of PCFD for early detection of subtle ankle instabilities/deformities even with mild PCFD deformities.[23]

This research has various limitations that must be considered. First, since it was retrospective research, the real linear progression of the PCFD could not be evaluated. Second, even though there was a statistically significant association between deformity components, no sample calculation or power analysis was conducted beforehand, therefore the study could be underpowered, and some existing correlations could be overlooked. Third, the WBCT is currently not widely available, limiting the generalizability of the findings.

This study was able to identify relationships between PCFD deformity components with the exception of ankle valgus (Class E). It was found that measurements established to one class were impacted by others, in some cases with remarkable strength. The reported data may support the hypothesis that PCFD is a three-dimensional complex deformity and show a probable relationship between its allegedly separate features. In addition, these findings may support the notion that a particular component correction may influence additional misalignments, hence potentially reducing the need for several adjuvant operations. This might have a direct impact on clinical practice, altering how clinicians evaluate PCFD and design their treatment plans.

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A CASE FOR ACUTE PROXIMAL ROW CARPECTOMY FOR PERILUNATE INJURIES

Kathryn C. Yeager, MD[1]; Kate M. Parker, MD[1]; Nathan T. Morrell, MD[1]

ABSTRACT

Background: Perilunate injuries are complex injuries typically arising from high-energy injuries to the wrist. Standard treatment involves open reduction and internal fixation with ligamentous reconstruction; however, outcomes are fraught with complications including pain, stiffness, and arthrosis. Several case reports have demonstrated the role of proximal row carpectomy as a salvage procedure for complex carpal trauma in the setting of significant cartilage injury or bone loss. The authors believe that proximal row carpectomy may be an appropriate acute treatment in certain patient populations, with functional results similar to those obtained with ligamentous reconstruction.

Methods: A retrospective review of two cases with perilunate dislocations managed with primary proximal row carpectomy are presented.

Results: At greater than 1-year follow-up, both patients had stable radiocarpal alignment. QuickDASH scores were 22.7 and 27.3.

Conclusion: Primary proximal row carpectomy is a treatment option in the acute setting for perilunate injuries in elderly, lower-demand patients. Functional results are similar to those obtained with ligamentous reconstruction, with a shorter recovery period.

Level of Evidence: IV

Keywords: perilunate, carpal, wrist, proximal row carpectomy, dislocation

INTRODUCTION

The scaphoid, lunate, and triquetrum make up the proximal carpal row of the wrist, commonly referred to as the intercalary segment. These three bones are linked via the scapholunate (SL) and lunotriquetral (LT) interosseous ligaments, respectively. These ligaments do not function in isolation; there is an extrinsic ligamentous complex that consists of volar and dorsal radiocarpal and ulnocarpal ligaments that provides additional stability to the proximal carpal row. Injuries to the wrist vary in severity by the degree and number of stabilizing ligaments disrupted.[1,2]

Perilunate dislocations (PLD) typically arise from a high energy mechanism. The mechanism responsible for most scapholunate and perilunate injuries is wrist extension, ulnar deviation, and carpal supination.[1] Mayfield described a progression of perilunate instability, traveling from radial to ulnar around the lunate: stage I involves disruption of the scapholunate articulation, stage II adds lunocapitate disruption, stage III adds lunotriquetral disruption, and finally, stage IV involves dislocation of the lunate from the radius.[1] Conversely, wrist extension, radial deviation, and intercarpal pronation create a reverse-progression of intercarpal disruption, starting with lunotriquetral disruption and working from ulnar to radial.[3] As such, isolated scapholunate and lunotriquetral ligament injuries are within the greater perilunate spectrum.

Perilunate dislocations can be described as greater arc or lesser arc injuries. Greater arc injury, also known as perilunate fracture dislocation (PLFD), involves fractures of the radius, ulna, or carpal bones in addition to ligamentous disruption. The most common of these injuries is the dorsal transscaphoid perilunate fracture dislocation. In contrast, a lesser arc perilunate dislocation is a purely ligamentous injury.[4,5]

Patients with a chronic perilunate dislocation may suffer from chronic wrist pain, decreased range of motion, and symptoms of carpal tunnel syndrome.[6] The literature reports rates of carpal tunnel syndrome at around 50% in patients with acute perilunate dislocation. Unfortunately, a quarter of these are reported to be missed at initial evaluation.[7-9] Mayfield stage IV injuries are most commonly associated with acute carpal tunnel syndrome.[1]

Initial management of perilunate injuries generally involves prompt recognition of the injury and closed reduction, if feasible. Standard anteroposterior and lateral radiographs of the wrist are typically sufficient for diagnosis. Immediate recognition of disruption of Gilula's lines should be identified on radiographs. The reduction maneuver is performed with a reversal of the

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injury mechanism, with radial deviation, palmar flexion, and intercarpal pronation.[1] Emergent surgical intervention is indicated in the setting of irreducible dislocations. Standard operative management includes open reduction internal fixation of the associated fractures and repair or reconstruction of ligamentous injuries, with or without carpal tunnel release.

Given that up to 25% of perilunate dislocations may be missed at their initial presentation, delayed diagnosis and treatment is not uncommon. In the chronic management of perilunate dislocation, open reduction internal fixation with ligament reconstruction has been described; however, outcomes are significantly worse when performed in chronic or missed injuries.[8] However, non-operative treatment is not often recommended due to the high risk of recurrent instability and poor functional outcomes.[8] The literature reports recurring dislocation rates of around 59% in patients treated conservatively.[2] Reports of patients presenting with chronic injury (more than 6 weeks) with no treatment complain of chronic pain, symptoms of carpal tunnel syndrome, other nerve symptoms, or tendon rupture.[6,10] Salvage procedures, such as proximal row carpectomy or wrist arthrodesis, are thus advocated for in these settings. The success of proximal row carpectomy is dependent on an intact proximal capitate. Therefore, significant trauma to the capitate directs salvage procedure selection toward arthrodesis.

After these injuries, outcomes can be poor, regardless of treatment, especially in higher demand patients or when the dominant arm is affected.[9] Return of full function, even with surgical treatment is unlikely, with reduced range of motion and grip strength being common.[9] The authors believe that there is a role for primary proximal row carpectomy as a “salvage surgery” in the acute treatment of PLD/PLFD injuries. We present two patients who were managed with proximal row carpectomy in the acute setting for perilunate dislocation.

CASE #1

A 69-year-old right hand dominant male presented after a ground level fall onto his right outstretched hand, sustaining a right perilunate fracture dislocation (image 1). He also presented with median nerve neuropraxia. Successful closed reduction was performed in the Emergency Department (image 2). The patient was diagnosed with a mixed lesser arc-greater arc injury with perilunate ligamentous disruption of the proximal carpal row and fractures of the radial and ulnar styloid. After discussion of management options, the decision was made to proceed with proximal row carpectomy, which was undergone 6 days post-injury. He also underwent carpal tunnel release at the time of the index procedure.

The patient was immobilized in a short arm cast for a total of 6 weeks and transitioned to a removable orthosis thereafter. He had limited access to occupational therapy, and therefore did not complete a formal regimen of post-operative therapy. The numbness to his index, middle, and ring fingers resolved by 6 weeks post-operative. At his final follow up 4 months postoperatively, the patient had intact nerve function, functional range of motion, and no pain. He demonstrated 30° wrist extension and 35° wrist flexion compared to 55° flexion and extension on the contralateral side. His 1-year follow up quickDASH score was 22.7, with main limitations being opening tight jars or heavy household chores where he reported moderate difficulty.

CASE #2

A 67-year-old male who was involved in a motorcycle crash, sustaining a right distal radius fracture-dislocation with ipsilateral perilunate dislocation (Moneim type II radiocarpal fracture dislocation). Closed reduction was performed in the Emergency Department. Seven days post-injury, the patient was treated with operative fixation of the distal radius and ulnar styloid and proximal row carpectomy.

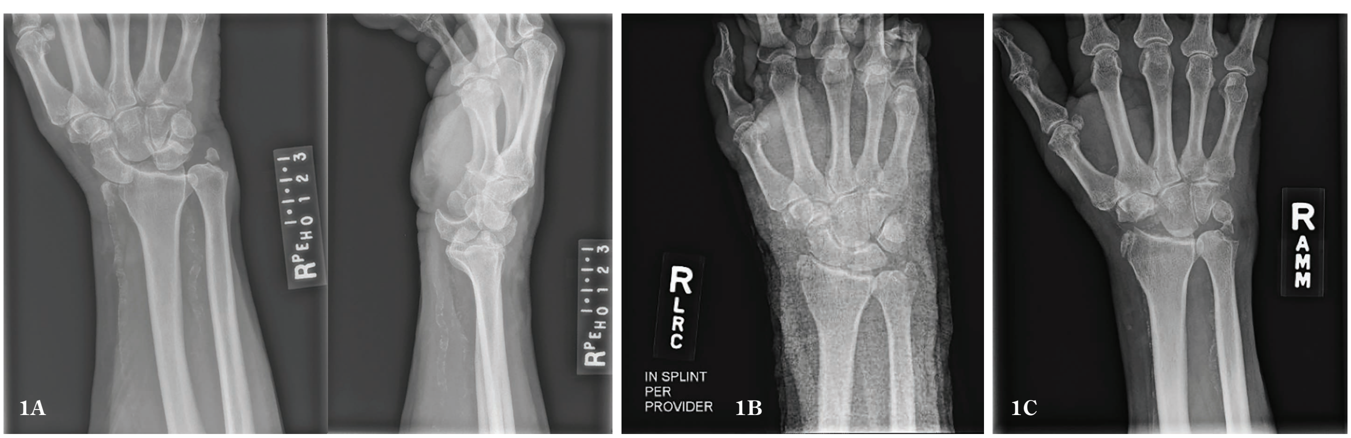

Figure 1A to 1C. Case #1: Injury XRs (1A), Post reduction XR (1B), Follow up XR (1C)

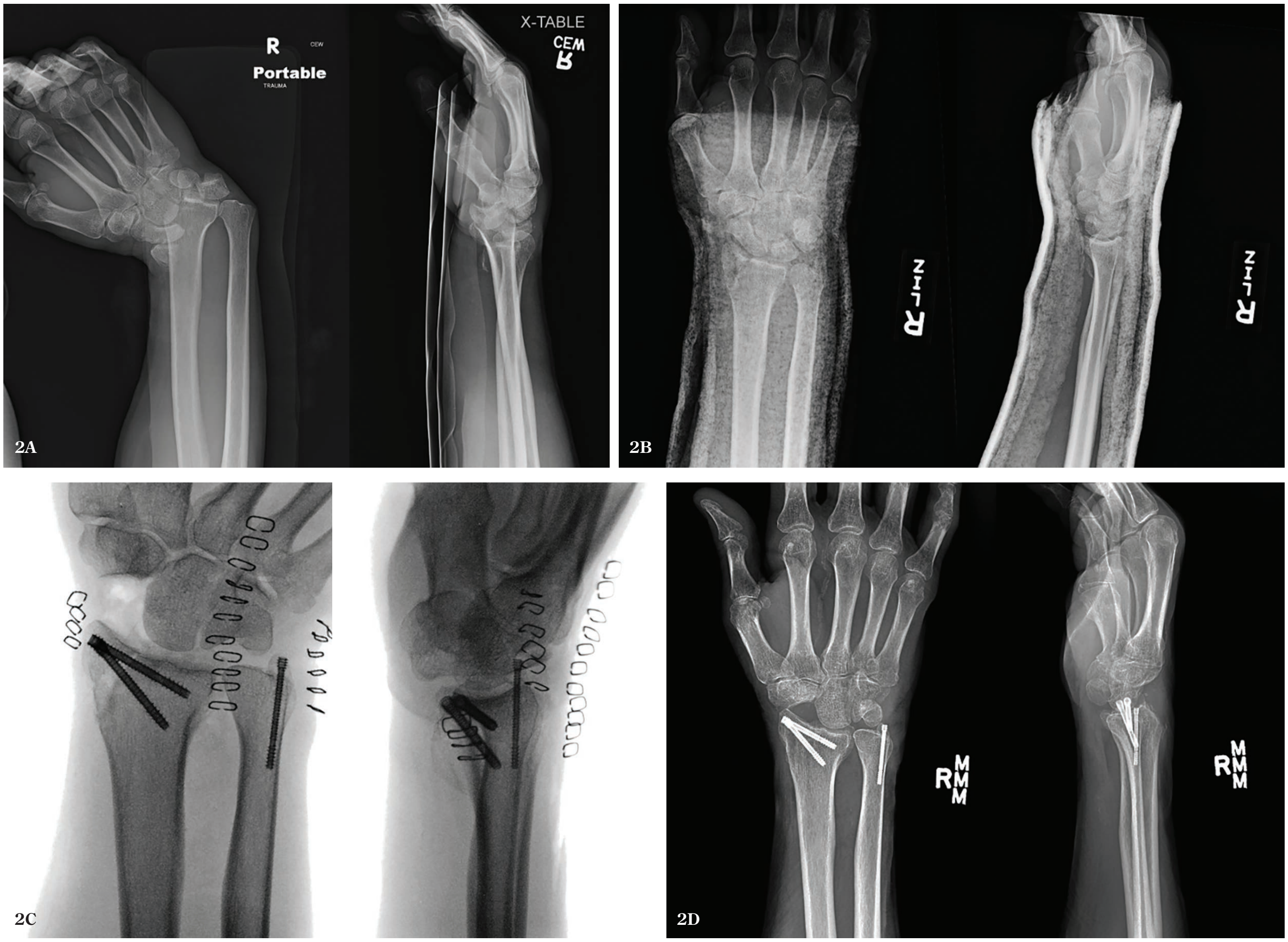

Figure 2A to 2D. Case #2: Injury XRs (2A), Post reduction XR (2B), Post-operative XRs (2C), Follow up XRs (2D)

Post-operatively, the patient was immobilized for 6 weeks, after which he began range of motion and occupational therapy. At his 5-month follow up, he reported improvement in wrist ROM and pain. On physical exam he was able to achieve 20˚ flexion and 20˚ extension. No sensorimotor insufficiencies were noted. At 3-year follow up, quickDASH score was 27.3, with his primary limitations related to work and recreational activities.

DISCUSSION

Following open reduction and internal fixation of perilunate injuries, patients often continue to suffer from limitations in range of motion (ROM), grip strength and decreased overall function.[9,11,12] This is especially the case in elderly populations, those with severe comminution, those with concurrent injuries, and those who sustained perilunate dislocation or fracture-dislocation injuries to their dominant hand.[9] Patients may require further surgical intervention to address pain and functional difficulties, such as proximal row carpectomy or arthrodesis.

Forli et al. published a retrospective review in 2010 of 18 patients, average age 34 years (12-63), who suffered either perilunate dislocation or transscaphoid perilunate fracture dislocations treated with ligament reconstruction and operative fixation.[11] They achieved follow up of 13 years, assessing Mayo wrist score, ROM, and radiologic evidence of arthritis. Most of their patients did fair or poor, with Mayo wrist scores expressing 3 poor, 7 fair, 3 good, and 5 excellent results. Their reported average flexion-extension at 13 years for perilunate dislocation patients to be 44˚ flexion, 54˚ extension, with grip strength of 75%-87% of their contralateral side. These functional findings were similar to other studies evaluating patients at shorter follow up periods.[13,14] Most patients (67%) demonstrated degenerative changes radiographically, however they concluded the presence of arthritis with static carpal instability did not cause reduced function. The rate of radiographic arthritis was also similar to other studies evaluating patients at 8-year follow up.[8]

In 2016, Griffin et al. published a prospective review of 16 patients, average age of 34 years (15-58 range) with perilunate injuries treated with ligament and fracture repair focusing on PROMs and functional exams.[12] At 24 months, VAS satisfaction score was 7.9 (range 0-10), pain at rest 1.9 (range 0-6), and activity 3.3 (range 1-6). Disability of the arm, shoulder, and hand (DASH) and patient-rated wrist evaluation (PRWE) scores were also reported. The mean DASH score of 25.2 (range 7.5-91.7) and PRWE score of 36.2 (range 14.5-77.3) demonstrated a wide range of patient function, pain, and satisfaction. Mean grip strength was around half compared to the contralateral side (59%), with a mean range of flexion-extension presenting at 71% compared to contralateral wrist. Fourteen of the 16 patients returned to work, 12 returning to the same level of work prior to injury at around 6.4 months (range 3-12 months). Ten of 16 patients returned to sport at an average of 8 months, and 7 were able to return to play at their prior level. While they concluded these patients did overall well, a significant difference compared to contralateral uninjured hand in ROM and grip strength was reported.

In 2018, Dunn et al. reported on outcomes after open reduction and internal fixation (ORIF) of 40 patients who suffered PLD or PLFD in the U.S Military.[9] Average age of the patient cohort was 28.8 years. While patients reported a decent postoperative ROM of around 74% contralateral side, grip strength lagged to 65% of the contralateral side, and about 78% reported pain with activity. Only 55% remained on active duty at final follow-up of 2 years. The reported complication rate was overall low, with only 7.5% of patients requiring re-operation; one hardware removal and two scaphoidectomies with four-corner fusion. They concluded high-demand patients may expect worse functional results after PLD/PLFD with higher degrees of limitation post op.

While outcomes were not perfect, these studies demonstrate ORIF for PLD/PLFD injuries as a reasonable treatment option in younger patients. While the literature shows ORIF maintains functional ROM and grip strength, PROMs are variable and the risk of requiring subsequent surgery is not negligible. Despite this, it has been shown to be an effective treatment for young patients in long-term follow up studies.

Proximal row carpectomy (PRC) is rarely performed in the acute setting for perilunate dislocations. This is in part due to the relatively successful outcomes with ORIF. However, patients who suffer severe comminution in PLD/PLFD with or without concomitant wrist or hand injuries may benefit from acute PRC as a management strategy to achieve functional ROM and grip strength that has been shown to be equivalent to acute ORIF in certain patients.

Proximal row carpectomy has been shown to be a successful motion-sparing procedure for patients at long-term follow ups. Wall et al. reported on 16 patients, average age 36 years with 20 years follow up after PRC for a variety of conditions. Flexion-extension arcs averaged 68°, and grip strength 72% of the contralateral side. Eleven (65%) wrists underwent no further surgery, and 10 patients went on to radiocarpal arthrodesis with an average time to conversion of 11 years. They concluded that PRC provided satisfactory results at 20-year follow-up with a survival rate of 65%, and while PRC for younger patients <35 years old may have higher rates of failure, they should not be excluded as PRC candidates.

Chim et al. published a retrospective case series that analyzed success of PRC in patients followed for a minimum of 10 years between 2003 and 2012. The study included 147 patients who underwent PRC for a variety of reasons including arthritis, scaphoid nonunion advanced collapse (SNAC), scaphoid lunate advanced collapse (SLAC), Kienböck disease, rheumatoid arthritis, chronic perilunate dislocation (2 patients), and chronic perilunate fracture dislocation (10 patients). They reported a post operative flexion/extension arc averaging 73.5°, and grip strength averaging 68.4% of contralateral side. Among studies reporting patient-reported outcome measures (PROMs), they found the average DASH score (weighted mean) was 21.5, PRWE was 28.7, and Mayo wrist score was 66.9 (all scores n=79).[15]

While it is difficult to directly compare results of ORIF vs PRC as there is a paucity in the literature of studies describing acute PRC for PLD/PLFD, the general outcomes at long-term follow ups between these two interventions appear to be relatively similar in ROM and grip strength. One study published in 2017 does directly compare ORIF vs PRC in acute treatment of PLD. Muller et al. published a retrospective study to compare the results of ORIF vs PRC in the acute management of perilunate dislocations between 2006 and 2011.[16] The cohort consisted of 21 male patients, average age of 33 years, with isolated or fracture associated PLDs. Thirteen were treated with ORIF and 8 by PRC with no significant differences in age range in each group, and achieved an average follow up of 35 months. They found similar results in pain rating (ORIF 3/10, PRC 1/10), strength (ORIF 77%, PRC 73%), QuickDASH (ORIF 27/100, PRC 16/100), PRWE (ORIF 43/150, PRC 15/5/150), and only slight differences in ROM, with the PRC group demonstrating two-thirds of the motion of the ORIF group. They also found the PRC operative time and immobilization time to be shorter. Thus, they concluded acute treatment of perilunate dislocations by PRC led to medium term results at least as good as ORIF treatment.

The results of these studies and the outcomes of the patients presented above have led the authors to advocate for the use of PRC as the primary treatment of PLD in patients over the age of 65, or those who are low demand. As discussed above, patients undergoing acute PRC vs ORIF for PLD have shown similar ROM and grip strength at long-term follow ups, and similar PROMs. However, Muller found ROM within the PRC patients to be 60% that of the ORIF group.[16] This is concerning when treating young and active patients.

Differences in PROMs at follow-up between elderly or lower-demand patients, and younger or high-demand patients when undergoing PRC also point toward avoiding PRC in younger or more active patients. Ali et al.'s 2012 long-term outcome study of PRC for arthritis found poor patient satisfaction scores, which they attributed to the high percentage of manual laborers within their study, and how they could not return to their prior level of performance.[17] The results of their study led them to become more cautious in offering PRC to young laborers, something that has been reported before by Dacho and others.[18]

Revision rates also play a role in the decision of surgical approach, as younger patients (<35 yrs old) treated with PRC showed higher revision rates of 65% at 20-year follow up in Wall et al.'s 2013 paper.[19] Notably, this study did not include ORIF of PLD/PFLD patients as a comparison and thus could not comment on the difference between survival rate of ORIF vs PRC in young patients.

Finally, the length of surgery is also significantly different between PRC and ORIF, with PRC typically taking around 45 minutes in our experience, versus ORIF with ligamentous reconstruction taking 90 minutes or longer. Elderly patients may be less tolerant of the longer surgery and rehabilitation required for ORIF, another reason PRC may be a better choice for this patient demographic. Finally, elderly patients with acute PLD are more likely to have pre-existing degenerative conditions of the wrist. Therefore, initial management with PRC may be the best option for their overall clinical picture.

CONCLUSION

Though classically considered an option for chronic perilunate dislocations or a salvage procedure in the setting of significant or cartilage and/or bone loss, proximal row carpectomy is a reasonable treatment option for the acute management of perilunate dislocation with satisfactory functional outcomes in older patients, or those with lower activity demand. The cases presented above demonstrate how acute proximal row carpectomy can be utilized in the initial management of complex fracture perilunate type injuries. Ligament reconstruction is often fraught with pain and stiffness post-operatively, to the degree that the motion lost in proximal row carpectomy is essentially equivalent.

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CONSIDERATION FOR LIMB SALVAGE IN PLACE OF AMPUTATION IN COMPLEX TIBIAL FRACTURE WITH NEUROVASCULAR INJURY: A CASE REPORT

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ABSTRACT

High-energy tibial fractures often present with associated soft tissue injuries, including neurovascular damage, complicating the treatment decision. A 33-year-old male presented with Gustilo Anderson type IIIA fracture of the left distal tibia and fibula with associated closed calcaneus fracture and tibial nerve transection. Amputation was discussed, but the decision was made for limb salvage with nerve allograft. The patient displayed satisfactory functional recovery at 29 months postoperatively without need for major revision, grafting, arthrodesis, or amputation. This case report provides an example of successful limb salvage utilizing tibial nerve allograft in a complex high-energy lower extremity injury.

Level of Evidence: IV

Keywords: limb salvage, lower extremity trauma, open tibial fracture, neurovascular injury, peripheral nerve allograft, tibial nerve injury

INTRODUCTION

Management options for open, high-energy distal tibia fractures with associated neurovascular injury remain highly controversial, as current literature suggests either amputation or limb salvage with neither yielding significantly greater outcomes.[1,2] Amputations are far more common in this setting, having demonstrating outcomes leading to fewer reoperations and hospitalizations.[3,4] The choice between amputation or limb salvage largely rests on surgeon judgement and shared-decision making with patients, and is influenced by numerous factors including patient's preinjury status, associated soft tissue damage, injury location, resources available, and patient wishes.[1]

High-energy tibial fractures often present with associated soft tissue injuries, including neurovascular damage, complicating decision making. In the context of nerve transection, amputation is strongly considered over limb salvage with complex nerve reconstruction.[3] Compared to that of the upper extremities, the literature on outcomes following allograft nerve reconstruction in the lower extremities is limited and remains controversial. In a study evaluating the rate of meaningful recovery of nerve repairs in different regions of the body, Safa et al. found that 53% of patients with repair of lower extremity nerves experienced meaningful recovery, defined as Medical Research Council Classification (MRCC) sensory and motor scale ≥ S3/M3, versus 100% and 83% in the head/neck and upper extremities, respectively.[5] With the recovery rate of lower extremity nerve repair significantly lower than that of other regions, and amputations potentially yielding fewer complications and faster recovery, amputation is a reasonable treatment.[4]

However, with recent advances in surgical care, the possibility of limb salvage with nerve allograft reconstruction should not be immediately excluded in favor of amputation, as it can potentially yield similar or improved outcomes.[3] Here we describe a patient with a high-energy tibial fracture and associated tibial nerve transection who experienced satisfactory outcomes following limb salvage and tibial nerve allograft reconstruction.

The patient described in this case report was informed that their case would be submitted for publication and provided verbal consent.

CASE REPORT

A 33-year-old male roofer presented to the emergency department at our university-associated level-one trauma center following a fall from height while working. The patient sustained a Gustilo-Anderson type IIIA fracture of the left distal tibia and fibula, as well as a closed calcaneus fracture, among other injuries (Figure 1a, b, c). Physical examination was significant for a 2cm posterolateral wound over the left lower extremity with exposed tibial bone fragments. He had a palpable dorsalis pedis pulse. Sensation to light touch was intact in the saphenous, sural, and superficial peroneal nerve distributions, but noted to be absent over the plantar foot and first webspace of the dorsal foot. He exhibited no active plantarflexion or dorsiflexion at the ankle.

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Within 8 hours of presentation, the patient was taken to the operating room (OR) for wound exploration, irrigation, debridement, and external fixation of the distal tibia. The posterior tibial artery and tibial nerve were found to be completely transected upon exploration of wound (Figure 1d). The neurovascular bundle was identified, noted to be bleeding, and ligated with suture.

Following his initial surgery, amputation of the limb was strongly considered given his neurovascular injury, however, limb salvage was pursued at the strong desire of the patient and presence of intact sensation to the extremity. After 72 hours after his initial surgery, perfusion to the foot remained and he returned to the OR for tibial nerve reconstruction using allograft. This was performed under microscopic guidance by a microsurgery-trained orthopaedic hand surgeon. Debridement of the open fracture site was repeated, and both ends of the transected tibial nerve were identified. Portions of the nerve were resected until healthy, budding fascicles were observed. The patient's tibial nerve was noted to be large, spanning 10mm in diameter with two separate nerve anastomoses. Therefore, the initial 5 x 70mm nerve allograft was cut in half and two separate allografts were utilized to reconstruct the nerve with 8-0 nylon suture, resulting in a 3cm graft gap (Figure 1e). Once the allograft was in place, minimal tension on the nerve was ensured and two submucosal nerve protectors were utilized. After wound closure, the foot remained well perfused.

Four days following tibial nerve allograft, revision fixation of the left distal tibia and fibula were performed. Fibular fixation was achieved using a 3mm flexible intramedullary rod, while the articular segment of the distal tibia was reconstructed using a 4.0 cannulated screw. A 3-ring circular frame with hind foot extension was used to span the tibia and calcaneus fractures in order to maintain alignment. The minimally displaced calcaneus fracture was fixated to the frame with two crossed tension wires, allowing for maintenance of reduction.

At two months postoperatively, the patient was ambulatory and reported sensation to light touch over the lateral left foot. At seven months, further improvement of sensation was observed, however, imaging revealed lack of appropriate bone healing. Results of a bone biopsy were negative for infection. The external frame was removed at this time, the fracture was debrided, and a spacer was placed at the tibial defect site. At 20 months postoperatively, radiographs demonstrated appropriate interval bone healing and the patient returned to limited work duties with slight pain during active ankle motion. He was provided with a dynamic ankle orthosis, which does provide additional comfort and support. At 22 months from his injury, protective plantar sensation had returned. At 29 months, maximal medical improvement was determined.

Figure 1A-1E. Anteroposterior (A) and lateral (B) radiographs of left ankle and lateral radiograph of the foot (C) demonstrating comminuted intraarticular distal tibial, fibular, and calcaneal fractures. Intraoperative image of tibial nerve and posterior tibial artery transection (D) and tibial nerve allograft placement (E).

Although he continued to experience limited range of motion at the ankle and ambulates with an antalgic gait, the patient attained his treatment goal - to be ambulatory on a salvaged limb rather than amputation. The tibial fracture demonstrated healing on radiology, and the patient had a functional lower extremity with intact sensation and motor function of deep peroneal, superficial peroneal, tibial, and sural nerves (Figure 2). There were no clinical indications of infection, and the patients is able to work 2-3 hours per day in a strenuous occupation.

Figure 2A-2D. Anteroposterior (A) and lateral (B) radiographs at 4 years postoperatively demonstrating well healed fractures. Clinical image of patient demonstrating dorsiflexion (C) and ambulation (D).

DISCUSSION

We describe a Gustilo-Anderson type IIIA distal tibia and fibula fractures, closed calcaneus fracture, posterior tibial artery injury, and tibial nerve transection. Given the patient's severe soft tissue damage, neurovascular injury with loss of plantar sensation, and prolonged ischemia (>6 hours), there were strong indications for amputation.[1,3] Although absence of plantar sensation remains a controversial contraindication to limb salvage,[2,6] a confirmed tibial nerve transection is widely considered contraindicative for limb salvage due to a loss of protective foot sensation and functional foot musculature.[1,4] In their analysis of 527 patients with mangled lower extremity injuries, MacKenzie et al. found that soft tissue injury and plantar foot sensation were the most important predictive factors of successful limb salvage.[7] Even when tibial nerve grafting is attempted to restore plantar sensation, Nunley et al. demonstrated poor functional nerve recovery or prolonged recovery time.[8] In the first long-term prospective study comparing amputation to limb salvage after severe lower extremity injury, Bosse et al. demonstrated no significant difference in functional outcomes at two years postoperatively.[11] The authors did report a significantly greater rate of complications, reoperations, and repeat hospitalizations in patients undergoing reconstruction. However, this literature does not account for recent improvements in surgical techniques nor improved understanding of these injuries and inadequately evaluated patient quality of life.[12] The recent literature provides improved outcomes in these cases, in part due to further understanding of the injuries and reconstruction techniques. Important technical considerations in nerve reconstruction include reducing allograft tension, shortening gap lengths,[5,9] and resection of the damaged nerve which is noted by bleeding within the budding fascicles.[8]

Currently, we have a better understanding of outcomes of allograft nerve reconstruction. The literature displays consistently satisfactory outcomes despite a lack of clarity on the indications for repair or reconstruction.[5,13] In a case series of traumatic lower extremity injuries with tibial nerve lacerations, Momoh et al. found that while patients treated with tibial nerve allograft experienced mild pain and decreased ankle range of motion, they were able to become ambulatory without aids and experienced minimal disability when performing daily activities.[2]

The meta-analysis by Garg et al.[13] reported that 81% of nerve graft reconstruction cases achieved good outcomes across a heterogenous sample of tibial nerve injuries. Kurozumi et al.[14] reported significantly higher functional and mental health scores in severe lower extremity fracture cases treated with limb salvage compared to amputation at a minimum of nine months postoperatively.

Other studies have demonstrated similar results further supporting nerve reconstruction.[9] Consistent with these findings, our patient achieved satisfactory results with evidence of functional nerve recovery within 6 months postoperatively with presence of plantar sensation, adequate bone healing on imaging, and ability to ambulate. The patient regained protective plantar sensation and with extensive physical therapy, returned to limited work duties within 20 months of surgery. Severe open tibial fractures are often associated with high infection and malunion rates resulting in subsequent procedures and prolonged recovery time.[6] However, in addition to a satisfactory functional result, the current case did not result in infection or major complication.

Given the complexity of this case and limited resources of our hospital, amputation could have been implemented and most likely resulted in a shorter recovery process with an acceptable functional outcome. However, this undermines the preferences of the patient, who expressed strong desire to pursue limb salvage over amputation. Furthermore, he possessed the resources to pursue more complex surgical management, which likely contributed to his favorable outcome. Ultimately, the patient remains pleased with his treatment course and is extremely delighted about having a functional limb rather than a prosthetic.

The strengths of the current case presentation are the clinical term of follow up, and the thorough description of treatment which provided excellent functional recovery despite the severity of injury. Amputation is a reasonable option in these complex cases. This information is intended to add to the literature regarding these complex injuries.

In conclusion, this case report provides an example of successful limb salvage utilizing tibial nerve allograft in a complex high-energy lower extremity injury.

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QUANTITATIVE ANALYSIS OF ANESTHESIA UTILIZATION IN AMBULATORY HAND SURGERY

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ABSTRACT

Background: Though evidence demonstrating benefits of local anesthetic continues to compound, a consensus among surgeons regarding optimal anesthetic modality has not been reached. General and regional anesthetic may still be preferred for patient anxiety, concomitant procedures, increased complexity, or poor patient pain tolerance. Therefore, the primary purpose of this study was to analyze trends in anesthetic utilization using a large-scale state healthcare database for common outpatient hand procedures. We hypothesize that over the 10 years between 2010-2019, local anesthetic [including Wide-Awake Local Anesthesia with no Tourniquet (WALANT)] utilization use for common hand procedures has increased, while the use of general and regional anesthesia has decreased.

Methods: A cross-sectional analysis was performed using the Texas Healthcare Information Collection Outpatient Database between 2010-2019. The de-identified data was queried for reported Current Procedure Terminology (CPT) anesthetic and associated procedure codes for the following ambulatory techniques: open carpal tunnel release, endoscopic carpal tunnel release, trigger finger release, De Quervain's release, partial palmar fasciectomy, and hand mass excision. Anesthetic options included: regional anesthesia (RA), local or WALANT anesthesia (LA), and general anesthesia (GA).

Results: There were 340,117 procedures performed during the study period. 98.14% of patient records reported LA application, while GA and RA only accounted for 0.41% and 1.45%, respectively. No significant growth was found for each form of anesthetic individually [LA: -0.12%, RA: 0.09%, and GA: 0.03%]. However, a significant difference in proportional growth is present when comparing all anesthetics (Figure 1, p<0.001). Commercial/private insurance was the most common payer regardless of anesthesia type, though Medicaid payment source covered a larger proportion of procedures performed under GA [Medicaid: 2.48%, Medicare: 0.37%, worker's compensation: 0.12%, commercial/private insurance: 0.20%].

Conclusion: LA was the most utilized modality over the study period, though a significant proportion of usage has shifted back towards RA and GA over time. Commercial/private insurance was the most frequent reimbursement source for all procedures, though Medicaid covered disproportionately more procedures utilizing GA. RA use was noted to be disproportionately higher in mid-sized population centers (2-4 million in population).

Level of Evidence: IV

Keywords: ambulatory surgery, hand surgery, anesthesia, orthopedic surgery

INTRODUCTION

Upper limb and hand surgeries are common procedures in plastic and orthopaedic surgery. Many procedures and most surgical specialties have transitioned to ambulatory surgery over the past two decades because of healthcare insurance influences, Medicare initiatives, advancements in medical technology, improved anesthetic techniques, and physician practice trends. As a result, many hand tendon, nerve, bone, joint, vascular, and other soft tissue procedures are now routinely performed as outpatient surgeries. Tourniquet use during these procedures is frequently employed to minimize blood loss, and historically RA or GA were the preferred anesthetic methods for hand surgery.[1]

To further define anesthetic modalities, regional block anesthetic (RA) involves the injection of an anesthetic near a nerve that supplies a specific body region. Common regional anesthetic techniques utilized in hand surgery include the brachial plexus block or axillary block. Conversely, local anesthesia (LA) involves the injection of anesthetic directly into the area of the procedure. In hand surgery, local anesthesia is often utilized for low

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acuity procedures such as removing a cyst or performing a biopsy. This modality can also be employed in conjunction with sedation or general anesthesia. Finally, general anesthesia (GA) involves the administration of medication that causes the patient to become unconscious and unable to feel pain during surgery. In hand surgery, general anesthesia may be advantageous for complex procedures, such as tendon repairs or joint replacements.

In a 1987 survey study of American Society for Surgery of the Hand (ASSH) members, most carpal tunnel release (CTR) procedures utilized regional anesthesia on an outpatient basis.[2] Now, newer subsequent studies estimate that CTR performed under local anesthesia with monitored anesthetic care (MAC) is the most common practice utilized by hand surgeon society members.[3-5] Conversely, conflicting database studies examining CTR, De Quervain release and trigger finger release indicate a majority of RA and GA usage with a growing trend in LA utilization.[6-7]

With the transition of many hand procedures to outpatient surgery, anesthesia trends have also transformed. One such transformation in the past fifteen years has been the implementation of a LA with epinephrine.[8] This breakthrough has given surgeons another tool to opt for multiple hand operations to transition into the minor procedure room. As a result, this method has gained notoriety due to increased efficiency, convenience, and reduced cost.[9-11] Now, it is estimated that 62% of hand surgery society members incorporate WALANT into their practice.[12]

Research demonstrating the benefits of LA continues to compound, though there remains no consensus regarding an optimal modality. RA and GA may still be preferred in cases of patient anxiety, concomitant procedures, increased complexity, or poor pain tolerance.[13-14] Therefore, the primary purpose of this study was to analyze anesthetic choice in common ambulatory hand procedures using a large-scale healthcare database. We hypothesized that local anesthetic utilization in ambulatory hand surgery has increased. Furthermore, we analyzed anesthetic administration during procedures with respect to patient sex, race, ethnicity, age, primary insurance designation, and patient-reported place of residence (metropolitan, micropolitan, or rural).

METHODS

Study Design

This study was exempt from Institutional Review Board (IRB) approval. A study population of 340,117 deidentified outpatient surgical records was obtained from the publicly available Texas Health Care Information Collection (THCIC) database through the Texas Department of State Health Services (TDSHS) for retrospective cross-sectional analysis.[15] The cohort from 2010 to 2019 was selected to avoid any COVID-19 pandemic effects on elective surgery. According to the United States Census Bureau, Texas is the second most populated state with over 29 million documented residents (2019), and represents a diverse ethnic and socioeconomic population. Records were identified through query of the database using Current Procedure Terminology (CPT) codes for the following common ambulatory hand procedures: trigger finger release, De Quervain's release, endoscopic carpal tunnel release, open carpal tunnel release, hand mass excision, and partial palmar fasciectomy (in association with Dupuytren's contracture). Anesthetic received (local, general, or regional) was then determined through a search of those respective CPT codes. The resulting records included demographic characteristics, insurance coverage, and patient county of residence. Counties of residence were then subcategorized based on population size (Rural: < two million, Micropolitan: > two – 3.9 million, Metropolitan: > four million). State-wide trends in anesthetic utilization for six common ambulatory hand procedures were then analyzed.

Table 1. Ambulatory Hand Procedure and Associated Anesthetic CPT Codes

Procedure	CPT Code
ECTR	29848
Open CTR	64721
Trigger Finger Relese	26055
1st Compartment Release	25000
Mass Hand Excision	26116
Open Dupuytren's Partial Palmar Fasciectomy	26123
Regional Anesthetic	**CPT Code**
Injection, anesthetic agent; brachial plexus, single	64415
Injection, anesthetic agent; brachial plexus, continuous infusion by catheter (including catheter placement)	64416
Injection, anesthetic agent; axillary nerve	64417
Injection, anesthetic agent; suprascapular nerve	64418
Injection, anesthetic agent; intercostal nerve, single	64420
Injection, anesthetic agent; intercostal nerves, multiple, regional block	64421
Injection, anesthetic agent; carpal tunnel	20526
General Anesthetic	**CPT Code**
	01810
Local Anesthetic	**CPT Code**
Injection, anesthetic agent; peripheral nerve/ digital	64450
	No Code

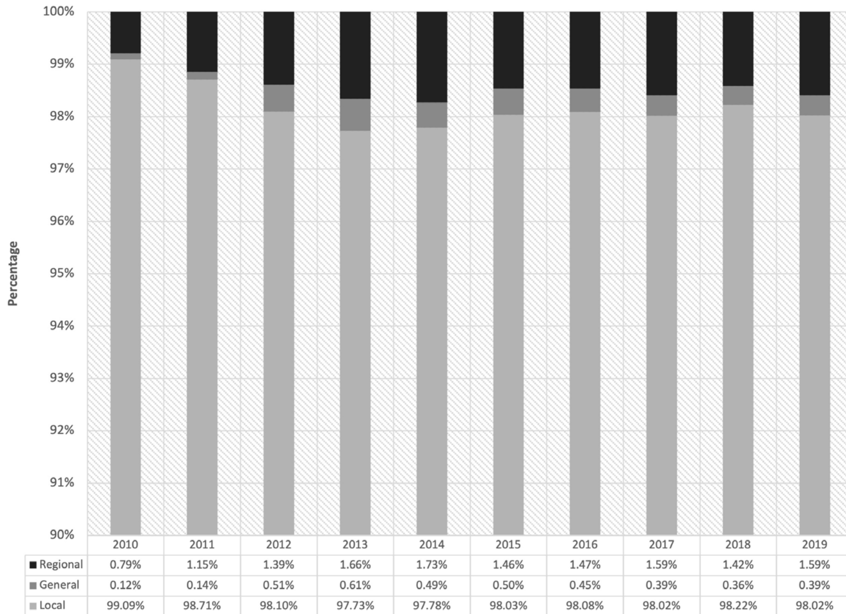

Figure 1. Trends in Anesthesia use Across Six Common Ambulatory Hand Procedures: 2010-2019.

Study Population

Table 1 summarizes the CPT codes used in this study. Outpatient surgical procedures occurring between 2010 and 2019 were queried using the CPT codes 29848, 64721, 26055, 25000, 26116, and 26123. Likewise, outpatient anesthetic administration occurring between 2010 and 2019 was queried using the CPT codes 01810, 64450, 64415, 64416, 64417, 64418, 64420, 64421, 64999, and 20526. Procedures with no corresponding anesthetic code were assumed to employ a pure local anesthetic or WALANT, as this administration is not directly coded. To prevent record duplication, only the primary reported procedure was analyzed. A total of 340,117 procedures performed between 2010 and 2019 were included in the final analysis.

Statistical Analysis

All statistical analyses were performed using STATA version 17.0. Count data were expressed as frequencies and percentages and Fisher Exact tests were utilized for comparisons. Mantel-Haenszel test was utilized to analyze the growth of respective anesthesia groups over the 10-year period (2010-2019). The Cochran-Armitage test for linear trend of proportions was used to compare the trends of anesthesia use in all three groups within the same period. All analyses were performed with an alpha level of 0.05, indicating statistical significance as less than 0.05.

RESULTS

There were 340,117 procedures performed in the ambulatory outpatient surgical setting over a 10-year period (2010-2019). In terms of usage, 98.14% of these records met the criteria for LA application, while GA and RA only accounted for 0.41% and 1.45%, respectively. Over time, local anesthetic usage saw a slight average annual decline -0.12% during this study period (Figure 1). Conversely, the average annual growth rate of regional and general anesthetic usage saw an uptick in the same time frame [regional (0.09%), general (0.03%)]. Mantel-Haenszel test demonstrated that these individual growth rates for each form of anesthetic were insignificant. However, Cochran-Armitage test shows a significant difference in proportional growth when comparing all three anesthetics ($p<0.001$). A complete breakdown of anesthetic received for each procedure can be found below (Table 2).

Insurance designation was reported in 316,022 records, while only 268,062 noted county or state health regions of residence. Commercial/private insurance was found to be the most common payer regardless of anesthetic choice [local (62.39%), general (39.76%), and regional anesthetic (63.09%), $p<0.001$]. However, Medicaid payment source covered a larger proportion of procedures performed under general anesthetic (2.48%), in comparison to Medicare (0.37%), worker's compensation (0.12%), or commercial/private insurance (0.20%, $p<0.001$) (Table 3). Local anesthetic was the most uti-

Table 2. Relative Anesthetic Utilization in Hand Procedures

	Local	General	Regional	Total
Endoscopic Carpal Tunnel Release	75,263	206	1,580	77,049
	97.68%	0.27%	2.05%	100%
Open Carpal Tunnel Release	138,074	688	2,260	141,022
	97.91%	0.49%	1.60%	100%
Trigger Finger Release	84,175	392	549	85,116
	98.89%	0.46%	0.65%	100%
1st Compartment Release	20,117	61	219	20,397
	98.63%	0.30%	1.07%	100%
Hand Mass Excision <1.5cm	4,642	11	20	4,673
	99.34%	0.24%	0.43%	100%
Open Dupuytren's Partial Palmar Fasciectomy	11,535	25	300	11,860
	97.26%	0.21%	2.53%	100%

lized anesthetic in every county and state health region [metropolitan (98.48%), micropolitan (97.22%), and rural (98.64%), p<0.001]. Micropolitan counties were notable for a higher percentage of regional anesthetic use compared to metropolitan and rural counties [metropolitan (1.10%), micropolitan (2.34%), and rural (1.05%), p<0.001] (Table 4).

There were 333,795 records reporting age, which show that most procedures were performed in age groups between the ages of 50 and 69 across all forms of anesthesia. Patient's age at the time of procedure did not influence anesthesia choice. Finally, female patients were found to outnumber male patients in this study (214,990 versus 123,969, p<0.001).

DISCUSSION

From 2010-2019, local anesthetic was far more often utilized in common ambulatory hand procedures. Although LA was the dominant anesthetic of choice for hand surgery in this cohort, all modalities were found to be growing/falling at insignificant rates. However, a significantly higher proportion of anesthesia utilization is trending towards general and regional modalities over time. We, therefore, reject our study hypothesis.

Foster and colleagues previously concluded that 80.5% of CTR procedures employed general or regional anesthesia between 2007-2011, while only 19.5% of procedures were performed using LA. However, LA usage was found to increase substantially from 2010-2011 by 4.7%.[6] Similarly, Kamnerdnakta et al. concluded that approximately 80% of CTR, De Quervain release, and trigger finger release involved anesthesiologist-administered anesthesia services. The use of anesthesia services was found

Table 3. Insurance Coverage for Anesthesia

	Local	General	Regional	Total
Medicare	99,539	371	1418	101,328
	98.23%	0.37%	1.40%	100%
Medicaid	8,327	215	124	8,666
	96.09%	2.48%	1.43%	100%
Workers' Compensation	8,883	11	159	9,053
	98.12%	0.12%	1.76%	100%
Commercial	193,673	394	2,908	196,975
	98.32%	0.20%	1.48%	100%

Table 4. Utilization of Anesthetic by State Population Grouping

	Local	General	Regional	Total
Metropolitan (> four million)	160,843	695	1790	163,328
	98.48%	0.43%	1.10%	100%
Micropolitan (two – 3.9 million)	97,029	446	2,331	99,806
	97.22%	0.45%	2.34%	100%
Rural (< two million)	75,934	242	807	4,928
	98.64%	0.31%	1.05%	100%

to decline by 3.9 % over their study period (2010-2015).[7] These findings stand in contrast to our results, and we instead concur with previous survey studies which estimate that CTR performed with a local anesthetic is the most common practice.[3-5] Although a recovery trend back towards RA and GA use was found during our ten-year study period, LA (including WALANT) still dominated anesthetic utilization (>97% of all cases) year over year.

Our study also demonstrated a majority of commercial/private insurance reimbursement, which is consistent with the literature. Odom and colleagues previously identified a majority of private insurance reimbursement (54.7%), followed by Medicare (26.3%), worker's compensation (10.5%), and Medicaid (8.5%).[16] Our study also identified a similar pattern [commercial/private (62.3%), Medicare (32.1%), worker's compensation (2.9%), and Medicaid (2.7%)]. However, a higher proportion of Medicaid coverage for GA is notable in our study, as previous research has implicated LA as the least costly modality across the 6 procedures in this study.[6,17-24] Therefore, a small, albeit significantly higher proportion of low-income bracket patients are likely incurring more expensive procedures. Excessive use of anesthesia services has been previously demonstrated and may be attributable to our current fee-for-service system.[7] However, further study is needed to ascertain the causation of this identified trend. Additionally, regional anesthetic use is disproportionally higher in Micropolitan counties (2.34%, p<0.001), though the reason for this remains unclear. Potential explanations include a higher volume of concomitant procedures, anxious patients, or poor patient pain tolerance.[13-14]

As Texas is the 2nd most populous state representing a broad base of demographics, this study adds to previous literature providing clarity on preferred nationwide anesthesia methods in commonly performed ambulatory hand surgical procedures. However, as with any retrospective review of a healthcare database, our findings may be limited by documentation, coding, and data submission errors. As a state healthcare database intended for administrative use, detailed clinical information was not available. As a result, treatment outcomes, certain population demographics, or procedure indications were not obtainable in this study. In addition, this study did not examine treatment patterns by surgical specialty, fellowship training received, or board certification. It is unclear if these factors may have affected our data. Further work is also needed to address the proposed regional and socioeconomic disparities in care.

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DID RAPID EXPANSION OF SAME DAY DISCHARGE HIP AND KNEE ARTHROPLASTY DURING THE COVID-19 PANDEMIC INCREASE EARLY COMPLICATIONS?

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ABSTRACT

Background: The COVID-19 pandemic has had a lasting impact on patients seeking total hip and knee arthroplasty (THA, TKA) including more patients undergoing same day discharge (SDD) following total joint arthroplasty (TJA). The purpose of this study was to assess whether expansion of SDD TJA during the COVID-19 pandemic resulted in more early complications following TJA. We anticipated that as many institutions quickly launched SDD TJA programs there may be an increase in 30-day complications.

Methods: We retrospectively queried the ACS-NSQIP database for all patients undergoing primary elective TJA from January 1, 2018, to December 31, 2020. Participants who underwent THA or TKA between January 1, 2018 and March 1, 2020 were grouped into pre-COVID and between March 1, 2020 and December 31, 2020 were grouped into post-COVID categories. Patients with length of stay greater than 0 were excluded. Primary outcome was any complication at 30 days. Secondary outcomes included readmission and re-operation 30 days.

Results: A total of 14,438 patients underwent TKA, with 9,580 occurring pre-COVID and 4,858 post-COVID. There was no difference in rates of total complication between the pre-COVID (3.55%) and post-COVID (3.99%) groups (p=0.197). Rates of readmissions for were similar for the pre-COVID (1.75%) and post-COVID (1.98%) groups (p=0.381). There was no statistically significant difference in respiratory complications between the pre-COVID (0.41%) and post-COVID group (0.23%, p=0.03). A total of 12,265 patients underwent THA, with 7,680 occurring pre-COVID and 4,585 post-COVID. There was no difference in rates of total complication between the pre-COVID (3.25%) and post-COVID (3.49%) groups (p=0.52). Rates of readmissions for were similar for the pre-COVID (1.77%) and post-COVID (1.68%) groups (p=0.381). There was no statistically significant difference in respiratory complications between the pre-COVID (0.16%) and post-COVID group (0.07%, p=0.26). Combined data to include THA and TKA patients did not find a statistical difference in the rate of complications or readmission but did note a decrease in the rate of combined respiratory complications in the post-COVID group (0.15% vs. 0.30%, p=0.028).

Conclusion: Rapid expansion of SDD TJA during the COVID-19 pandemic did not increase overall complication, readmission, or re-operation rates.

Level of Evidence: IV

Keywords: covid, total joint arthroplasty, NSQIP, total knee arthroplasty, total hip

INTRODUCTION

With an aging population, the American Academy of Orthopedic Surgeons has estimated an increase of up to 180% in hip and knee arthroplasty in the next 10 years.[1] The SARS-CoV-2 (COVID-19) pandemic has had a lasting impact on patients seeking total hip and knee arthroplasty (THA, TKA). In mid-March of 2020, the American College of Surgeons (ACS) and the Centers for Medicare and Medicaid Services (CMS) proposed postponing or cancelling all "elective" or "non-essential" procedures.[2] As a result, many patients scheduled to undergo THA and TKA procedures had their surgeries postponed. It has been estimated approximately 30,000 primary total joint arthroplasty (TJA) procedures and 3,000 revision TJA procedures were cancelled per week.[3] One of the primary reasons for delaying non-essential procedures was to limit hospital occupancy in the event beds were necessary to care for patients with COVID-19-related symptoms. In 2018, CMS removed TKA from the inpatient-only list, followed by THA in 2020, allowing these procedures to be completed as a same day discharge (SDD), defined as length of stay (LOS) 0 days. As the COVID-19 pandemic continued, many hospitals allowed same day discharge procedures to be performed which allowed patients improved access to

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care without increasing hospital census. This change led to a rapid and unprecedented expansion in SDD programs by arthroplasty surgeons at many institutions.[4] Prior to this, SDD occurred in approximately 2.9% of patients undergoing primary TKA and 2.2% of patients undergoing primary THA.[5]

While inpatient length of stay continues to decrease there is still persistent concern that complications such as uncontrolled pain, post-operative medical, and wound complications would go unnoticed in patients undergoing SDD.[6,7] SDD following TJA has previously reported to be safe, effective, and cost saving.[8-10] Studies have shown equivalent or even improved outcomes with SDD TJA.[11] Patients also benefit from recovering in a familiar environment without increased exposure to nosocomial organisms, including COVID-19.[12] However, many of these procedures are performed at highly specialized centers that have refined perioperative care pathways including patient selection, education, pain management regimens, and close post-operative telephone follow-up.[10,13-15] It is unknown whether similar results can be expected with the rapid expansion in TJA with SDD driven by the COVID-19 pandemic. Therefore, the purpose of this study was to assess whether expansion of SDD TJA during the COVID-19 pandemic resulted in more early complications following TJA. We anticipate that as many institutions quickly launched SDD TJA programs there may be an increase in 30-day complications. We hypothesize that the indications for outpatient TJA may also have been expanded allowing patients with more comorbidities to undergo outpatient TJA when they previously would have been denied the option.

METHODS

We retrospectively queried the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) database for all patients undergoing primary elective TJA from January 1, 2018, to December 31, 2020. The ACS-NSQIP database is a nationally validated, risk-adjusted, outcomes based program that collects data from over 700 hospitals. ACS-NSQIP collects over 300 variables per patient including principal diagnosis, demographics, comorbidities, and surgical outcomes. Routine auditing provides assurance of high-quality data with a disagreement rate of less than 1.8%.[16] Further details of ACS-NSQIP are available elsewhere.[16,17] This study was deemed exempt by the University of Iowa IRB. No external funding was used in this study.

Patients were identified based on Current Procedural Terminology (CPT) codes 27447 and 27130. Only patients who underwent primary, elective TJA were included. ACS-NSQIP provides the length of stay (LOS) of each patient which they define as the LOS from admission to discharge with 0 being considered same day discharge. Patients with length of stay greater than 0, revision arthroplasty, arthroplasty for fracture or neoplasm, patients with unrelated concurrent CPT codes, and patients under 18 years of age were excluded.

Primary outcome was any complication at 30 days including, deep surgical site infection, wound disruption, pneumonia, unplanned intubation, pulmonary embolism, progressive renal insufficiency, acute renal failure, urinary tract infection, stroke/CVA, cardiac arrest requiring CPR, myocardial infarction, transfusions, DVT requiring therapy, sepsis, septic shock, and death. Secondary outcomes included readmission and re-operation 30 days. All outcomes were assessed using standard definitions as defined by NSQIP.[16]

The ACS and CMS guidelines were set in place in March of 2020 which we used as our definition as the start of the COVID-19 pandemic impact on United States healthcare. Since, ACS-NSQIP does not report which month surgeries were performed in we classified all procedures taking place after the start of the second quarter to be within the COVID-19 era.

Participants who underwent THA or TKA between January 1, 2018 and March 1, 2020 were grouped into pre-COVID and between March 1, 2020 and December 31, 2020 were grouped into post-COVID categories. Characteristics were compared between pre- and post-COVID groups by surgical procedure and with all procedures combined. Continuous variables were described using mean ± standard deviation and compared between groups using independent t-tests. Frequencies (percentages) were used to describe categorical variables and between-group differences were evaluated using chi-square or exact tests. The frequency of post-operative complications and readmissions were evaluated using chi-square tests for all procedures combined and separately for THA and TKA procedures. Outcomes included any complication, respiratory complication and readmission. Analyses were completed using R Statistical Software (v4.1.2; R Core Team 2021) and Microsoft Excel (2021).

RESULTS

A total of 14,438 patients underwent TKA, with 9,580 occurring pre-COVID and 4,858 post-COVID. There was no statistically significant difference between groups when assessing age, sex, BMI, history of smoking or diabetes. The pre-COVID group had more patients with history of severe COPD, (1.84% vs 1.38% $p=0.034$). The post-COVID group had significantly less patients with ASA score of 2 (62.9 vs 59.1, $p<0.001$) and significantly more patients with an ASA score of 3 (34.8 vs 38.1, $p<0.001$). More patients in the post-COVID group had

Table 1. Total Knee Arthroplasty

Characteristic	Pre-COVID	Post-COVID	Relative Difference	p-Value
N	9580	4858		
Avg Age	66.12	64.98	-1.73%	0.9263
- Std Dev	8.73	8.74		
% Female	54.6%	52.9%	-3.00%	0.0621
Race				
% Asian	5.50%	3.77%	-31.52%	0.0000
% Black	6.57%	8.13%	23.84%	0.0008
% White	80.1%	75.8%	-5.34%	0.0000
% Hispanic	10.87%	9.45%	-13.05%	0.0071
Avg BMI	31.35	31.99	2.05%	0.9365
- Std Dev	5.49	5.89		
% Diabetic	15.0%	15.0%	-0.16%	0.9688
% Smoker	5.51%	5.91%	7.19%	0.3347
% Dyspnea	2.08%	2.47%	18.91%	0.1398
% Dependent due to health	0.21%	0.10%	-50.70%	0.1061
% With severe COPD history	1.84%	1.38%	-24.93%	0.0343
% Ascites	0.00%	0.02%	-	0.3173
% CHF	0.04%	0.14%	245.10%	0.0791
% Hypertension	55.3%	56.8%	2.87%	0.0699
% Acute renal failure	0.00%	0.02%	-	0.3173
% On dialysis	0.11%	0.08%	-28.29%	0.5457
% Steroid use	2.37%	2.70%	13.80%	0.2420
% Weight loss	0.17%	0.06%	-63.02%	0.0551
% Bleeding disorders	1.33%	1.63%	22.67%	0.1638
ASA Classification				
% No Disturb	1.85%	2.18%	18.10%	0.1823
% Mild Disturb	62.9%	59.1%	-6.05%	0.0000
% Severe Disturb	34.8%	38.1%	9.62%	0.0001
% Life Threat	0.44%	0.62%	40.86%	0.1719
Principal anesthesia technique				
% Epidural	0.68%	0.66%	-2.92%	0.8901
% General	25.0%	28.3%	13.47%	0.0000
% MAC / IV Sedation	9.7%	17.4%	78.96%	0.0000
% Regional	0.63%	1.44%	130.07%	0.0000
% Spinal	63.8%	52.0%	-18.62%	0.0000
Avg. Total Operation Time	81.95	85.92	4.84%	0.9141
- Std Dev	25.55	26.49		

procedures completed under general anesthesia (25.0% vs 28.3%), MAC/IV sedation (9.7% vs 17.4%), and regional anesthesia (0.63% vs 1.44%) as compared to pre-COVID group in which more spinal anesthesia was utilized (63.8% vs 52.0%, p<0.001 for all). (Table 1)

For TKA, there was no difference in rates of total complication between the pre-COVID (3.55%) and post-COVID (3.99%) groups (p=0.197). Rates of readmissions for were similar for the pre-COVID (1.75%) and post-COVID (1.98%) groups (p=0.381). There was no statistically significant difference in respiratory complications between the pre-COVID (0.41%) and post-COVID group (0.23%, p=0.03). (Table 2)

A total of 12,265 patients underwent THA, with 7,680 occurring pre-COVID and 4,585 post-COVID. There was no statistically significant difference between groups when assessing age, sex, BMI, history of smoking or diabetes. The post-COVID group had more patients with history of severe COPD, (1.92% vs 1.30% p=0.034), patients with hypertension (45.9 vs. 42.3, p<0.01), and patients on dialysis (0.24% vs 0.07%, p=0.025). The post-COVID group has significantly more ASA 3 (30.0% vs. 26.5%, p<0.01) and ASA 4 (0.74% vs. 0.43%, p=0.03). (Table 3)

For THA, there was no difference in rates of total complication between the pre-COVID (3.25%) and post-COVID (3.49%) groups (p=0.52). Rates of readmissions for were similar for the pre-COVID (1.77%) and post-COVID (1.68%) groups (p=0.381). There was no statistically significant difference in respiratory complications between the pre-COVID (0.16%) and post-COVID group (0.07%, p=0.26). (Table 4)

Table 2. Total Knee Arthroplasty

Any complication?	Pre-COVID	Post-COVID		
No	9240	4664		
Yes	340	194	ChiSq	1.6643
Rate	3.55%	3.99%	p-Value	0.197
Readmission?	Pre-COVID	Post-COVID		
No	9412	4762		
Yes	168	96	ChiSq	0.76912
Rate	1.75%	1.98%	p-Value	0.3805
Respiratory complication?	Pre-COVID	Post-COVID		
No	9541	4847		
Yes	39	11	ChiSq	2.5477
Rate	0.41%	0.23%	p-Value	0.1105

Table 3. Total Hip Arthroplasty

Characteristic	Pre-COVID	Post-COVID	Relative Difference	p-Value
N	7680	4585		
Avg Age	62.88	62.51	-0.59%	0.9801
- Std Dev	10.46	10.54		
% Female	48.6%	46.9%	-3.57%	0.0624
Race				
% Asian	3.59%	3.18%	-11.39%	0.2219
% Black	5.92%	7.59%	28.11%	0.0005
% White	76.3%	73.1%	-4.19%	0.0001
% Hispanic	4.64%	4.71%	1.63%	0.8480
Avg BMI	29.15	29.56	1.39%	0.9579
- Std Dev	5.25	5.57		
% Diabetic	7.5%	8.2%	8.67%	0.1956
% Smoker	8.24%	9.23%	11.93%	0.0636
% Dyspnea	1.61%	1.85%	14.82%	0.3301
% Dependent due to health	0.44%	0.17%	-60.59%	0.0060
% With severe COPD history	1.30%	1.92%	47.40%	0.0102
% Ascites	0.00%	0.00%	-	-
% CHF	0.03%	0.11%	318.76%	0.1111
% Hypertension	42.3%	45.9%	8.48%	0.0001
% Acute renal failure	0.04%	0.04%	11.67%	0.9050
% On dialysis	0.07%	0.24%	268.51%	0.0248
% Steroid use	1.94%	2.42%	24.78%	0.0817
% Weight loss	0.16%	0.26%	67.50%	0.2301
% Bleeding disorders	0.68%	0.83%	22.41%	0.3530
ASA Classification				
% No Disturb	5.95%	4.93%	-17.16%	0.0146
% Mild Disturb	67.2%	64.3%	-4.23%	0.0014
% Severe Disturb	26.5%	30.0%	13.43%	0.0000
% Life Threat	0.43%	0.74%	72.58%	0.0339
Principal anesthesia technique				
% Epidural	0.36%	0.65%	79.47%	0.0351
% General	24.6%	28.0%	13.97%	0.0000
% MAC / IV Sedation	10.6%	18.7%	77.21%	0.0000
% Regional	0.44%	1.81%	308.90%	0.0000
% Spinal	64.0%	50.8%	-20.71%	0.0000
Avg. Total Operation Time	81.29	85.16728	4.77%	0.9191
- Std Dev	25.87	28.06		

Table 4. Total Hip Arthroplasty

Any complication?	Pre-COVID	Post-COVID		
No	7430	4425		
Yes	250	160	ChiSq	0.41847
Rate	3.26%	3.49%	p-Value	0.5177
Readmission?	Pre-COVID	Post-COVID		
No	7544	4509		
Yes	136	76	ChiSq	0.15525
Rate	1.77%	1.66%	p-Value	0.6936
Respiratory complication?	Pre-COVID	Post-COVID		
No	7668	4582		
Yes	12	3	ChiSq	1.2664
Rate	0.16%	0.07%	p-Value	0.2604

Combined data including THA and TKA patients did not find a statistical difference in the rate of complications pre-COVID (3.42%) compared to post-COVID (3.75%, p=0.17). There was also no statistically significant difference in readmission rates (1.76% pre-COVID vs. 1.82% post-COVID, p=0.76.) There was a decrease in the rate of combined respiratory complications in the post-COVID group (0.15% vs. 0.30%, p=0.028. However, there was no significant difference when evaluating respiratory complications individually. (Tables 5, 6) (Figure 1)

DISCUSSION

The COVID-19 pandemic led to unprecedented changes to the healthcare system and had a profound effect on hip and knee arthroplasty. The guidelines recommended by the ACS and CMS lead to restrictions on which procedures could be completed during the beginning of the pandemic era. As a results, many institutions quickly developed programs for same-day discharge. The goal of this study was to evaluate if rapid expansion of same day discharge TJA during the COVID-19 pandemic increased early complications.

Prior literature has evaluated the effects of anesthesia and surgery on the immune system and describe a transient immunosuppression following procedures.[18-20] Quinlan et al. performed a large data base study evaluating patient susceptibility to viral illness following TJA. They concluded that there was no increased incidence of influenza in patients who recently underwent TJA.[21] Our study revealed that there was no increase in respiratory complications during the post-COVID era when evaluating TKA and THA separately. There was a decrease in respiratory complications when combining THA and TKA data.

Table 5. Total Knee Arthroplasty + Total Hip Arthroplasty

Characteristic	Pre-COVID	Post-COVID	Relative Difference	p-Value
N	17260	9443		
Avg Age	64.68	63.78	-1.39%	0.9477
- Std Dev	9.67	9.73		
% Female	51.9%	50.0%	-3.71%	0.0026
Race				
% Asian	4.65%	3.48%	-25.11%	0.0000
% Black	6.28%	7.87%	25.28%	0.0000
% White	78.4%	74.5%	-4.98%	0.0000
% Hispanic	8.09%	7.15%	-11.68%	0.0050
Avg BMI	30.37	30.81	1.44%	0.9567
- Std Dev	5.49	5.86		
% Diabetic	11.7%	11.7%	0.01%	0.9972
% Smoker	6.73%	7.52%	11.78%	0.0169
% Dyspnea	1.87%	2.17%	16.01%	0.0998
% Dependent due to health	0.31%	0.14%	-56.00%	0.0022
% With severe COPD history	1.60%	1.64%	2.65%	0.7936
% Ascites	0.00%	0.01%	-	0.3173
% CHF	0.03%	0.13%	265.56%	0.0189
% Hypertension	49.5%	51.5%	4.11%	0.0015
% Acute renal failure	0.02%	0.03%	82.78%	0.4913
% On dialysis	0.09%	0.16%	71.36%	0.1600
% Steroid use	2.18%	2.56%	17.64%	0.0510
% Weight loss	0.16%	0.16%	-2.08%	0.9474
% Bleeding disorders	1.04%	1.24%	19.47%	0.1419
ASA Classification				
% No Disturb	3.67%	3.52%	-4.29%	0.5076
% Mild Disturb	64.8%	61.6%	-4.88%	0.0000
% Severe Disturb	31.1%	34.2%	10.00%	0.0000
% Life Threat	0.43%	0.68%	55.97%	0.0132
Principal anesthesia technique				
% Epidural	0.54%	0.66%	21.85%	0.2393
% General	24.8%	28.2%	13.65%	0.0000
% MAC / IV Sedation	10.1%	18.0%	78.69%	0.0000
% Regional	0.54%	1.62%	197.51%	0.0000
% Spinal	63.9%	51.4%	-19.63%	0.0000
Avg. Total Operation Time	81.66	85.56	4.78%	0.9171
- Std Dev	25.69	27.27		

Table 6. Total Knee Arthroplasty + Total Hip Arthroplasty

Any complication?	Pre-COVID	Post-COVID		
No	16670	9089		
Yes	590	354	ChiSq	1.8593
Rate	3.42%	3.75%	p-Value	0.1727
Readmission?	Pre-COVID	Post-COVID		
No	16956	9271		
Yes	304	172	ChiSq	0.094142
Rate	1.76%	1.82%	p-Value	0.759
Respiratory complication?	Pre-COVID	Post-COVID		
No	17209	9429		
Yes	51	14	ChiSq	4.8587
Rate	0.30%	0.15%	p-Value	0.02751

Courtney et al. completed a NSQIP database study evaluating the 30-day complication rate, readmission rate, and reoperation rates for patients undergoing SDD TJA. They found that outpatient TJA alone was not a risk factor for readmission or reoperation and was a negative risk factor for complications. They did report that patients over 70 years of age, those with malnutrition, cardiac history, smoking history, or diabetes mellitus are at higher risk for readmission and complications following TJA.[22] Our study found no difference in readmission, reoperation, or overall complication rates between the pre-COVID and post-COVID groups.

The limitations to this study are similar to other large database studies. First, we are unable to define an exact timepoint at which institutions prohibited or reduced the number of TJA performed and likewise we are unable to define a timepoint when SDD TJA was allowed as it was variable throughout the country. While we are not able to define an exact timeline the ACS and CMS made their recommendations concurrently and thus, we assume the majority of institutions followed these guidelines at approximately the same time. Second, we cannot separate institutions that have had established SDD programs from those that started SDD programs during the pandemic. Theoretically, institutions that began SDD during the pandemic could have an increased rate of readmission, reoperation or 30-day and 90-day complication which could be outweighed by practices with established SDD programs. Since this is a large database study, any miscoding or misbilling could lead to potential sources of error that could affect the quality of the study.

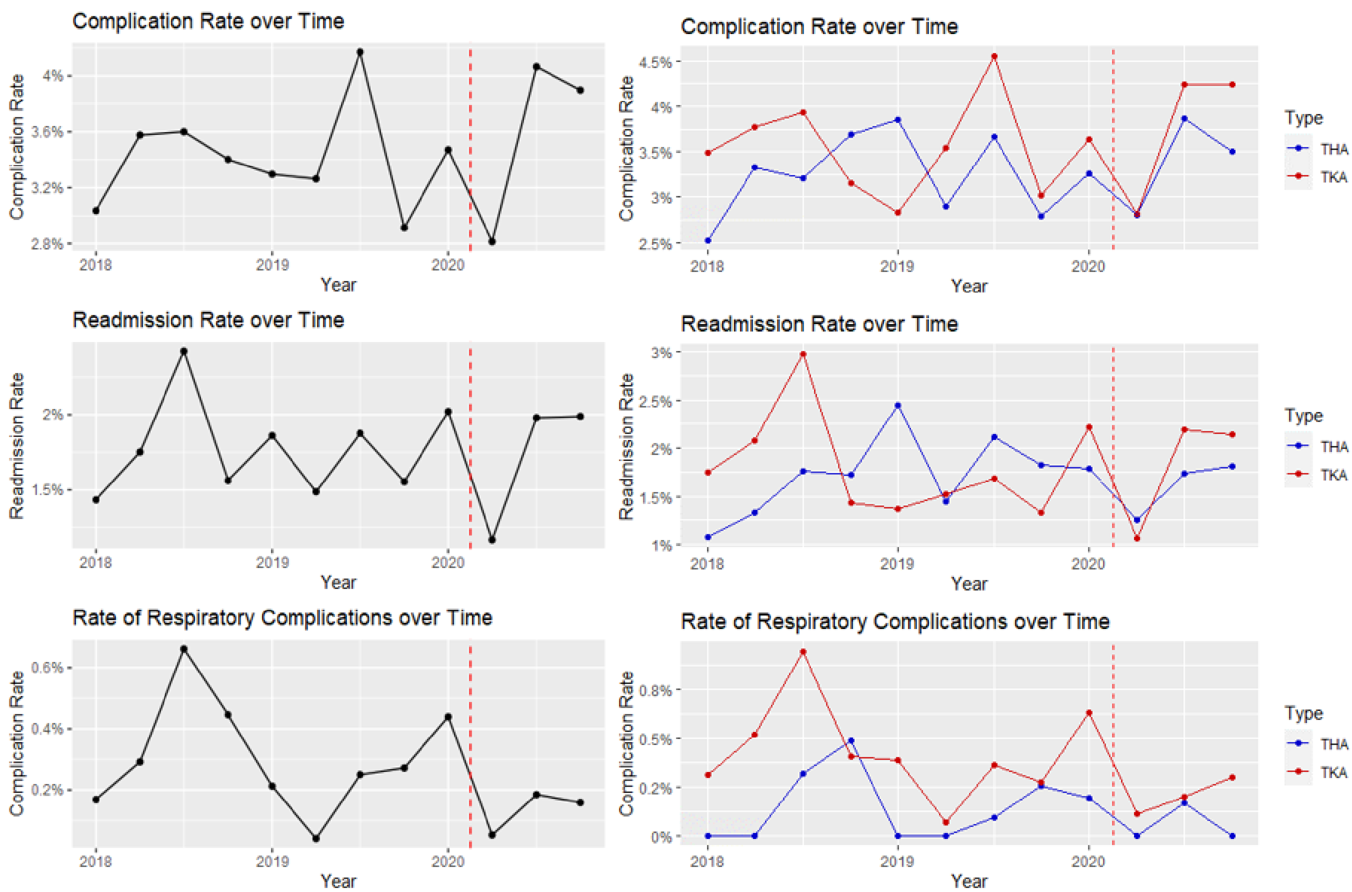

Figure 1. xxxxxxxxxxxxxxxxxx.

CONCLUSION

While there has been increased interest in same day discharge following total joint arthroplasty for several years, the COVID-19 pandemic caused institutions to rapidly integrate SDD TJA programs. The goal of this study was to evaluate early complications of SDD TJA in the pre-COVID and post-COVID era. We did not find any increase in the readmission, reoperation, and overall complication rates between groups. There was a decrease in respiratory complications when combining TKA and THA data which could reflect an increased diligence in pre-operative respiratory optimization.

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OUTCOMES OF REVISION TOTAL HIP ARTHROPLASTY IN PATIENTS 60 YEARS AND YOUNGER

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ABSTRACT

Background: The annual volume of patients requiring revision total hip arthroplasty prior to age 60 is projected to increase considerably. Despite this, outcome data for revision THA in these younger patients remain limited. The purpose of this study was to define implant survivorship, identify risk factors for re-revision, and determine clinical outcomes of revision THA in patients aged ≤60 years.

Methods: We identified 191 revision THAs performed in patients aged ≤60 years. Minimum 4-year follow-up was obtained in 141 (73.8%) hips (mean 10.3 years [range, 4–20]). Mean age was 48 years (range, 20–60). Forty-five hips (32%) had previously been revised. Indications for index revision included aseptic loosening (28%), polyethylene wear (26%), dislocation (20%), and infection (14%). Outcome measures were Kaplan-Meier survival free from re-revision and patient-reported outcome scores (mHHS, UCLA).

Results: Survivorship free from re-revision for any cause was 78% [95% CI=70–85] at five years and 71% [62–78] at ten years. The most common indication for re-revision at both five and ten years was dislocation (12% [8–19], 16% [10–23]), followed by infection (6% [3–12], 10% [5–18]) and aseptic loosening (2% [1–7], 4% [1–11]). Mean scores were improved from baseline at six (mHHS +21.4, UCLA +0.9) and twelve years (mHHS +13.4, UCLA +0.5).

Conclusion: Revision THA in patients less than 60 years of age was associated with considerably lower rates of early loosening-related failure than historically reported. Recurrent dislocation and infection appear to remain challenges in this population. Despite improvements in survivorship from earlier studies, patient-reported functional improvements remained relatively unchanged.

Level of Evidence: IV

Keywords: revision, hip, arthroplasty, THA, young, younger

INTRODUCTION

Younger age at the time of primary total hip arthroplasty (THA) has historically been associated with increased risk for revision surgery.[1-3] With contemporary implants and surgical technique, revision-free survivorship of primary THA in younger patients has approached that of older patients,[4] and THA continues to be utilized increasingly in younger patients.[5]

With more than half of all primary THAs projected to be performed in patients <65 by the end of the decade, and with the greatest increase expected among patients aged 45–55, the volume of patients that can be anticipated to require revision surgery prior to age 60 is considerable.[5-8] Understanding the indications and prognoses of revision surgery in this population is critical to providing realistic expectations to these patients and to mitigating risk for re-revision surgery.

Despite this importance, outcome data for revision THA in young patients have remained extremely limited. Ten-year failure rates have ranged from 37–52%, with high observed rates of early aseptic loosening.[9-11] However, the majority of series published to date include more historical fixation (cemented, early cementless) and bearing surfaces (conventional polyethylene, early ceramics). Thus, the purpose of this study was to provide a more contemporary overview of implant survivorship, risk factors for re-revision, and clinical outcomes of revision THA in patients 60 years of age or younger.

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METHODS

Following institutional review board approval, a retrospective review of our institutional total joint arthroplasty registry was performed to identify patients who underwent revision THA at 60 years of age or younger between 2000 and 2016. Revision THA was defined as reoperation with exchange of one or more components of a prior THA. Patients with prior hemi- or resurfacing arthroplasty were excluded. Oncologic cases were also excluded. We initially identified 191 revision THAs. Of these, 141 (73.8%) had minimum 4-year follow-up (mean 10 years [range, 4–20 years]) or were re-revised and were the focus of this report.

Mean age at the time of index revision THA was 48 years (range, 20–60), mean body mass index (BMI) was 29 (range, 19–53 kg/m^2), and 65% were female. Prior ipsilateral revision THA was noted in 45 (32%) hips (mean 1.7 previous revisions [range, 1–6]). The most common indications for index revision surgery were aseptic loosening (28%), polyethylene wear (26%), dislocation (20%), and periprosthetic joint infection (PJI) (14%). Aseptic loosening was of the acetabular component in 26 (67%) hips, femoral component in 3 (8%) hips, and of both components in 10 (26%) hips. Comorbidities included rheumatoid arthritis (13%), systemic lupus erythematous (12%), sickle cell anemia (1%), and HIV/AIDS (1%).

Among the 141 included revision surgeries, acetabular revisions were most common (43%, n=61), followed by femoral and acetabular revision (25%, n=35), isolated head and liner exchange (24%, n=34), and femoral revision (8%, n=11), Table 1. Both head and liner were exchanged in all cases. Heads were predominantly cobalt chromium (93%, n=121), with ceramic used in the remainder (7%, n=20). Median head size was 32mm (range, 22–40) and 86% of polyethylene liners were highly cross-linked. Constrained liners were used in 39% (n=11/28) of hips undergoing index revision for dislocation. A posterolateral approach was used in all cases. Postoperatively, all patients were instructed to follow posterior hip precautions for three months, and abduction bracing used selectively.

Table 1. Components Used in the 141 Included Revision THAs

Components	% used
Acetabular	
Zimmer Trabecular Metal Modular™	68%
Zimmer Trilogy®	30%
Howmedica Osteonics	2%
Femoral	
Zimmer VerSys® Beaded Fullcoat	72%
DePuy Solution System®	14%
Zimmer VerSys® Heritage®	7%
Howmedica Osteonics	2%
Stryker GMRS™ Global Modular Replacement System	2%
Smith & Nephew Spectron™	2%

Clinical follow-up was recommended at 6 weeks, 6 months, 1 year, 2 years, 5 years, 10 years, and 15 years. Patients with less than 4-year clinical follow-up were contacted by phone or mail for updates on their clinical status. Follow-up was completed predominantly in person (81%). Correspondence by phone or mail was used to obtain follow-up in 19% of patients.

All intra- and post-operative complications were recorded, as well as all reoperations and re-revisions. Re-revision was the primary study endpoint and was defined as exchange of one or more components and/or open reduction and internal fixation of the femur or acetabulum. Survivorship free from re-revision was calculated at 5 years and 10 years using Kaplan-Meier survivorship estimation.[12] Failure rates at 5- and 10-year were reported as the difference between 1 and the Kaplan-Meier survival estimate.

Clinical outcomes were assessed through patient-reported outcome scores gathered preoperatively, at minimum 4-year follow-up, and at latest follow-up. These included the modified Harris Hip- (mHHS)[13] and UCLA Activity[14] scores. Scores in patients who underwent index revision for infection were not included in our report or analysis of scores.

Statistical Analysis

Statistical analysis was performed to assess patient factor differences (age, sex, BMI, comorbidities, prior revision history, bone defect, femoral head size, bearing material) between surviving hips and those that were re-revised (for any reason, and for each of the most common re-revision indications). Categorical variables were compared using Chi-square tests and continuous variables with two-tailed t tests. A p value less than 0.05 defined significance.

RESULTS

At 10-year mean follow-up (range, 4–20), forty hips (27.8%) had been re-revised. Indications for re-revision included dislocation (13.5%, n=19), PJI (7.8%, n=11), aseptic loosening of the acetabular (2.8%, n=4) or femoral (0.7%, n=1) component, periprosthetic femur fracture (1.4%, n=2), component failure (1.4%, n=2), and polyethylene wear (0.7%, n=1). The two component failures included a fractured femoral stem, and a fractured constrained liner secondary to a fall. As such, the 10-year survivorship free of re-revision for any cause was 78% at 5 years

Table 2. Reasons for Re-Revision

Failure in Overall Cohort		
	5-year Failure	10-year Failure
	% [95% CI]	% [95% CI]
Full Cohort		
Any Reason	22.3 [14.8-30.2]	29.3 [22.1-38.1]
Loosening	2.4 [0.8-7.4]	3.9 [1.4-10.5]
Instability	12.1 [7.6-19.1]	15.5 [10.0-23.4]
Infection	6.0 [3.0-11.7]	9.7 [5.4-17.8]
Excluding Index Indication: Infection)		
Any Reason	20.1 [13.9-28.5]	27.0 [19.6-36.5]
Loosening	2.8 [0.9-8.5]	4.5 [1.6-12.1]
Instability	11.3 [6.7-18.7]	15.1 [9.5-23.7]
Infection	5.2 [2.4-11.2]	7.8 [3.9-15.2]
Failure by Index Revision Indication		
Wear +/- Osteolysis		
Any Reason	8.1 [2.7-23.1]	8.1 [2.7-23.1]
Loosening	5.4 [1.4-19.9]	5.4 [1.4-19.9]
Instability	2.8 [0.4-18.1]	2.8 [0.4-18.1]
Infection	-	-
Loosening		
Any Reason	8.5 [2.8-24.1]	12.5 [4.8-30.4]
Loosening	3.1 [0.4-20.2]	3.1 [0.4-20.2]
Instability	-	4.3 [0.6-27.1]
Infection	5.6 [1.4-20.4]	5.6 [1.4-20.4]
Instability		
Any Reason	54.3 [37.6-69.3]	74.3 [56.9-88.9]
Loosening	-	14.3 [2.1-66.6]
Instability	40.8 [24.6-62.4]	52.5 [33.4-74.5]
Infection	10.0 [3.3-27.9]	25.7 [10.5-55.0]
Infection		
Any Reason	35.0 [18.5-59.7]	42.2 [23.4-67.7]
Loosening	-	-
Instability	10.8 [2.8-36.9]	17.2 [5.8-44.6]
Infection	10.8 [2.8-36.9]	20.7 [10.6-54.0]

(95% Confidence Interval [CI]=70%–85%) and 71% at 10 years (95% CI=62%–78%). When excluding index revisions performed for PJI, survivorship free of re-revision was 80% at 5 years (95% CI=72%–86%) and 73% at 10 years (95% CI=64%–80%).

The greatest overall contributor to failure at both five and ten years was dislocation (12% [95% CI=8–19%], 16% [95% CI=10–23%]), followed by PJI (6% [95% CI=3–12%], 10% [95% CI=5–18%]) and aseptic loosening (2% [95% CI=1–7%], 4% [95% CI=1–11%]), Table 2.

Survivorship free from re-revision differed considerably by index revision indication and was greater for indications of wear/osteolysis (92% at 10 years [95% CI=77–97%]) and aseptic loosening (88% [95% CI=70–95%]) compared to dislocation (26% [95% CI=11–43%]) and PJI (58% [95% CI=32–77]), Figure 1.

There were eight (6%) complications that did not require re-revision. These included: four dislocations that were closed reduced with no sequelae thereafter, two hematomas treated with I&D, one superficial infection treated with I&D, and one DVT. All other complications were those resulting in re-revision.

Factors Associated with Re-revision

Prior ipsilateral revision surgery was found to be a significant risk factor for re-revision (Relative Risk [RR] 2.65 [95% CI=1.56–4.50], p<0.005). Hips with at least one prior revision for dislocation were considerably more likely to undergo re-revision for dislocation (RR 5.41 [95% CI=2.57–11.41], p<0.001), and hips with at least one prior revision for PJI were more likely to undergo re-revision for PJI (RR 4.33 [95% CI=1.32–14.17], p=0.016). Female sex was associated with elevated risk for re-revision for dislocation (RR 3.44 [95% CI=1.06–11.20], p=0.040). There were no associations between failure (for any reason, or for any specific reason) and age, BMI, comorbidities, femoral head size, or presence or absence of an acetabular or femoral defect for which bone graft was used, Table 3.

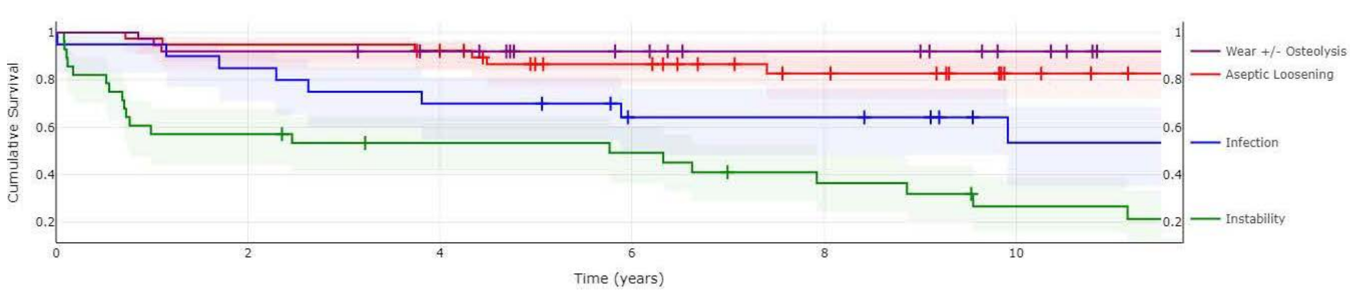

Figure 1. Survivorship by index revision indication (80% confidence intervals).

Table 3. Risks Factors for Re-revision

Risk Factors for Re-revision									
Re-Revision for:		Any Cause n=40		Loosening n=5		Instability n=19		Infection n=11	
	Nonrevised	Revised	p=	Revised	p=	Revised	p=	Revised	p=
Age									
Average	48.6	48.0	0.691	44.2	0.276	48.6	0.994	48.1	0.520
>40	81%	85%	0.593	80%	0.380	84%	0.047	73%	0.425
<50	47%	50%	0.365	20%	0.245	63%	0.184	45%	0.946
Sex									
Female	60%	80%	0.026	80%	0.380	84%	0.047	73%	0.425
BMI									
Average	29.4	29.2	0.851	27.1	0.454	29.4	0.728	28.5	0.704
>30	41%	33%	0.437	20%	0.344	40%	0.924	33%	0.700
Comorbities									
Any	30%	23%	0.389	20%	06.42	26%	0.766	18%	0.422
Rheumatoid Arthritis	15%	10%	0.447	-	-	10%	0.620	18%	0.770
Lupus	12%	13%	0.920	20%	0.589	16%	0.637	-	-
Prior Ipsi. Revision									
Any	27%	60%	<0.005	40%	0.516	68%	<0.005	82%	<0.005
Instability	2%	23%	<0.001	20%	0.018	42%	<0.001	18%	0.013
Infection	4%	15%	0.021	20%	0.099	11%	0.228	27%	<0.001
Bone Deficiency									
Acetabular	29%	20%	0.289	50%	0.368	16%	0.234	27%	0.904
Femoral	11%	8%	0.544	-	-	5%	0.453	9%	0.854
Femoral Head Size (mm)									
Median	32	32	-	32	-	32	-	32	-
Mean	32.3	31.8	0.225	32.6	0.857	32.5	0.658	32.2	0.708
<32	21%	35%	0.078	20%	0.966	37%	0.129	27%	0.619
Polyethylene Liner*									
Conventional	12%	23%	0.137	20%	0.568	29%	0.086	-	-
Highly Crosslinked	88%	77%		80%		71%		100%	

*Constrained liners excluded.

Index Revision Indication: Dislocation

Among the 28 patients who underwent index revision for dislocation, 20 (71%) were re-revised at a mean of 3 years (median 0.75) for dislocation (39.3% [58% of all re-revisions for dislocation]), PJI (17.9%), and aseptic loosening (7.1%). Though head diameter was not associated with failure in the overall cohort, hips that underwent index revision for dislocation that were re-revised for dislocation had smaller head diameters than those that survived (median 28mm vs 34mm, p=0.016). All non-revised hips in this group had a head size ≥32mm, while 55% of those re-revised for dislocation had a head size <32mm (p=0.012). Rates of re-revision for dislocation were similar between those with and without a constrained liner (36% vs. 41%, p=0.799), though those that received a constrained liner had more commonly failed previous revision surgery. No other factors, including age (49±8 vs 48±9, p=0.915) or BMI (30.1±8 vs 29.3±7, p=0.653), were associated with elevated risk of re-revision for recurrent dislocation within this group.

Function

Among surviving hips, mean mHHS improved from 49.7 preoperatively to 71.1 at 6 years (n=66, range, 24–100) and 63.1 at 12 years (n=66, range, 15–100). At these same intervals, UCLA Activity scores had improved from 4.1 preoperatively to 5.0 (n=66, range, 2–10) and 4.6 (n=66, range, 2–10), Table 4.

Score improvements and final scores were comparable between index indication groups. Groups were similar with respect to age, sex, years between primary THA and index revision, and revision history, Table 5.

Table 4. PRO Scores

PRO Clinical Status Changes (Full Cohort)			
	Preoperative	6 Years	12 Years
mHHS	49.7	71.1	63.1
Score >70	13%	60%	40%
Score >80	5%	43%	26%
Improvement >20	-	50%	34%
Score >70 OR Improvement >20	-	71%	48%
UCLA	4.1	5.0	4.6
>5	39%	49%	27%
8-10	7%	19%	19%

DISCUSSION

As the volume of younger patients undergoing THA continues to increase,[5-7] the importance of understanding the indications and prognoses of revision surgery in this population has grown considerably.[8] Despite this importance, published outcome data has remained largely limited to surgeries performed prior to the wide adoption of more durable fixation techniques and bearings, Table 6.

In our series, re-revision free survivorship was 80% and 73% at 5 and 10 years, which is notably higher than rates previously reported. At 10-year mean follow-up, Stromberg et al. reported on 59 revision THAs performed for aseptic loosening in patients less than 55 years of age years with a first-generation cementing technique. Survivorship free from re-revision for aseptic loosening was 86% at four years and 48% at ten years (acetabular 65%, femoral 61%).[9] In a similar cohort of 70 hips, the same authors reported this rate to be 76% at eight years with a second-generation cementing technique (acetabular 80%, femoral 85%).[10] At 11-year mean follow-up, Lee et al. reported on 151 revision THAs performed primarily

Table 5. PRO Scores and Patient Characteristics by Index Revision Indication Group

Patient-Reported Outcome Scores and Patient Characteristics by Index Revision Indication Group												
	mHHS			UCLA								
	Baseline	6 Years	12 Years	Baseline	6 Years	12 Years	n hips (% of survivors)	Mean age at surgery	%F	Years from THA Mean (SD)	Prior Revision	n (mean)
All	49.7	71.1	63.1	4.1	5.0	4.6	66 (72%)	49	65%	11.3 (8)	23%	1.4
Loosening	45.0	70.8	69.6	3.9	4.9	4.5	27 (79%)	47	62%	10.9 (8)	26%	1.7
Wear	52.8	70.4	64.8	4.7	5.5	5.1	25 (73%)	50	65%	13.6 (7)	17%	1.5
Instability	28.9	56.4	48.4	3.0	4.0	3.0	6 (75%)	50	50%	11.9 (12)	50%	1.0

Table 6. Studies Reporting 10-Year Survivorship of Revision THA in Younger Patients

	Study Year	Age (mean) [rng]	Surgery Dates	n hips	Follow-up (years)			Survivorship free from re-revision for:			
								Any Cause		Aseptic Loosening	
					Min.	(mean)	[range]	5 year	10 year	5 year	10 year
Stromberg	1994	<55 (47) [31-55]	1979-1982	59	8	(10)	[8-13]	-	-	86%	48%
Stromberg	1996	<55 (47) [29-55]	1984-1986	70	4	(7)	[4-10]	-	-	-	76%
Lee	2013	<50 (43) [22-50]	1983-2008	151	2	(11)	[2-26]	-	63%	-	74%*
Kuijpers	2020	<55 (49) [18-54]	2007-2018	1037	0.1	(4)	[0.1-12]	78% [75-81]	72% [67-76]	95% [92-96]	90% [85-94]
Present Study	2022	<60 (48) [20-60]	2000-2016	141	4	(10)	[4-20]	78% [70-85]	70% [62-78]	98% [93-99]	96% [90-99]

*Approximated (70% failures due to aseptic loosening).
Survivorship data presented as % [95% CI].

for aseptic loosening (86%) in patients less than 50 years of age with cementless components. Survivorship was 88% at five years and 63% at ten years (acetabular 71%, femoral 80%), with failures again due primarily to aseptic loosening (70% of failures).[11] In contrast, we observed considerably lower rates of failure due to aseptic loosening, with only a 4% failure rate due to aseptic loosening at 10 years.

Our results are comparable to those of one of the only studies to evaluate similarly modern revision THA outcomes in this younger population. Kuijpers et al. reported outcomes of 1,037 revision THAs in the Dutch Arthroplasty Register in patients less than 55 years of age for index indications aseptic loosening (32%), dislocation (20%), infection (16%), and cup/liner wear (4%). They reported re-revision-free survivorship rates of 78% and 72% at five and ten years. Five- and ten-year failure due to aseptic loosening was 5% (acetabular 3.1%, femoral 2.3%) and 10% (7.0%, 2.7%).[15]

Owing to these lower rates of early loosening-related failure, re-revision-free survivorship in the current study and the study of Kuijpers et al. was considerably higher than rates previously reported in this younger population, and compared favorably to rates reported in general revision THA populations at both five (81–83%)[16-17] and ten (72%)[18] years. Overall 10-year failure rates for both instability (16%) and infection (10%), were comparable to rates reported in general revision THA populations at similar intervals (dislocation 1–27%, infection 1–22%).[19-22]

To our knowledge, the current study is the first to report clinical outcome scores in a large contemporary series of revision THAs in this younger population. Despite improvements in survivorship from earlier studies, patients reported similarly modest[23-25] improvements in outcome scores at 6 years (mHHS +21.4, UCLA +0.9) and 12 years (mHHS +13.4, UCLA +0.5). In contrast, a 2003 meta-analysis of revision THA outcomes in the general population (mean age 67), noted a mean mHHS improvement of 37.3 [95% CI 34.7–39.9] at 5-year mean follow-up.[26] This lag of scores behind survivorship improvements over time was similarly observed by a meta-analysis of primary THA outcomes in patients less than 30 years of age, where it was suggested to be due to the higher incidence of systemic disease in very young patients undergoing THA. Our similar finding in this broader age range (<60) of younger patients may highlight the significance of an independent effect of higher demands or expectations in younger populations in limiting felt improvements. We did not observe a significant relationship between age and reported score improvement within this cohort. Incidence of previously studied comorbidities were low and these were not found to be significantly associated with either re-revision rates or score improvements.

There are several limitations to this study. First, THA surgery is continuously evolving, and it is possible that outcomes of today's revision surgeries differ meaningfully from those reported by this study. However, in a recent report on revision THAs performed between 2010 and 2016 in a cohort similar to the current study's, re-revision-free survivorship at 5 years (81% [95% CI 76–86%]) was similar to that in the current study (80% [95% CI 72– 86%]), and instability was similarly the leading indication for re-revision (44%) in that study (5-year instability-related failure rate of 8%, vs. 11% in the current study).[27] Second, this patient population was treated at a high-volume tertiary care center and may represent comparatively more severe revision cases than the average young patient undergoing revision THA. Third, radiographic data may have allowed for detection of more subtle outcome differences and risk factors for re-revision. Finally, a larger cohort may have permitted multivariate determination of risk factors for re-revision, which would have been valuable given the number of potentially influential factors and the complexity of their relationships with one another.

CONCLUSION

Revision THA in patients less than 60 years of age was associated with considerably lower rates of early loosening-related failure than historically reported. Recurrent dislocation and infection appear to remain challenges in this population for which an improved understanding of risk factors and mitigation strategies would be of benefit. Despite improvements in survivorship from earlier studies, patient-reported functional improvements remained relatively unchanged.

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A PILOT STUDY OF NUTRITIONAL SUPPLEMENTATION IN SOFT TISSUE SARCOMA PATIENTS

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ABSTRACT

Background: Wound healing is particularly important for sarcoma patients who undergo neoadjuvant radiation therapy. Previous studies have demonstrated wound complications in this population approaching 35%. With this high rate of wound healing issues, identifying treatment modalities to minimize these complications is of paramount importance.

Methods: All patients with high grade bone and soft tissue sarcoma received 15 days of twice daily amino acid supplementation starting in the immediate post-operative period. We documented the healing status of the surgical wound, the primary outcome, at all follow up appointments until six months after surgery. Non-healing wounds were defined as any wound requiring 1) a return visit to the OR for debridement, 2) IV antibiotics (ABX), and 3) unhealed wounds at 6 months post-operatively.[1] For each patient, we collected biometrics with lean body mass analysis at pre-operative appointment, and two and six weeks postoperatively. The proportion with non-healing wounds was compared with a historical patient cohort using the chi-square test. In a subgroup of participants with body composition measurements, we also compared changes in mean fat mass, lean mass, and psoas index from pre-operative baseline to 6 months post-operative using generalized linear models.

Results: A total of 33 consecutive patients were supplemented with a branched chain amino acid (BCAA) formulation. The historical cohort included 146 participants from the previous 7 years (2010-2017). 26% of patients in the historical cohort experienced wound complications compared to 30% in the supplemented group. (p=0.72) When focusing specifically on lower extremity sarcomas treated with neoadjuvant radiation therapy, 46% of patients in the supplemented group experienced wound healing complications compared to 39% in the non-supplemented group (p=0.68). BCAA supplementation was found to be protective with regards to decreasing muscle wasting with no difference in psoas index measurements throughout the study period compared to a 20% muscle loss in the historical cohort (p=0.02).

Conclusion: In our limited sample size, there was no difference in wound healing complications between sarcoma patients who received post-operative BCAA supplementation compared to a historical cohort who were not supplemented. Patients who did not receive supplementation had a significant decline in post-operative psoas index following operative sarcoma removal.

Level of Evidence: III

Keywords: sarcoma, sarcopenia, tumor, nutrition, supplement, protein

INTRODUCTION

In recent years, there has been a push to optimize patient nutritional status through optimized dietary regimen and nutritional supplementation. Recent attempts to measure the severity of malnutrition have shown great promise in predicting post-surgical complications.[2] Much of this focus has been centered on pre-operative diagnosis of sarcopenia, or decreased muscle mass, which has been demonstrated to be an independent risk factor for injuries such as osteoporotic fractures.[3] Several studies have specifically investigated the impact of nutritionally supplementing patients with an amino acid formulation in the immediate post-operative period.[2,4]

Amino acid supplementation has shown promise in prior wound healing studies.[5,6] Many of these studies have centered on conditionally essential amino acids (CEAAs) which are normally produced by the body but must be supplemented in times of increased physiologic stress when demand outweighs production.[5,6] Two such CEAAs are glutamine and arginine. L-Arginine specifically has been shown to improve overall immune function during the wound healing process through a variety of

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mechanisms, including increased T-lymphocyte, macrophage, and splenocyte functioning as well as improved splenic blood flow.[6] Supplementation with arginine and glutamine has been shown to improve parameters of wound healing such as length of hospital stay and mortality rate.[5] Meanwhile larger formulations such as arginine, β-hydroxy-β-methyl butyrate (HMB), and glutamine supplementation have been demonstrated to significantly enhance deposition of wound collagen[6] and have also shown promise in improving wound healing for diabetic foot ulcer patients with poor limb perfusion or low albumin.[7] Finally, CEAA supplementation has shown efficacy in reducing the malnutrition- associated post-operative complications in studies on total knee arthroplasty and fracture fixation.[4,8-10]

While many recent studies have focused on the trauma patient population, there is no literature regarding nutritional supplementation of the soft tissue sarcoma patient population. Sarcomas are mesenchymal tumors which commonly arise from the soft tissues.[11] This category of cancers affects just over 13,000 individuals in the US annually and is often treated with a combination of radiation therapy and surgical excision.[1,12] The addition of radiation therapy is beneficial for its ability to target microscopic extensions of sarcoma tumor, reduce tumor size pre-operatively, and sterilize the tumor margin post-operatively,[13,14] resulting in a lower rate of local recurrence. Previous studies examining patients with combined excision and preoperative radiation therapy have demonstrated wound complications rates approaching 35%,[1] compared to 20% when radiation is delivered postoperatively. However, this typically requires a larger field of radiation and increased treatment dose and results in increased complications from radiation such as stiffness, swelling, pain, and increased risk of secondary malignancy.[1] Considering the high rate of wound healing issues experienced by the sarcoma population, especially in cases of combined excision and neoadjuvant radiation therapy, finding alternative low cost and low risk treatment modalities that minimize poor wound outcomes is of great importance.

The primary purpose of this study is to determine whether supplementation with a branched chain amino acid (BCAA) formulation results in fewer wound healing complications for sarcoma patients in the post-excision period when compared to a control cohort that did not receive supplementation. Secondary aims include evaluating for changes in overall muscle mass and body mass index after nutritional intervention in the supplemented group.

METHODS

We designed this pilot trial to include one year of consecutive patients, between June 2020 and May 2021, with high grade bone and soft tissue sarcomas receiving care in our department. Each patient received 15 days of BID amino acid supplementation starting on postoperative day 1. This study was originally launched as a quality improvement project with IRB approval obtained retroactively for data analysis purposes. Funding for the project was obtained from the University of Iowa Sarcoma Multidisciplinary Oncology Group in the form of a research grant used to cover the expense of the nutritional supplement, which was provided to the patients without charge. Inclusion criteria for the study were patients with intermediate and high-grade soft tissue sarcomas of greater than 5cm in diameter. Exclusion criteria included low grade sarcomas, sarcomas <5cm in diameter, and non-sarcoma cancers. We assessed patients for sarcopenia (low muscle mass) utilizing standard-of-care sarcoma staging chest/abdomen/pelvis CT scans to measure baseline psoas index. The validated psoas index (PI) is defined as the sum of the cross-sectional areas (CSA, cm2) of the psoas muscles divided by the patient's height squared (m2). Psoas CSA was measured at the level of L4 on pre-operative axial CT pelvis or, if unavailable, axial CT chest.[15] In addition to this, we utilized a body composition analyzer, InBody 770 to determine baseline body mass composition.

Immediately after surgical excision (post-operative day one) we started twice daily nutritional supplementation with Juven Therapeutic Nutrition Powder for 15 days (a total of 30 doses). The nutritional supplement Juven was selected due to its promising wound healing effects established in the diabetic patient population, as well effects of minimizing muscle wasting in the cancer patient population.[6,7] We selected this protocol of nutritional supplementation as this was the most consistent algorithm that could be used in our prospective patient cohort given variability in neoadjuvant radiation and systemic therapy. Additionally, we reasoned that the time of most importance of supplementation would be the first two weeks after surgery as the process of wound healing initiated. This protocol was also modeled after previous studies that had shown benefits to nutritional supplementation in the trauma patient population.[4]

At the two week follow up appointment, patients were asked to fill out a questionnaire indicating how many doses they missed. Additionally, at this appointment we measured body composition using the InBody device and conducted a grip strength evaluation. Body composition was also obtained at the 6-week post-op appointment. We analyzed wound healing at the 2, 6, 12, 24 week follow up appointments. Non-healing wounds were defined as any wound requiring packing or continued dressing changes at 6 months post operatively, any wound requiring a return to the operating room (OR) for debridement, or any wound requiring admission for intravenous antibiotics (ABX). This was based off of criteria previously outlined by O'Sullivan et al.[1] We also measured psoas indices on CT chest, abdomen, and pelvis obtained at 12 and 24 week follow up appointments and compared those measurements to preoperative values (Figure 1).

We performed a retrospective comparison of the supplemented group and group of 146 soft tissue sarcoma patients to serve as a historical control prior to nutritional supplementation which represented a 7-year, retrospective chart review. These patients were matched for similar disease processes and type of radiation therapy. The proposed study protocol timeline is included in Figure 1.

Statistical Analysis

Prior to data collection, our team completed a power analysis with the premise that the rate of wound healing complications would be 35% in in the control group and 17% in the supplement group, a rate equal to that of individuals undergoing postoperative radiation therapy.[1] We determined that 100 participants per group would provide ~80% power to detect this difference at an alpha level of 0.05 (2-sided test). Based upon this, a total enrollment of 100 patient's in both the supplemented and the historical control groups was intended for enrollment.

As enrolling 200 sarcoma patients, a monumental effort that would require many years and multi-institutional collaboration, we designed this study as a pilot trial to determine if we could discover a trend or a particular clinical scenario that would make a greater effort worthwhile. We chose to enroll consecutive qualifying and willing patients for one year.

Participant characteristics were described by group using mean ± standard deviation for continuous variables and frequency (percentage) for categorical variables. Between group differences in characteristics and complication rates were evaluated using independent t-tests for continuous variables and chi-square tests for categorical variables. The change in baseline to week 24 psoas index in the historical control group was evaluated using a generalized linear model in those not missing baseline or week 24 data (n=39).

RESULTS

Our historical cohort consisted of 146 patients for the non-supplemented group and 33 for the group receiving supplemental BCAA therapy. The control and treatment groups were similar across most characteristics (Table 1). There were no significant differences between groups with regards to mean age, mean BMI, gender, or smoking history. Notable differences include a larger mean tumor size and proportionally more grade 2 tumors for the supplemented group. Of note, the non-supplemented group did have an increased percentage of high-grade sarcomas. There was also a significant difference in the

Baseline (Pre-Op)
- Body Composition
- CT/CAP
- Wound Evaluation

2 Week Post-Op
- Body Composition
- Wound Evaluation

6 Week Post-Op
- Body Composition
- Wound Evaluation

12 Week Post-Op
- CT/CAP
- Body Composition
- Wound Evaluation

24 Week Post-Op
- CT/CAP
- Wound Evaluation

Figure 1. Study protocol.

Table 1. Participant Characteristics

Participant Characteristics	Did Not Receive Therapeutic Nutrition N = 146	Received Therapeutic Nutrition N = 33	P-value
Mean Age (years)	59.1 (SD18.3)	59.4 (SD17.8)	0.917
Male	84 (58%)	21 (64%)	0.520
Female	62 (42%)	12 (36%)	0.258
Smoking History	51 (35%)	15 (45%)	0.886
Mean BMI	29.7 (SD6.8)	29.5 (SD5.3)	0.024
Mean Tumor Size (cm)	10.3 (SD6.6)	13.5 (SD7.2)	0.378
Primary Tumor	131 (90%)	31 (94%)	0.001
Recurrent Tumor	7 (5%)	2 (6%)	0.192
Metastatic Tumor	8 (5%)	0 (0%)	0.395
Tumor Grade1	17 (12%)	1 (3%)	0.001
Tumor Grade 2	19 (13%)	13 (39 %)	
Tumor Grade 3	110 (75%)	19 (58%)	
Tumor Depth Deep	119 (82%)	30 (91%)	
Tumor Depth Superficial	27 (18%)	3 (9%)	
Upper Body Tumor	26 (18%)	8 (24%)	
Lower Body Tumor	120 (82%)	25 (76%)	
Neoadjuvant Radiation	53 (36%)	23 (70%)	0.001

proportion of patients that received neoadjuvant radiation therapy, which was 70% for the supplemented group compared to 36% for the non-supplemented group.

When examining the entire cohort, our results showed no significant difference with regards to wound complications between the non-supplemented and nutritionally supplemented groups. Similarly, when examining only those patients who had received neoadjuvant radiation therapy, there was no significant difference in wound complication rates between the non-supplemented and supplemented groups (Table 2).

When examining the most high-risk group, lower extremity soft tissue sarcoma patients treated with neoadjuvant radiation therapy, there was again no difference noted with regards to wound healing complication rates with the supplemented group having a 46% complication rate compared to 39% in the non-supplemented group (p=0.680).

For the supplemented group, average body composition measures such as BMI and Lean Mass remained relatively stable during the 24 week follow up period (Figure 2).

Figures 3 and 4 demonstrate the change in psoas index measurements over time for each group. In the supplemented group, the psoas index measurements remained stable from pre-operative measurement (mean value 7.8) to 6 month follow up (mean value 7.9). For the non-supplemented cohort, psoas index measurements decreased overtime from 8.9 pre-operatively to 7.1 at 6-month follow-up. This represented a 20% loss in psoas index measurements over the course of 6 months that was not demonstrated in patients with nutritional supplementation (p=0.021).

Looking further into the supplemented group and variations with patient compliance, 30% of the supplemented group missed at least one dose and 12% missed up to 15 doses (Figure 4). This variation in supplementation compliance could have influenced the results. When we standardized these results based upon compliance, we separated participants who were greater than 80% compliant from the rest. This demonstrated similar results to the non stratified data with a 28% wound complication in the non supplemented group compared to 36% in the supplemented group (p=0.421). This is shown in Figure 5.

Table 2. Wound Outcomes

Wound Outcomes	Did Not Receive Therapeutic Nutrition	Received Therapeutic Nutrition	P-value
Wound Complications: Whole Cohort	41/146 (28%)	12/33 (36%)	0.347
Wound Complications: Neoadjuvant Radiation Therapy Group	14/53 (26%)	7/23 (30%)	0.719

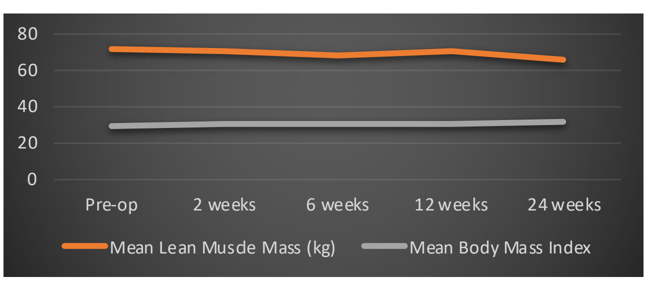

Figure 2. Body Composition Supplemented Group.

DISCUSSION

In a small prospective pilot trial, we found that sarcoma patients treated with nutritional supplementation in the immediate postoperative period did not demonstrate an improvement in wound complication rates. Wound

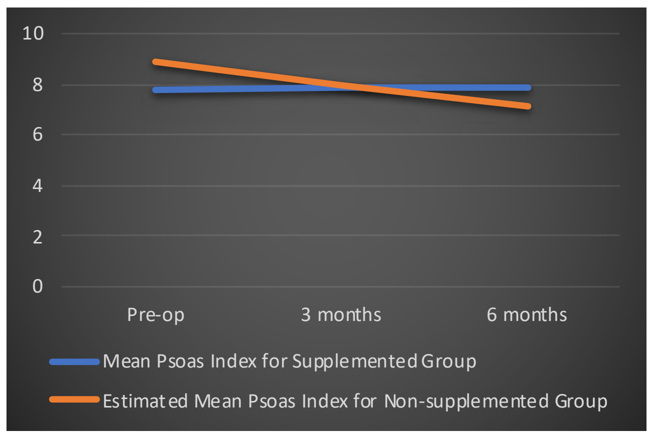

Figure 3. Psoas Index Measurements.

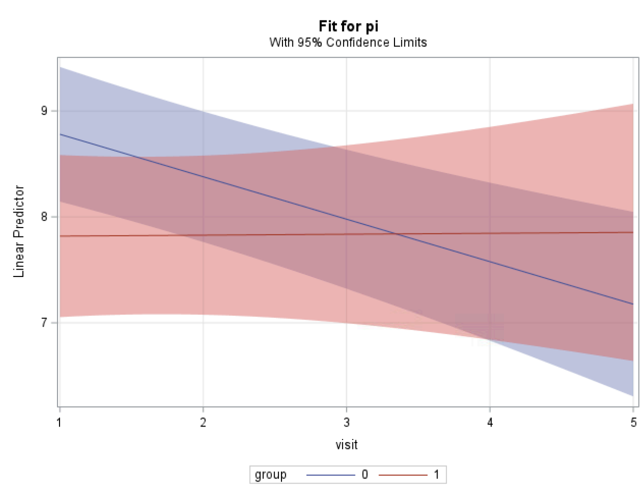

Figure 4. Confidence intervals for psoas index comparison. P=0.0213 for group.

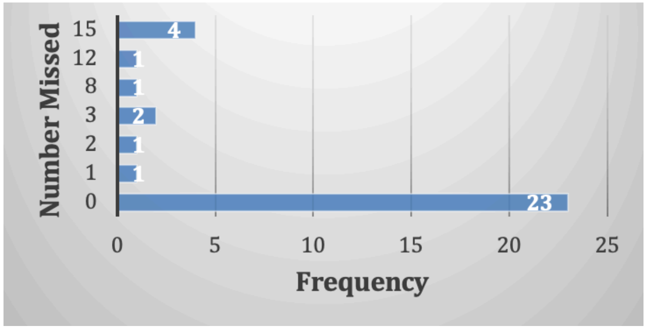

Figure 5. Missed Supplementation Doses.

Table 3. Wound Complications

Group	Wound complication		Totals
	No	Yes	
Non-supplemented	105 (71.9%)	41 (28.1%)	146
Supplemented	16 (64%)	9 (36%)	25
p-value	0.4213		

healing complications in the sarcoma population are well documented, particularly for those patients treated with neo-adjuvant radiation therapy. Although demonstrably effective at improving local control, radiation therapy has a profoundly damaging effect on the local soft tissue and can compromise wound healing. It is notable that significantly more patients in the supplemented group received radiation therapy at 70% versus the historical group at 36% (Table 3). Our investigation revealed several findings that warrant further discussion.

Neo-adjuvant radiation therapy is known to significantly elevate the risk of wound complications for sarcoma patients undergoing surgical excision.[1,16] Other known risk factors for wound complications among sarcoma patients include tumor depth and size.[16,17] Therefore, it is notable that the supplemented group also had a larger mean tumor size of 13.5 cm, and tumors larger than 10 cm have previously been associated with increased risk of wound complications.[17]

Interestingly, our results suggested that BCAA supplementation may have a protective effect against post-operative muscle wasting. A comparable historical cohort demonstrated a 20% loss in their average psoas index (PI) during the follow-up period. By contrast, the supplemented group PI values were essentially unchanged in the immediate 6-month postoperative period. Lean muscle mass (LMM) was also shown to be stable during follow up for the supplemented group. The potential for reduced muscle wasting with BCAA supplementation is encouraging and a potential benefit considering the high-risk profiles of the STS patient population.

While nutritional supplementation has been demonstrated to help prevent muscle wasting, we did not observe a similar benefit in wound healing. There are a number of potential explanations. First, our study was underpowered given the rarity of the diagnosis, study design based on a consecutive sample of clinical convenience, and the substantial number of patients with missed supplementation doses (30%). Next, we elected to include all patients with soft tissue sarcoma. It is likely that nutritional supplementation is of most benefit to a select subset of high-risk patients, such as patients with measurable sarcopenia or lower extremity tumors treated with neoadjuvant radiation. Further review of our specific interventional cohort revealed a number of extraordinarily difficult healing situations, such as large tumors involving the leg, foot, groin, and multiply comorbid patients. It is possible that our limited cohort is not representative of this population at large and does not conclusively prove that nutritional supplementation has no utility. Finally, our decision to supplement starting postoperative day 1 is perhaps not the most effective time for this intervention. For example, it may be that nutritional supplementation for several weeks prior to surgery would provide the components needed to successfully heal a wound at risk. This would be a reasonable study design for patients receiving neoadjuvant radiation, as there are several weeks available for intervention.

Our study was limited in the following ways. First, we recognize that our study was underpowered. The final treatment group of 33 participants was far less than the targeted 100, which was determined by our initial power analysis. Unfortunately, the relative scarcity of soft tissue sarcomas and consequential slow participant enrollment rate hampered efforts to reach the goal sample size. Thus, this study was vulnerable to type II error, where had the authors reached the target sample size a significant relationship may have been demonstrated. Regarding the study design, we used a retrospective analysis to create the historical control group while prospectively enrolling the treatment group. Although we attempted to match the control group and experimental groups, it is difficult to account for all variances between groups. In fact, our experimental cohort demonstrated a larger proportion of radiated tumors and tumors >10 cm, both factors associated with increased wound healing complications. Thus, it is possible that the mixed-design was unable to control for confounding patient factors, which may have impacted the eventual outcomes accordingly. Specifically, regarding the wound complication results which showed no significant difference between groups, it is possible that a protective effect of BCAA supplementation was masked by the unbalanced distribution of radiation therapy treatment and large tumor size.

CONCLUSION

In our limited sample size, there was no difference in wound healing complications between sarcoma patients who received post-operative BCAA supplementation and those who were not supplemented. However, patients who did not receive supplementation experienced significant decline in post-operative psoas index following operative tumor removal. By contrast, this decline in muscle mass was not seen in the BCAA supplemented group. Further work is warranted to investigate alternative approaches in BCAA nutritional supplementation that may be more effective at limiting wound healing complications.

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A SYSTEMATIC REVIEW AND META-ANALYSIS OF NEGATIVE WOUND PRESSURE THERAPY USE IN SOFT TISSUE SARCOMA RESECTION

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ABSTRACT

Background: Negative wound pressure therapy (NWPT) may reduce the wound complication (WC) risk in soft tissue sarcoma (STS) and is often utilized for large and/or irradiated wounds, extensive dissections, or wounds at risk of impaired drainage. However, data on WCs after NWPT in STS are lacking. This study systematically reviewed the available literature on NWPT in STS.

Methods: A query of the Cochrane Central Register of Controlled Trials (1976-2022), Cochrane Database of Systematic Reviews, MEDLINE (1946-2022), Scopus, and PubMed (1964-2022) was performed. Eight studies met inclusion.

Results: One-hundred eighty-six cases were analyzed. Among studies with available data, myxofibrosarcoma (n=32/131; 24.4%) and undifferentiated pleomorphic sarcoma (n=29/131; 22.1%) were the most common subtypes, 83.3% (n=90/108) were lower extremity STS, and 51.9% (n=82/158) were preoperatively irradiated. The overall WC rate was 10.8% (n=20/186). Pooled-analysis (three studies) demonstrated a lower WC risk with NWPT versus conventional dressings (OR, 0.133; 95% CI, 0.050-0.351; p<0.001; I^2=0%). Subsequent analysis (two studies) found no increased local recurrence risk versus conventional dressings (OR, 1.019; 95% CI, 0.125-8.321; p=0.99), with high heterogeneity.

Conclusion: NWPT appears to lower the WC risk in STS without increasing the recurrence risk, and may be suitable for primary, recurrent, or positive margin resections, staged reconstructions, and while awaiting histologic margin assessment. However, larger, randomized-controlled trials of NWPT in STS are warranted.

Level of Evidence: III

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Keywords: sarcoma, negative wound pressure therapy, wound complications

INTRODUCTION

Soft tissue sarcomas (STS) are rare tumors that comprise nearly 1% of adult malignancies.[1] STS commonly arise in the extremities, and treatment typically involves wide-margin resection with radiation and/or chemotherapy. Wound complication (WC) rates in extremity STS resection range from 16% to 53%, and are strongly associated with age, tumor size, and neoadjuvant radiation.[2-6] Negative wound pressure therapy (NWPT) devices are believed to reduce the risk of WCs, and are often utilized in STS for large and irradiated wounds, extensive dissections, or wounds at risk of impaired drainage.[6,7] Despite this practice, however, there are limited evidence-based data on the WC risk after NWPT in STS.

NWPT reduces bacterial colonization by removing excess fluid from surgical wounds, and few STS studies have suggested a lower WC risk with NWPT versus conventional postoperative dressings.[8-10] However, these data are derived from retrospective case series and small-sampled prospective investigations, thus limiting the evidence for routine use of NWPT in clinical practice. Conversely, randomized-controlled trials of NWPT in vascular procedures, high-risk fracture treatment, and gynecologic and breast surgery have independently demonstrated reduced wound infection rates, warranting further investigation of NWPT in STS which often involves a more extensive soft tissue dissection and larger residual dead space.[11-14]

Therefore, the primary goal of this investigation was to conduct a systematic review of the current literature that describe NWPT after STS resection. Targeted metrics included WCs, reoperations, local recurrence, and functional outcomes, if available. The secondary goal of this study was to perform pooled-analyses for use of NWPT versus conventional dressings to compare WC rates and oncologic outcomes.

METHODS

Search Strategy

This systematic review was conducted according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement of 2009. A systematic review of the literature was performed in August 2022 to identify all studies that described NWPT use following STS resection. The current review was registered with the PROSPERO International Prospective Register (National Institute for Health Research; CRD42022354991). The initial search was conducted using the following Boolean terms: Soft Tissue Sarcoma AND (Drainage OR Negative Wound Pressure Therapy OR Vacuum OR Prevena). Each phrase was applied to the following databases: Cochrane Central Register of Controlled Trials (1976 to 2022), Cochrane Database of Systematic Reviews, Ovid MEDLINE (1946 to 2022), Scopus, and PubMed (1964 to 2022).

Inclusion and Exclusion Criteria

All titles queried from each individual database were compiled and systematically screened by two independent authors to increase inter-observer reliability. First, titles were screened for duplicate entries and those written in a non-English language. Second, article titles were screened for relevance to negative wound pressure therapy (NWPT) in soft tissue sarcoma (STS). Indistinct titles were retained for eligibility screening. Remaining titles were screened for those that recorded wound outcomes associated with NWPT in STS. Editorials, commentaries, reviews, instructional course lectures, case reports, and techniques were excluded. Eligible articles underwent a full-text review. To meet final inclusion criteria, each article needed to provide evidence that NWPT was used following surgical resection of STS, with specific documentation of subsequent wound complications (WCs). Among those articles that met final inclusion, each bibliography was reviewed, and pertinent articles not included in the original query scope were added post hoc. If screening authors did not mutually agree a study should be included, it was excluded. If there was mutual agreement and the study met eligibility criteria, it was included for data extraction.

Data Extraction

For each study, the authors and publication year, study design and quality, sample size, pertinent clinicopathologic characteristics, and available oncologic, functional, and wound outcomes were recorded in a custom data extraction table (Table 1).[15] For extraction, the primary goal was to identify WC rates among included patients from eligible studies. A WC was defined as a non-oncologic WC requiring operation, prolonged wound care, documented infection, or the need for postoperative antibiotics due to a wound issue. Studies that compared WCs and oncologic outcomes of NWPT to conventional dressings were assessed using pooled-analysis. Local recurrence was reviewed as a measure of oncologic outcome.

Table 1. Description of Included Studies

Study, Year	N	Design	Age (years)[a]	Predominant Histology	Predominant Location	Quality of Study[1]	WC Rate	LR Rate	FU (months)[a]	Notes
Siegel et al., 2016	16	R	52.0 (17.7-86.3)	NA	NA	NA	6.3% (1/16)	NA	NA	Temporizing for staged reconstruction
Senchenkov et al., 2007	17	R	65 (42-82)	UPS (6/17)	LE (14/17)	NA	11.8 (2/17)	5.9% (1/17)	NA	Primary resection
Chen et al., 2016	5	R	44.4 (17.8)	UPS (2/5)	LE (3/5)	NA	0%	20% (1/5)	26 (12-36)	Primary resection
Nakamura et al., 2021	7	P	61.4 (11.5)	DFSP (4/7)	LE (3/7); UE (3/7)	NA	0%	NA	NA	Primary resection
Shields et al., 2021	10	P	56 (13.7)	UPS (3/10); Liposarcoma (3/10)	LE (7/10)	2	20% (2/10)	30% (3/10)	24 (10.7)	Primary resection vs. conventional dressings
Bedi et al., 2018	39	R	54.3 (15.3)	NA	NA	NA	7.7% (3/39)	0%	39.6 (15-98)	Primary resection vs. conventional dressings
Dadras et al., 2021	30	P	59.9 (14.2)	ALT (10/30)	LE (24/30)	2	3.3% (1/30)	NA	NA	Primary resection vs. conventional dressings
Fourman et al., 2021	62	R	62.2 (22.3)	MFS (32/62)	NA	NA	17.7% (11/62)	8.1% (5/62)	51.6 (33.6)	Temporizing histologic margin assessment.

R, retrospective; P, prospective; UE, upper extremity; LE, lower extremity; USP, undifferentiated pleomorphic sarcoma; DFSP, dermatofibrosarcoma protuberans; ALT, atypical lipomatous tumor; MFS, myxofibrosarcoma; NWPT, negative wound pressure therapy; NA, not available; WC, wound complication; LR, local recurrence; FU, follow-up.

[a]Reported as mean and standard deviation, median and range, or mean and range.

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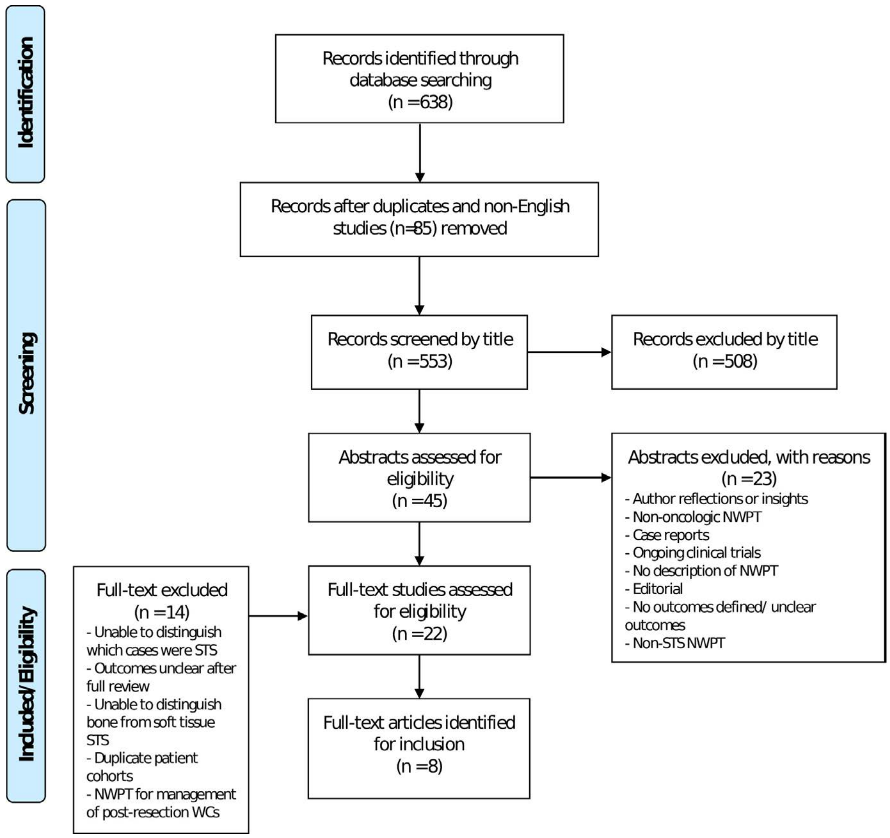

Figure 1. Study flowchart using the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) selection process. NWPT, negative wound pressure therapy; STS, soft tissue sarcoma; WC, wound complication.

Statistical Analyses

Statistical methods were performed using Microsoft Excel (Microsoft, WA, USA), and R-Studio version (RStudio: Integrated Development for R. RStudio, PBC, Boston, MA, USA). All missing data were given a 'null' value, and continuous variable testing was performed using weighted means and the rule of thumb for estimating standard deviations, or among range and median values.[16,17] Pooled analysis was performed for variables among studies with sufficient data using chi-squared and I-squared (I^2) tests for heterogeneity. For visual representation, these data are shown as forest plots with odds ratios (OR) and associated 95% confidence intervals (CI) (OpenMeta[Analyst]). A p-value <0.05 was considered statistically significant.

RESULTS

Literature Search

The initial search yielded 638 articles. 85 were excluded without English translation, or as duplicate entries. Each abstract and title was then carefully reviewed to determine study relevance, resulting in a total of 22 papers eligible for full-text review. A PRISMA flowchart of the initial study identification and subsequent screening criteria is highlighted in Figure 1. There were five retrospective and three prospective studies (eight total) that met final inclusion.[2,8-10,18-21]

Three of eight studies assessed NWPT outcomes with skin grafting only.[2,18,19] Two of eight assessed incisional NWPT outcomes only.[9,10] One of eight assessed NWPT-temporization to stage tumor beds requiring complex reconstructions only.[21] The remaining two studies included combined cases of incisional NWPT, NWPT with skin grafting, and NWPT-temporized wounds requiring complex staged reconstructions only.[8,20] One of the above-mentioned studies specifically temporized NWPT while awaiting histologic assessment of margins.[20] Among the eight included studies, three distinguished WC rates between NWPT and conventional dressings, and two of those three studies also compared local recurrence rates between NWPT and conventional dressings.[8-10] These studies did not compare outcomes by radiation usage or other clinicopathologic characteristics.

Sample Characteristics

The included articles, data extraction characteristics, descriptions of common histologies, and anatomical locations are recorded in Table 1. A total of 186 patients (eight studies) were analyzed. The mean (SD) age of included patients was 57.09 (5.39) years, with a mean (SD) follow-up time of 25.5 (18.9) months. Among six studies with available histology data, the most common subtypes were myxofibrosarcoma (MFS; n=32; 24.4%), undifferentiated pleomorphic sarcoma (UPS; n=29; 22.1%), dermatofibrosarcoma protuberans (DFSP; n=12; 9.2%), and atypical lipomatous tumors (n=10; 7.6%).[2,9,10,18-20] Among six studies that recorded anatomic location, 83.3% (n=90) were lower extremity STS, 10.2% (n=11) were upper extremity STS, and 6.5% (n=7) were trunk or back STS.[2,8-10,18,19] Among five studies that recorded radiation therapy characteristics, 51.9% (n=82) received neoadjuvant radiation, and 27.4% (n=31) received adjuvant radiation.[8-10,19,20] Five studies recorded NWPT duration, which ranged from five to ten days of use after surgery.[2,8,9,18,19]

Wound Complications

All Studies

The overall WC rate among the eight included studies with NWPT after STS resection was 10.8% (n=20/186). A summary of the WCs occurring in the included studies is shown in Table 2.

Negative Wound Pressure Therapy versus Conventional Dressings

Three studies compared NWPT (n=79) to conventional dressings (n=121).[8-10] 7.6% (n=6/79) developed a WC in the NWPT group, and 39.7% (n=48/121) developed a WC in the conventional dressing group. Pooled-analysis showed a statistically significantly lower risk of WCs with NWPT than conventional dressings, with low heterogeneity (OR, 0.133; 95% CI, 0.050-0.351; $p<0.001$; $I^2=0\%$) (Figure 2). The high heterogeneity of data otherwise limited pooled-analyses with respect to clinicopathologic characteristics and adjuvant treatments in these three studies, such the use of radiation which is a known risk factor for infection.

Table 2. Description of Wound Complications Among Included Studies

Study, Year	WC Rate	Notes
Siegel et al.	6.3% (1/16)	One unspecified bleeding episode requiring return the operating room.
Senchenkov et al.	11.8 (2/17)	Two repeat operations, specific wound complications unspecified.
Chen et al.	0%	NA
Nakamura et al.	0%	NA
Shields et al.	20% (2/10)	Two superficial surgical site infections, one requiring oral antibiotics only, one requiring debridement 21 days postoperatively.
Bedi et al.	7.7% (3/39)	Unplanned reoperation, prolonged wound care, or antibiotics within 6 months of resection. Individual wound complications unspecified.
Dadras et al.	3.3% (1/30)	Deep wound infection requiring operative revision.
Fourman et al.	17.7% (11/62)	Unplanned return to the operating room for deep infection (4/11) or aseptic wound complication requiring debridement (7/11).

WC, wound complication; NA, not applicable.

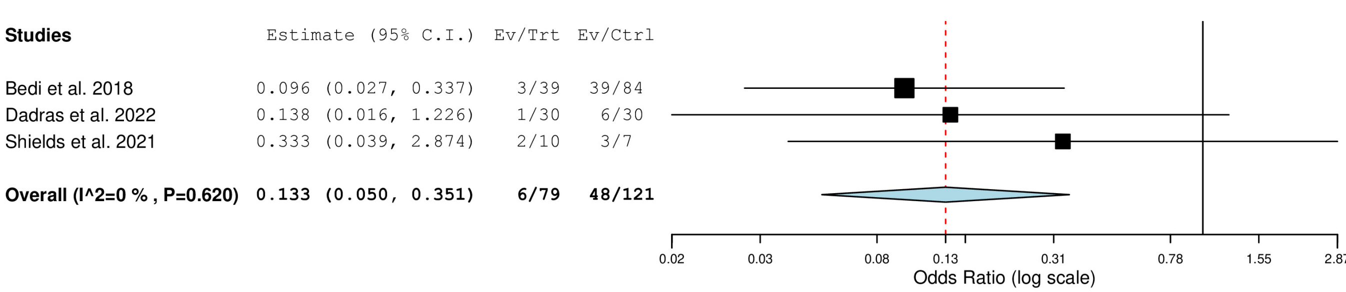

Figure 2. Pooled analyses of wound complication rates among studies that compared negative wound pressure therapy to conventional dressings (p<0.001).

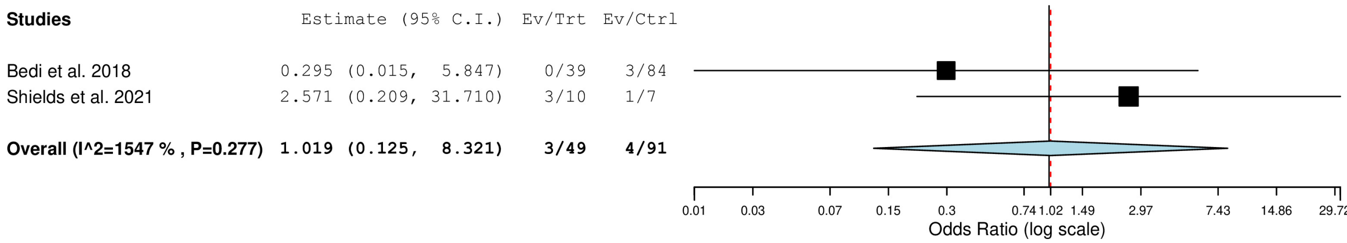

Figure 3. Pooled analyses of local recurrence rates among studies that compared negative wound pressure therapy to conventional dressings (p=0.99).

Local Recurrence

Local recurrence was reported in five of the nine studies.[8,10,18-20] The overall local recurrence rate was 7.5% (n=10/133) with NWPT. Two of the nine studies compared local recurrence between NWPT and conventional dressings.[8,10] 6.1% (n=3/49) of patients treated with NWPT developed a local recurrence, while 4.4% (n=4/91) with conventional dressings only developed a local recurrence. Pooled-analysis of these two studies showed no significant difference with high heterogeneity for local recurrence risk between NWPT and conventional dressings (OR, 1.019; 95% CI, 0.125-8.321; p=0.99; I^2=1547%) (Figure 3).

DISCUSSION

Despite advancements in the medical and surgical treatments of STS, the rate of postoperative WCs remains high. Recent meta-analysis data by Slump et al. suggest an overall WC rate of 30.2% and a reoperation rate of 13.4% for patients undergoing extremity STS resection.[6] These patients are often at a high risk for delayed wound healing and infection given extensive dissection, local tissue invasion, impaired drainage, and the effects of radiation. There exist a variety of strategies to minimize WCs, including the use of NWPT devices. However, there are no current practice guidelines regarding NWPT use in STS. The current investigation therefore comprehensively and systematically reviewed the available literature that describes wound outcomes with NWPT in STS. The findings of this study suggest NWPT is associated with a lower WC risk than conventional dressings with no increased local recurrence risk. Furthermore, it appears NWPT may be suitable for primary, recurrent, or positive margin resections, staged reconstructions, and while awaiting histologic margin assessment.

NWPT was introduced as a wound closure adjuvant around 2006, and in recent years has been reliably shown to reduce WCs in randomized controlled trials of inguinal vascular reconstructions, gynecologic and breast tumor procedures, and fracture management.[11,12,14] In STS, NWPT is often used for incisional closures or open wounds, often in conjunction with skin grafting or tissue flaps. Bickels et al. and Siegel et al. were among the first to describe the use of vacuum-assisted closure in STS. Despite limited samples, these two studies compared NWPT to conventional dressings and found that NWPT was associated with shorter hospital stays, fewer repeat operations, and higher primary closure rates without the need for soft tissue transposition.[22,23] For the purposes of this review, however, the articles by Bickels et al. and Siegel et al. were not included because their cohorts included STS wounds, trauma wounds, and infected postoperative wounds, without any explicit distinction of STS WC outcomes. Since these initial investigations, very few studies have evaluated the use of NWPT in STS, and only eight articles met final inclusion per PRISMA guidelines outlined in Figure 1. Currently, there are five ongoing clinical trials examining the effects of NWPT on WCs and clinical outcomes after STS resection (NCT04960332; NCT03900078; NCT03175718; NCT02901405; NCT02638298).

The overall WC rate for cases with NWPT in STS per this review was 10.8%.[2,8-10,18-21] Overall, the large heterogeneity of data and small samples with nondescriptive data limited meaningful pooled-analyses, such as assessment of WCs by adjuvant therapy, age, tumor size, and other known risk factors. However, this review did identify three studies in which a total of 79 NWPT cases were compared to 121 cases of conventional dressings.[8-10] The WC risk was statistically significantly lower with NWPT use than conventional dressings in pooled-analyses, with low heterogeneity (Figure 2). These data suggest NWPT use during STS resection may be associated with a lower WC risk.

Among the three studies that compared NWPT to conventional dressings, Bedi et al. specifically assessed WC rates with preoperative radiotherapy in lower extremity STS. They considered a WC to include reoperation, prolonged wound care, or antibiotic use after resection for wound issues.[8] They reported a lower rate of WCs with NWPT (8%) versus conventional postoperative dressings (43%), as well as a 9% vs. 46% difference in medial thigh compartment WCs treated with NWPT than conventional dressings, respectively. Shields et al. also compared NWPT to dressings, and defined WC as a surgical site infection within 30 days.[10] They had two (20%) WCs in the NWPT group, compared to three (42%) in the conventional dressings group. However, the relatively limited time frame may not have captured the true WC rate given short follow-up of only 30 days. Dadras et al. was the third study to compare NWPT and dressings, and defined a WC according to the Clavien-Dindo classification.[9,24] They only recorded one WC in the NWPT group (3%), compared to six (20%) in the conventional dressings group. However, it was unclear whether this complication occurred in an STS patient since their cohort included patients with lipomas, aggressive fibromatosis, and "other benign tumors". Therefore, although the current systematic review demonstrates a statistically significant lower risk of WCs with NWPT than with conventional dressings in pooled-analyses, larger randomized-controlled trials with longer follow-up, strict criteria, and stratification by clinical factors and adjuvant therapies are necessary to address confounding variables.

NWPT has been shown to induce inflammatory cell infiltration as well as vascular endothelial growth factor production and angiogenesis due to reduced tissue perfusion from negative pressure suction.[25] Therefore, local effects of NWPT mirror tumorigenesis, and it is not unreasonable to associate NWPT with an increased local recurrence risk. However, this systematic review did not observe an increased local recurrence risk with NWPT over conventional dressings in pooled-analysis of two studies, though with high heterogeneity.[8,10] Among all eight included studies, five documented oncologic outcomes, and there were a total of ten total local recurrences reported. Therefore, while it appears that NWPT provides a benefit with no compromise of local control, follow-up in most included studies was either limited or not clearly defined. Future prospective studies with longer and more detailed follow-up are needed to assess the oncologic outcomes of STS patients treated with NWPT, especially given variable late recurrence patterns of some histologic subtypes.

Anagnostakos & Mosser were among the first to describe the use of NWPT-temporization in STS, however their study was not included in the final eligible articles.[26] This concept was further studied by Fourman et al., Chen et al., and Siegel et al., who each vac-temporized in patients undergoing STS resection.[18,20,21] Chen et al. temporized NWPT in five patients with ulcerating STS or with impending ulceration, all with skin grafts, and found only two needed a future flap with no overall WCs and one local recurrence. Siegel et al. temporized NWPT in 16 STS cases requiring complex staged reconstructions, with only one WC but no mention of oncologic outcomes. Last, Fourman et al. temporized NWPT while awaiting histologic assessment of margins. They predominantly used NWPT in DFSP and MFS, two subtypes with fingerlike histologic projections and a proclivity for local recurrence. They recorded five local recurrences with a reoperation rate of 17.7% due to WCs. Together, the findings from each of these studies support the potential benefits of NWPT as a temporizing measure until final margins are achieved or following with skin grafting or until delayed reconstruction can be successfully and safely performed.

LIMITATIONS

The limitations of this review involve the limited samples of included studies and heterogeneity of data across all studies that limit generalizability of the results. This variability is likely due to the rarity of STS producing studies with a small N and the under-reporting of NWPT outcomes in the STS literature. There was also no consistent definition of what constitutes a WC across all studies, nor specific information regarding NWPT details (incisional, console settings, volume, etc.). Furthermore, most studies were retrospective and assessed small cohorts which limited the ability to perform meaningful meta-analyses. However, to our knowledge, this pooled comparison is unique and provides evidence that NWPT may be associated with lower WCs than regular dressings during resection of STS. An additional limitation worth noting is the lack of data on WCs by age, preoperative radiation, and tumor size. These are all known risk factors for infection, and it would otherwise be important to distinguish these as confounding variables in future investigations.

CONCLUSION

Systematic review and pooled analyses of available evidence suggests that compared to conventional dressings, NWPT was associated with a lower risk for WCs without a higher risk of local recurrence after STS resection. However, these results should be interpreted and applied while considering limitations related to a relatively small number of eligible studies, heterogeneity of data, and small study populations. Given this relative paucity of data on use of NWPT in STS, this review warrants larger randomized-controlled trials to provide evidence-based guidelines regarding the use of these treatment modalities.

List of abbreviations

WC, wound complications; STS, soft tissue sarcoma; NWPT, negative wound pressure therapy; DFSP, dermatofibrosarcoma protuberans; MFS, myxofibrosarcoma.

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T_2* IMAGING ASSESSMENT OF NEOADJUVANT RADIATION THERAPY COMBINED WITH PHARMACOLOGICAL ASCORBATE IN EXTREMITY SOFT-TISSUE SARCOMAS: A PILOT STUDY

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ABSTRACT

Background: Extremity soft-tissue sarcomas (STS) are commonly treated with neoadjuvant radiation therapy followed by surgical resection. However, the pathological near-complete response rate is low (9-25%). Noninvasive imaging assessment that predicts treatment response before and during treatment is desirable to optimize treatment regimens. This pilot study aimed to investigate the application of a quantitative MRI parameter, T_2*, in assessing neoadjuvant radiation therapy combined with pharmacological ascorbate in extremity STS.

Methods: This prospective cohort study included seven patients diagnosed with extremity STS and scheduled to receive neoadjuvant radiation therapy combined with pharmacological ascorbate. T_2* maps were obtained from each patient before treatment (baseline MRI), two weeks after initiating treatment (on-treatment MRI), and before surgery (pre-surgery MRI). The T_2* values within the tumor region were transformed into z-scores with respect to the normal- appearing tissue region. The voxel-wise z-scores within the tumor region were thresholded to generate masks representing significantly high (z-score>1.96) and low z-score (z-score<-1.96) voxels. The means of the total z-scores and within each of the significantly high and low z-score mask were computed. Their correlations with percent necrosis from pathological examination were evaluated using Spearman's rank correlation coefficient r. A correlation was considered as moderate or strong when r is higher than 0.6 and 0.8, respectively. A correlation was considered as fair or weak when r is below 0.6.

Results: For the baseline and on-treatment MRIs, the means of the significantly high z-scores of the T_2* measurements showed moderate correlations with percent necrosis (r = 0.68 and 0.6; p = 0.11 and 0.24). For the pre-surgery MRI, the means of the total and significantly high z-scores showed strong correlations with percent necrosis (r = 0.8 and 0.9; p = 0.13 and 0.08). Tumor volume and baseline MRI-based percent necrosis showed fair or weak correlations (r = 0.3-0.54; p = 0.24-0.68).

Conclusion: T_2* measurements prior to treatment, two weeks after initiating treatment, and before surgery showed moderate to strong correlations with percent necrosis. These results support the potential for using T_2* mapping to predict and assess response to neoadjuvant radiation therapy combined with pharmacological ascorbate in extremity STS.

Level of Evidence: IV

Keywords: soft-tissue sarcomas, treatment assessment, response, MRI, T_2*, necrosis

INTRODUCTION

Soft-tissue sarcomas (STS) encompass a group of rare and heterogenous tumors of mesenchymal origin that predominately arise in the extremities or retroperitoneal regions. They have more than 100 histological subtypes and represent less than 1% of all malignant tumors in adults.[1,2] A common treatment for localized STS is neoadjuvant radiation therapy (RT) followed by surgical resection. Despite a high risk of acute wound complications, neoadjuvant RT potentially reduces tumor burden, improves limb-sparing resection rates, and leads to a better functional outcome.[3,4] Current assessment of neoadjuvant treatment response relies on pathological examination after surgical resection. Nonetheless, the pathological near-complete response rate, defined as ≥95% necrosis or ≤5% viable tumor, is low (9-25%).[5-7]

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Therefore, early prediction of treatment response before or during treatment may help identify patients who would benefit from neoadjuvant treatment. In theory, serial biopsies can be performed to assess treatment response throughout the treatment, but the procedure is invasive and subject to sampling errors in heterogeneous tumors. A non-invasive tool, such as magnetic resonance imaging (MRI), is desirable to predict treatment response before and early during treatment to reduce the need for exploratory biopsies.

Previous studies have used structural MRI images to measure changes in tumor volume following neoadjuvant RT based on the anticancer effect from RT to decrease tumor volume. However, most studies fail to find correlations between tumor volume changes and pathological response.[8-11] Tissue changes that are accompanied with a favorable pathological response include necrosis, fibrosis, hemorrhage, and cystic regions.[9-12] These changes may not necessarily correspond to a decrease in tumor volume.[9-12]

Quantitative MR parameters that provide measures of diffusion, perfusion, and relaxation times of water molecules in tissue may help better characterize the RT effects than volumetric measures.[13-17] Recent studies have shown that diffusion and perfusion measures derived from diffusion-weighted MRI (DWI) and dynamic contrast-enhanced (DCE-MRI) before or early during treatment correlate with pathological response.[18-21] The MR relaxation time, T_2*, has been used to detect RT-induced hypoxia in animal models[22,23] and study regional cellularity in human STS.[16] The utility of T_2* in predicting and assessing response to neoadjuvant RT has not been investigated.

This pilot study aimed to investigate the feasibility of using T_2* mapping to assess neoadjuvant RT combined with pharmacologic ascorbate (P-AscH-) in seven patients with extremity STS. Preoperative T_2* measurements were obtained from each patient before, during, and after neoadjuvant treatment to study their correlations with percent necrosis from pathological examination.

METHODS

Patients

This prospective cohort study was approved by the Institutional Review Board of the University of Iowa (IRB# 201901810). Patients receiving pharmacological ascorbate concurrently with radiation were treated on the Phase 1b/2 clinical trial (NCT03508726). Fourteen patients were enrolled in the study from January 2020 to December 2022. Informed written consent was obtained from all the patients. Seven of these patients (2 females and 5 males; 62 ± 15 years old, mean ± standard deviation (SD)) had completed at least one baseline MRI scan. Their data were eventually included in the analysis (Table 1). The inclusion criteria were as follows: pathologically confirmed diagnosis of locally advanced extremity STS through biopsy; prescribed neoadjuvant RT; ECOG performance status scale of 0, 1, or 2. Patients were excluded if they were unable to undergo MRI scans. All subjects received five-week RT (50 Gy in 25 fractions) combined with P-AscH$^-$ infusions (75 g infusion three times per week). Surgical resection was scheduled approximately four weeks following the completion of RT. After surgical resection, gross estimation of percent necrosis was recorded by an anatomic pathologist with a treatment goal of ≥95% necrosis (pathological near-complete response).

Magnetic resonance imaging

The imaging protocol consisted of five MRI scans (Fig. 1a). One baseline MRI scan was collected two weeks prior to the start of RT. Three on-treatment MRI scans were collected on the same day two weeks after the start of RT combined with P-AscH$^-$ (Fig. 1b); the first scan before daily therapy (pre), the second scan one hour after P-AscH$^-$ infusion but before RT (post P-AscH$^-$), and the third scan one hour after RT (post RT). One pre-surgery MRI scan was collected two to four weeks after the completion of RT and one day before surgery. Among the seven patients, five patients completed all five MRI scans. Two patients completed only a subset of the five MRI scans: four and three of the five MRI scans, respectively.

MRI scans were performed on a 3 Tesla MRI scanner (Siemens TIM TRIO, Erlangen, Germany). Each MRI scan included a 3D multi-echo gradient-echo (GRE) sequence for T_2* measurements. The parameters for the 3D multi-echo GRE sequence were as follows: voxel size of 1.2 × 1.2 × 3 mm^3, pixel bandwidth of 260 Hz, flip angle of 17°, repetition time of 80 ms, 8 echo times of 7-56 ms in increments of 7 ms, and number of averages: 1. The baseline MRI scan also included post-contrast T_1-weighted (T_1+C) and T_2-weigthed sequences with Dixon method. The parameters for the T_1+C sequence were as follows: voxel size of 0.9 × 0.9 × 3 mm^3, pixel bandwidth of 965 Hz, flip angle of 9°, echo times of 2.46 and 3.69 ms, repetition time of 5.5 ms, and number of averages: 1. The parameters for the T_2-weighted sequence were as follows: voxel size of 0.94 × 0.94 × 3.5 mm^3, pixel bandwidth of 340 Hz, flip angle of 101°, echo times of 59.04 and 60.27 ms, repetition time of 4950 ms, and number of averages: 1.

Table 1. Demographics and Clinical Information of Seven Patients with STS

No.	Age	Gender	Diagnosis	Site	Percent necrosis
001	42	M	Undifferentiated pleomorphic sarcoma grade 2	Thigh	53
002	39	F	Myxoid liposarcoma	Thigh	99
003	69	M	Extraskeletal myxoid chondrosarcoma	Thigh	48
004	72	M	Extraskeletal osteosarcoma	Thigh	92
005	69	F	Myxofibrosarcoma grade 3	Arm	18
006	69	M	Undifferentiated pleomorphic sarcoma grade 2	Thigh	90
007	74	M	Undifferentiated pleomorphic sarcoma grade 2	Thigh	77

Data analysis

T_2* maps were generated by fitting a mono-exponential decay to the signals of the multi-echo GRE images using Matlab (Mathworks, Inc.). For region-of-interest (ROI) analysis, the tumor ROI was defined as gross regions with abnormal T_2* values on the T_2* map (Fig. 2a). The normal-appearing tissue ROI was selected on a spherical region (15 mm radius) with normal T_2* values, avoiding regions treated with RT (Fig. 2b). To account for tumor heterogeneity and minimize inter-subject variability, T_2* values within the tumor ROI were transformed into z-scores with respect to the normal-appearing tissue ROI; $\text{z-score}_{tumor} = (T_2{*}_{tumor} - \text{mean } T_2{*}_{normal})/\text{SD of } T_2{*}_{normal}$ (Fig. 2c,d).[24,25] The voxel-wise z-scores within the tumor ROI were thresholded to generate masks representing significantly high (z-score > 1.96) and significantly low z-score (z-score < -1.96) voxels. The z-score thresholds (1.96 and -1.96) were determined based on a 95% confidence interval. The mean of the total z-scores, as well as the means within the significantly high and significantly low z-score masks, were computed to evaluate their correlations with percent necrosis. Additionally, the correlations of tumor volume and baseline MRI-based percent necrosis, defined on the hyperintense signals within the tumor ROI on the T_2-weighted images without enhancement (Fig. 2a), with percent necrosis were evaluated. Correlations were assessed using Spearman's rank correlation coefficient r. A correlation was considered as moderate or strong when r is higher than 0.6 and 0.8, respectively.[26-28] A correlation was considered as fair or weak when r is below 0.6.

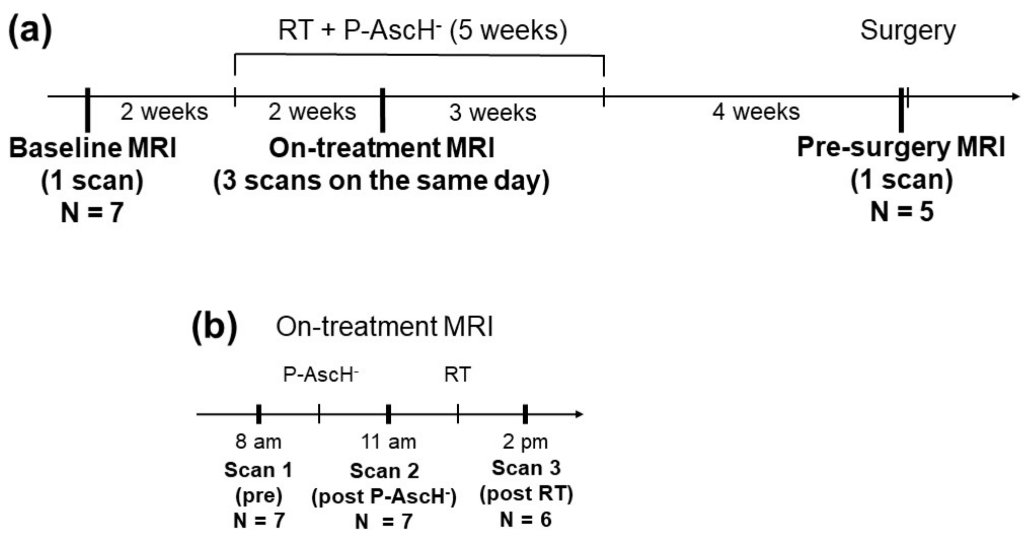

Figure 1A-1B. (1A) The imaging protocol consisted of five MRI scans. One MRI scan was collected before the treatment (baseline MRI). Three MRI scans were collected two weeks after the start of five-week RT+P-AscH⁻ treatment (on-treatment MRI). One MRI scan was collected two to four weeks after the completion of RT and 1 day before surgery (pre-surgery MRI). (1B) Three on-treatment MRI scans consisted of one scan before daily therapy (pre), one scan after P-AscH⁻ treatment but before RT (post P-AscH⁻), and one scan after RT (post RT).

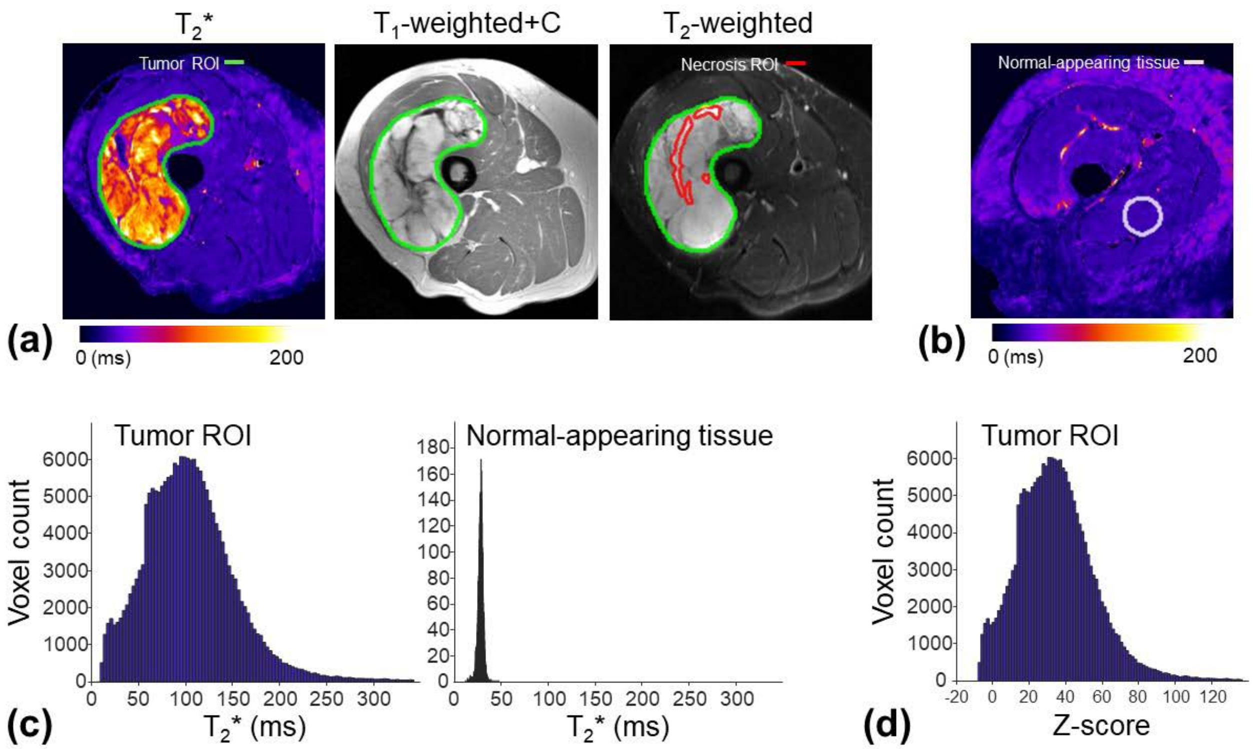

Figure 2A-2D. (2A) The tumor and necrosis ROIs overlaid on the T_2* map, T_1+C, and T_2-weighted images obtained from a baseline MRI scan of a patient. The tumor ROI was defined on gross regions with abnormal T_2* values. The necrosis ROI was defined on hyperintense signals within the tumor ROI on the T_2-weighted images without enhancement. (2B) The normal-appearing tissue ROI overlaid on the T_2* map. The normal-appearing tissue ROI was defined on the regions with normal T_2* values, avoiding regions treated with RT. (2C) Histograms of the T_2* values within the tumor and normal-appearing ROIs. (2D) The voxel-wise z-scores was computed by normalizing the T_2* values of the tumor ROI to those of the normal-appearing tissue ROI; z-score$_{tumor}$ = ($T_2{}^*_{tumor}$ - mean $T_2{}^*_{normal}$)/SD of $T_2{}^*_{normal}$.

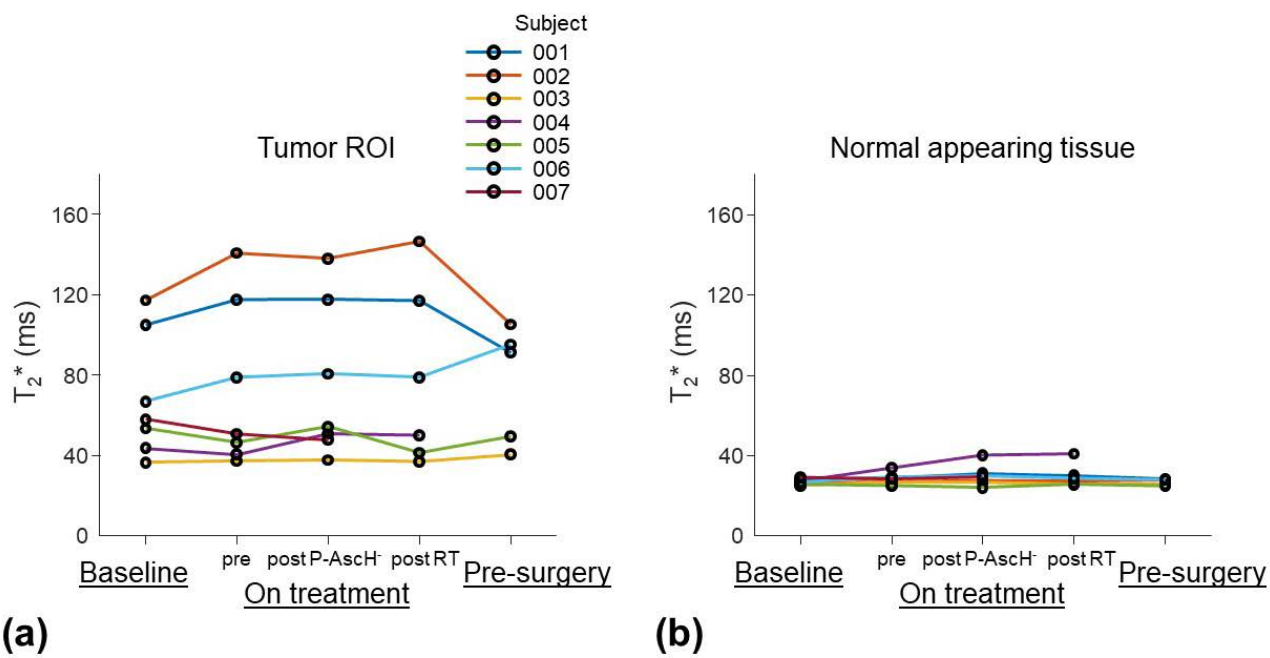

Figure 3A-3B. Changes of the mean T_2* values within the tumor (3A) and normal-appearing tissue ROIs (3B) of the 7 patients across baseline, on-treatment, and pre-surgery MRI scans.

RESULTS

Compared with the normal-appearing tissue ROI, the tumor ROI showed a larger inter-subject variation (SD: 36.9 ms versus 3.4 ms Fig. 3a,b) and a larger intra-subject temporal variation of the T_2* measurements (SD: 8.1 ms versus 1.7 ms). Similarly, the *z*-scores within the tumor ROI showed large inter-subject and intra-subject temporal variations (Fig. 4). These effects are likely reflective of tumor heterogeneity. The variability observed temporally may be the result of treatment-induced tissue changes.

For the baseline MRI scan, the mean of the significantly high *z*-scores of the T_2* measurement showed a moderate correlation with percent necrosis from pathological examination ($r = 0.68$; $p = 0.11$) (Fig. 5b). For the on-treatment MRI scans, the mean of the significantly high *z*-scores of the post-RT T_2* measurement showed a moderate correlation with percent necrosis ($r = 0.6$; $p = 0.24$) (Fig. 5b). For the pre-surgery MRI scan, the means of the total and significantly high *z*-scores of the T_2* measurement showed strong correlations with percent necrosis (r = 0.8 and 0.9; p = 0.13 and 0.08) (Fig. 5a,b). These correlations trended toward statistical significance despite the small sample size. Other imaging measures, including significantly low *z*-scores of the T_2* measurement, tumor volume and baseline MRI-based percent necrosis, only showed fair or weak correlations (r = -0.54-0.54; p = 0.24-0.92) (Fig. 5c and Fig. 6).

DISCUSSION

The prediction of response to treatment plays an essential role in patient management by allowing to identify patients who would benefit from the treatment. In this study, the observed moderate or strong correlations between the T_2* measurements and percent necrosis determined histologically support the potential of using T_2* mapping to predict and assess response to neoadjuvant RT combined with $AscH^-$ in extremity STS. In particular, the pre-surgery T_2* measurements obtained after the completion of neoadjuvant therapy showed a strong correlation with percent necrosis (r = 0.8 and 0.9; p = 0.13 and 0.08), suggesting that the effect of five-week neoadjuvant therapy together with $AscH^-$ on tumors contributes to pathological findings. Notably, the baseline and on-treatment post-RT T_2* measurements showed a moderate correlation with percent necrosis (r = 0.68 and 0.6; p = 0.11 and 0.24), suggesting that the T_2* measurements obtained before and during active treatment may contain information on predicting response to neoadjuvant therapy. The predictive information of the T_2* measurements may arise from different histological phenotypes of STS. Less aggressive phenotypes of STS are more likely to respond to neoadjuvant therapy[29] and may reveal lower tumor activity on imaging before or early during treatment.[19,21]

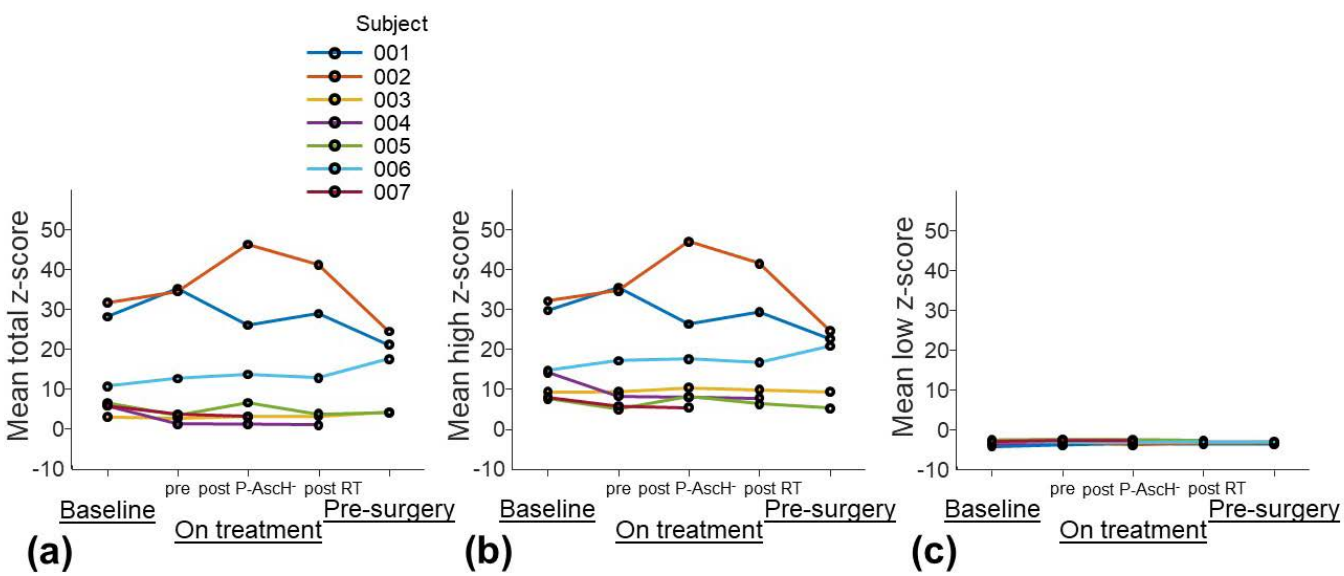

Figure 4A-4C. Changes of the mean of the total z-scores (4A), the means of the significantly high (4B) and low z-scores (4C) within the tumor ROI of the 7 patients across baseline, on-treatment, and pre-surgery MRI scans. The significantly high (z-score > 1.96) and low z-scores (z-score < -1.96) were determined based on a 95% confidence interval.

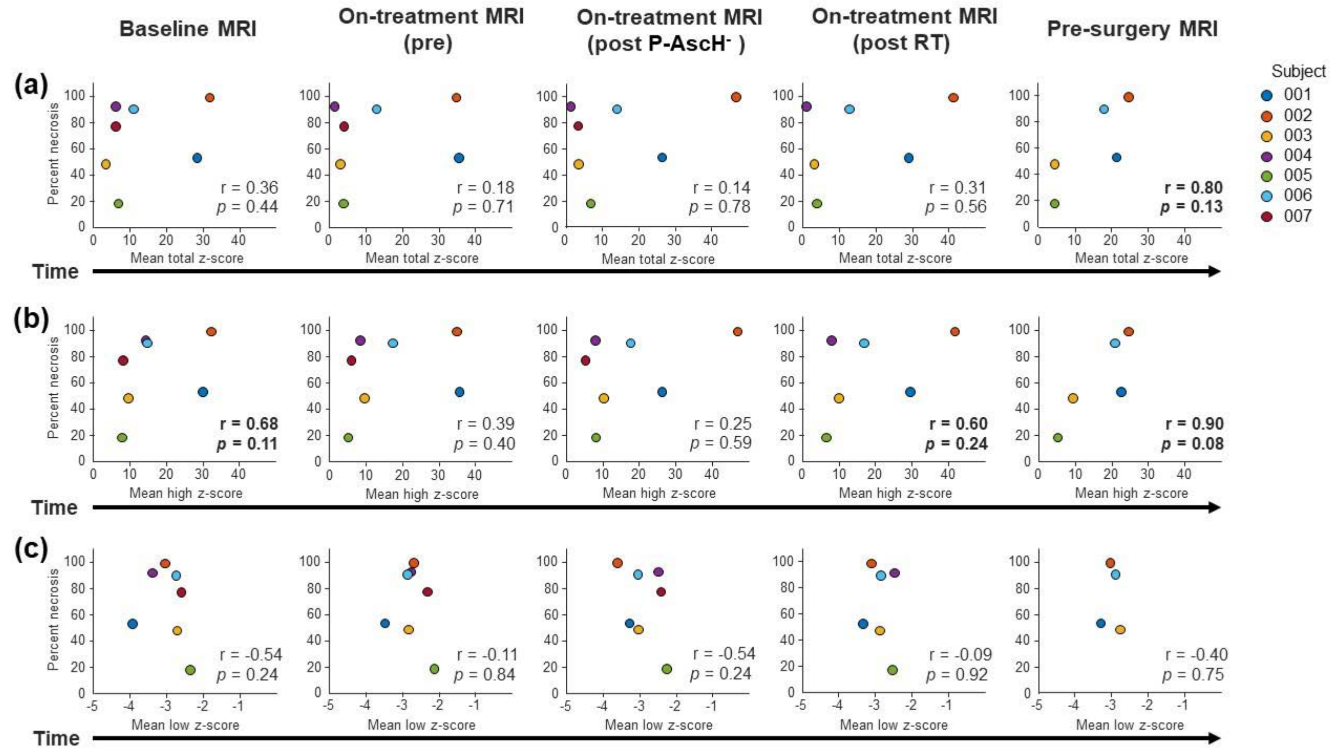

Figure 5A-5C. Correlations of the mean of the total z-scores (5A), the means of the significantly high (z-score > 1.96) (5B) and low z-scores (z-score < -1.96) (5C) with the percent necrosis from pathological examination across baseline, on-treatment, and pre-surgery MRI scans. Bold indicates a moderate or strong correlation (r > 0.6). The data of subject 005 was absent for the significantly low z-scores of the pre-surgery MRI because subject 005's z-scores of the pre-surgery T_2* measurements were all above -1.96.

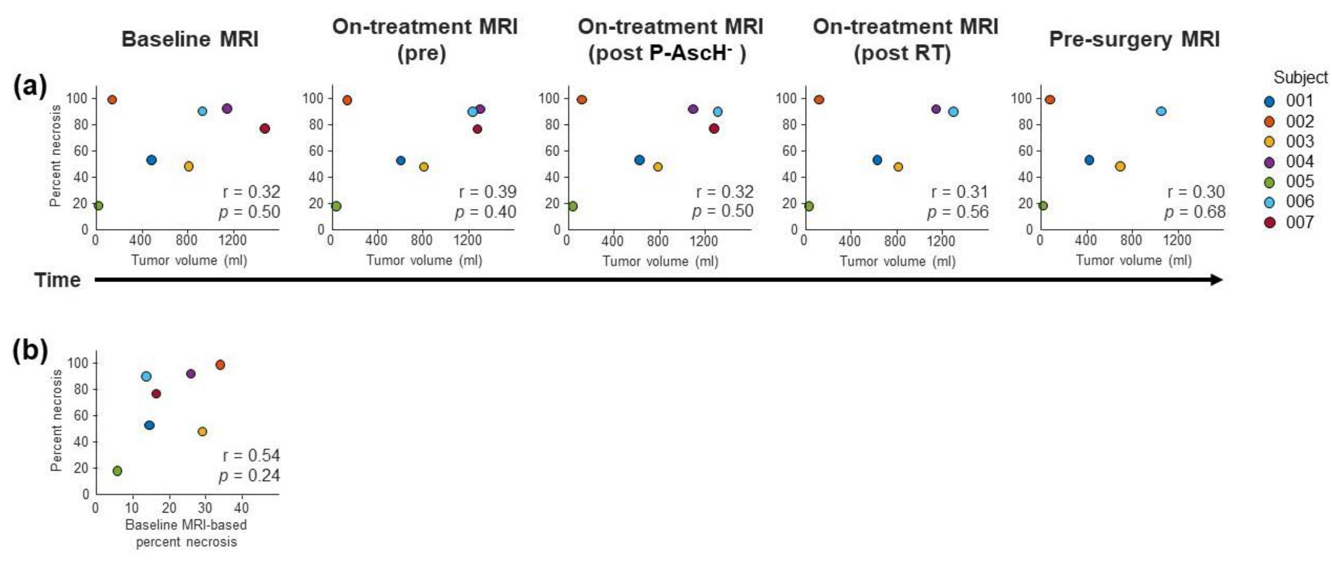

Figure 6A-6B. Correlations of the tumor volume (6A) and baseline MRI-based percent necrosis (6B) with the percent necrosis from pathological examination across baseline, on-treatment, and pre-surgery MRI scans. Baseline MRI-based percent necrosis was determined by the proportion of hyperintense signals of the tumor ROI on the T_2-weighted images without enhancement. MRI-based percent necrosis was absent for on-treatment and pre-surgery MRI scans, because T_1+C and T_2weighted images were unavailable.

STS with higher percent necrosis following treatment moderately correlated with longer T_2* relaxation times in the baseline and on-treatment post-RT MRI scans in our study. A long T_2* relaxation time indicates the presence of microenvironments with freely moving water molecules, such as necrosis and cysts.[30,31] Solid tumors with viable tumor cells show a shorter T_2* relaxation time.[30,31] Therefore, our finding suggests that tumors before or during treatment may contain higher content of freely moving water, such as necrosis and cysts, and a lower proportion of viable, actively proliferating tumor cells, leading to overall longer T_2* relaxation times and a higher likelihood to respond to neoadjuvant therapy. Similarly, previous DWI and DCE-MRI studies have suggested that less aggressive imaging phenotypes of STS before and early during treatment are more likely to respond pathologically to neoadjuvant therapy.[19,21] Higher diffusivity, lower perfusion and vascular permeability measures corresponding to lower tumor cellularity and vascularity[32,33] have been correlated with higher percent necrosis or a lower viable tumor fraction.[19,21] On the other hand, sarcomas at baseline with a higher percent necrosis determined through biopsies tend to be high-grade sarcomas.[1,2] Given the small sample size of this study, it is impossible to determine the impact of baseline percent necrosis on the correlation between T_2* measurements and response to neoadjuvant therapy. Furthermore, baseline percent necrosis determined from biopsies may not reflect the percent necrosis of gross tumors. Taken together, these quantitative MR parameters reveal different aspects of tumor activity and may aid in predicting response to neoadjuvant therapy before and early during treatment in STS based on biochemical rather than structural changes.

Tumor volume and baseline MRI-based percent necrosis only showed fair or weak correlations with percent necrosis ($r = 0.3$-0.54; $p = 0.24$-0.68). Our finding is consistent with previous studies using volumetric measurements to study response to neoadjuvant therapy in STS.[8-11] Except for myxoid liposarcomas, most subtypes of STS do not show a correlation between reduced tumor volume and favorable pathological response.[3,14] A revised guideline has incorporated changes in the contrast enhancement on the T_1+C images to evaluate response to neoadjuvant therapy.[12,34,35] However, the assessment remains qualitative because the contrast enhancement on the T_1+C images also depends on the acquisition delay.[36] Alternatively, the quantitative MR parameters, such as T_2* relaxation time, allow more objective assessment of response to neoadjuvant therapy in STS.

Many tissue entities within a heterogeneous tumor of STS influence the T_2* relaxation time in different ways. As opposed to necrosis and cysts with a long T_2* relaxation time, hemorrhage or tissue iron in tumors induces a short T_2* relaxation time.[37] Using the *z*-score analysis to stratify the measured T_2* values within the tumor ROI, our study demonstrates that the strong or moderate correlations ($r = 0.6$-0.9; $p = 0.08$-0.24) were observed between the significantly high *z*-scores and percent necrosis. All the significantly low *z*-scores showed fair or weak correlations ($r = -0.54$–-0.09; $p = 0.24$-0.92). These findings suggest that alternations of the significantly high *z*-scores of the tumor predominately contribute to percent necrosis. This is consistent with previous studies showing long T_2 relaxation times in necrosis[30,31] and highlights the importance of stratification to account for tumor heterogeneity in STS. Further stratification can be achieved by using T_2* along with other imaging measures to create imaging habitats and reveal region-specific treatment response.[38]

In addition to changes in the tissue microenvironment, macroscopic magnetic field inhomogeneities, such as regions near air-tissue interfaces, influence T_2* relaxation times and increase variations of the T_2* measurements. In our study, the intra-subject variations of the T_2* measurements across the total five MRI scans were 5.2 and 10.2% within the normal-appearing tissue and tumor ROIs, respectively. Regarding the three on-treatment MRI scans performed on the same day, the intra-subject variations of the T_2* measurements were 3.7 and 5% within the normal appearing tissue and tumor ROIs, respectively. These variations are comparable with the previously reported variation of R_2* ($1/T_2$*) measurements in STS (13.7%).[16] However, the intra-subject temporal variation of the T_2* measurement in our study was contributed by the combined effects from macroscopic magnetic field inhomogeneities, as well as treatment (RT combined with P-AscH$^-$) and possible tumor progression. To quantify the repeatability of the T_2* measurements, repeated T_2* measurements on the same day under the same condition are required to minimize the effects from treatment and tumor progression.[16] Furthermore, optimized B_0 shimming and a small image voxel size may help mitigate the macroscopic field effect and improve the repeatability of the T_2* measurements.[39]

A previous study has demonstrated that neoadjuvant RT combined with P-AscH- enhances the efficacy of RT using animal models of fibrosarcoma and liposarcoma.[40] In our study with a small sample size (N =7), pathological near-complete response rate (percent necrosis ≥95%) to combined RT and P-AscH$^-$ was 13%, which is within the range of previously reported pathological near-complete response rate (≥95% necrosis or ≤5% viable tumor) to neoadjuvant RT (9-25%).[5-7] Considering the variety of subtypes of STS, a larger sample size is needed to study the benefit of combined RT and P-AscH$^-$. Additionally, different pathological responses to the combined RT and P-AscH⁻ among patients may be related to differences in iron metabolism. One of the major contributors for the enhanced RT through P-AscH⁻ is related to higher levels of labile iron and H_2O_2 in tumors, inducing selective toxicity and DNA damage.[41] Protein expression levels that are related to iron storage and uptake have been shown to be different among STS treated with combined RT and P-AscH⁻,[37] suggesting that iron metabolic heterogeneities may provide differential responses to combined RT and P-AscH⁻.

This study has several limitations. First, the small sample size may contribute to a lack of statistically significant findings. Given the various subtypes of STS with different clinical and pathological presentations, future studies with a larger sample size and histology specific trials are warranted to confirm the findings of this study. Second, this study enrolled a single cohort of patients treated with RT combined with P-AscH⁻. Given that P-AscH⁻ may influence the efficacy of RT,[40] it could alter the tumor microenvironment and affect T_2* measurements and pathological findings. Whether our results can be generalized to patients treated with RT alone requires a further investigation. Third, this study focused on imaging assessment of neoadjuvant therapy. For imaging assessment of adjuvant therapy, T_2* measurements are also influenced by the prior neoadjuvant therapy and surgery. The imaging assessment of adjuvant therapy will need to consider the impact of prior treatments on imaging. Fourth, the volumetric measurements of STS based on T_2* signal abnormalities may be inaccurate. Volumetric measurements typically rely on structural MRI images, including T_1-weighted, T_1+C and T_2-weighted images, which were unavailable for the on-treatment and presurgery MRI scans. Despite these limitations, this study may inform future studies on quantitative imaging assessment of response to neoadjuvant therapy.

In conclusion, the T_2* measurements of tumors obtained before treatment, two weeks after initiating treatment, and before surgery showed moderate or strong correlations with the percent necrosis from pathological findings. A longer T_2* relaxation time may indicate a presence of a larger proportion of necrosis and cysts, associated with less aggressive imaging phenotypes and favorable pathological response to treatment. These results support the promise of using T_2* mapping to predict and assess response to neoadjuvant RT combined with P-AscH⁻ in patients with extremity STS.

ACKNOWLEDGEMENTS

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MECHANICAL GAINS ASSOCIATED WITH VIRTUAL PROPHYLACTIC INTRAMEDULLARY NAIL FIXATION IN FEMURS WITH METASTATIC DISEASE

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ABSTRACT

Background: Many patients with metastatic bone disease (MBD) of the femur undergo prophylactic surgical fixation for impending pathologic fractures; intramedullary nailing (IMN) being the most common fixation type. However, surgeons often question if IMN fixation provides sufficient improvements in mechanical strength for particular metastatic lesions. Our goal was to use patient-specific finite element (FE) modeling to computationally evaluate the effects of simulated IMN fixation on the mechanics of femurs affected with MBD.

Methods: Computed tomography (CT) scans were available retrospectively from 48 patients (54 femurs) with proximal femoral metastases. The CT scans were used to create patient-specific, non-linear, voxel-based FE models of the femur, simulating the instant of peak hip joint contact force during normal walking. FE analyses were repeated after incorporating virtual IMN fixation (Smith and Nephew, TRIGEN INTERTAN) into the same femurs. Femur strength and load-to-strength ratio (LSR; lower LSR indicates lower fracture risk) were compared between untreated and IMN conditions using statistical analyses.

Results: IMN fixation resulted in a very modest average 10% increase in mechanical strength ($p<0.001$), which was associated with a slight 7% reduction in fracture risk ($p<0.001$). However, there was considerable variation in fracture risk reduction between individual femurs (0.13-50%). In femurs with the largest reduction in fracture risk (>10%), IMN hardware directly passed through a considerable section of that femur's metastatic lesion. Femurs with lytic (10%) and diffuse (9%) metastases tended to have greater reductions in fracture risk compared to femurs with blastic (5%) and mixed (4%) metastases ($p=0.073$).

Conclusion: Given the mechanically strong baseline condition of most femurs in this cohort, evident by the low fracture risk at the time of CT scanning, the relative increase in stiffness with the addition of the IMN hardware may not make a substantial contribution to overall mechanical strength. The mechanical gains of IMN fixation in femurs with MBD appear most beneficial when the hardware traverses an adequate section of the lesion.

Level of Evidence: III

Keywords: metastatic bone disease, prophylactic intramedullary nailing, finite element analysis, femur strength, mechanical fracture risk

INTRODUCTION

Metastatic bone disease (MBD) is a common and costly condition.[1] The femur is a common site for MBD,[1] and demonstrates a higher risk of impending pathologic fracture compared to other sites in the appendicular skeleton.[2] It is important to prevent pathologic femur fractures in cancer patients to avoid further morbidity and loss in quality of life, and potentially improve survival.[2] Prophylactic surgical fixation for impending pathologic fractures is commonly performed in patients with femoral metastases.[3] However, there is only moderate agreement amongst surgeons regarding when and what surgical treatment is needed in these medically compromised patients.[4] While the choice of surgical fixation depends on the surgeon's evaluation of clinical factors, the primary methods implemented are intramedullary nailing (IMN) and endoprosthetic reconstruction.[3] The questions of whether to use IMN fixation (versus hemiarthroplasty, for example) or when is IMN fixation mechanically insufficient, remain to be answered.

Finite element (FE) analysis is a non-invasive tool that is attractive for evaluating the subject-specific mechanics of metastatic femurs. Computed tomography (CT)-based FE models have been validated for predicting the mechanical behavior of femurs with MBD using cadaveric femurs with real or artificial lesions.[5-9]

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These validated models have shown reduced bone strength and higher probability of fracture in patients with femoral metastases.[10-13] FE models have also been widely implemented to virtually evaluate the efficacy of various surgical methods, such as short-stem implants for total hip replacement,[14] and anti-rotation/antegrade IMN for fracture treatment in femurs without MBD.[15-19]

A few FE studies on prophylactic surgical treatment efficacy in patients with femoral MBD have shown that femoroplasty can provide an improvement in femur strength.[20] Experimental studies using synthetic femurs with artificial lesions have similarly shown improvements in femur stiffness and strength after IMN fixation.[21] However, these mechanical improvements are variable, and they depend on lesion characteristics such as type (lytic versus blastic, for example) and location (femoral neck versus intertrochanteric, for example).[20-22] Surgical treatment with resection and reconstruction is associated with slightly higher patient survival compared to nailing in patients with femoral metastases, but with higher rates of complications.[2] Therefore, it is important to understand the mechanical gains associated with IMN fixation to elucidate situations where IMN stabilization is inadequate and the severity of the defect is better addressed with resection and reconstruction. FE models are time- and computationally-efficient tools to process large datasets simulating various disease and fixation conditions, and an automated FE modeling pipeline would be useful to evaluate the mechanical gains of IMN fixation in a clinical population.

The goal of our study was to computationally evaluate the mechanical effects of virtual prophylactic IMN fixation in patients with femoral metastases using a validated, patient-specific, CT-based, automated FE model of the proximal femur. Our primary hypothesis was that mechanical improvements would be observed with virtual IMN fixation, but the gains would depend on the baseline mechanical significance of the defect and hardware coverage of the lesion. A secondary hypothesis was that greater mechanical improvements would be observed after IMN fixation in femurs with destructive lesions.

METHODS

2.1. Patient Data

With Institutional Review Board approval, retrospective data were collected over three years from 48 consecutive patients (64±13 years; range 27 to 90 years) diagnosed with MBD of the proximal femur. Whole-femur diagnostic CT scans (Siemens, Forchheim, Germany; 120 kVp, 150 mAs, in-plane pixel size 0.3906 mm, slice thickness 0.6 mm) were available for 54 femurs from the 48 patients (6 bilateral). To retain an adequate sample size given the timeframe of data collection, the inclusion restrictions were only limited to proximal femur lesions and no femoral fracture at initial presentation. The cohort included 24 femurs with lytic metastases, 19 femurs with mixed metastases, 6 femurs with diffuse metastases, and 5 femurs with blastic metastases. Since our goal was to characterize the mechanical effects of virtual IMN fixation within the broad context of metastatic disease, to minimize treatment bias, we did not exclude femurs with blastic lesions from our analysis, even though these femurs are infrequently indicated for prophylactic stabilization and considered to be at minimal risk for impending pathologic fracture.

2.2. Finite Element Model Geometry

Patient-specific femur geometries were segmented from the CT scans (Fig. 1) based on a density threshold (0.15 g/cm^3)[5] using Mimics (Materialise, Leuven, Belgium). Manual corrections to the periosteal boundary around lesion and epiphyseal regions were performed only as necessary. Lesion boundaries within each femur were separately identified and manually segmented to evaluate lesion volume change. Surface representations of commercially available cephalomedullary nail (130°, 11.5 mm × 34 – 44 cm) and lag screw (11 mm × 80 – 110 mm) hardware (Smith and Nephew TRIGEN INTERTAN, Watford, UK) were produced in Geomagic (3D Systems, Rock Hill, SC, USA). For patients that had undergone prophylactic IMN stabilization after the initial CT scan, the generic geometries were scaled to the implanted nail and lag screw lengths. If the patient had not already undergone prophylactic stabilization, the lengths of the nail and lag screw were determined by the size of the femur and matched the commercially available lengths. Virtual fixation was manually performed using Geomagic and Mimics to position the IMN surfaces within the surface model of the femur. Effective IMN orientation was achieved when the nail was centered in the femoral canal while avoiding overlap with substantial amounts of cortical bone, and the lag screw was placed in the middle of the femoral neck and center-center in the femoral head, 5 – 10 mm from the articular surface. Sizes and placement were verified by a board certified, fellowship-trained orthopedic surgeon (BJM). The geometry of the distal locking screw was excluded in the present analysis because simulating the interaction of the locking screw with the nail and bone was beyond the current scope. The constraint provided by this screw was instead simulated with specific FE boundary conditions (see Section 2.5).

2.3. Finite Element Model Mesh

Two models were created for each femur: (1) pathologic intact femur without IMN fixation, and (2) pathologic femur incorporating virtual IMN fixation (Fig. 1). For each model, voxel meshes of linear hexahedral elements with 1.5 mm isotropic edge length were automatically generated using custom code (Matlab, Mathworks, Natick, MA). Voxel meshes are commonly implemented in femur FE simulations,[23,24] and have been shown to accurately reproduce experimental measurements of femur mechanical behavior (R^2 = 0.88 – 0.96).[5,25] For the intact model, the segmented femur geometry was directly converted into a voxel mesh. For the model incorporating IMN fixation, the region enclosed by the IMN surfaces was first subtracted from the femur region. Then, the subtracted femur, nail, and lag screw geometries were converted into voxel meshes. Since our goal was not to evaluate local mechanical behavior related to contact interactions, but rather to model whole-bone/global mechanical behavior, the use of a voxel mesh was appropriate for our virtual fixation application.[25]

2.4. Finite Element Model Material Behavior

A calibration phantom (QRM, Moehrendorf, Germany) included in each of the CT scans was used to convert CT Hounsfield units into bone density (R^2 = 0.99). Patient-specific bone density information was then used to determine patient-specific non-linear material properties (including post-yield behavior) using empirical density-elasticity relationships specific to the femur (R^2 = 0.99).[24] Assuming isotropy (ν = 0.3),[26] inhomogeneous material properties were assigned to each bone element, specific to whether an element belonged to either a low (apparent density ≤ 1.0 g/cm3 corresponding to trabecular bone) or high (apparent density > 1.0 g/cm^3 corresponding to cortical bone) density bone region.[27,28] A minimum modulus (0.01 MPa) was assigned to elements with modulus values < 0.01 MPa,[29] and a maximum modulus (25 GPa) was assigned to surface elements that were prescribed external loads in order to prevent excessive local mesh distortion.[24] Bone yield was simulated using the von Mises yield criterion.[24] IMN components were assigned standard linear elastic properties of titanium alloy (E = 113.8 GPa, ν = 0.342).

2.5. Finite Element Model Setup (Loads, Boundary Conditions, Constraints)

Since pathologic fractures typically occur during daily activities,[9] we simulated boundary conditions associated with the instance of maximum hip joint contact force during normal walking (near heel-strike).[10] This was done by aligning femurs to the Bergmann local coordinate system and applying muscle forces scaled to patient bodyweight as concentrated loads on surface nodes corresponding to muscle insertion locations.[30,31] A ramped compressive displacement was simultaneously applied to the surface of the femoral head in the direction of the resultant hip joint contact force, and femur displacements were physiologically constrained.[32]

For the femur model incorporating IMN fixation, additional constraints were prescribed to simulate load transfer between the hardware and the bone voxel mesh regions. The lag screw-bone interface was modeled as a tied interface.[17-19] The interface between the lag screw and the nail was also modeled as a tied interface as the set screw in the nail would prevent any relative motion between the two components. Due to the stair-step nature of the voxel mesh surface (Fig. 1), the nail-bone interface was not modeled as a typical contact interface. Instead, the nail surface was tied along regions expected to be in tight contact with the endosteal bone surface (Fig. 1). The distal nail surface was tied to the neighboring cortical bone to account for the mechanical contribution of the distal locking screw, the geometry of which was not explicitly modeled.

FE models with a smooth geometric mesh are typically used for evaluating bones with implanted hardware, where the interaction between the bone and implant components is simulated using a contact interface. To verify the constraints used in our voxel mesh models, which are not typically the type of FE model used for evaluating bones with implanted hardware, we modeled a sample femur with a smooth geometric mesh (Fig. 2) using both tied interfaces (same as our voxel mesh approach) and contact interfaces. Concordance of the global mechanical behavior was evaluated by comparing the correlation between the resulting force-displacement curves from the two interface conditions. The global mechanical behavior was found to be highly correlated (cross correlation r = 0.999) between the smooth geometric mesh model using contact interfaces versus the smooth geometric mesh model using tied interfaces (Fig. 2). Therefore, we concluded that our simplification of the bone-IMN component surface interactions using tied constraints provided an adequate representation of virtual fixation global mechanical behavior.

2.6. Outcome Variables and Statistical Analyses

All FE simulations were performed in Abaqus (Dassault Systemes Simulia Corp, Johnston, RI). For two of the femurs modeled, the FE analysis terminated before the simulation completed, and these were omitted from further analyses.

The peak resultant reaction force achieved at the femoral head was defined as the femur strength,[24] where a higher femur strength indicates a stronger femur. The ratio of patient-specific joint contact force to femur strength was defined as load-to-strength ratio (LSR),[10] where a lower LSR indicates lower fracture risk. To determine the change in lesion volume, the volume of lesion traversed by IMN hardware, if any, was first subtracted from the original lesion volume. Then the volume

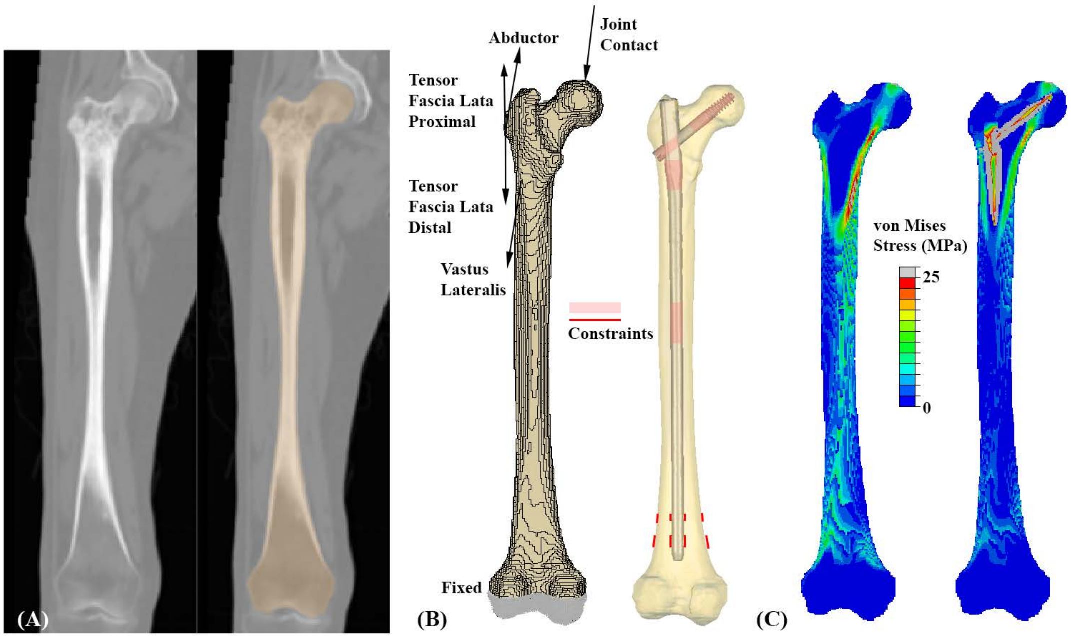

Figure 1A-1C. Patient-specific finite element model of an example metastatic femur with and without virtual intramedullary nail fixation (1B) created from computed tomography scans (1A), and distribution of von Mises stress through the proximal cross-section (1C). Please refer to the online version for interpretation of color.

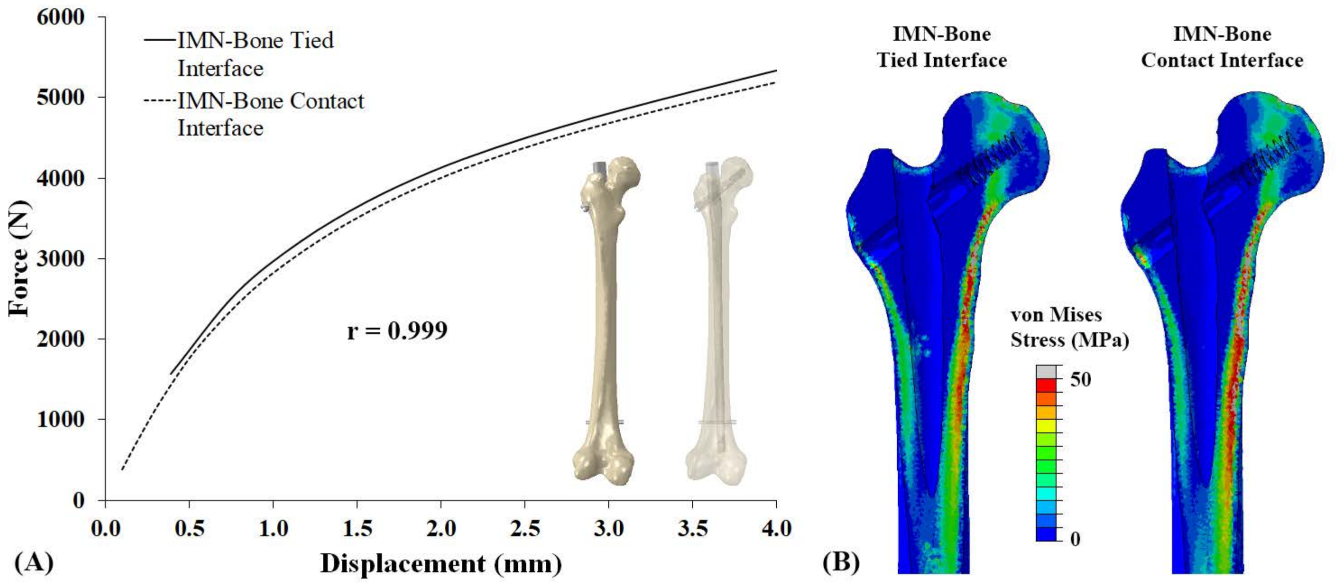

Figure 2A-2B. (2A) Agreement between computed mechanical behavior using a smooth (tetrahedral element) geometric mesh (inset) with either contact interactions between the IMN hardware and bone (coefficient of friction $\mu = 0.3$)[16] or tied constraints between the IMN hardware and bone (same as the voxel mesh model). Material behavior, loads, and boundary conditions were the same as the voxel mesh model. Global mechanical behavior was highly correlated between the two interface conditions (cross correlation r = 0.999). (2B) Distribution of von Mises stress through the proximal cross-section showing qualitative similarity between the two interface conditions. IMN hardware not shown for clarity. Please refer to the online version for interpretation of color.

change was determined from the ratio of the reduced lesion volume to the original lesion volume expressed as a percentage.

Femur strength and LSR were compared between the pathological intact femur models (without IMN fixation), and the same femur models incorporating virtual IMN fixation, using comparison of means and percentile analysis. Paired t-tests (normal data) or Wilcoxon signed-rank tests (non-normal data) were used for comparison of whole-cohort means while Kruskal-Wallis tests (non-parametric one-way ANOVA) were used for comparison of multiple means (SPSS, SPSS Inc., Chicago, IL). An alpha level of 0.05 was defined as statistically significant.

RESULTS

Most femurs (71%; 37/52) were determined to be at relatively low fracture risk (LSR ≤ 0.5) at the time the CT scans were acquired. IMN fixation resulted in a very modest average 10% increase in mechanical strength (4333±1422 versus 4748±1588 N for intact femurs and femur with IMN fixation, respectively; $p < 0.001$). This increase in mechanical strength was associated with an average 7% reduction in (LSR) fracture risk ($p < 0.001$). However, these whole-cohort averages do not adequately reflect the considerable variation in the reduction in fracture risk between individual femurs, which varied between 0.13 – 50% (Fig. 3). In femurs with the largest reduction in fracture risk (> 10%; Fig. 3), IMN fixation hardware directly passed through a considerable section of that femur's metastatic lesion (Fig. 4; 24±8% change in lesion volume). Whereas the lesions in femurs with the smallest reduction in fracture risk (< 2%) were minimally spanned by the IMN fixation (12±12% change in lesion volume). Percent increase in femur strength after IMN fixation was strongly related to the percent decrease in fracture risk ($R^2 = 0.999$), as expected, but the mechanical gains appeared to have a diminishing effect (Fig. 5).

Reduction in fracture risk appeared preferential ($p = 0.073$) based on the type of metastases (Fig. 6). Greater reductions in fracture risk tended to be observed in femurs with lytic (10%) and diffuse (9%) metastases, compared to femurs with blastic (5%) and mixed (4%) metastases. Overall reduction in fracture risk was similar ($p = 0.17$) regardless of whether the metastases were located in the femoral head-neck (8%), intertrochanteric (6%), or subtrochanteric (7%) regions of the femur. However, femurs with lytic lesions located in the femoral head-neck region tended to have a higher fracture risk (LSR = 0.65), compared to femurs with lytic lesions located in the intertrochanteric (LSR = 0.53) and subtrochanteric (LSR = 0.34) regions.

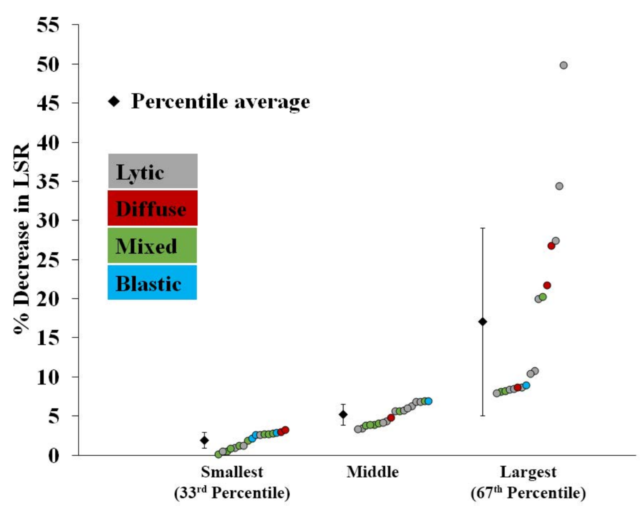

Figure 3. Variation in the reduction of load-to-strength ratios (LSR) after virtual intramedullary nail fixation grouped according to smallest, middle, and largest percentiles. Error bars indicate standard deviations. Femurs with lytic, diffuse, mixed, and blastic metastases are indicated with gray, red, green, and blue dots, respectively. There are more lytic (gray) and diffuse (red) metastases in the group with the largest reduction of fracture risk. Please refer to the online version for interpretation of color.

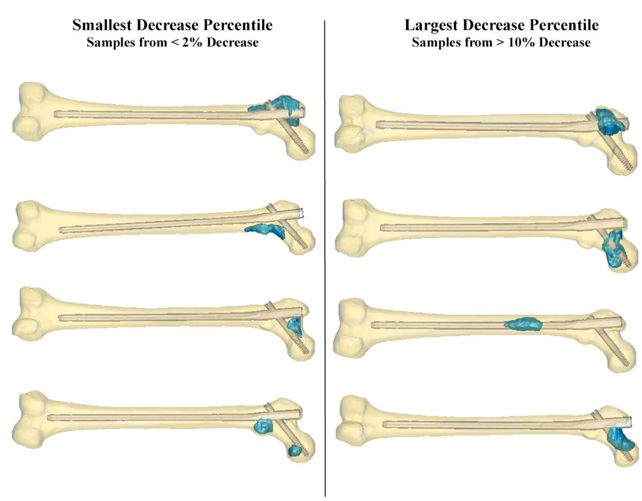

Figure 4. Sample virtual intramedullary nail (IMN) hardware coverage of lesion geometries. IMN hardware passed directly through a considerable section of the lesion in femurs with the largest reduction in fracture risk (right). Lesions in femurs with the smallest reduction in fracture risk were minimally spanned by the IMN fixation (left).

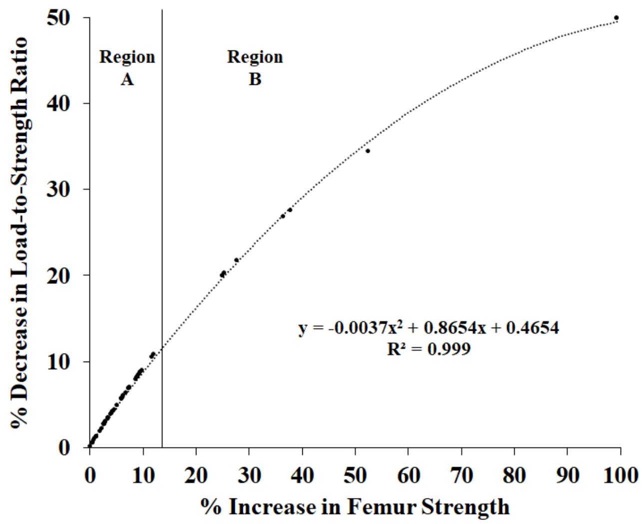

Figure 5. Relationship between percent increase in femur strength and percent decrease in load-to-strength ratio after virtual IMN fixation, showing a potential diminishing effect in the mechanical gains. Dotted line indicates a polynomial fit. The vertical line indicates a transition from a direct relationship between increasing strength and decreasing fracture risk (Region A), to a relationship where an increase in strength does not cause a proportional decrease in fracture risk (Region B).

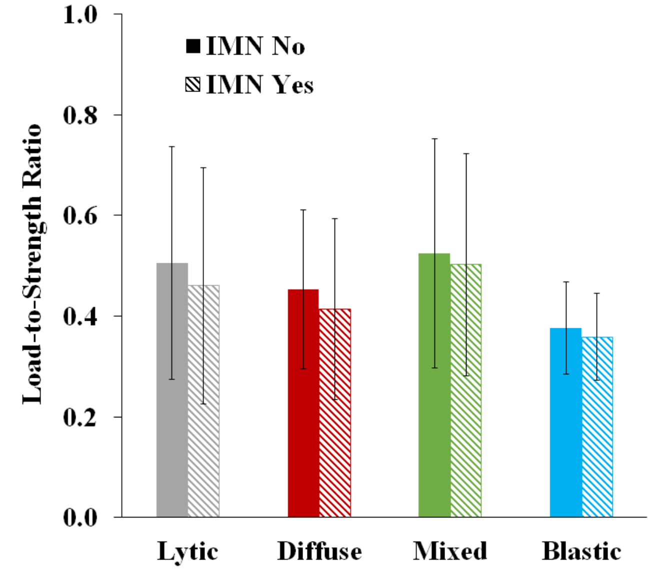

Figure 6. Load-to-strength ratios of pathological femurs without IMN fixation, and femurs incorporating virtual IMN fixation grouped according to lesion type. Error bars indicate standard deviations. Addition of IMN fixation only moderately decreased fracture risk for all lesion types.

DISCUSSION

Femurs with metastatic bone disease are at a higher risk for fracture,[2] and prophylactic intramedullary nailing is commonly performed to prevent impending pathologic fractures.[3] However, the mechanical efficacy of IMN fixation in patients with femoral metastases is still not well understood. Using a validated, patient-specific, CT-based, automated FE model of the proximal femur, we evaluated the mechanical effects of virtual prophylactic IMN fixation in 48 patients with femoral metastases. We found modest mechanical gains after virtual IMN fixation in our patient cohort (10% increase in femur strength; 7% reduction in fracture risk), and the reduction in fracture risk varied considerably across femurs. The IMN fixation hardware was observed to directly pass through the lesion in femurs with the largest reductions in fracture risk (> 10%). Femurs with lytic and diffuse lesions tended to benefit the most mechanically after virtual IMN fixation (10% and 9% reduction in fracture risk, respectively).

We observed only modest mechanical gains with virtual IMN fixation in our patient cohort. Given the mechanically strong baseline condition of most femurs in this cohort, evident by the low fracture risk at the time of CT scanning, the small increases in stiffness with the addition of the IMN hardware may not make a substantial contribution to overall mechanical strength in many cases. A similar effect was found in an IMN fixation study using synthetic femurs, where femurs with artificial lesions that did not perforate the cortical bone had mechanical strength equivalent to intact femurs, and subsequent IMN fixation of these femoral defects also resulted in no further improvement in mechanical strength.[21] Our findings of greater increases in strength after IMN fixation occurring when the hardware spans the lesion were also paralleled in the study using synthetic femurs.[21] That experimental work found that smaller calcar lesions which were minimally spanned by the IMN hardware had no gains in mechanical strength, while larger lesions partially spanned by the IMN hardware had over twice the gains in mechanical strength compared to the defect state, albeit only achieving 40% of the intact state strength.[21] Largest reduction in fracture risk for our cases with more hardware coverage of the lesion implies that the mechanical gains of IMN fixation in femurs affected by MDB appear most beneficial so long as the hardware stabilizes an adequate section of the lesion.

Femurs with destructive (lytic, diffuse) lesions were observed to have greater reductions in fracture risk with virtual IMN fixation. Prior studies evaluating the efficacy of cement augmentation have also shown that improvements in mechanical strength were only observed in femurs with a critical lesion.[22] Cement augmentation has also been shown to benefit femurs with head-neck lesions and provide no definite improvement in mechanical strength for femurs with trochanteric lesions.[20] Though femurs with lytic lesions located in the head-neck region were observed to be weaker in our study, similar reductions in overall fracture risk in femurs with head-neck lesions compared to the other two locations could be due to grouping lesion types. This was necessary for our data, which were not sufficiently powered for a multi-factor analysis. As expected, femurs with metastases characterized by abnormal bone formation were less mechanically compromised. Femurs with lytic and diffuse lesions appear to benefit the most mechanically after virtual IMN fixation, but the diminishing effect of the mechanical gains (Fig. 5) likely depends on the interaction between lesion type and location.

Simulating virtual IMN fixation using a voxel mesh was a limitation of our study. However, the automated voxel mesh FE methodology was intentionally selected for this work as it allows for the efficient processing of large clinical datasets, and our voxel-based femur strength results corroborate well with published data.[23-25] And while contact interactions are needed to realistically simulate the local mechanics at the nail-bone interface,[15-19] the ability of voxel meshes to capture global mechanics[25] allowed us to achieve our goal of making mechanical comparisons at the global/whole-bone level. Furthermore, we carefully verified the use of appropriate modeling constraints to best replicate the nail-bone contact interaction for our application. Another limitation of our study was the assumption of femur strength and fracture risk only at the time-point the CT scans were acquired. MBD is a dynamic process, and while changes in bone density may be minimal in the short-term,[33] the long-term applicability of a single point-in-time mechanical fracture risk prediction requires further investigation. Lastly, in this work, we focused on a common physiologic activity – walking, which provided a low fracture risk estimate for most femurs. Mechanical effects of IMN fixation may vary based on the activity modeled (for instance, stair ascent, sideways fall), particularly for loading mechanisms the IMN hardware was not designed to resist.

In conclusion, using a validated patient-specific, CT-based, automated FE model of the proximal femur, we found that the reduction in mechanical fracture risk after virtual prophylactic IMN fixation varies considerably across femurs with metastatic bone disease. In general, femurs with lytic and diffuse lesions that are directly spanned by some element of the IMN fixation hardware are most likely to benefit mechanically from prophylactic IMN fixation. The results from this study suggest a framework to provide surgeons with additional mechanical information to assist in making treatment decisions, potentially improving the outcome of prophylactic IMN fixation in patients with femoral MBD.

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BACK TO BASICS: PEDIATRIC CASTING TECHNIQUES, PEARLS, AND PITFALLS

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ABSTRACT

Cast application is a critical portion of pediatric orthopaedic surgery training and is being performed by a growing number of non-orthopaedic clinicians including primary care physicians and advanced practice providers (APPs). Given the tremendous remodeling potential of pediatric fractures, correct cast placement often serves as the definitive treatment in this age population as long as alignment is maintained. Proper cast application technique is typically taught through direct supervision from more senior clinicians, with little literature and few resources available for providers to review during the learning process. Given the myriad complications that can result from cast application or removal, including pressure sores and cast saw burns, a thorough review of proper cast technique is warranted. This review and technique guide attempts to illustrate appropriate upper and lower extremity fiberglass cast application (and waterproof casts), including pearls and pitfalls of cast placement. This basic guide may serve as a resource for all orthopaedic and non-orthopaedicproviders, including residents, APPs, and medical students in training.

Level of Evidence: IV

Keywords: casting, pediatric orthopaedics, resident education, technique guide

INTRODUCTION

Closed reduction and casting is a central component of acute orthopaedic management of many fractures in children. Historically, this care has been provided by orthopaedic surgeons and their trainees. However, as access points to medical care diversify, a variety of non-orthopaedic clinicians may provide these initial treatments. These non-orthopaedic clinicians include physician assistants (PAs), nurse practitioners (NPs), primary care physicians, non-operative sports medicine physicians, and emergency physicians.

Proper closed reduction and casting may serve as definitive treatment if the fracture is adequately reduced with a well-molded cast. However, if a patient is discharged with an inadequate reduction or a poorly-molded cast, the child will likely require further manipulation and casting.[1,2] Worse than requiring repeat manipulation and casting, poor casting technique can also result in devastating complications such as compartment syndrome, cast burns, and pressure sores.[3] Therefore, proper casting technique is extremely important in the nonoperative treatment of pediatric fractures.

Closed reduction and casting of fractures in the pediatric emergency room is often performed by junior trainees[4,5] in a directly supervised setting before they are responsible for performing these tasks independently. As a result, many casting pearls are either demonstrated or passed down verbally from senior to junior clinicians. This informal mentoring has left little published on proper casting technique.

While trainee competence for closed reduction and casting is often presumed after a certain amount of time taking consults under supervision, the COVID-19 pandemic and associated changes to resident and APP rotation schedules may have created a situation where providers are progressing from direct supervision with less casting experience than in previous years.[6] In addition to junior residents, closed reduction and casting is also being performed by other emergency room, urgent care, and primary care providers.[7-11] While the authors advocate for a competency-based system in which a provider demonstrates the ability to cast safely before doing so without direct supervision, we also feel that a review of proper casting technique is warranted.

The purpose, then, of this review is to provide clinicians who see children for acute orthopaedic care – both orthopaedic specialists and non-orthopaedic providers – with a technique guide for commonly-placed fiberglass casts, including pearls and pitfalls of cast placement. It is critical that these providers develop competence in the initial management of pediatric fractures so that the patient receives optimal care in a timely fashion. This

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review may serve as a basic guide for all. Specific indications for casting, reduction maneuvers, and plaster cast and splint placement are outside the scope of this review.

UPPER EXTREMITY CASTING

Set-up

1. For most children, it is best to position them supine on a stretcher with the shoulder at the edge of the bed. The hips and legs should remain centered in the bed for patient safety. In some instances when a reduction is not needed, it may be acceptable for a child to be sitting upright in their parent's lap, or an older child sitting independently.
2. It is optimal to have an experienced assistant to hold the patient by the fingers while the cast is being placed. The elbow is typically held in 90 degrees of flexion, although a more extended position is sometimes warranted. Flexion past 90 degrees is to be avoided.
3. Have all necessary material in the room for cast placement, including cast padding, cast material, a cast saw (if bivalving or univalving the cast), a bucket of water (room temperature), gloves, and trauma shears.
    a. The authors advocate for use of a mini C-arm during a reduction under sedation to minimize reduction attempts. If using a mini C-arm, a lead apron should be placed over the child.
4. If casting under sedation, once adequate sedation has been induced, bring the patient's ipsilateral shoulder to the very edge of the stretcher to allow room for manipulation and casting of the arm (see Figure 1A). The patient's hips and legs should be left in the center of the stretcher. An assistant should be tasked with making sure the patient remains centered in the bed and that the C-arm does not bump the patient when being moved.

Long Arm Cast Placement

The indications for placing long arm casts include closed forearm and elbow fractures. Young infants and toddlers, typically those under 3 years, should always be placed in a long arm cast (rather than a short arm cast) if an upper extremity cast is required. This is due to the short length of the forearm and the abundance of subcutaneous fat at this age, which make it more likely for a short arm cast to shift position and even slide off completely.

Steps for fracture reduction and placement of a long arm cast are explained below. However, these general steps can be followed even without a reduction. It is helpful to have an assistant available who can maintain a single position of the elbow during casting to prevent bunching of cast material in the antecubital fossa.

1. Reduction: If a reduction is required, reduce the fracture manually prior to cast application. Biplanar fluoroscopic views using a C-arm should be used to ensure an adequate reduction is attained.
2. Place stockinette: When the reduction is satisfactory and you are ready to place the cast, roll the stockinette down and over the arm so that it is almost to the axilla proximally and just distal to the fingertips distally. Cut a hole for the thumb and a hole in the antecubital fossa to prevent bunching of material in the elbow flexion crease (Figure 1B).
3. Roll the cast padding: Padding is applied as shown in Figure 1C-H. Two-inch or three-inch webril is preferred depending on the age of the child and size of the arm.
    a. Start distally at the level of the metacarpal heads. As you roll proximally, overlap each previous layer by 50% with each successive roll around the arm. The total number of layers should be 4 or more to prevent thermal injury during cast removal.[12]

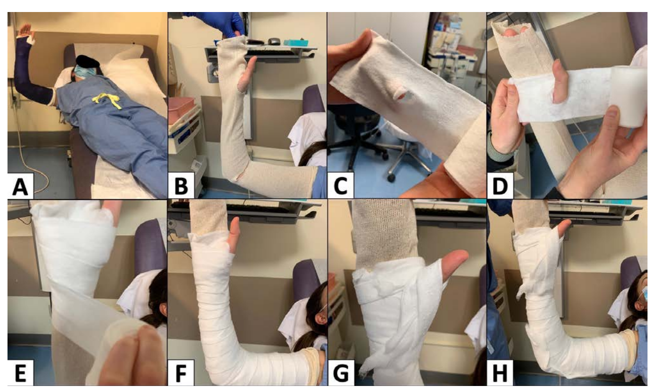

Figure 1A-1H. Upper Extremity Cast Padding Application. (1A) The optimal position of the patient during long arm cast placement is lying supine with the ipsilateral shoulder off of the table to allow room to work. The hips and feet should be towards the center of the table to prevent the patient from falling. (1B) Stockinette should be placed to the axilla proximally and just distal to the fingertips distally. A hole is cut for the thumb and in the antecubital fossa to prevent bunching of material in the flexion space. (1C) A hole is made in the center of the cast padding a few inches from the end of the roll. (1D) The patient's thumb is placed through the hole and the padding at the end of the roll pads the metacarpal heads. (1E) The cast padding is rolled starting distally at the level of the metacarpal heads and overlapping the previous layer by 50% with each successive roll around the arm. The roll is held on the sides using the thumb and index finger to keep the cast padding taut while rolling to prevent wrinkles. (1F) Demonstrating the arm after 4 layers of padding have been placed. (1G) Cuffs of padding are made proximally, distally, and around the thumb by folding the cast padding in thirds. (1H) Three to four extra layers of padding are placed over the olecranon.

b. Hold the roll of webril gently on the sides using the thumb and index finger to keep the padding taut while rolling and avoid wrinkles. Be careful to avoid creating a tourniquet effect by stretching the webril as it is wrapped circumferentially. Wrap webril up proximally just short of the axilla – the cast always ends up shorter than you expect at this point.
c. Make cuffs of padding proximally, distally, and around the thumb by folding the cast padding in half or thirds. Pad the bony prominences of the olecranon and epicondyles of the elbow with an extra 3-4 layers of padding.
d. If the padding in the antecubital fossa appears to be bunching, some can be torn away to decrease the bulk. In practice, we have a low threshold to do this.
e. Of note, if placing a waterproof cast, stockinette is not used, and the waterproof undercast liner is placed in the same manner as the cast padding, overlapping the previous layer by 50% and placing cuffs proximally, distally, and around the thumb. The total number of layers should be 2-3 for a waterproof cast.
    i. Place a blue woven safety strip on each of the volar and dorsal aspects of the padding to prevent cast saw burns during removal of the cast (Figure 2A-B). The location of these strips should be visible at the proximal and distal ends of the cast after application. The waterproof cast is not as resistant to the cast saw heat and shear as cotton undercast padding and the strips must be used to prevent skin injury on removal. Additionally, a plastic zip cutting stick may be placed underneath the cast to aid in soft tissue protection during cast removal (Figure 2C).
    ii. The authors do not recommend waterproof cast placement in the acute setting, but waterproof casts may be considered at subsequent cast exchanges. Note that the proper application of a well-fitting waterproof cast is substantially more challenging than a standard cotton lined cast and should be performed only by those with sufficient casting experience.

4. Fiberglass placement: Make sure gloves are worn while working with fiberglass as it is not easily removed from hands. It is advisable to keep 1-2 extra pairs of gloves at bedside in case you need to change gloves during the procedure.
    a. Remove the fiberglass cast roll from its package and dip it in a bucket of room temperature water, holding it under water until it stops bubbling (this ensures that the water has fully penetrated the roll).
    b. Now, roll the cast material. Again, two- or three-inch is preferred depending on the age of the child and size of the arm.
        i. Make initial wrist and thumb wraps – The authors' preferred technique is to start rolling on the dorsal aspect of the distal forearm away from the thumb and cut a rectangle of cast material out at the thumb so that a layer is left in the first webspace (Figure 3A-D). However, there are several acceptable ways to work around the thumb. One alternative is to twist the cast material multiple times as opposed to cutting if a thicker cast is preferred in the first webspace.

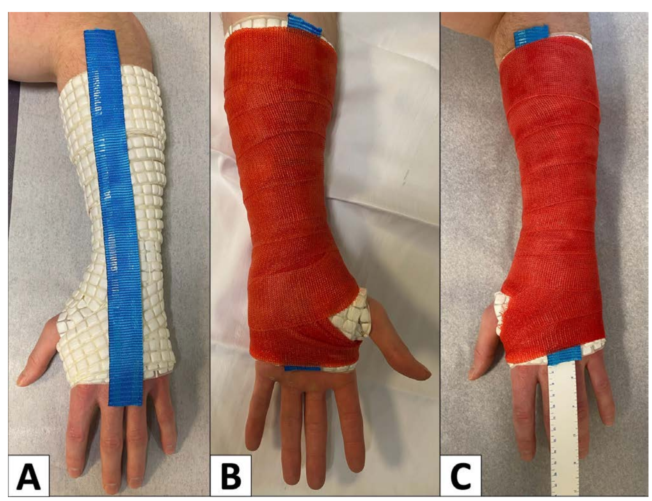

Figure 2A-2C. Waterproof Cast Application. (1A) Two to three layers of waterproof cast padding are used for a waterproof cast, with padding cuffs similarly applied proximally and distally. A blue woven safety strip must then be applied to the volar and dorsal aspects of the forearm to aid in future cast removal to prevent thermal injury. (1B) After fiberglass application, the blue safety strips must be visible at the cast edges for later identification and removal. (1C) A plastic stick (Zip Stick, BSN Medical and Essity Company, Hamburg, Germany) seen here can be used as another measure to protect against cast saw burns and is placed beneath the cast in line with the blue safety strip when using the cast saw.

1. The most important point is that thumb motion is not restricted after cast placement. Cast material should be just proximal to the metacarpal heads to allow for full finger flexion (Figure 4E). In younger children (infants and toddlers) keeping the cast this short can be challenging and it is acceptable for casts to end beyond the metacarpal heads in this age group.
2. The cast material should always be placed onto cast padding and should never touch unpadded skin. Similar to the cast padding, hold the roll gently on the sides using the thumb and index finger to pull the fiberglass taut while rolling to prevent wrinkles.

ii. Wrap proximally – As with the webril, each successive layer of fiberglass should overlap the prior layer by 50%. Again, be careful to avoid stretching the fiberglass around the arm, which can result in a tourniquet effect.

1. Some authors advocate for the use of stress-relaxation – unrolling a small amount of cast material and laying it on without tension – to prevent excessive constriction. We believe that stretching the roll away from the extremity may actually increase the risk for constriction, so our preferred technique is to roll the material directly onto the extremity with care taken to avoid excessive tension.

iii. Wrap around the elbow – When wrapping around the elbow on the first pass, it is acceptable to proceed in a figure-of-eight fashion, leaving an area over the posterior elbow uncovered by cast material. Such a technique is employed to prevent wrinkles during the first roll, and open areas are covered with successive wraps (either immediately or with the next roll of fiberglass).

iv. Finish proximally – The first roll of cast material should be finished proximally at the cuff of webril placed near the axilla. As with the hand and thumb, make sure there is about 5-10mm of uncovered webril adjacent to the end of the fiberglass, which allows for sufficient padding to roll back with the stockinette to create soft cuffs.

v. Add layers – When finished with the first roll of fiberglass, fold the stockinette over the cast material proximally and distally. Distally, cut another thumb hole in the stockinette (Figure 3E-G).

1. Place another roll of cast material in a similar fashion as the first, making sure to reinforce any areas that may feel weak (such as the posterior elbow).

c. When all of the cast material is applied, there should be 4-5 layers of fiberglass throughout the cast. Remember that the cast material must be applied relatively quickly to allow time for proper molding of the cast before the fiberglass hardens.

5. Molding: The most important molds in short and long arm casts are the interosseous mold and the three-point fracture reduction mold.

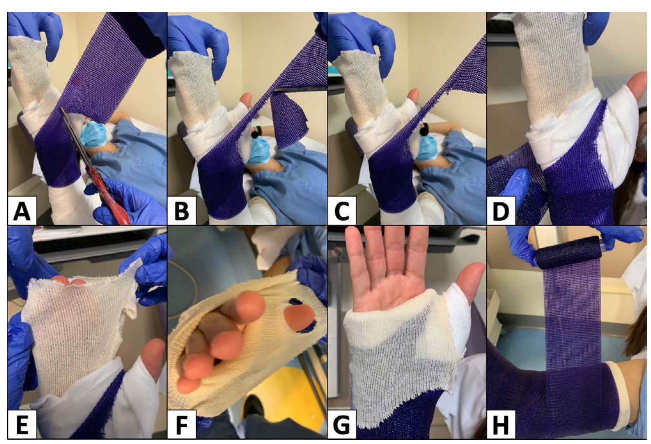

Figure 3A-3H. Figure 3. Upper Extremity Cast Fiberglass Application. (3A-3D) Start rolling on the dorsal aspect of the distal forearm and cut a rectangle of cast material out at the thumb so that a layer is left in the first webspace. Thumb motion should not be restricted after cast placement. (3E-3G) When finished with the first roll, distally cut another thumb hole in the stockinette and roll back the stockinette over the cast material proximally and distally. (3H) Hold the roll on the sides using the thumb and index finger to allow for some tension while rolling to prevent wrinkles. Bring the cast material away from the arm prior to laying the cast material down (stress-relaxation) to prevent constriction of the cast.

a. Interosseous mold: The interosseous mold is obtained by placing the heels of the palms on the dorsal and volar aspects of the forearm, interlocking the fingers together, and squeezing the palms together (Figure 4A). The hands should be constantly moving up and down the forearm while the cast is hardening to prevent wrinkles or pressure points in any given area. Indentations or pressure points from the fingers of the person performing the reduction can lead to pressure sores beneath the cast. The cast should take the shape of the arm with cast index <0.8 when it has been adequately molded and should not look like a tube (Figure 5). The cast index is measured by dividing the inner anteroposterior diameter of the cast by the inner lateral diameter of the cast, both at the fracture level.[13]

b. Three-point mold: The position of the hands and leg for the three-point mold depends on the fracture angulation. For a dorsally angulated forearm or wrist fracture, the physician's leg should be placed on the dorsal, proximal aspect of the forearm near the elbow. The heels of the hands are again placed on the dorsal and volar aspects of the forearm, similar to the interosseous mold, but for a three-point mold the hands are not at the same level. The distal hand is placed dorsally and just distal to the fracture site. The proximal hand is placed volarly just proximal to the fracture site and acts as a fulcrum (Figure 4B). This allows for a net volar force to reduce and hold the dorsally angulated distal fracture segment.

   i. Again, this position should not be held statically for the entire time while the cast is hardening, but rather the hands must be constantly moving to prevent rigid prominences inside the cast that could lead to pressure sores while also molding to allow for maintenance of reduction.

c. Ulnar border mold: A flat or straight ulnar border can be obtained by compressing the heel of the hand over the ulna in sequential fashion to avoid indentation or by pressing the ulnar forearm against the backside of a firm plastic object (such as one of the plastic basins used in hospitals for patient hygiene) placed against the provider's chest as an interosseous mold is applied. This mold prevents ulnar angulation and displacement.

Figure 4A-4G. Upper Extremity Cast Molding and Valving. (4A) The interosseous mold is obtained by placing the heel of both palms on the dorsal and volar aspects of the forearm, interlocking the fingers together, and squeezing the heel of both palms together. (4B) Example of a three-point mold for a dorsally angulated fracture. The physician's leg should be placed on the dorsal, proximal aspect of the forearm (see arrows). The distal hand is placed dorsally and just distal to the fracture site (fracture site demarcated by black line without arrow). The proximal hand is placed volarly just proximal to the fracture site and acts as a fulcrum. This allows for a net volar force to reduce and hold the dorsally angulated fracture. (4C) A supracondylar mold is obtained by squeezing the heels of both hands together over the supracondylar humerus. (4D-4E) Cast material should be just proximal to the metacarpal heads to allow for finger flexion. (4F) Valving should be performed with the arm on a stable surface. Preferred positioning for valving the dorsal aspect of the cast is with the arm over the patient's body. (4G) The shoulder can be abducted and externally rotated to valve the volar part of the cast.

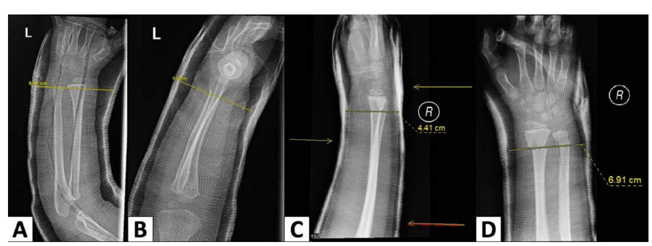

Figure 5A-5D. Cast Index. (5A-5B) Example of a poorly molded long arm cast for a distal radius buckle fracture. The cast index is measured at 0.85, and the cast takes the shape of a tube. (5C-5D) Example of a well molded long arm cast. The cast index is 0.64 and the cast is molded to the shape of the arm. The arrows in image C indicate the three-point mold that was performed for this initially dorsally angulated distal both bone fracture.

d. Supracondylar mold (for long arm casts): A supracondylar mold is obtained by gently squeezing the heels of both hands together over the supracondylar region of the distal humerus (Figure 4C). This mold prevents the cast from slipping down the arm. Always use the heel of the palm to mold the cast and never use fingers, as fingerprints can cause pressure points in the cast.
    i. When applying this mold, there is a tendency for the posterior border of the cast above the elbow to bow out, which would then allow the elbow to extend more than intended. To avoid this, pressure may be held over the posterior border of the cast as the supracondylar mold is applied.

e. It should be recognized that there is a discrete working time of about 4-5 minutes during which fiberglass can be molded - this is the window during which the reduction maneuver should be held. As the cast hardens it will become tacky and more difficult to mold with replacement of hands. A small amount of water or soap can be applied to the cast to counter the tackiness of the fiberglass and allow for continuous hand movement and molding while the cast hardens.
    i. Make sure the position of the elbow does not change while the cast is hardening; this prevents bunching of cast material or creasing of the fiberglass in the antecubital fossa. If there is concern for such mistakes, the cast should be removed and a new one applied.

f. Hybrid plaster and fiberglass casting: An alternative technique combines the greater molding capability of plaster casts with the strength of lighter-weight fiberglass.[14] In this method, 2-3 layers of plaster are applied over a layer of padding as previously described. While this is still wet/curing, 1-2 layers of fiberglass are applied on top with the appropriate molds obtained. However, this method has the potential downside of preventing effective heat dissipation from the plaster as it is covered in synthetic fiberglass and magnifies the exothermic reaction, increasing the risk of burns while the cast is curing, and may also increase the risk of cast saw burns upon removal. Therefore, it is not the favored technique at our institution.

6. Trimming edges: Trim excess cast material around the thumb which may have jagged edges when hard. Always protect the patient's skin when using shears on a cast.
7. Cast Valving: Once the cast has hardened completely, it may be univalved (one cut) or bivalved (two cuts) and taped to allow for swelling, though the impact of splitting to avoid increased compartment pressures is controversial. Valving should be performed with the arm on a stable surface.
    a. Preferred positioning for valving the dorsal aspect of the cast is with the arm internally rotated, resting over the patient's abdomen (Figure 4F). The shoulder can be abducted and externally rotated to valve the volar aspect of the cast (Figure 4G).
    b. The cast should never be cut in a flexion crease (i.e. antecubital fossa). If univalving or bivalving, make sure the cast has been completely cut. In general, fractures in which further swelling is not expected and those in which a reduction has not been performed may not require cast valving.

Short Arm Cast Placement

Short arm casts are applied in a manner similar to long arm casts but end just distal to the elbow. Short arm casts should not restrict elbow motion.

LOWER EXTREMITY CASTING

Set-up

1. It is optimal to have an experienced assistant to hold the patient by the foot and thigh while the cast is being placed. The ankle is typically held in neutral dorsiflexion unless this interferes with fracture reduction.
    a. For short and long leg casts, the patient should be lying supine with the assistant holding the 2nd and 3rd metatarsal heads with one hand (with the thumb and index/long fingers) and the other hand stabilizing the thigh.
    b. For short leg casts, the knee can be flexed to 90°. For long leg casts, the knee should be maintained at 30-45° of flexion.
2. Have all necessary material in the room for cast placement, including cast padding, cast material, a cast saw if bivalving or univalving the cast, a bucket of water (room temperature), gloves, trauma shears.
    a. Similar to upper extremity casting, use of a mini C-arm during a reduction under sedation can minimize reduction attempts. A lead apron should again be placed over the child.

3. If casting under sedation, once adequate sedation has been induced, bring the patient down to the end of the stretcher so that the feet are at the edge. Have your assistant hold the foot and thigh so that the knee is at approximately 30 degrees of flexion and the ankle is at neutral dorsiflexion.
    a. An alternative position, particularly for short leg casts, is abduct the leg at the hip and allow the lower leg to flex at the knee such that the calf hangs off of the bed.

Long Leg Cast Placement

Long leg casts should be applied for all injuries that require immobilization of the knee to prevent flexion, extension, or rotation. Additionally, long leg casts should be placed in all infants and toddlers (up to approximately age 2) who require a lower extremity cast due to the short, stout, cylindrical nature of the patient's lower legs and relatively large amount of subcutaneous fat, which predispose them to slipping out of a short leg cast.

There are several different techniques described for placing long leg casts. Some advocate for placing a short leg cast first, molding the short leg cast, and transitioning to a long leg cast once the short leg cast has hardened.[8] One must be very cautious using this technique and ensure the end of the short leg part of the cast is distal to the popliteal fossa when first placed and there is abundant padding at the transition, so that the edge of the short leg cast does not compress the fossa at the junction. This can lead to skin breakdown and compartment syndrome. Because of this concern, the authors' preferred technique is to place the entire long leg cast at once. However, the knee must be held in the same position during the entire casting process to prevent bunching of material in the popliteal fossa with flexion or wrinkling of the cast anteriorly with extension.

Regardless of which technique is chosen, an assistant is required for the placement of a long leg cast. The authors' preferred technique for long leg cast placement is described below. Again, it is presented as if a reduction is being performed, though the same steps can be followed without a reduction.

1. Reduction: If a reduction is required, reduce the fracture using C-arm manually prior to cast application to ensure adequate reduction.
2. Place stockinette: When the reduction is satisfactory and you are ready to place the cast, roll an appropriately-sized stockinette over the leg so that it is as proximal as possible (almost to the groin) and just distal to the toes distally (Figure 6A). A hole may be cut in the popliteal fossa and over the dorsum of the ankle to prevent bunching of material in these flexion creases.
3. Roll the cast padding: three or four-inch webril is preferred for the lower extremity depending on the age of the child and size of the leg.
    a. Start distally at the level of the great toe, angled obliquely to match the cascade of the toes (Figure 6B). Ensure that the cast padding extends beyond the end of the toes. Wrap several times around the toes and then travel proximally, overlapping the previous layer by 50% with each successive roll around the leg (Figure 6C-D). The total number of layers should again be 4-5 throughout the cast.
    b. Make cuffs of padding proximally and distally. Pad the bony prominences of the heel, malleoli, and anterior knee with an extra 3-4 layers of padding (Figure 6E).
    c. When finished applying cast padding, some of the cast padding in the popliteal fossa and over the dorsum of the ankle can be removed to prevent bunching of material in these flexion areas.
4. Fiberglass placement:
    a. Remove the fiberglass cast roll from its package and dip it in a bucket of room temperature water, holding it under water until it stops bubbling. Again, 3- or 4-inch is preferred depending on the age of the child and size of the leg.
    b. Roll the cast material.
        i. Make initial foot wraps – Start rolling distally at the end of the toes (if the preference is for toes to be covered). Roll obliquely to follow the cascade of the toes. The end of the cast should extend to the ends of the toes so they

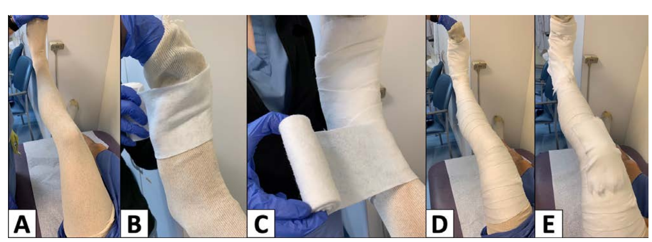

Figure 6A-6E. Lower Extremity Cast Padding. (6A) Roll the stockinette over the leg so that it is as proximal as possible (almost to the groin) and just distal to the toes distally. (6B-6D) Roll the cast padding starting distally at the level of the great toe and angled obliquely to match the cascade of the toes. Overlap the previous layer by 50% with each successive roll around the leg. (6E) Make cuffs of padding proximally and distally. Pad the bony prominences of the heel, malleoli, and anterior knee with an extra 3-4 layers of padding.

do not curl over the edge (Figure 7A). The tips of all the toes should still be visible by looking into the end of the cast after placement. Three or four layers of fiberglass should be laid over the foot.

ii. Wrap around the ankle – When wrapping around the ankle, it is recommended to proceed in a figure-of-eight fashion, initially leaving an area over the posterior calcaneus uncovered by cast material, then doubling back to cover this area.

iii. Wrap proximally – As with the upper extremity, successive layers of cast material should be placed, overlapping each prior layer by 50%. Again, ensure that the fiberglass is not constricting the extremity. A second roll of fiberglass will likely be needed as you roll proximally. The knee is usually wrapped in the typical overlapping fashion.

iv. Finish proximally – The fiberglass should be carried up to the cuff near the groin, leaving approximate 1cm of uncovered padding proximally. When finished with the initial layers of the fiberglass from toes to groin, roll back the stockinette over the cast material proximally and distally (Figure 7B). At this point there is usually about 2-3 layers of cast material.

v. Add layers – After folding back the stockinette, add more layers of fiberglass in a similar fashion. There should be 5-6 layers of fiberglass in total at the end of casting.

5. Molding: In addition to any fracture reduction mold, the most important molds in long leg casts are the supramalleolar and supracondylar molds to prevent cast slippage.
   a. Supramalleolar mold: This is performed by placing the heel of both palms just proximal to the medial and lateral malleoli, interlocking the fingers together, and squeezing the heel of both palms together (Figure 7C).
   b. Supracondylar mold (for long leg casts): This is performed by squeezing in the coronal plane just proximal to the medial and lateral femoral condyles, again using the palms. Unlike upper extremity casts, there is no interosseous mold.
   c. Heel mold: This mold is performed by using one palm to "cup" the heel above the calcaneal tuberosity and apply gentle pressure. This is done to prevent pressure sores on the heel.
   d. Other molding pearls:
      i. The distal aspect of the cast should also be compressed with the heels of the palms on the dorsal and plantar aspects of the foot. This "pancaking" of the cast helps to open up the cast around the great and small toes and prevent abrasion. In addition, as the cast is drying, the opening for the toes can be spread in the coronal plane of the foot to ensure adequate space, especially for the small toe which can easily be compressed by the cast.
      ii. The ankle should be kept in a neutral position and out of equinus. However, equinus may be acceptable in cases of distal tibial fractures where dorsiflexion of the ankle displaces the fracture into recurvatum.
      iii. Care should be taken to maintain position of the ankle and knee while placing the cast padding and fiberglass, as movement can cause wrinkles and bunching of material in flexion creases.
6. Trimming edges: Trim excess cast material around the toes and groin, which may have jagged edges when hard. Always protect the patient's skin when using shears on a cast.

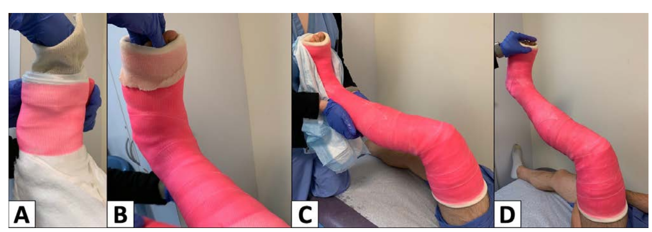

Figure 7A-7D. Lower Extremity Cast Fiberglass Application. A: Start rolling the cast material distally just proximal to the cast padding. The tips of all the toes should be visible after cast placement. Overlap each layer by 50%. B: When finished with the first roll, roll back the stockinette over the cast material proximally and distally. C: The supramalleolar mold is performed by placing the heel of both palms just proximal to the medial and lateral malleoli, interlocking the fingers together, and squeezing the heel of both palms together. The foot can also be placed against the physician's chest during this step to prevent equinus. The position of the knee must be carefully monitored to prevent creases. D: Final position of the long leg cast with the toes visible, the ankle in neutral dorsiflexion, and the knee in 30-45 degrees of flexion.

7. Cast Valving: Once the cast has hardened completely, it may be univalved or bivalved and taped according to preference. This should be done on medial and/or lateral sides of the cast and not along the anterior or posterior sides.

Short Leg Cast Placement

Short leg casts are applied in a manner similar to long leg casts, but these should end distal to the tibial tuberosity and should not restrict knee motion. Care should be taken that they also do not impinge on the head of the fibula to reduce risk of peroneal nerve compression. A discussion of the various indications for applying a short leg cast, rather than a long leg cast, are beyond the scope of this review. However, a long leg cast is generally preferable for tibia fractures, if rotational control of an ankle fracture is required or if the child's leg is not amenable to a short leg cast due to size and morphology.

DISCUSSION

Properly placed casts are essential for maintaining pediatric fracture reduction and preventing complications. Cast placement and removal are core orthopaedic skills that should not be overlooked in orthopaedic residency or APP education.[2] Additionally, these skills are increasingly being used by emergency room, primary care, and urgent care providers to manage pediatric patients with acute fractures. While often considered a rather "benign" treatment, errors in cast application can result in serious complications. Therefore, cast placement, manipulation, and removal must be performed with great attention to detail. Common "Pearls and Pitfalls" of cast placement are listed in Table 1.

Skin complications, including pressure sores and skin maceration, can occur with casting. These complications can be avoided with proper technique and counseling of the patient and parents. Pressure sores are most common at bony prominences and flexion creases, but

Table 1. Pearls and Pitfalls of Placing Fiberglass Casts

Pearls	Pitfalls
Use 4 layers of padding (rolling up and down extremity once while overlapping by 50%) plus 3-4 extra layers over bony prominences.	Not enough padding around prominences or excessive cast padding that prevents proper molding and risks loss of reduction
Constantly move hands up and down the extremity while molding the cast to prevent wrinkles and pressure points.	Wrinkling of the cast causing pressure points
Always mold cast with heel of palm to prevent pressure points.	
Maintain position of joints while casting to prevent material bunching in flexion creases.	Material in creases can cause skin breakdown and increase risk for compartment syndrome.
Always wait until cast material is hard before univalving or bivalving.	Cast saw burns
Never use the cast saw in a flexion crease.	
Never use a cast saw with a dull blade.	
Always stop the cast saw periodically (every ~3 passes depending on thickness of cast) to cool the blade.	
Use extra caution removing a cast that was placed at another institution or by another provider.	
LAC: interosseous mold, three-point mold, flat ulnar border, supracondylar mold	
SAC: interosseous mold, three-point mold, flat ulnar border	
LLC: supramalleolar and supracondylar mold, three-point mold	
SLC: supramalleolar mold	Poor molding of the cast causing it to slip or lose reduction
Ensure there is sufficient padding at the proximal and distal ends of the cast as well as the thumb to protect the skin from the sharp edges of the cast. Leave a cuff of about 1 cm of cast padding proximally and distally free from fiberglass when rolling. Always check around edges of cast, especially around the thumb, to ensure sharp edges do not need to be trimmed or covered.	Sharp edges of cast material around the thumb causing skin lacerations
Ensure that fiberglass is rolled without tension to prevent excessive constriction.	Compartment syndrome
Do not cast the elbow/knee at > 90˚flexion.	Extremity ischemia, compartment syndrome
Always warn patients and parents about the signs and symptoms of compartment syndrome and next steps to take if they experience them	

LAC = long arm cast, SAC = short arm cast, LLC = long leg cast, SLC = short leg cast.

they can also occur in areas of cast wrinkling. Areas of increased pressure result in decreased perfusion which in turn causes sore formation.[4] Pressure sores can be avoided by 1) placing a sufficient amount of cast padding (4-6 layers), 2) leaving a sufficient cuff of padding at the proximal/distal aspects of the cast and around the thumb, 3) proper molding of the cast with the heels of the palm as opposed to the fingers, and 4) ensuring that the extremity remains in one position while casting so that wrinkles are not created during flexion/extension of the joint after casting. Skin maceration, irritation and abrasion can also easily occur if the cast gets wet or the child sticks objects into the cast for itching. The patient and family should be extensively counseled about this risk and instructed to return to clinic if either of these scenarios occurs so that the cast can be changed before skin maceration occurs.

Sores can also occur as a result of crowding of the toe in lower extremity casts. This can be avoided by placing the cast padding and material obliquely, in-line with the cascade of the toes so that after cast placement, all of the toes are visible. Additionally, one can create more room in the lateral distal end of the cast after placement by placing both index fingers inside the cast near the great and small toes and spreading the cast to create more lateral space for the small toe. Cast slippage is another complication that can occur if not molded properly or a short arm or short leg cast is placed in a toddler who has a short and cylindrical extremity which predisposes the cast to slip.

Proper casting technique not only results in a visually-appealing cast, but it also optimizes the patient's chances of a successful outcome with initial closed fracture treatment. While proper technique also aims to avoid injuries from cast application and removal including skin complications as outlined above, the use of appropriate materials in appropriate ratios helps to avoid thermal injury to the skin while the cast cures. Prior work has shown that decreased cast padding, increased cast thickness, the use of hot dip-water (above room temperature), and cooling of a cast while lying on a pillow are risk factors for thermal injury to the patient while the cast dries.[9,10]

As many casts placed in the acute care setting are valved, safe cast saw technique is another important consideration that should be thought of as part of proper casting technique. Poorly-kept saws and sawblades, inadequate padding, and bad technique raise the risk for cast saw burns when a cast is being valved or removed. Cast saws are used commonly while on-call in the pediatric emergency room for univalving, bivalving, and removing cast. Cast saw injuries, including both thermal and abrasive injuries, occur in 0.1- 0.7% of cases and often result in permanent scarring.[11] Using a cast saw with a dull blade, a thick cast, and minimal cast padding all predispose to cast saw injuries.

One should never use a cast saw with a dull blade. In the case of a thick cast, one should pause periodically (approximately every 3 passes) and cool the blade with a damp cloth moistened with water or isopropyl alcohol before continuing. An "in and out" motion – never a "dragging" motion – should be used when cutting a cast. One should also never use a cast saw in a flexion crease, as the saw will have penetrated the fiberglass at the proximal and distal aspects of the crease (in contact of the skin) while the center of the cast saw has not yet penetrated the fiberglass at the deepest aspect of the crease.[11] This can cause burns at the proximal and distal aspects of the crease.

Clinicians working with casts should exercise extreme caution when removing a cast not placed at their institution, as it is impossible to know how much padding was used or if the person who placed the cast was well-trained. However, one can usually tell whether waterproof or cotton undercast was used. Waterproof undercast is much less resistant to the heat and shear produced by the cast saw than cotton (and thus much more likely to be associated with cast saw burns). However, these casts are typically placed with blue woven strips that prevent burns while removing the cast as described previously. One should therefore be observant for the location of these strips proximally and distally as these indicate where the casts should be cut to prevent burns.[11] A cast removal aid such as a zip stick can also be placed down the cast to provide a barrier between the saw and the skin if it is unknown how much or what type of cast padding was used.

CONCLUSION

Proper casting technique is critical in optimizing outcomes in the treatment of pediatric fractures. While casting is often performed outside of the operating room by APPs, junior residents, and emergency department or urgent care providers, it should be taken seriously given the potential for serious complications.

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MEDICAL LITERATURE IN THE TREATMENT OF CLUBFOOT 1997 – 2021: THE EMERGENCE AND SPREAD OF THE PONSETI METHOD OVER 23 YEARS

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ABSTRACT

Background: The Ponseti method of treatment for clubfoot which utilizes serial manipulations and casting in order to achieve correction of the deformity has become increasingly popular due to its robust track record of success without the need for surgical intervention and is considered the gold standard for clubfoot treatment. Exposure of new technology in the scientific literature is associated with the diffusion and adoption of that technology in clinical practice. The aim of this study sought to identify tendencies in the thematic changes in medical literature regarding the treatment of congenital clubfoot over a period of twenty-three years, from 1997 to 2021.

Methods: The Medline databases were searched for articles containing the keyword "clubfoot". Articles from 1997 to 2021 were identified and analyzed by institutions which published the articles, and whether treatment was with the Ponseti method or surgical interventions. We also observed in order the geographic diffusion of the Ponseti method.

Results: 2067 articles were found in Pubmed referencing clubfoot, and in these publications 577 addressed the Ponseti method and 273 articles discussed surgical treatment. From 1997 – 2000, the only articles discussing the Ponseti Method were from Iowa,in the United States. The increasing number of publications about the Ponseti method and the decrease in publications about surgical treatment for clubfoot occurred after 2003. In 1997, only one country had a publication regarding the Ponseti method; by 2018, 24 countries published articles on the method.

Conclusion: These results suggest a trend of dissemination of knowledge to additional countries, reflecting the more widespread usage of the method throughout the world, and global outreach as a result of the work of Ponseti International Association.

Level of Evidence: II

Keywords: ponseti method, clubfoot, database, impact

INTRODUCTION

In recent years, the Ponseti method of treatment for clubfoot has become increasingly popular due to its high level of efficacy[1-10] and better long-term results than invasive surgical treatment.[11] The Ponseti method utilizes serial manipulations and castings in order to achieve correction of the deformity, which is frequently followed by a minimally invasive Achilles tenotomy, as well as the use of an abduction brace for 4-5 years.[12-13] Previously, the most common form of conservative treatment was the Kite technique,[14] which used serial casts for a much longer time (from six months to one year), with the majority of cases followed by a posteromedial release, an extensive orthopedic surgery. The extensive surgical approach is associated with greater complications and longer recuperation.[15-17]

As the Ponseti method has become more widely used throughout the world, research has become necessary in order to track the dissemination of the method. Medical innovation encounters difficulties changing traditional paradigms.[18-22] Organizational disciplines attempt to correlate the production of scientific interest with trends in clinical practice that reflect the approaches adopted by the doctors viewed as a whole.[18] This information is generally used in planning health initiatives, hospital and budget management, or even for individual use.[20] As health decisions regarding the utilization of different procedures and practical equipment and in medicine are increasingly reliant on evidence-based medicine, scientific publications have an important role in this analysis.[21]

In the United States, the dissemination of knowledge about the treatment of clubfoot with the Ponseti method has been slow, despite being the country where the technique was first developed and described. In 1963, the first publication about the technique described a series of consecutive cases from 1948 to 1956. One of the possible reasons that this publication did not have a major impact in the medical community was due to the fact

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that despite reporting a good correction of the treated feet, more than half of the patients had recurrences after 36 months. The average time spent with the abduction brace after the correction was now modified to be worn until the age of 4-5 with less relapses. In addition, the angle of the abduction brace following correction was less than 60 degrees, now considered inadequate to prevent recurrences.[12]

The article that contributed to the true beginning of the dissemination of the method was published in 1995, when the results of a thirty-year study were reported by Dr. Ponseti.[9] The study made a careful and complete evaluation of patients, including clinical aspects (joint mobility, podobarometry, gait analysis, muscle strength, size and strength of calf muscle), radiographic elements, a satisfaction survey, an analysis of activities, and electrogoniometry.

A comprehensive assessment of these patients was compared to the evaluation of patients randomly selected from the waiting room of the ophthalmology clinic of the same hospital, and showed that the feet were anatomically and functionally comparable to the clubfeet treated by the Ponseti method. The internet diffusion increased the popularity of the method, and the successfully treated patients helped to disseminate it.

This study sought to identify tendencies in the thematic changes in medical literature regarding the treatment of congenital clubfoot over a period of twenty three years, from 1997 to 2021. One database was searched on the subject: PubMed with English-language publications. By recognizing patterns in the distribution of medical literature regarding clubfoot, the authors identified the geographical trends associated with the technique.

METHODS

The Medline databases were searched for articles containing the keyword "clubfoot". In the Medline Database (PubMed), articles from 1997 to 2021 were analyzed by the abstract and/or the article, and divided into the following thematic categories: articles advocating the Ponseti method of treatment, articles advocating surgical treatment for clubfoot, recurrences and evolution of the deformity, conservative treatment, different treatment comparisons, images, epidemiology, genetics, pathologic anatomy, syndromes, pre-natal diagnosis, and revisions.

From the works found in the PubMed database regarding clubfoot, the authors looked to identify not only whether the treatment was by the Ponseti Method or surgical, but which institutions published the articles, in order to observe the geographic diffusion of the Ponseti method.

RESULTS

2067 articles were found in the Pubmed (Medline Database) from 1997 – 2021 referencing clubfoot, of which were indexed into 15 categories. Only two categories were chosen for this study: Ponseti management and surgical treatment. Over the twenty three years period, the authors found 577 articles about the Ponseti method and 273 articles about surgical treatment (fig 2).

From 1997 – 2000, the only articles discussing the Ponseti Method were from Iowa, United States, by Dr. Ponseti's own group of researchers, with one article each in 1997 and 2000. The published articles, by year and country, are available in Figure 3. There has been a steady increase in the number of articles published regarding the Ponseti Method since 2001, while the number of articles published regarding surgical treatment for clubfoot has diminished.

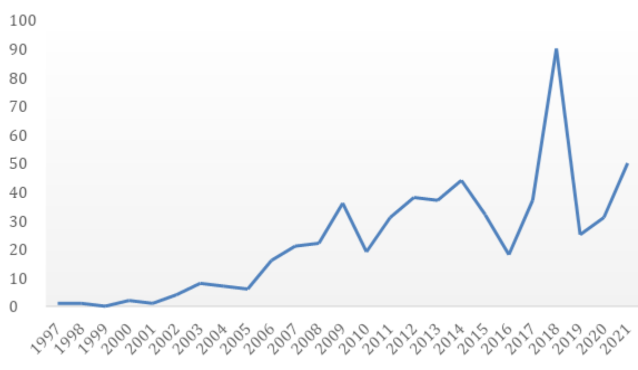

Figure 1. Ponseti method. Number of articles published from 1997 to 2021 with reference to "clubfoot" and classified from Ponseti Method.

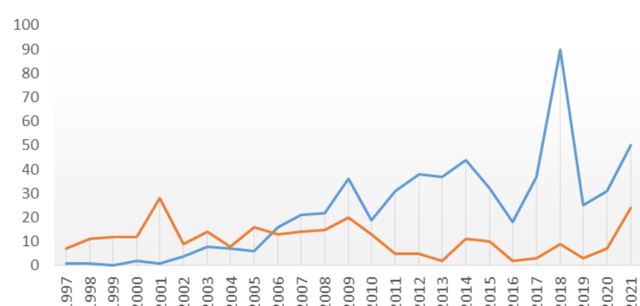

Figure 2. Ponseti method and surgical treatment from 1997-2021. Comparison of trends in the number of articles per year: Ponseti method and surgical treatment from 1997 – 2021.

COUNTRIES	PUBLICATION YEARS	COUNTRIES	PUBLICATION YEARS
Australia	2009; 2013-2014;2016-2017;2021	Mexico	2012;2013
Austria	2003;2006-2007; 2013-2013;2021	Nepal	2009;2013
Bangladesh	2013;2016	Netherlands	2015;2018;2021
Belgium	2008	New Zealand	2007;2010;2014;2018
Brazil	2009;2011;2013;2016-2018;2020-2021	Nigeria	2010;2015;2017
Canada	2001;2008-2009;2011;2013-2014;2018	Norway	2011-2012;2014;2017
Catar	2014	Pakistan	2007;2014;2016-2017;2020-2021
China	2008-2012;2014;2018;2020-2021	Peru	2015
Czech Republic	2009;2012-2013;2018;2021	Poland	2004;2007-2008;2011;2017;2018
Emirados arabes	2009	Portugal	2009;2021
Egypt	2008-2009;2011-2012;2015;2021	Romania	2013-2014;2018
England	2018-2019	Servia	2018
France	2002;2008;2011-2012;2015-2016;2019-2021	South Korea	2015
Germany	2006-2010;2012-2013;2007;20189-2021	Southern Africa	2014
Ghana	2021	Spain	2013;2018
India	2008,2010-2021	Sweden	2015;2017
Iran	2014-2017;2021	Switzerland	2011;2013;2019
Ireland	2012-2013	Taiwan	2017;2021
Israel	2005-2007;2009;2011-2012;2016-2017;2021	Thailand	2017
Italy	2003;2009;2012-2014;2016-2017;2019;2021	The Netherlands	2017
Japan	2003;2012-2013;2018;2020	Tunisie	2008
Kenia	2015	Turkey	2002;2006;2008-2011;2015;2018;2020-2021
Korea North	2009;2013;2020-2021	Ukraine	2020
Kuwait	2010	Uganda	2007
Madagascar	2016	Unite States	1997-1998;2000;2002-2021
Malawi	2005-2007;2011;2018	United Kingdom	2005-2018
Malaysia	2014;2016;2018;2020-2021	Zâmbia	2018
Maroc	2007		

Figure 3. Publications per year regarding the Ponseti method by country, Pubmed 1997-2021.

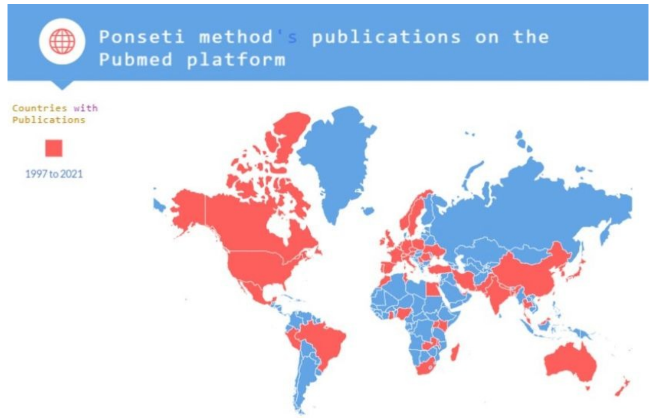

Figure 4. Worldwide publications listed in the Pubmed database regarding the Ponseti method.

The increasing number of publications about the Ponseti method and the decrease in publications about surgical treatment for clubfoot occurred after 2003, with a plateau observed in the graph of the series of publications by 2005 (Figure 1). In these three years, the groups most active in Ponseti publications were those in the United States, especially Iowa, New York, St. Louis, Dallas, New Orleans, and San Francisco. European groups soon followed suit, and developing countries began to publish articles in 2005, beginning with Malawi, Africa, in collaboration with researchers from the United Kingdom. In 2006, India published an article regarding the use of the technique for older children, which was also the case of Brazil, Turkey, Uganda and Nepal in the following two years. Chile, India, Egypt, South Korea and China have also joining the ranks of Ponseti publications. This observation indicates a clear trend of dissemination of knowledge to additional countries, reflecting the more widespread usage of the method throughout the world. In 1997, only one country had a publication regarding the Ponseti method; by 2009, 26 countries published on the method: 2 in North America, 2 in South America, 14 in Europe, 4 in Africa, 2 in Asia and 2 in Oceania. By 2018, 90 articles are published on the method from 24 countries. The geographical distribution is clear (Figure 3).

In 2014, as in 2018, there was a great increase in publications on the Ponseti method (44 and 90 articles). Surgical treatment also increased in the same years, but in smaller number compared to Ponseti (11 and 09 article). However, publication about surgical treatment has reduced in recent years.(Fig 1 and 2).

DISCUSSION

The increase in the number of publications about the Ponseti Method, may represent a trend of increasing interest to the international medical literature regarding the Ponseti method. The transforming influence of the medical literature in clinical practice or as a reflection of changes in clinical practice has been the subject of various studies,[23,24,26,19] and the Ponseti method's trend of increasing publications reflects this diffusion, both in the number of articles as well as with regard to geographical expansion of the publications.

In 2003, a cross-sectional study was conducted on the treatment of clubfoot in the United States: 65% of physicians responding to the survey reported that they used the Ponseti method, and 31% of those had recently switched to the Ponseti method from other forms of treatment. However, the study also pointed out that the rate of correction with conservative treatment was small (26.2%); as a result, 56% of all respondents used extensive surgical releases of the foot.[26] A recent publication objectively reflects a reduction in the number of posterior-medial releases (from 70% to 10%) observed after comparing American health statistics from 1996 to 2006.[27] Comparing the trend found in the increase of publications (Figure 2) with the observed reduction in the number of surgeries, one could hypothesize that the medical literature and clinical practice are similarly indicating a higher level of interest in the use of the Ponseti method.

In Brazil, a survey completed in Rio de Janeiro in 2009 during the 41st Brazilian Conference of Orthopedics and Traumatology reported that 88% of 88 orthopedists interviewed used the Ponseti method.[28]

In 2010, research was done on the use of the Ponseti method for the Brazilian Pediatric Orthopedic Conference in June 2010. 80% of orthopedic surgeons who completed the questionnaires reported using the Ponseti method for the treatment of clubfoot. More than half of the physicians surveyed treated children with syndromes or myelodysplasia; this indicated that physicians are beginning to utilize the Ponseti method for non-idiopathic clubfoot, reflecting an increased use of the method for a wider range of patients.

In a search of the international database (PubMed), five multicenter studies were found on the Ponseti method. One of the studies is a collaboration between the United States (Baltimore) and Israel (Afula), with four studies (Herzenberg 2002, Bor et al., 2006, Bor, et al., 2007, Bor, et al., 2009) with a series of cases with increasing follow-up times. Another multicenter study was completed in Brazil with Spain (Barcelona) and Portugal (Funchal, Ilha da Madeira) regarding the treatment of previously operated clubfeet.[29] This international collaboration demonstrates that different centers in different parts of the world can achieve the same good results in patients whose feet are difficult to treat following previous surgical manipulation. Furthermore, international partnerships reflect an interest in the method that transcends international borders, and demonstrate the existence of a network of studies regarding the technique.

In a developing country like India, where there was a dearth of proper operative facilities in remote areas, this technique is a very safe, easy, result-oriented, economical method of clubfoot management.[8] Between 1997 – 2021, 356 publications were found by authors in developing countries. In 2014 and 2015 (14 and 18 articles) there is an increase in publications in developing countries (32%), since these years were found 97 publications in Ponseti method and surgical. Between 1997 and 2021, we found 12 publications from African countries and 21 articles from Latin America. Include that 80% of clubfoot cases take place in the developing world, and a cost-effective treatment such as the Ponseti method can preferentially benefit poorer countries as this method uses low-cost casting materials as the primary treatment. Achilles tenotomy is typically performed in the office, thus avoiding costly surgical costs.

Another interesting finding is the growing base of literature indicating that extensive surgical treatment for clubfoot can have poor long term results. In 2006, Dobbs reported the results of patients with congenital clubfoot who were treated with extensive surgical release, averaging 25 years of follow-up. These patients had multiple surgeries, stiffness, and pain, and a quality of life similar to patients in renal failure on dialysis or patients with heart disease. In 2006, a German institution that had previously published a work advocating posteromedial release as the gold standard of treatment published an article about the preliminary results of its use of the Ponseti technique.[10]

Simultaneously, growing evidence of the effectiveness of the Ponseti method began to reflect the changing trend of surgical treatment for the now-preferred Ponseti method.

However, despite the trend observed in the literature, we cannot presume that there is a direct relationship between clinical practice and scientific publications, as these publications are not responsible for the dissemination of knowledge. In evaluating how doctors obtain information that modifies their clinical practices, several other factors come into play: adherence to standards of conduct for institutions and universities, resistance to change, and a lack of credibility for research perceived as having commercial interests.[19]

As a limitation, our study extracted data only from Pubmed, which possibly could have missed some important papers.

The diffusion of medical knowledge depends on the innovation and perceptions of those implementing change, as well as the advantages this innovation presents compared to the current method of treatment.[18] These advantages are observed with respect to efficacy and reproducibility;[1-10] additionally, better diffusion is associated with longer follow-up time for studies, efficiency of treatment, and time of treatment in relation to cost, as compared to conventional treatment.[11,30]

Orthopedic physicians exposed to the Ponseti method, either practically through courses or theoretically through conferences, scientific articles and books, act as promoters for the new technique after achieving good results.[19] Moreover, the so-called informal opinion of leaders and champions of the cause can be transformative and influential. The health system can participate in the dissemination by seeking a less expensive and more effective treatment option than extensive surgeries. Factors influencing the change in medical management could be related to the need for change due to difficulty solving the frequent problems and complications derived from surgical treatment.[15,30,21]

Social pressure for change, especially in the case of clubfoot, can take place through the parents of children with the deformity who are seeking treatment. The internet can play an important role in the case of parents researching potential treatment options for their children, as it is a great disseminator of knowledge and available to entire communities. In clinical practice, it has become an important source of health information, and is frequently used by patients and parents.[31,33] A clear involvement of the internet with relation to the adoption of the Ponseti method has been demonstrated.[13] Research done by the parents of children with clubfeet investigating the role of the internet in choosing a method of treatment (Symposium of Ponseti International Association – Washington, 2009) found that about half of American parents seek a second opinion for their child's treatment, and a growing number of parents outside the United States also sought second opinions or other treatment options.[10]

In 2014 Shabatai et al. point out that despite the benefits of this technique, we found that only 34 of 193 (18%) UN countries have published their experience using the Ponseti method. In another 7 countries we found abstract submissions related to this topic and another 72 countries where the Ponseti method is apparently performed on a clinical basis. This total of 113 countries represents only 59% of the countries in the world.

CONCLUSION

The data presented suggests a trend toward the Ponseti method for the treatment of children with clubfoot, worldwide and also in Brazil. This technique replaced treatment by the Kite method. Future studies should indicate whether this trend will continue, and if such practice will be incorporated into the public health system (SUS) and private sector of Brazil. In this period there is an increase in the number of publications, thereby demonstrating the increase in cases that were treated by Ponseti method. However the number of articles cannot be directly correlated to the diffusion of knowledge regarding that subject, despite the different areas of research, tending to a strong correlation.

Some health technologies have spread at impressive speed, changing the paradigms in the attention to certain diseases. The technologies developed do not always have a relevant clinical role, and some simply do not have significant clinical applicability and quickly pass from the diffusion phase to the obsolescence phase. Duarte, in 2009, discussed the introduction of electron beam computed tomography; that became obsolete because it was an ineffective technology and was replaced by other image technology as multidetector computed tomography.[23]

It is evident, therefore, how important the theme "technological diffusion" is nowadays, and the adequate use of technology in health constitutes a great challenge for modern societies. However, assessing the patterns of technological diffusion is not an easy task due to the scarcity of data in this area and the limited availability of such data in several countries.[19,20] The number of published articles will not always mean that that technology will become clinically applicable like the Ponseti method. However, we can observe that there is a tendency for the scientific community to publish less about the technologies of the past and to give more attention to that technology that is being applied clinically, as in the case of the Ponseti method.

Therefore, we can conclude that medical literature indicates Ponseti method as the gold standard treatment for patients with clubfoot. In addition to recent studies showing good results and being an easy-to-apply and low-cost method, Ponseti International Association and non-governmental organizations provide resources for healthcare professionals in low- and middle-income countries to apply the Ponseti method.

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MANAGEMENT OF ADULT ATLANTOAXIAL ROTATORY FIXATION: CASE SERIES WITH LITERATURE REVIEW

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ABSTRACT

Background: Atlantoaxial rotatory fixation (AARF) is extremely rare in adults, and there is no consensus on the ideal treatment of adult AARF because of its rarity. We presented a case series of three adult AARFs and reviewed the literature on adult AARFs. We suggest treatment guidelines for the injury based on the literature review.

Methods: We compiled a series of three adult AARFs seen in our hospital. We also utilized the NCBI library to retrieve literature on adult AARF from 2000 to 2021. We included articles on adult AARF, which described the number of days from injury to diagnosis, Fielding classification, occurrence of associated cervical injuries, and details of treatment and the results.

Results: Thirty adult AARFs reports fulfilled the criteria and 32 patients were analyzed. Eighteen patients had Fielding Type 1 AARF and were diagnosed within 1 month of injury. Among them, 13 cases healed with conservative treatment. Patients with acute AARF of Fielding Type 1 who underwent manual reduction healed successfully. All patients that required more than 1 month from injury to diagnosis underwent surgery. All cases with AARF Fielding Types 2, 3, and 4 failed conservative treatment.

Conclusion: The case series and literature review suggest that early diagnosis of adult AARF is essential for successful closed reduction, and the Fielding classification may help determine treatment strategy. Furthermore, this study showed that not only traction but also manual reduction may be a useful treatment for early diagnosed AARF Fielding Type 1 without complications.

Level of Evidence: III

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INTRODUCTION

Atlantoaxial rotatory fixation (AARF) is defined as torticollis caused by atlantoaxial subluxation. Generally, AARF is common in children and is generally triggered by traumatic events or upper respiratory infections.[1] However, the occurrence of AARF is extremely rare in adults compared to children because of adult features such as well-developed musculature, decreased elasticity, and relative ankylosis of the joints caused by degenerative changes.[2] Moreover, diagnosis and treatment of the adult condition are often delayed because of its rarity, and delayed diagnosis of AARF decreases the success rate of closed reduction.[3] Furthermore, adult AARF is frequently caused by high-energy trauma, and patients can present with complications such as articular cartilage lesions, articular process fractures, or spinal cord lesions.[4,5] Therefore, surgical stabilization is recommended for AARF cases where closed reduction fails, there is a complicated cervical injury, or dislocation recurs.[5-8] However, there is no consensus on the ideal treatment of adult AARF due to the rarity of the condition. Therefore, the purpose of this study was to present a case series of three adult AARFs, review the literature on adult AARFs, and propose treatment guidelines for the injury.

METHODS

Literature Review

We utilized the NCBI library to retrieve literature on adult AARF, and we limited our search to those in English language from 2000 to 2021. Search terms and phrases included "atlantoaxial rotatory fixation," "adult and atlantoaxial rotatory fixation," "atlantoaxial rotatory dislocation," "adult and atlantoaxial rotatory dislocation," "atlantoaxial rotatory subluxation," and "adult and atlantoaxial rotatory subluxation." The obtained papers were screened by title and abstract. In addition, we selected studies that described adult AARF, including the number of days from injury to diagnosis, Fielding classification,[6] the occurrence of associated cervical injuries, details of treatment, and the results. Cases with unspecified details, children, infection, and rheumatoid arthritis were excluded.

Case Series

Three patients were diagnosed with adult AARF between January 2019 and December 2021 at Fukuchiyama city hospital (an emergency medical center in Japan).

Case 1

A healthy 23-year-old Japanese man was involved in a traffic accident while walking on a crosswalk where he was hit by a car—he fell head-first, hitting the ground. He was brought to our emergency department by an ambulance with a chief complaint of posterior neck pain. He was conscious, had no neurological deficits, and his head was in the "cock robin" position—it was rotated to the left and could not be moved from that position. Cervical spine computed tomography (CT) revealed that the atlas was rotated to the left without displacement between the anterior arch of the atlas and the dens of the axis (Figs. 1a and b).

The patient was diagnosed with Fielding Type 1 AARF without fractures. Manual manipulation was performed while the patient was awake by holding the patient's mandible to provide traction in the cephalic direction. This was done to ensure that the patient did not develop pain or palsy in the upper extremities. The mandible was further slowly rotated to the right to induce a feeling of reduction. Immediately after reduction, the cervical pain and cock robin positioning disappeared.

No neurological complications were observed. Subsequent CT and magnetic resonance imaging (MRI) confirmed anatomical reduction, intact transverse and alar ligaments, and no spinal cord lesions (Figs. 2a and b). Fixation was performed with a Philadelphia collar. A CT scan 3 weeks after the injury showed no recurrent dislocation, and the collar was subsequently removed. In addition, the patient had no cervical pain, limited range of neck motion, or neurological deficits at 2 year after the injury.

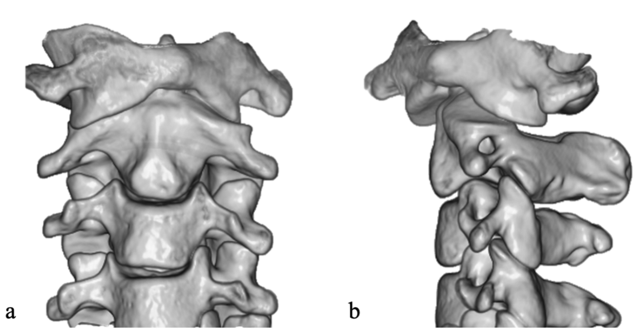

Figure 1A-1B. Three-dimensional computed tomography of case 1 shows adult atlantoaxial rotatory fixation of Fielding type 1.

Case 2

A 64-year-old Japanese man was involved in a traffic accident when he fell asleep while driving and crashed into a roadside tree. He was transported to our emergency department by an ambulance; his chief complaint was chest pain. The patient was disquiet and had no neurological deficits. A full-body CT showed bilateral hemothorax; therefore, the patient was intubated to insert chest drains. After intubation, the CT scan was rechecked—suspected abnormal alignment of the atlas and axis was observed; therefore, the emergency physician consulted us.

The patient's head was in the "cock robin" position rotated to the right (Fig. 3), and it was unclear whether he had posterior cervical pain because he was intubated and sedated. The CT revealed that the atlas was rotated to the right without displacement between the anterior

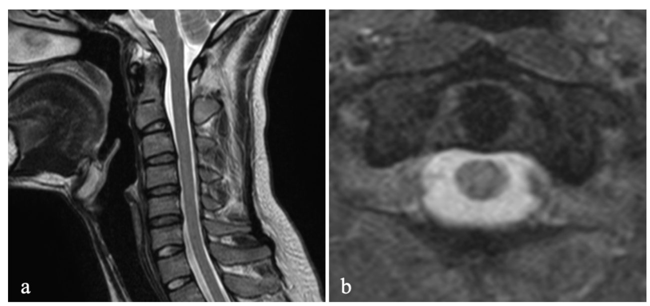

Figure 2A-2B. Post-reduction magnetic resonance imaging of case 1 shows intact transverse and alar ligaments and no spinal cord lesions. (2A) Sagittal view. (2B) Axial view of odontoid process.

Figure 3. The patient's photograph of case 2 shows cock robin position.

arch of the atlas and the dens of the axis (Figs. 4a and b). The patient was diagnosed with Fielding Type 1 AARF without fractures. Manual manipulation was performed under sedation, which involved holding the patient's mandible to provide traction in the cephalic direction, and then it was rotated slowly to the left to induce a feeling of reduction. Immediately after reduction, the cock robin position was resolved, and no neurological complications were observed. A subsequent CT and MRI confirmed anatomical reduction, intact transverse and alar ligaments, and no spinal cord lesions (Figs. 5a and b). Fixation using a Philadelphia collar was performed. A CT scan 3 weeks after the injury showed no recurrent dislocation, and the collar was subsequently removed. The patient had no cervical pain, limited range of neck motion, or neurological deficits at 15 months after the injury.

Case 3

A healthy 47-year-old Japanese man was involved in a traffic accident when he fell asleep while driving—he swerved onto oncoming traffic and collided head-on with an oncoming truck. He was brought to our emergency department by an ambulance. His chief complaints were posterior neck and abdominal pain. He was conscious and had no neurological deficits. His head was in the cock robin position rotated to the left, and he could not move it from this position. CT of the cervical spine revealed that the atlas was rotated to the left without displacement between the anterior arch of the atlas and the dens of the axis (Figs. 6a and b).

MRI confirmed that the transverse and alar ligaments were intact, and there were no spinal cord lesions. Moreover, a fracture was observed in the seventh cervical vertebral arch (Figs. 7a and b), and an abdominal CT showed mesenteric injury. Therefore, an emergency gastrointestinal surgery was performed. The case was diagnosed as Fielding Type 1 AARF with a seventh cervical vertebral arch fracture. Manual manipulation was not performed because the patient had a fracture complication in the other vertebra.

First, a Philadelphia collar was used for fixation. A CT scan 3 days after the injury showed that the dislocation had improved without complete reduction. Therefore, a halo vest was used for further fixation, and the patient's neck was immobilized in traction. A repeat CT scan confirmed that the atlantoaxial joint was adequately reduced. A CT scan 4 weeks after the injury showed no recurrent dislocation, and fixation using a Philadelphia collar was performed again. The collar was removed 12 weeks after the injury, and the patient had no cervical pain, limited range of neck motion, or neurological deficits at 1 year after the injury.

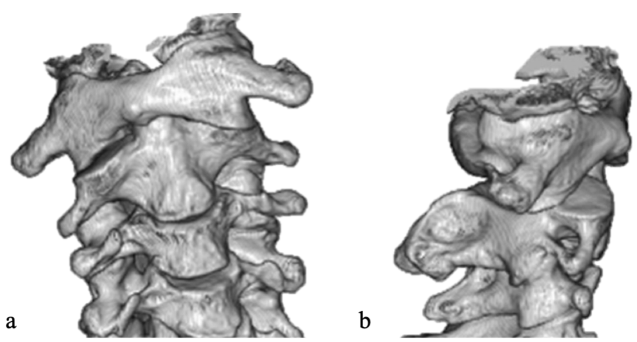

Figure 4A-4B. Three-dimensional computed tomography of case 2 shows adult atlantoaxial rotatory fixation of Fielding type 1.

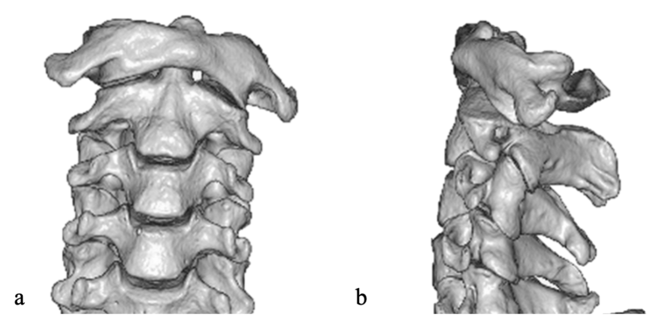

Figure 6A-6B. Three-dimensional computed tomography of case 3 shows adult atlantoaxial rotatory fixation of Fielding type 1.

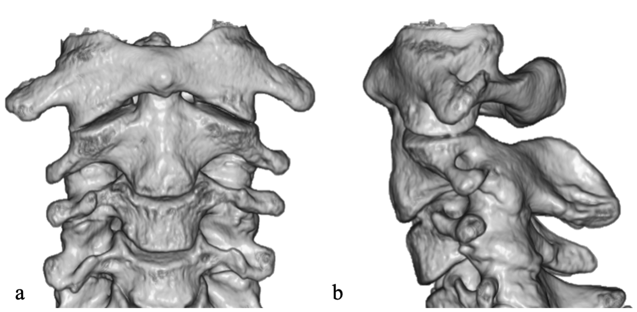

Figure 5A-5B. Post-reduction three-dimensional computed tomography of case 2 shows disappearance of C1-C2 subluxation.

Figure 7A-7B. Computed tomography of case 3 shows the seventh cervical vertebral arch fracture. (7A) Axial view. (2B) Sagittal view.

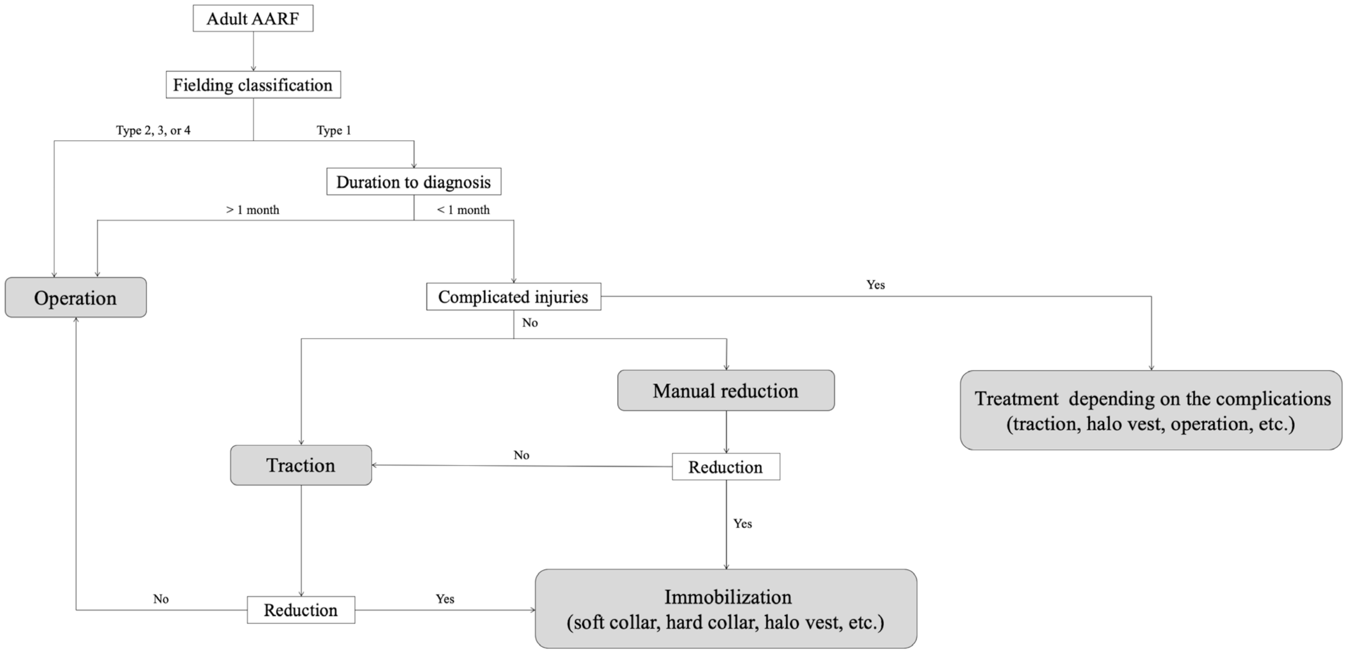

Figure 8. Treatment flowchart for adult atlantoaxial rotatory fixation.

RESULTS

A review of the literature on adult AARF is provided in Table 1.[2,4,5,7-33] From 2000 to 2021, 30 reports have shown the time from injury to diagnosis, imaging findings, treatment strategies and results for adult AARF. We analyzed 32 patients (14 males and 18 females; mean age: 36 years).

Eighteen patients had Fielding Type 1 AARF and were diagnosed within 1 month of injury.[4,8-23] Complications included epidural hematoma and C5/6 disc protrusion in one case[12] and C2 facet fracture in one case.[16] As for the initial treatment, one patient underwent C1-C2 posterior fusion,[13] and the remaining 17 cases were treated conservatively. Traction was performed in 10 cases,[8-11,14,19,20,22,23] and immobilization by hard collar was selected in two patients.[15,17] Five patients initially underwent manual reduction,[4,12,16,18,21] and three were treated with the procedure secondarily.[8,19,22] Thirteen of 17 cases healed with conservative treatment.[4,8-12,16-19,21,22] Three patients were treated surgically due to failed closed reduction by traction, the duration from injury to diagnosis was 0 days, 11 days, and 1 month, respectively.[14,20,23] One case underwent surgery because of worsening neck pain after successful closed reduction by immobilization.[15] After successful closed reduction, 12 patients underwent immobilization with a hard collar, soft collar or halo vest.[4,8-12,16-19,22] The remaining one case was not immobilized after manual reduction under general anesthesia.[21] Consequently, rotation limitation remained in two cases,[10,14] headaches remained in one patient,[10] and occipital neuralgia remained in one case.[10]

There were six cases with Fielding Type 1 AARF that took more than 1 month from injury to diagnosis.[2,24-27] All patients were initially treated with traction or manual reduction. Two cases succeeded in closed reduction; however, they underwent surgical treatment because of concerns about a high risk of recurrence with only neck orthosis.[26,27] The remaining four patients who failed in nonsurgical treatment were operated on with C1-C2 posterior fusion,[2,24,25] and the result was good in all cases.

There were three patients with AARF of Fielding Types 2,[28-30] two of Type 3,[31,32] and three of Type 4,[5,7,33] respectively. In addition, five cases were complicated by odontoid fracture, including all three Fielding Type 4 patients.[5,7,28,32,33] Five cases were treated nonoperatively; however, no cases were successfully treated regardless of the duration from injury to diagnosis.[5,7,28-30] All patients underwent surgery except for one case.[5,7,29-33] In addition, C1-C2 posterior fusion was performed in six cases,[5,7,29,30,32,33] and the remaining one patient was treated with occipitocervical fusion (C0-C3).[31] In one case, traction and halo vest was performed but failed; however, no additional treatment was given, and torticollis remained.[28]

Table 1. Summary of the Previous Studies Describing Adult AARF

Author	Age	Sex	Mechanism	Duration to diagnosis	Fielding type	Associated cervical injuries	First treatment	Reduction by conservative treatment	Following treatment	Duration of immobilization	Results
Singh, 2009[9]	25	F	MVA	0 day	1	None	A few days of Crutchfield skull traction	Succeeded	Halo vest	4 weeks	Good
Venkatesan, 2012[10]	20	F	MVA	0 day	1	None	4 days of skull traction	Succeeded	Hard collar	8 weeks	Headaches
	52	F	MVA	0 day	1	None	5 days of halo traction	Succeeded	Hard collar	8 weeks	• Occipital neuralgia • Rotation limitation
Hawi, 2016[11]	34	F	MVA	0 day	1	None	2 weeks of halo traction	Succeeded	Hard collar	6 weeks	Good
Meza, 2012[12]	19	F	MVA	0 day	1	• Epidural hematoma • C5/6 disc protrusion	Reduction by cautious rotation under traction	Succeeded	Soft collar	6 weeks	Good
Min Han, 2014[5]	22	M	MVA	0 day	1	None	Manual reduction while awake	Succeeded	Philadelphia collar	1 month	Good
Horsfall, 2020[13]	65	F	Fall down	0 day	1	None	C1-C2 posterior fusion	-	NA	NA	Good
Eghbal, 2018[14]	21	M	MVA	0 day	1	None	2 days of Gardner-Wells spinal traction and muscle relaxant	Failed	C1-C2 posterior fusion	NA	Rotation imitation
Marti, 2011[8]	24	F	Streching neck	1 day	1	None	Gardner-Wells spinal traction and closed reduction	Succeeded	Halo vest	3 months	Good
Ng, 2021[15]	28	F	MVA	2 days	1	None	Several days of hard collar	"Succeeded (worsening of neck pain)"	C1-C2 posterior fusion	NA	Good
Bellil, 2014[16]	56	F	MVA	3 days	1	C2 facet fracture	Manual reduction while awake	Succeeded	Halo vest	3 months	Good
Jeon, 2009[17]	25	F	MVA	5 days	1	None	A few hours of Philadelphia collar	Succeeded	Soft collar	6 weeks	Good
Greenberg, 2020[18]	38	F	Forceful move	5 days	1	None	Reduction at the bedside	Succeeded	Cervical collar	2 weeks	Good
Garcia-Pallero, 2019[19]	28	F	MVA	6 days	1	None	Cervical traction and manual reduction	Succeeded	Hard collar	16 weeks	Good
Eghbal, 2017[20]	35	M	Fall down	11 days	1	None	Gardner-Wells spinal traction	Failed	C1-C2 posterior fusion	NA	Good

Table 1. Summary of the Previous Studies Describing Adult AARF Continued

Isogai, 2021[21]	42	F	None	18 days	1	None	Closed reduction under general anesthesia	Succeeded	None	None	Good
Castel, 2001[22]	41	M	Rugby injury	1 month	1	None	10 days of skull traction follwed by manipulation	Succeeded	Minerva jacket	6 weeks	Good
Tarantino, 2014[23]	34	F	Epileptic seizure	1 month	1	None	Cervical traction, Philadelphia collar and muscle relaxant	Failed	C1-C2 posterior fusion	6 months of cervical collar	Good
Akiyama, 2020[24]	50	M	None	6 weeks	1	None	3 weeks of Glisson traction	Failed	C1-C2 posterior fusion	NA	Good
Singla, 2020[25]	25	M	MVA	1.5 month	1	None	Awake manipulation	Failed	C1-C2 posterior fusion	NA	Good
Rahimizadeh, 2019[3]	33	F	MVA	2 months	1	Cervical spine injury	2 weeks of neck traction and manipulation under anesthesia	Failed	C1-C2 posterior fusion	NA	Good
	56	M	MVA	3 months	1	None	3 days of Gardner-Wells spinal traction	Failed	C1-C2 posterior fusion	NA	Good
Elsissy, 2019[26]	30	M	Work-related accident	1 year	1	None	2 days of Gardner-Wells spinal traction and muscle relaxant	Succeeded	C1-C2 posterior fusion	NA	Good
Kia, 2020[27]	64	F	Stumble fall	2.5 years	1	None	2 days of halo traction	Succeeded	"C1-C2 posterior fusion (Considering the risk of recurrence)"	NA	Good
Oh, 2010[28]	37	M	Neck hit with falling brick	0 day	2	• Odontoid fracture • C2 facet fracture	2 days of skull traction follwoed by 3 months of halo vest	Failed	No additional treatment	-	Mild torticolis
Kim, 2007[29]	34	M	Fall down	1 day	2	C2 facet fracture	Skull traction followed by manipulation under general anesthesia	Failed	C1-C2 posterior fusion	8 weeks of Philadelphia collar	Good
Barimani, 2019[30]	66	F	Forceful move	2 weeks	2	None	1 week of head halter cervical traction and hard collar	Failed	C1-C2 posterior fusion	NA	Rotation limitation

Table 1. Summary of the Previous Studies Describing Adult AARF Continued

Maida, 2012[31]	27	M	MVA	few days	3	None	Occipitocervical fusion (C0-C3)	-	Philadelphia collar	60 days	Good
Gahlot, 2020[32]	47	M	Fall down	3 weeks	3	Odontoid fracture	C1-C2 posterior fusion	-	Hard collar	3 months	Good
Opoku-Darko, 2018[33]	20	F	MVA	0 day	4	• Odontoid fracture • Vertebral artery dissection	C1-C2 posterior fusion	-	NA	NA	Good
Goel, 2010[7]	28	M	Fall down	1 day	4	Odontoid fracture	Head traction	Failed	C1-C2 posterior fusion	NA	Good
Fuentes, 2001[6]	24	M	Fall down	1 month	4	Odontoid fracture	Traction and manipulation under general anesthesia	Failed	C1-C2 posterior fusion	3 months of Philadelphia collar	Good
case 1	23	M	MVA	0 day	1	none	Manual reduction while awake	Succeeded	Philadelphia collar	3 weeks	Good
case 2	64	M	MVA	0 day	1	none	Manual reduction under sedation	Succeeded	Philadelphia collar	3 weeks	Good
case 3	47	M	MVA	0 day	1	C7 arch fracture	3 days of Philadelphia collar followed by 4 weeks of halo vest	Succeeded	Philadelphia collar	8 weeks	Good

Case Series

In our case series, all three cases were injured with Fielding Type 1 AARF and were diagnosed on the day of injury. Cases 1 and 2 had no associated neck injuries and underwent manual reduction followed by 3 weeks of immobilization. In contrast, case 3 had the seventh cervical vertebral arch fracture and was treated with a hard collar followed by 4 weeks of halo vest. Closed reduction was successful in all cases with good results.

DISCUSSION

The results showed that early diagnosis of adult AARF is essential for successful closed reduction, and Fielding classification may help determine treatment strategy. Furthermore, the case series and literature review suggested that manual reduction may be a useful treatment for early diagnosed AARF Fielding Type 1 without complications.

AARF in adults is extremely rare and is frequently caused by high-energy trauma such as traffic accidents or falls.[4,9] However, such trauma may cause immediate death because of damage to the medulla or vertebral arteries.[2] Therefore, it is likely that very few adults survived high-energy trauma and suffered from AARF. Moreover, the rarity of the injury can cause delayed diagnosis. A previous study reported that chronic AARF, caused by delayed diagnosis and subsequent delayed management, is more refractory to conservative treatment than early diagnosed and treated AARF.[2] Our literature review revealed that all patients that required more than 1 month from injury to diagnosis underwent surgery. Moreover, our results suggested that early diagnosis of adult AARF is important as in the past reports. Furthermore, this study showed that adult AARF Fielding Types 2, 3, and 4 are refractory to conservative treatment. Therefore, even if diagnosed early, surgical treatment should be considered for Fielding Types 2, 3 and 4 AARF.

Fortunately, the patients described in this report survived the accidents, although they showed typical positions of painful torticollis with lateral neck flexion and contralateral rotation in the cock robin position. Furthermore, CT and MRI revealed Fielding Type I AARF in which the atlas was rotated with intact transverse and alar ligaments without displacement between the anterior arch of the atlas and the dens of the axis. Moreover, the clinical and imaging findings enabled an early diagnosis of AARF, which resulted in successful conservative treatment.

Manual reduction can be a useful treatment for early diagnosed AARF Fielding Type 1. Table 1 shows that the standard of conservative treatment is traction; however, there are several reports of manual reduction for AARF.[2,4,5,8,12,16,18,19,21,22,25,29] Among them, all acute AARF Fielding Type 1 were resolved successfully with manual reduction.[4,8,12,16,18,19,21,22] In addition, Han, Bellil, and Isogai described the detailed methods of manual reduction: holding the mandible, providing traction in the cephalic direction, and rotating it slowly to the opposite direction to that of the torticollis to obtain a feeling of reduction.[4,16,21] Moreover, several reports showed that they performed manual reduction with the patient awake to confirm that the patient did not develop pain or palsy in the upper extremities.[4,12,16]

The patients in cases 1 and 2 in this study presented with very acute cases of AARF without complications, including no fractures or neurological symptoms, and we attempted manual manipulation. Reduction was not possible in the awake state in case 2 because the patient was intubated. However, the patient in case 1 could be manually manipulated while awake; consequently, the patient was assessed to determine whether he developed neurological symptoms in the upper extremities. AARF Type 1 has no disruption or laxity of the transverse and alar ligaments. As such, we hypothesized that a satisfactory feeling of reduction was achieved, and the atlantoaxial vertebra regained strong ligamentous stability when the subluxated facet was reduced. In addition, we suspect that the rigid ligamentous stability improved neck pain and prevented recurrence.

However, there are only a few reports on manual manipulation, and their safety remains uncertain.[4,12,16,21] Fortunately, no reports described that patients who underwent manual reduction showed worsening of neurological deficits. However, Isogai suggested that manual manipulation should be avoided in adult AARF patients with neurological symptoms or complicated injuries.[21] The patient in case 3 not only had AARF but also experienced a seventh cervical vertebral arch fracture. Manual manipulation was contraindicated because of concerns of worsening neurological symptoms or fracture dislocation. Han recommended the performance of an awake manual reduction by experienced or appropriate surgeons in the right place as soon as possible.[4]

We suggest treatment strategies for adult AARF based on the review according to the following criteria: 1) surgical treatment should be performed for AARF that require more than 1 month for diagnosis or Fielding Types 2, 3, or 4 cases; 2) AARF associated with neurological symptoms or complicated injuries should be treated depending on the complications (traction, halo vest, surgery, etc.) and manual reduction should not be performed; 3) the standard treatment for acute AARF of Fielding Type 1 without associated neck injuries is traction; however, manual reduction can also be the treatment option; 4) If closed reduction is successful, immobilization is performed; if not, surgery should be performed (Figure 8). However, there is a need for further studies to test our findings in a large population.

CONCLUSION

AARF can occur in adults, and early diagnosis is important for successful conservative treatment. A patient complaining of posterior neck pain due to high-energy trauma should be considered to have AARF and assessed appropriately. Fielding classification, as well as the duration from injury to diagnosis, can be a factor in determining the treatment strategy. Moreover, manual reduction could be a useful treatment for early diagnosed AARF cases, although the indications for this procedure should be carefully determined and considered. Further study is required to determine treatment guidelines for the injury.

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RISK FACTORS FOR BLOOD TRANSFUSIONS IN ELECTIVE SINGLE-LEVEL ANTERIOR LUMBAR INTERBODY FUSION FOR DEGENERATIVE CONDITIONS

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ABSTRACT

Background: ALIF (anterior lumbar interbody fusion) and other spinal fusion surgeries are among the most common orthopaedic procedures requiring blood transfusions. However, blood transfusions have been associated with various complications, including adverse reactions and infections. The present study aims to identify independent risk factors for blood transfusions in patients undergoing single-level ALIF specifically to better identify high risk patients and optimize perioperative management.

Methods: All patients who had undergone single-level ALIF patients for the treatment of degenerative spinal conditions, excluding traumatic, pathologic, and infectious etiologies, were identified by querying a multi-institutional surgical registry from 2005 to 2018. Multi-level fusions, PLIF/TLIF, and posterior procedures were also excluded. Mann-Whitney-U-Tests were used to analyze continuous variables, while Fisher's-Exact-Tests/Bonferroni-Corrected-Tests were used for categorical variables. Multivariate logistic regression analysis with alternating backward stepwise elimination and forward entry was implemented to identify significant predictors for blood transfusions within 72 hours after incision. The predicted probabilities were used in post-regression diagnostics to generate a Receiver Operating Characteristic (ROC) curve to assess model performance.

Results: 4,792 single-level ALIF patients met inclusion criteria – 183 (3.82%) had received blood transfusions within 72 hours after incision and 4,609 (96.18%) had not. Age ≥60 years (OR 1.954, p<0.001), preoperative transfusions (OR 33.758, p=0.023), extended operative times (≥197.0 minutes; 75th percentile) (OR 4.645, p<0.001), ASA≥3 (OR 1.395, p<0.001) and preoperative hematocrit levels (Hct) 30.00-37.99 (OR 1.562, p=0.016) and Hct <30.00 (OR 6.334, p<0.001) were shown to be significant independent risk factors for perioperative blood transfusions. The area under the ROC curve (AUROC; C-statistic) was 0.759 (p<0.001), indicating relatively strong discriminatory ability/predictability of the final model.

Conclusion: Several independent risk factors including age ≥60 years, preoperative blood transfusions and extended operative times increased risk for blood transfusion following single-level ALIF. The present study aims to help surgeons identify high-risk patients to better communicate postoperative expectations and optimize patients to reduce the risk of transfusions and secondary complications.

Level of Evidence: III

Keywords: ALIF, transfusion, complications, outcomes, risk factors

INTRODUCTION

Anterior lumbar interbody fusion (ALIF) is widely viewed as an effective surgical option for patients experiencing pain or neurologic dysfunction due to degenerative disc disease (DDD), spondylolisthesis, pseudarthrosis, sagittal malalignment, and lumbar lateral listhesis.[1-6] The ALIF approach to the lumbar spine pro-

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vides several advantages compared to other approaches, such as the posterior lumbar interbody fusion (PLIF) or transforaminal lumbar interbody fusion (TLIF). In many cases, ALIF is superior to PLIF and TLIF in restoring disc/foraminal height, potentially contributing to greater nerve decompression depending on the underlying pathology. The anterior approach also provides greater visualization of the intervertebral disc space during the operation and allows for preservation of posterior spinal musculature.[7,8] Despite these advantages, ALIF carries unique risks not typically associated with PLIF or TLIF. As the lumbar spine is accessed through the abdomen or retroperitoneal space, risks for visceral injury, vascular injury, sympathetic dysfunction, and retrograde ejaculation must be taken into careful consideration.[5,9] Additionally, there is risk for postoperative anemia inherent to ALIF, with sources of bleeding including the soft tissues, vertebral endplates, and in rare cases, injury to the great vessels.

Blood transfusions in spine surgery have been the focus of many studies and quality improvement initiatives, as spinal fusion has been recognized as among the top ten surgical cases that result in blood transfusion.[10-13] Such transfusions have been associated with an increased risk for infection in patients following spine surgery.[14] High rates of transfusion in spine surgery patients have also been associated with increased length of stay and higher rates of perioperative morbidity.[11] Furthermore, blood transfusions incur increased costs, as each unit of red blood cells (RBCs) can cost from $700-1,200, with additional costs for the treatment of transfusion-related complications.[13,15] Previous reports in the literature have examined factors that predict blood transfusion requirements in spine surgery overall, for a wide variety of indications.[16,17] However, to the authors' knowledge, there are no reports in the literature on risk factors for blood transfusion in single-level ALIF for specifically degenerative indications (i.e. degenerative spondylolisthesis, DDD, etc.). Furthermore, few of these studies have considered the specific indication for the ALIF performed.[16,17] It is important to identify the existence of potential risk factors for blood transfusions in efforts to mitigate their incidence and associated complications. As ALIF can be performed for other etiologies including traumatic, infectious, or oncologic, identifying a specific subset of patient populations is imperative to guide pre-operative discussions and risk assessments most accurately. Given the inherent risk for blood loss during ALIF, the present study aims to identify independent risk factors for blood transfusion in patients undergoing single-level ALIF for degenerative conditions to optimize perioperative management and better risk-stratify patients prior to surgical intervention.

METHODS

Patient Selection

The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database was queried to identify all patients who had undergone single-level anterior lumbar interbody fusions (ALIF) from 2005 to 2018 by Current Procedure Terminology (CPT) codes.[18] Patients with CPT code 22558 were included in this study, while patients with other or concurrent CPT codes 22585 (multi-level ALIFs), 22630 (PLIF/TLIF), 22612 (posterior fusion), and 22840 (posterior spinal instrumentation) were excluded. Patients were further isolated and selected for by ICD-9 and ICD-10 codes corresponding to degenerative conditions, excluding traumatic, infectious, pathologic etiologies (Supplemental Table A). Patients with missing demographic and preoperative comorbidity data were also filtered–428 patients were further excluded for emergent status or missing values in their age, BMI, gender, ASA classification, operative times, or preoperative hematocrit levels. After all inclusion/exclusion criteria were applied, a total of 4,792 patients who underwent elective single-level ALIF were stratified into two separate cohorts: control (no blood transfusion; n=4609, 96.18%) and those who received transfusions within 72 hours after incision (n=183, 3.82%). The current study met exemption criteria for IRB review approval as it utilized a publicly available, de-identified database.

Variables

The outcome of interest, "intra/postoperative blood transfusions" was defined by the ACS-NSQIP as, "At least 1 unit of packed or whole red blood cells given from the surgical start time at incision up to and including 72 hours postoperatively. If the patient received shed blood, autologous blood, cell saver blood or pleurovac postoperatively, this was counted in terms of equivalent units for the sake of this variable. For a cell saver, every 500 mL of fluid was equal to 1 unit of packed cells. If there are less than 250 ml of cell saver, round down and report as 0 units. If there are 250 cc, or more of cell saver, round up to 1 unit. The blood may be given for any reason."[19-21]

Patient demographics, such as age, gender, and body mass index (BMI) data, and preoperative comorbidities were analyzed to better characterize the patient cohort. Preoperative blood transfusions were defined as, "Preoperative loss of blood necessitating any transfusion (minimum of 1 unit) of whole blood/packed red cells transfused during the 72 hours prior to surgery start time, including any blood transfused in the emergency room."[20] Perioperative variables such as type of anesthesia, American Society of Anesthesiologists (ASA) classification, operative times, and total length of hospital stay were also included. Extended operative times (≥197.0 min) were defined as those in the first quartile of the cohort for reported procedure duration. Patients were stratified by preoperative hematocrit (Hct) levels according to previously published studies by Almeida et al. in 2020 as: normal (Hct 38.00+), mild anemia (Hct 30.00-37.99), and moderate-severe anemia (Hct<30.00).[22,23]

Statistical Analysis

The current study sought to analyze differences in patient demographic features and preoperative comorbidities between the transfused and non-transfused cohorts. Pearson's chi-squared tests and Fisher's exact tests were implemented for categorical variables, while Mann-Whitney-U-Tests were used for continuous variables, such as age and time parameters.

In identifying predictors for perioperative blood transfusions, the current study implemented multivariate logistic regression analysis with alternating backward stepwise elimination and forward entry (entry: 0.05; removal: 0.10). The remaining variables were entered into the final multivariate logistic regression model to identify significant predictors for blood transfusions while controlling for demographic features and comorbidities. The predicted probabilities given by the logistic regression model were used to generate a receiver operating characteristic (ROC) curve to assess the discriminatory ability of the regression model in assigning patients into the transfused or non-transfused cohorts based on the controlled variables. Post-regression diagnostics were assessed using the area under the ROC curve (AUROC), reported as the C-statistic.

All statistical findings with p-values less than or equal to 0.05 were considered significant in this analysis. All statistical analyses were performed using the IBM SPSS® Statistics Version 25 software (IBM Corporation, Armonk, NY) and R© Version 3.3.3.

RESULTS

A total of 4,792 patients who had undergone single-level ALIF from 2005 to 2018 met inclusion criteria for this study, of which 183 (3.82%) had received blood transfusions within 72 hours after incision and 4,609 (96.18%) patients in the control cohort had not. The transfused cohort was significantly older ($\bar{x}$=61.22 years ± 12.481) than the control cohort ($\bar{x}$=54.14 years ± 13.563; p<0.001). A larger proportion of the transfused cohort (59.56%) was 60 years or older than the control cohort (36.43%; p<0.001). The transfused cohort was comprised of more female patients, though not significant (59.34% vs. 51.03%; p=0.128) and those who self-identified as Asian or Pacific Islander (4.37% vs. 1.13%; p<0.05) in comparison to the control cohort. No significant differences were observed in mean BMI (p=0.098) or when stratified by classes of obesity (p=0.113; Table 1).

Those receiving blood transfusions presented with significantly higher rates of preoperative diabetes mellitus (p=0.028), insulin-dependent diabetes mellitus (p<0.05), dyspnea (p=0.030), hypertension requiring medication management (p=0.003), hematologic disorders (p=0.035), and preoperative blood transfusions (within 72 hours before the start of surgery) (p<0.001). (Table 1). The transfused cohort demonstrated greater rates of ASA ≥ 3 (p<0.001) and consisted of a larger proportion of cases with extended operative times, considered to be 197.0 min (75th percentile) or longer in length (59.56% vs. 23.26%; p<0.001). In comparing mean operative times, those requiring blood transfusions had significantly longer mean operative times ($\bar{x}$=273.13 min ± 161.620; p<0.001) than those in the control cohort ($\bar{x}$=149.81 min ± 90.605). No significant differences were noted in the type of anesthesia administered, with most undergoing general anesthesia (p=0.597; Table 2). There was a significant difference noted in the mean preoperative hematocrit levels between the two cohorts, with the transfused cohort demonstrating a significantly smaller mean hematocrit level ($\bar{x}$=39.19 ± 5.367) than the non-transfused cohort ($\bar{x}$=41.50 ± 4.228; p<0.001). A significantly larger proportion of the transfused cohort was considered anemic according to preoperative hematocrit levels (Hct < 38.00; 33.88%) in comparison to the cohort who was not transfused (17.70%, respectively; p<0.001; Table 2).

Multivariate logistic regression analyses with alternating backward stepwise elimination and forward entry identified several factors associated with the incidence of blood transfusion. Age ≥60 years (Odds Ratio [OR] 1.954, 95% Confidence Interval [CI] 1.396-2.734; p<0.001), preoperative blood transfusions (OR 33.758, 95% CI 1.629-699.403; p=0.023), extended operative times (≥ 197.0 minutes) (OR 4.645, 95% CI 3.403-6.340; p<0.001), ASA ≥ 3 (OR 1.395, 95% CI 1.000-1.947; p=0.050), mild anemia (Hct 30.00-37.99; OR 1.562, 95% CI 1.085-2.249; p=0.016), and moderate-severe anemia (Hct <30.00; OR 6.334, 95% CI 2.737-14.661; p<0.001) were shown to be significant independent risk factors for intraoperative/postoperative blood transfusions within 72 hours after incision (Table 3). The area under the ROC curve (AUROC) (C-statistic) was 0.759 (95% CI 0.722-0.796; p<0.001), indicating relatively strong discriminatory ability and predictability of the logistic regression model (Figure 1).

Table 1. DEMOGRAPHICS and COMORBIDITIES in Transfused vs. Non-Transfused Patients

	No Transfusions (n=4609)		Transfused (n=183)		P-Value
DEMOGRAPHICS					
Age (Mean ± SD)[a]	54.14 ± 13.563		61.22 ± 12.481		<0.001#
Age Categories (years)					<0.001
x < 40.00	722	15.67%	12	6.56%	*
40.00-49.99	1020	22.13%	19	10.38%	*
50.00-59.99	1188	25.78%	43	23.50%	
60.00-69.99	1020	22.13%	59	32.24%	*
x ≥ 70.00	659	14.30%	50	27.32%	*
Gender					0.128
Female	2456	53.29%	108	59.02%	
Male	2153	46.71%	75	40.98%	
Race/Ethnicity					0.006
American Indian/Alaska Native	16	0.35%	0	0.00%	
Asian/Pacific Islander	52	1.13%	8	4.37%	*
Black/African American	384	8.33%	12	6.56%	
Hispanic	5	0.11%	0	0.00%	
White/Caucasian	3920	85.05%	154	84.15%	
Other	232	5.03%	9	4.92%	
Body Mass Index (kg/m^2) (Mean ± SD)[a]	30.17 ± 6.197	29.44 ± 6.206	0.098		
Body Mass Index (kg/m^2)					0.113
Normal	925	20.07%	50	27.32%	
Overweight	1554	33.72%	55	30.05%	
Class I Obese	1225	26.58%	46	25.14%	
Class II Obese	603	13.08%	25	13.66%	
Class III Obese	302	6.55%	7	3.83%	
PRE-OPERATIVE COMORBIDITIES					
Diabetes Mellitus	620	13.45%	35	19.13%	0.028*
Diabetic Status					0.001
No Diabetes Mellitus	3989	86.55%	148	80.87%	*
Non-Insulin Dependent	434	9.42%	17	9.29%	
Insulin Dependent	186	4.04%	18	9.84%	*
Smoking History	1109	24.06%	33	18.03%	0.060
Dyspnea	198	4.30%	14	7.65%	0.030*
Ventilator Dependence	1	0.02%	0	0.00%	1.000
COPD	173	3.75%	12	6.56%	0.054
Ascites	3	0.07%	0	0.00%	1.000
Congestive Heart Failure	10	0.22%	0	0.00%	1.000
Hypertension	2023	43.89%	101	55.19%	0.003*
Acute Renal Failure	0	0.00%	0	0.00%	-
Dialysis	7	0.15%	0	0.00%	1.000
Disseminated Cancer	5	0.11%	0	0.00%	1.000

Table 1. DEMOGRAPHICS and COMORBIDITIES in Transfused vs. Non-Transfused Patients (Continued)

Wound Infection	10	0.22%	0	0.00%	1.000
Chronic Steroid Use	134	2.91%	6	3.28%	0.770
Weight Loss	10	0.22%	2	1.09%	0.074
Bleeding Disorders	43	0.93%	5	2.73%	0.035*
Preoperative Transfusions	1	0.02%	3	1.64%	<0.001*
Systemic Sepsis	17	0.37%	2	1.09%	0.163
Functional Status					0.073
Independent	4538	98.46%	177	96.72%	
Partially/Totally Dependent	71	1.54%	6	3.28%	

COPD: Chronic obstructive pulmonary disease.
[a] Values expressed as Mean ± Standard Deviation (SD); all other values expressed as (%) and N.
* Significant on Bonferroni comparison of proportions tests ($p<0.05$); # Significant on Mann-Whitney U-Test.

Table 2. PERIOPERATIVE VARIABLES in Transfused vs. Non-Transfused Cohorts

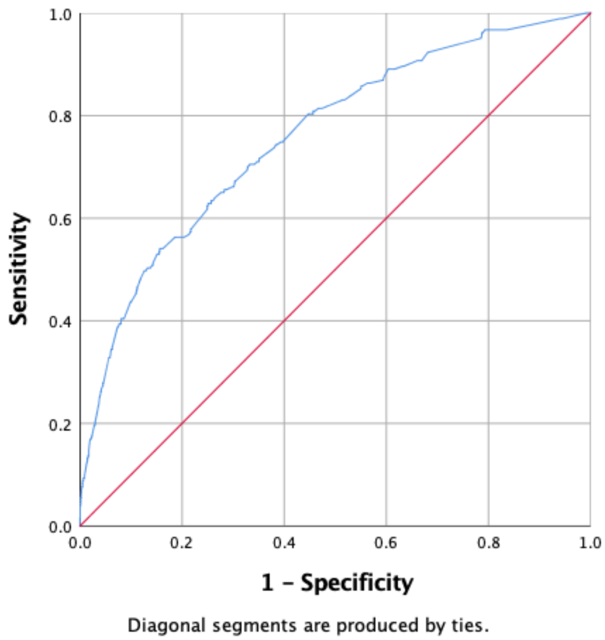
	No Transfusions (n=4609)		Transfused (n=183)		
PERIOPERATIVE VARIABLES					
Anesthesia Administered					0.597
General	4596	99.72%	182	99.45%	
Epidural/Spinal	3	0.07%	0	0.00%	
Local/Regional/Other	7	0.15%	1	0.55%	
MAC/IV Sedation	3	0.07%	0	0.00%	
ASA Classification					<0.001
1- No Disturb	232	5.03%	3	1.64%	*
2- Mild Disturb	2693	58.43%	81	44.26%	*
3- Severe Disturb	1623	35.21%	96	52.46%	*
4- Life Threat	61	1.32%	3	1.64%	
Operative Time (min) (Mean ± SD)[a]	149.81 ± 90.605	273.13 ± 161.620	<0.001#		0.006
Extended Operative Time (75th Percentile)					<0.001
x < 197.0 min.	3537	76.74%	74	40.44%	*
x ≥ 197.0 min.	1072	23.26%	109	59.56%	*
Preoperative Hematocrit (Mean ± SD)[a]	41.50 ± 4.228	39.19 ± 5.367	<0.001#	0.00%	
Anemia by Preoperative Hematocrit					<0.001
Normal (38.00+)	3793	82.30%	121	66.12%	*
Mild anemia (30.00-37.99)	784	17.01%	53	28.96%	*
Moderate to Severe Anemia (<30.00)	32	0.69%	9	4.92%	*

MAC: Monitored Anesthesia Care; IV: Intravenous; ASA: American Society of Anesthesiologists.
[a] Values expressed as Mean ± Standard Deviation (SD); all other values expressed as (%) and N.
* Significant on Bonferroni comparison of proportions tests ($p<0.05$); # Significant on Mann-Whitney U-Test.

Table 3. Risk Factors for Blood Transfusions in Single-Level ALIF Patients

RISK FACTORS	Odds Ratio	95% CI		P-Value
Age				
<60 years	Reference	-	-	-
≥60 years	1.954	1.396	2.734	<0.001
Sex				
Male	Reference	-	-	-
Female	1.207	0.873	1.671	0.256
Diabetes Mellitus				
No Diabetes Mellitus	Reference	-	-	-
NIDDM	0.634	0.370	1.085	0.097
IDDM	1.496	0.850	2.633	0.163
Smoking History	0.879	0.583	1.325	0.539
Dyspnea	1.372	0.745	2.528	0.310
COPD	1.181	0.611	2.285	0.621
Significant Weight Loss	3.510	0.678	18.175	0.134
Hematologic Disorders	2.185	0.816	5.852	0.120
Preoperative Transfusion (72 hr preop.)	33.758	1.629	699.403	0.023
Operation Duration (min)				
x < 197 min.	Reference	-	-	-
x ≥ 197 min.	4.645	3.403	6.340	<0.001
ASA Classification				
ASA 1 or 2	Reference	-	-	-
ASA 3 or 4	1.395	1.000	1.947	0.050
Anemia by Preoperative Hematocrit				
Normal (38.00+)	Reference	-	-	-
Mild anemia (30.00-37.99)	1.562	1.085	2.249	0.016
Moderate to Severe Anemia (<30.00)	6.334	2.737	14.661	<0.001

ALIF: Anterior Lumbar Interbody Fusion; CI: Confidence Interval; NIDDM: Non-insulin-dependent diabetes mellitus; IDDM: Insulin-dependent diabetes mellitus; COPD: Chronic obstructive pulmonary disease; ASA: American Society of Anesthesiologists.



AUROC	Std. Error	Significance	95% Confidence Interval	
0.759	0.019	**<0.001**	0.722	0.796
ROC: Receiver Operating Characteristic Curve; ALIF: Anterior Lumbar Interbody Fusion; AUROC: Area Under ROC Curve				

Figure 1. ROC Curve Assessing Multivariate Logistic Regression Model for Blood Transfusions in Single-Level ALIF.

DISCUSSION

Spinal fusion surgeries are among the most common orthopaedic procedures that require blood transfusions.[10-13] Blood transfusions are not without risk, as they have been associated with increased incidence of various adverse events in orthopaedic surgery including, but not limited to, infections, extended hospital length of stay, and increased overall perioperative morbidity.[11,13-15,24] Varshneya et al. had previously reported an annual increase of 24.1% in the incidence of ALIF procedures over eight years by analyzing a large-scale national database.[25] Given the increasing number of ALIF procedures being performed, it is essential to identify risk factors for blood transfusion in single-level ALIF in order to better guide perioperative management of these patients. At present, there is a paucity of data examining independent risk factors for blood transfusion in single-level ALIF, specifically for the treatment of degenerative pathologies. Using a large national database, our study found that age ≥60 years, preoperative blood transfusions, extended operative times (≥197.0 min), and ASA ≥ 3 were all independently associated with an increased risk for blood transfusion during or after ALIF. While some may present as non-modifiable risk factors, the current study presents important considerations for surgeons in patient counseling, preoperative optimization, and the postoperative management of patients undergoing single-level ALIF. While the current study reported an intra-/postoperative transfusion rate of 3.82%, lower than the 7.6% previously reported by Shillingford et al. in 2018 or 10.2% reported by Choy et al. in 2017, our study aimed to analyze a very specific subset of relatively healthy patients undergoing an elective, single level ALIF for the treatment of degenerative disease.[9,26]

Consistent with the orthopaedic literature, the present study identified increasing age, specifically ≥60 years, as an independent risk factor for blood transfusion needs in the intraoperative and immediate postoperative period following single-level ALIF. Elderly patients have previously been identified to be at increased risk for blood transfusions in multiple orthopaedic procedures, including total hip arthroplasty and total knee arthroplasty.[27-33] Berenholtz et al. had previously reported older age to increase the risk for allogeneic blood transfusions in spinal procedures.[34] Although unclear and likely multifactorial in etiology, this observation may likely be explained by the decreased rate of hematopoiesis within the bone marrow with increased age, potentially resulting in decreased preoperative and postoperative levels of RBCs.[28-30,35] In addition, the elderly population is thought to have a diminished overall physiologic reserve. Thus, clinicians typically utilize higher hemoglobin/hematocrit trigger points for initiating transfusion in these patients, as restrictive trigger points in the elderly have been associated with increased risk for morbidity and mortality.[31,36]

Prolonged operative time in major orthopedic procedures, including appendicular arthroplasty and lumbar spine surgery, has been associated with increased blood loss and a subsequent need for blood transfusion, and the current body of literature corroborates our findings demonstrating extended operative times (≥197.0 min), defined as those in the first quartile, to be independently associated with increased risk for perioperative blood transfusions. This finding is expected, as longer operative times would conceivably allow for more bleeding to occur within the surgical field. Furthermore, longer operative times may characterize more complex cases potentially with intraoperative complications, which may further increase the risk for blood loss. This is especially highlighted in the present report as the transfused cohort experienced on average two hours of additional operative time compared to the non-transfused cohort. (Table 2) While both cohorts experienced longer mean operative times than previously reported in the literature ranging from an average of 79 min reported by Mobbs 2016, they were closer to the previously reported 75th percentile of 247 minutes reported in a retrospective study of 1474 single-level ALIF patients by Choy et al. in 2017.[9,37] Intraoperative management of patients' coagulopathies with tranexamic acid (TXA) have previously been shown to mitigate blood loss in extended spine surgery cases. A recent meta-analysis by Lin et al. in 2022 demonstrated TXA to be a safe and effective treatment option to reduce intraoperative blood loss and transfusion rates (RR 0.41, $p<0.001$) in patients undergoing posterior lumbar interbody fusion (PLIF).[38] Clinical situations presenting indications for other blood products such as fresh frozen plasma (FFP) or cryoprecipitate in a patient with end stage renal disease may significantly impact patient outcomes. While the ACS-NSQIP database is limited in providing further information about intraoperative and perioperative bleeding, the increased risk seen with extended operative times further underscores the importance of streamlining care and expediting surgical processes in a safe and efficient manner to help mitigate the risk for transfusions and further morbidity in ALIF. Recently, enhanced recovery after surgery (ERAS) pathway protocols have been developed in spine surgery with the purpose of systematically streamlining care, reducing the rates of complications, and improving postoperative outcomes without compromising patient safety. These pathways have been shown to yield substantial benefits in various quality-driven metrics and patient-reported outcomes.[39-41] While ERAS pathways have not been developed for ALIF specifically, the standardization and implementation of such pathways for ALIF may improve operative efficiency and procedural workflow to reduce total procedure time and risk for blood transfusion needs. Future work examining the efficacy of ERAS pathway protocols on decreasing the risk for blood transfusions in ALIF specifically may serve to mitigate these risks.

Our analysis found several other independent risk factors for blood transfusion following single-level ALIF for degenerative conditions, including preoperative blood transfusions and higher ASA classification (> 3). Patients who had preoperative blood transfusions would conceivably be at a greater risk for needing one during or immediately after the procedure. This is further supported in the present report as the transfused cohort had significantly lower preoperative hematocrit levels compared to the non-transfused cohort. (Table 2) Our findings are in line with the current literature as numerous studies have previously established low preoperative hematocrit levels to be independently associated with perioperative blood transfusions in other spine procedures.[9,42,43] Those requiring preoperative transfusions were most likely transfused given their lower preoperative hematocrit levels. These patients may have presented with underlying chronic conditions that resulted in anemic states that contributed to lower hematocrit values that ultimately required transfusions. Finally, higher ASA class has been previously shown to be associated with an increased need for RBC transfusion in posterior lumbar fusion.[13] Higher ASA class may indicate worse overall health due to underlying disease processes that may compromise physiologic reserve or alter the coagulation cascade, and while the present study utilized robust logistic regression analyses to identify significant predictors for transfusions, the variables provided by the ACS-NSQIP database do not capture the entirety of each patient's medical history, highlighting a limitation in the granularity of information provided by large-scale databases.

There are various strengths to the present report. In this study, we sought to identify independent risk factors for increased perioperative blood transfusion requirements in a specific subset of patients who are generally healthy undergoing elective single-level ALIF, specifically for the treatment of degenerative spinal conditions. The identified preoperative hematocrit levels in this study present values that surgeons should take into consideration in optimizing patients for outpatient surgery. Preoperative hematocrit levels between 30 and 38 increased risk for need for intraoperative blood transfusion by ~56%, while preoperative hematocrit levels of less than 38 increased patients' risk more than six times that of a normal, non-anemic patient. Lower risk surgical candidates may have a higher threshold for preoperative transfusion needs; however, these results come with the understanding that as hematocrit levels drop closer to 30, patients are at an increased risk of 633%. By understanding patients' complete medical histories, etiologies for acute and/or chronic anemia, and their predicted need for intraoperative transfusions, surgeons may better optimize their patients' perioperative care and better counsel them on their risk associated with surgery. These values are consistent with the previously reported literature by Almeida et al. in 2020, reporting increased risk for morbidity specifically in geriatric patients undergoing spinal procedures.[22] Future randomized trials with specific parameters may be warranted to provide further clarification on and better lineate specific perioperative transfusion thresholds in single-level ALIF patients.

While the large sample size from a national database provides in-depth analyses with adequate power, the present study is not without limitations, including those inherent to all retrospective studies where inaccuracies in data collection and inputting may exert undue confounding influence on subsequent analyses. However, collaborators have bolstered the reliability of the ACS-NSQIP database, assessing the database for accuracy and providing insight into the vigorous data-collection process.[44,45] Those with missing information regarding demographics and comorbidities were excluded to mitigate the confounding effects posed by missing data. While the exclusion of these patients may have included some patients who had received transfusions, the authors felt it was important to reduce the confounding effects posed by missing information, given the relatively large sample size with complete information. In addition, the use of CPT codes (originally designed for insurance reimbursement claims rather than research purposes) in the present study could not control for the potential influence exerted by financial incentives or miscoding.[46] Further, the ACS-NSQIP does not record the specific spinal level at which the ALIF procedure was performed. This may represent another confounding variable, as the risk of major vascular injury and subsequent blood transfusion is partially dependent on the normal anatomy at each lumbar level at which ALIF is performed. Another limitation presented in this retrospective study centers around the lack of estimated blood loss for each patient, as well as the lack of data on the specific indication for transfusion. Estimated blood loss for a patient requiring one unit for extended operative time may differ significantly from that resulting from a vascular injury intraoperatively. However, while this inability to clearly delineate the specific indication for transfusion presents as a limitation, by selecting specifically for elective cases with postoperative diagnoses related to degenerative spinal conditions, the authors present a relatively reliable model identifying significant predictors for intraoperative transfusions. Limitations presented by a large-scale national database such as the ACS-NSQIP also include details on patients' perioperative care related to their transfusions (i.e. autologous transfusions from cell saver devices or preoperative stored blood).

CONCLUSION

As the first study to report on risk factors for blood transfusion following single-level ALIF for degenerative conditions, this analysis found that age ≥60 years, preoperative blood transfusions, extended operative times (≥197.0 min), ASA ≥ 3, and hematocrit levels < 38 were all independently associated with peri-/postoperative blood transfusion. By identifying these predictors, surgeons can better counsel patients prior to surgery, identify patients at higher risk for blood transfusions, and optimize surgical management of these patients appropriately.

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THE IMPACT OF ISOLATED PREOPERATIVE CANNABIS USE ON OUTCOMES FOLLOWING CERVICAL SPINAL FUSION: A PROPENSITY SCORE-MATCHED ANALYSIS

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ABSTRACT

Background: Cannabis is the most commonly used recreational drug in the USA. Studies evaluating cannabis use and its impact on outcomes following cervical spinal fusion (CF) are limited. This study sought to assess the impact of isolated (exclusive) cannabis use on postoperative outcomes following CF by analyzing outcomes like complications, readmissions, and revisions.

Methods: The New York Statewide Planning and Research Cooperative System (SPARCS) was queried for patients who underwent CF between January 2009 and September 2013. Inclusion criteria were age ≥18 years and either a minimum 90-day (for complications and readmissions) or 2-year (for revisions) follow-up surveillance. Patients with systemic disease, osteomyelitis, cancer, trauma, and concomitant substance or polysubstance abuse/dependence were excluded. Patients with a preoperative International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM) diagnosis of isolated cannabis abuse (Cannabis) or dependence were identified. The primary outcome measures were 90-day complications, 90-day readmissions, and two-year revisions following CF. Cannabis patients were 1:1 propensity score-matched by age, gender, race, Deyo score, surgical approach, and tobacco use to non-cannabis users and compared for outcomes. Multivariate binary stepwise logistic regression models identified independent predictors of outcomes.

Results: 432 patients (n=216 each) with comparable age, sex, Deyo scores, tobacco use, and distribution of anterior or posterior surgical approaches were identified (all p>0.05). Cannabis patients were predominantly Black (27.8% vs. 12.0%), primarily utilized Medicaid (29.6% vs. 12.5%), and had longer LOS (3.0 vs. 1.9 days), all p≤0.001. Both cohorts experienced comparable rates of 90-day medical and surgical, as well as overall complications (5.6% vs. 3.7%) and two-year revisions (4.2% vs. 2.8%, p=0.430), but isolated cannabis patients had higher 90-day readmission rates (11.6% vs. 6.0%, p=0.042). Isolated cannabis use independently predicted 90-day readmission (Odds Ratio=2.0), but did not predict any 90-day complications or two year revisions (all p>0.05).

Conclusion: Isolated baseline cannabis dependence/abuse was associated with increased risk of 90-day readmission following CF. Further investigation of the physiologic impact of cannabis on musculoskeletal patients may elucidate significant contributory factors.

Level of Evidence: III

Keywords: Cannabis, marijuana, cervical spinal fusion, outcomes

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INTRODUCTION

Cannabis is currently the third most commonly used psychoactive substance worldwide, following alcohol and tobacco. Globally, cannabis use disorder is the most common drug use disorder with 22.1 million cases estimated in 2016.[1] As of May 2021, a total of 36 states and four territories have initiated medical marijuana programs, with 18 states having legalized it for nonmedical use. The prevalence of patients diagnosed during an inpatient stay with cannabis use disorder has continued to rise in recent decades, with an increase from 0.52% to 1.34% between 2002 and 2011.[2] Such expansion may stem from the utilization of cannabis in various medical fields and/or from the easier accessibility to this substance. Cannabis-based medications have demonstrated clinical benefits for sleep disturbances, chemotherapy-associated nausea and vomiting, chronic pain, and multiple sclerosis management.[3] However, various adverse events have been observed, including cardiovascular accidents and strokes.[4-8]

Cervical spinal fusion is a common orthopaedic procedure, most often indicated for degenerative disk disease, cervical spondylosis, and symptomatic cervical spinal stenosis.[9] Rates of cervical fusion have been steadily increasing in recent decades.[9] The rates of complications after cervical fusion depend on surgical approach, with anterior cervical fusion associated with the lowest risk of complications, followed by posterior, and then combined. Previous studies have found the most common postoperative complications to be respiratory, dysphagia, sepsis, and major bleed, with older age being an independent risk factor for such complications.[9,10]

Public opinion regarding cannabis use is evolving, and the literature on the impact of cannabis consumption in orthopaedic surgery is scarce and inconclusive. One study has documented a high prevalence of marijuana use in total joint patients and its resulting postoperative complications.[11] Cannabis has also been associated with lower bone mineral density and increased risk of fracture.[12] A study by Moon et al.[8] using the National Inpatient Sample (NIS) found that among 9.5 million orthopaedic postoperative patients, the use of marijuana was associated with reduced postoperative mortality after total hip, knee, and shoulder arthroplasty and traumatic femur fixation, but increased risk of stroke and cardiac disease in patients undergoing spinal. Other studies have found cannabis to be associated with higher rates of perioperative thromboembolism, neurological complications, respiratory complications, sepsis, and lengths of stay after inpatient spine surgery.[13,14] It has also been shown that cannabis consumption increases the risk of myocardial infarction among patients undergoing a variety of common elective procedures.[15] In contrast, several studies have found no significant differences in postoperative complications or have recommended the use of marijuana as an analgesic in conjunction with standard postoperative care regimens in patients with musculoskeletal injuries.[16-18]

With the rising use of cannabis in the United States and the dearth of knowledge on its postoperative effects, it becomes essential to identify the impact of baseline cannabis use on surgical outcomes. This study sought to compare adverse outcomes between isolated baseline cannabis users (dependence or abuse) and non-users who underwent cervical spinal fusion and identify independent predictors of these outcomes. This study hypothesized that adverse outcomes would be comparable between the isolated cannabis use and non-use group.

METHODS

Data Source

The New York Statewide Planning and Research Cooperative System (SPARCS) was queried to retrieve patient-specific data. SPARCS is an all-payer comprehensive data-reporting system that collects patient characteristics, diagnoses, treatments, services, and charges for each inpatient stay and outpatient visit. Each patient is assigned a unique identifier that allows for longitudinal follow-up. Diagnostic and procedural data are classified according to the International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9-CM).

Patient Population

All patients who underwent primary anterior or posterior cervical fusion (ICD-9-CM codes 81.02, 81.03) between January 2009 and September 2013 were identified. Subjects were subsequently included if aged >18 years and if they had follow-up surveillance of 90 days for complications and all-cause readmissions. Subjects included in the analysis cohort also required minimum two-year follow-up surveillance for revision procedures. Within this cohort, isolated cannabis patients were identified with specific ICD-9-CM codes. Diagnoses included unspecified, continuous, and episodic cannabis dependence (304.30, 304.31, and 304.32, respectively) and abuse (305.20, 305.21, and 305.22, respectively) (Figure 1).

Exclusion Criteria

Patients were excluded for any of the following conditions or pathologies: osteomyelitis, traumatic fracture, pathologic fracture, any type of cancer or metastasis, rheumatoid arthritis, Charcot-Marie-Tooth disease, mucopolysaccharidosis, osteitis deformans, osteitis fibrosis cystica, osteoporosis, poliomyelitis, osteomalacia, Pott's disease, tuberculosis, scoliotic conditions such as spina bifida/myelomeningocele, neurofibromatosis, cerebral

Table 1. Comparison of Demographics Between Cannabis and Non-Cannabis Users Who Underwent Primary Cervical Fusion

		Non-Cannabis	Cannabis	p-value
Age		45.1 ±10.6	45.2 ±10.3	0.933
Sex	Male	70.8%	71.3%	0.916
	Female	29.2%	28.7%	
Race	White	66.2%	52.3%	0.001
	Black	12.0%	27.8%	
	Hispanic	10.2%	9.7%	
	Asian	2.8%	0.5%	
	Native American	0.0%	0.5%	
	Other	8.8%	9.3%	
Insurance	Medicare	8.8%	11.6%	<0.001
	Medicaid	12.5%	29.6%	
	Private Insurance	58.8%	37.5%	
	Self-Pay	2.8%	3.2%	
	No Charge	0.0%	0.0%	
	Other	17.1%	18.1%	
Length Of Stay (Days)		1.9 ±1.8	3.0 ± 4.5	<0.001
Total Charges (USD)		$41,267.88 ±$36,077.33	$48,422.29 ±$61,197.11	0.127
Surgical Approach	Anterior	90.3%	87.0%	0.288
	Posterior	9.7%	13.0%	
Charlson/Deyo		0.11±0.34	0.11 ±0.32	0.935
Tobacco		44.40%	50.0%	0.247

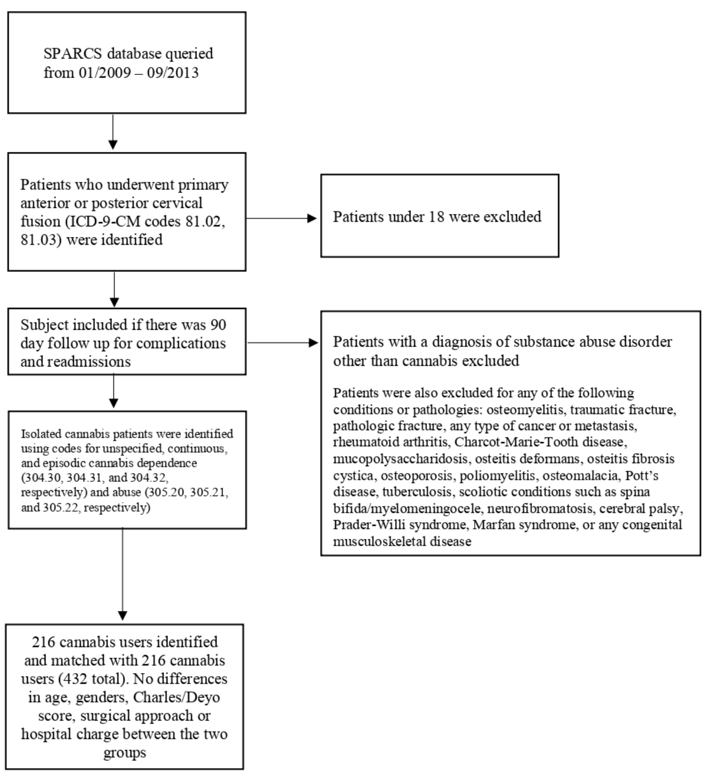

Figure 1. Flow diagram of the inclusion and exclusion criteria used in this study.

Table 2. Comparing the 90-Day Rates of Individual and Overall Complications, 90-Day Readmissions, and Any Revisions Between Cannabis and Non-Cannabis Groups

Medical Complications	Non-Cannabis	Cannabis	p-value
Acute renal failure	0.0%	0.5%	0.317
Acute myocardial infarction	0.0%	0.5%	0.317
Altered mental status	0.0%	0.0%	-
Anemia	0.5%	1.4%	0.315
Acute respiratory distress syndrome	0.0%	0.5%	0.317
Cardiac	0.0%	0.0%	-
Digestive	0.0%	0.0%	0.317
Deep vein thrombosis	0.5%	0.5%	-
Hematoma	0.5%	0.0%	0.317
Infection	0.5%	0.0%	0.317
Nervous	0.0%	0.5%	0.317
Pulmonary embolism	0.0%	0.0%	-
Pneumonia	0.5%	0.5%	-
Puncture	0.5%	0.0%	0.317
Peripheral vascular disease	0.0%	0.0%	-
Respiratory	0.5%	0.5%	-
Sepsis	0.0%	0.0%	-
Urinary	0.0%	0.5%	0.317
Any medical complication	2.8%	4.6%	0.308
Surgical Complications	Non-Cannabis	Cannabis	p-value
Hemorrhage	0.0%	0.0%	-
Wound disruption	0.0%	0.0%	-
Wound infection	0.5%	0.5%	-
Implant infection	0.0%	0.0%	-
Irrigation debridement	0.0%	0.0%	-
Postoperative dislocation	0.5%	0.0%	0.317
Implant-related complications	0.0%	0.5%	0.317
Central nervous system complications	0.0%	0.0%	-
Dural tear	0.5%	0.0%	0.317
Blood other transfusion	0.0%	0.0%	-
Other unspecified surgical complications	0.0%	0.4%	0.317
Any surgical complication	1.4%	0.9%	0.653
Total Complications	3.7%	5.6%	0.360
Readmissions	6.0%	11.6%	0.042
Revisions	2.8%	4.2%	0.430

palsy, Prader-Willi syndrome, Marfan syndrome, or any congenital musculoskeletal disease. Patients with a co-diagnosis or a prior diagnosis of any other substance use disorder (alcohol, cocaine, barbiturates, opioids, amphetamines, hallucinogens, antidepressants, and mixed/other substances) were also excluded from the analysis (Figure 1).

Data Collection

The data extracted included patient demographics (age, gender, race, and insurance), hospital-related parameters (length of stay, hospital charges), surgical approaches (anterior or posterior) and 90-day complication rates (individual and overall medical, individual, and overall surgical, and total complications). 90-day all-cause readmissions, and two-year revisions were recorded.

Statistical Analysis

A 1:1 propensity score-matching algorithm was first developed based on the patients' age, sex, race, Charlson/Deyo score, history of tobacco use, as well as the surgical approach employed for patients undergoing cervical spinal fusion. Patients were then stratified into two groups based on their consumption of cannabis (Cannabis and Non-Cannabis cohorts). Hospital-related parameters, 90-day complications, 90-day all-cause readmissions, and subsequent revision procedures were compared between both groups. Continuous and categorical variables were compared using Student's T-tests and Chi-square analysis, respectively. Multivariate binary stepwise logistic regression models were utilized to identify independent predictors of outcomes, while using age, sex, race, Charlson/Deyo score, and cannabis use as covariates. The threshold for statistical significance was defined as p-value <0.05. All analysis was performed using SPSS software version 24.0 (IBM Corp., Armonk, NY, USA).

RESULTS

During the study period, 216 cannabis users were identified and 1:1 propensity score-matched to 216 non-cannabis users (432 individuals in total). No significant differences were identified between both patient groups in terms of age (p=0.933), gender (p=0.916), Charlson/Deyo scores (p=0.935), surgical approach used (p=0.288), and hospital charges ($48,422 vs. $41,268, p=0.127) (Table 1).

Cannabis and non-cannabis cohorts experienced comparable rates of individual medical complications, including respiratory complications (p=1.000), acute respiratory distress syndrome (p=0.317), and pneumonia (p=1.000). Individual surgical complications were also comparable between both groups, including implant-related complications (p=0.317), dural tears (p=0.317), and wound infections (p=1.000). Similarly, overall complications (p=0.360) and revisions (p=0.430) did not statistically differ based on cannabis use. However, cannabis users had significantly higher rates of 90-day postoperative all-cause readmissions (11.6% vs. 6.0%, p=0.042). Individual and overall, medical and surgical complications are summarized in Table 2.

Isolated cannabis use was not associated with significantly increased risk of any 90-day individual medical or surgical complications, 90-day overall complications, or two-year revision cervical surgery ($p>0.05$). However, compared to non-cannabis use, isolated cannabis use was significantly associated with 90-day readmission (Odds Ratio [OR]=2.0, 95% CI: 1.004-4.1, p=0.049).

DISCUSSION

As cannabis is becoming more commonly legalized, it is important to elucidate its effects on surgical outcomes. This study sought to identify any association between isolated cannabis use and postoperative outcomes after cervical spinal fusion. The findings in this study are the first to demonstrate that cannabis was associated with 90-day readmissions following cervical fusion. Choy et al.[19] reported on risk factors for readmission following cervical spinal fusion and found age >70 years (OR=1.6, p=0.012), renal failure requiring dialysis (OR=3.7, p=0.011), anemia (OR=1.6, p=0.006), and multilevel fusion (OR=1.6, p=0.012) to increase the odds of readmission within 30 days. A previous meta-analysis by Bernatz et al.[20] noted that 30-day readmission following spinal surgeries ranged between 4.2% and 7.4%. The authors additionally reported readmission rates for single institutions (6.6%, 95%CI: 3.8%-11.1%) and multicenter registries (4.7%, 95%CI: 2.3%-9.7%).[20] Additional retrospective studies have identified similar 30-day readmission rates.[19,21] Compared to existing literature, this study found an increased rate of readmission among isolated cannabis users (11.6%). Bernatz and Anderson[20] reported the most common reasons for readmission to be surgical wound complications (39.3%), and medical (including deep venous thromboses, pulmonary embolisms, pneumonias, and urinary tract infections) complications (26.6%). Adogwa et al.[22] also reported readmission rates due to pain intolerance (19.7%) and noted that 26.5% of all readmissions required a revision. While there was no difference in individual medical and surgical complications between the cannabis and non-cannabis group, the increased rate of readmission among cannabis users may comprise of more severe complications. Further studies with prospective patient samples are warranted to identify the specific causes of readmission associated with cannabis consumption.

This study sought to determine the impact of cannabis use on postoperative complications in patients undergoing cervical spine fusions and found no significant difference in rates of complications and revision surgery between patients using and not using cannabis. A prior study found that isolated cannabis use in patient undergoing thoracolumbar spinal fusion was not associated with increased readmissions as well as surgical complications or revision.[23] That study also found a reduction in medical complications in the cannabis users.[23] Lumbar fusion was found to have increased re-operations but no increase in readmissions in cannabis patients.[24] This underscores the need for more research in this area. Prior research has shown a decrease in postoperative mortality associated with cannabis consumption, though an increase in the rate of medical complications in the post-operative period (stroke and DVT more specifically) in patients undergoing common orthopedic procedures.[8] Additionally, studies on trauma patients have also reported a beneficial effect of cannabis use on survival. Nguyen et al.[25] evaluated patients with positive cannabis toxicology tests and identified that positively tested patients carried lower odds of death following traumatic brain injury. A study by Singer et al.[26] reported ICU trauma patients also demonstrated lower mortality rates in patients with positive toxicology tests. The present study excluded patients with use of other substances besides cannabis allowing us to identify the effect of isolated cannabis use. This may account for many of the differences found by the present study. Excluding patients diagnosed with concomitant poly-substance use, a feature unique to this study, may have eliminated the associated increases in complications previously reported in drug-using TKA and THA patients.[8] Further research on the impacts of isolated cannabis use is warranted.

This study carries several limitations. It is a retrospective review of an administrative database. Although SPARCS is noted to collect outpatient data from ambulatory surgery, emergency departments, and hospital extension clinics, the database would not be able to comprehensively account for events that may have occurred outside of inpatient hospitalization, such as primary care or private practice clinics. Therefore, this study is unable to fully account for cannabis use diagnoses that may have occurred outside the inpatient setting. Additionally, this study could not consider variables that relate to cannabis use dependence/abuse. Such variables include the reason for cannabis use (medicinal or recreational), cumulative exposure, concentrations, as well as routes of administration (inhalation, vaporization, etc.).[7] With new changes to ICD-10-CM coding and DSM 5 classification systems, including broader diagnoses of cannabis use disorders, future studies may be better suited to stratify these patients. This study had an sample size of 216 patients for each cohort due to stringent exclusion of patients with any other documented substance use in order to reduce confounding. Additionally, given the legal status of cannabis at the time this data was recorded, cannabis use was likely underreported, and the percentage of users is likely higher than found in this study.[27,28] Patients who use tobacco were not specifically excluded, given they are not categorized as illicit substances. While its use may serve as a potential confounder, tobacco use was included as a variable in the propensity score-match to address this. Though the regression analysis controlled for age, sex, Charlson/Deyo score, and cervical surgical approach, the authors could not rule out the potential influence that economic and insurance status may have on the included patients. Li et al.[29] found that having private insurance was associated with a lower risk of perioperative medical and surgical complications for shoulder arthroplasty when compared with age-matched and sex-matched Medicaid, Medicare, and uninsured patients. Similar studies on hip arthroplasty have shown significantly higher complication rates in Medicaid and/or Medicare patients than in privately insured patients.[30] Race may also have been a potential confounder. A systematic review conducted by Schoenfeld et al.[31] found that following spine and joint replacement procedures, patients from ethnic and racial minority populations seemed to be at an increased risk of mortality and/or complications. Several studies have demonstrated controlling for hospital location or comorbidities could reduce this potential risk.[32-34] However, this study's propensity-score matching design helped mitigate confounding variables that could interfere with the analysis.

CONCLUSION

Isolated cannabis use was an independent predictor of 90-day readmissions, but not of revisions or any individual/overall medical or surgical complication(s) following cervical fusion. To the best of our knowledge, there is no currently available study that has investigated the relationship between cannabis use and readmission following cervical fusion. While noting an association between isolated cannabis consumption and readmission rates, this study can assist spine surgeons in optimizing operative outcomes and mitigating postoperative rates of complications, revisions, and readmissions among patients using cannabis. Of interest within this patient cohort is the postoperative analgesic requirements that could contribute to the increase in 90-day readmission rates. Further investigation is warranted to evaluate this further, as well as determine what physiologic impact cannabis has on musculoskeletal patients.

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PAIN CATASTROPHIZING, KINESIOPHOBIA, STRESS, DEPRESSION, AND POOR RESILIENCY ARE ASSOCIATED WITH PAIN AND DYSFUNCTION IN THE HIP PRESERVATION POPULATION

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ABSTRACT

Background: Psychiatric disorders are known to have a negative impact on outcomes attained from hip-preservation surgery. Psychosocial traits such as resiliency and pain avoidance likely also affect treatment outcomes, however these characteristics are less easily identified, and data is lacking supporting their presence and impact on related outcomes within the hip preservation population. We therefore evaluated hip preservation patients for a variety of maladaptive psychosocial traits and assessed patient-reported outcomes (PROs) in order to ascertain which specific traits were most associated with hip pain and dysfunction.

Methods: 62 subjects aged 15-49 years presenting for evaluation of a nonarthritic hip condition completed psychosocial questionnaires and patient reported outcome measures via electronic survey as listed in table one. Participants were tested again eight weeks later to evaluate the relationship between changes in physical function, pain, and mental health behaviors. Pearson correlation coefficients assessed association between hip PROs and psychosocial tests and analyses were corrected for multiple comparisons.

Results: Pain Catastrophizing (PCS), Kinesiophobia (TSK), Stress, and PROMIS-Global Mental Health (GMH) scores correlated with poor physical function and high pain scores at zero and eight weeks. Low resiliency (BRS) and depression were also associated with elevated pain on PRO tests as well as HOOS-Physical Function. There was a moderately strong correlation between improvement in PROMIS-Physical Function (PF) from zero to eight weeks and subjects initial scores for kinesiophobia, anxiety, and stress (r= -0.45, -0.41, -0.44, all p<0.05).

Conclusion: PCS, TSK, Stress, Depression, and low BRS are associated with pain and disability in hip preservation subjects. Elevated TSK, Anxiety and Stress may be predictors of failure to improve with nonoperative treatment. These psychosocial characteristics should be investigated further as predictors of clinical outcomes in the hip preservation population.

Level of Evidence: II

Keywords: hip preservation, patient reported outcomes, hip arthroscopy, psychosocial

INTRODUCTION

Over the last 30 years, there has been a drastic increase in the number of joint preservation surgeries performed for pre-arthritic hip conditions in the United States.[1] Despite advances in surgical technique and our understanding of the biomechanics of pre-arthritic hip conditions such as impingement and dysplasia, failure rates range from 5-20%[2,3] at early follow up, and can be even higher with continued monitoring.[4] These failures are often attributed to the presence of pre-operative osteoarthritis,[5] increased age,[6] or unaddressed structural deformity.[7,8] The influence of psychosocial factors on surgical and rehabilitative outcomes has been recognized in multiple populations but has largely been ignored in individuals with hip pathology, despite growing recognition by clinicians as to how psychosocial factors may contribute to patient outcomes.

Recent studies demonstrate that poor mental health is associated with lower physical function[9] and certain psychiatric diagnoses are being identified as independent factors associated with failure of hip arthroscopy.[10] Maladaptive psychological features such as anxiety, depression, pain catastrophizing, and kinesiophobia are known to negatively influence treatment outcomes in surgery.[11,12,13] Conversely, resiliency, self-efficacy, and grit appear to be positively associated with improvement during rehabilitation.[9,14] Unfortunately, approximately one third of young adult patients undergoing hip preservation surgery demonstrate maladaptive behavior patterns, with between 14-25% demonstrating mild to

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moderate depression or anxiety in prior studies.[2,15,16] Studies further demonstrate that mental health predicts baseline physical function in patients with symptomatic femoroacetabular impingement (FAI),[9,18] a common cause of hip pain in young adults; patients with FAI who have documented psychiatric comorbidities are 3 times more likely to fail hip arthroscopy and go onto require revision hip surgery.[10,19] Further investigation into the incidence of these psychosocial conditions and their contributions to surgical and non-surgical outcomes needs to be performed in musculoskeletal medicine, specifically in the developing field of hip preservation surgery.

We therefore evaluated hip preservation patients for a variety of maladaptive psychosocial traits and assessed patient-reported outcomes (PROs) to ascertain which specific traits were most associated with hip pain and dysfunction. We hypothesized that maladaptive psychosocial traits (low resiliency, self-efficacy, and grit, and high kinesiophobia, pain catastrophizing, and hazardous alcohol use) will be associated with higher pain scores and lower reported physical function (HOOS, PROMIS-PI, PROMIS-PB, PROMIS-PF).

METHODS

This prospective study was approved by the institutional review board. Patients between the ages of 15-49 years presenting for new or return appointment at an academic hip preservation clinic run by an open and arthroscopic hip surgeon (M.C.W, R.W.) were eligible for inclusion. Inclusion criteria included a chief complaint of hip pain or dysfunction and a diagnosis of a nonarthritic hip condition including labral tear, femoroacetabular impingement (FAI), snapping hip, femoral anteversion or dysplasia. Exclusion criteria included age <15 or >50 years, difficulty with written English, surgery scheduled within eight weeks or treatment for alternative conditions such as trochanteric bursitis, osteoarthritis, hip dislocation, avascular necrosis, or fracture. Patients were screened for inclusion by the medical provider or research assistant after receiving their medical care. Following enrollment demographic data including age, gender, athletic interests, education level, occupation, and contact information were collected using an electronic survey administered via RedCap electronic data capture tools.[2] Participants were then prompted to complete the following tests administered in a randomized order on a handheld electronic tablet: Visual Analog Scale (VAS)[17] for pain, Hip Disability Osteoarthritis Outcome Score (HOOS), PROMIS Physical Function computer adaptive tests (PROMIS PF-CAT), Depression Anxiety Stress Scale (DASS-21),[1] PROMIS Global Mental (GM),[1] Pain Behavior (PB) and Pain Interference (PI) adaptive tests,[1] Alcohol use Disorders Identification Test (AUDIT),[1] Short Tampa Scale for Kinesiophobia (TSK-11),[1] Brief Resiliency Scale (BRS),[1] Short Grit Scale (GRIT-S),[1] and Pain Catastrophizing Scale (PCS).[1] Patients who were unable to complete the testing during the visit due to time limitations were allowed to complete testing after the visit using an emailed link to the online surveys. The test closed automatically after 48 hours regardless of completion status. Eight weeks after enrollment participants received via email a link to a new RedCap survey repeating the same set of surveys to again evaluate pain, physical function, and mental health; surveys were electronically randomized so that participants received the tests in a new order. Study personnel monitored survey completion within the RedCap system and contacted participants via phone and/or email to confirm that the survey was received.

Statistical Analysis

Data analysis was performed by a statistician using SAS statistical software (SAS Institute, Cary, NC); P value of <.05 was considered statistically significant. Presence and severity of maladaptive traits, depression, and anxiety in young adults with hip pain was calculated. Pearson and Spearman Correlations were used to determine association between continuous variables, and multivariate analysis was conducted to evaluate for associations between individual tests and demographic and clinical features such as dysplasia severity (lateral center edge angle). Subgroup analysis was performed with ANOVA with post-hoc unpaired t- tests with a Bonferroni Holm correction to evaluate for differences between patients diagnosed with FAI versus dysplasia. Effect size, recruitment and retention rates were analyzed to guide the design and conduct of future interventions. Linear mixed models were used to evaluate for any significant difference in mental health, pain and function scores over the duration of the study; MDC for PROMIS PF-CAT, Pain Interference, Pain Behavior and HOOS were used as cutoffs to define clinically significant improvement. For PROMIS measures the established minimally importance difference (MID) in patients with back pain undergoing psychotherapy was used. Scoring and normative data for the psychological metrics are described in table one.

RESULTS

62 participants were consented and enrolled in this study. Of these, 50 participants completed initial testing and 12 did not. Following the eight-week period, 23 participants completed follow-up testing and a total of 27 did not (Figure 1). The mean age for our study group was 28.7±10.5 years and BMI was 25.4±5.2 kg/m^2. Of the 62 participants enrolled, 30 presented with right hip pain, 21 with left hip pain and 11 with bilateral hip pain

Table 1. Overview of Psychological Tests Administered

Measure	Test	Format	Scoring
Self-Efficacy	Generalized Self Efficacy Scale (GSE)[7]	10 item test 1-4 points each	10 (low SE) to 40 (high SE)
Grit	Short Grit Scale (Grit-S)[1]	8 item test 1-5 points each, divided by 8	1 (not at all gritty) to 5 (extremely gritty)
Pain Catastrophizing	Pain Catastrophizing Scale (PCS)[9]	13 item test 0-4 points each	0-52 >30 clinically significant level of pain catastrophizing, high risk of developing chronic pain and disability
Kinesiophobia	Shortened Tampa Scale for Kinesiophobia (TSK-11)[10]	11 item test 1-4 points each	11 (no kinesiophobia) – 44 (high kinesiophobia) no specific cutoff exists
Depression, Anxiety, Stress	Short Depression Anxiety Stress Scale (DASS21)[3]	21 item test 7 items for each subscale 0-3 points each	0-21 score for each subscale: 0-2: Normal 3-5: Mild 5-9: Moderate 10+ Severe
Resiliency	Brief Resiliency Scale (BRS)[8]	6 item test 1-5 points each divide by 6	1-5 score: 1.0-2.99: Low Resilience 3.0-4.3: Normal resilience 4.3-5.0: High resilience
Overall Mental Health and Wellbeing	PROMIS Pain interference (PI), Pain behavior (PB) Global Mental Health (GMH), and Physical Function (PF)[1]	Adaptive test T score output	40 One SD below mean 50 Mean 60 one SD above mean
Alcohol Misuse	AUDIT[6]	10 item test 0-4 points each	8+ harmful/hazardous drinking 13+ alcohol dependence (F) 15+ alcohol dependence (M)
Pain Rating	Visual Analog Scale (VAS)[17]	Scale from 0-10	1 (no pain) to 10 (extreme pain)

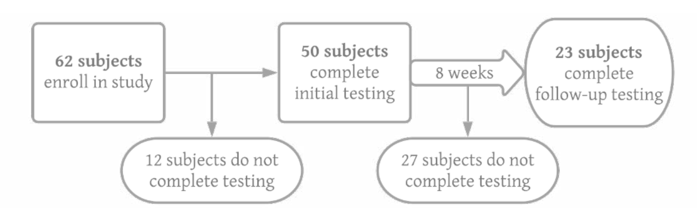

Figure 1. CONSORT diagram depicting study enrollment and timeline.

Table 2. Participant Demographics and Radiographic Measurements

Variable	Mean±SD (range)		p-value
Age (years)	28.7±10.5 (15-49)		NS
BMI (kg/m2)	25.4±5.2 (17.3-44.6)		NS
AA (degrees)	62.1±16.6 (25.0-90.0)		NS
LCEA (degrees)	27.7±9.7 (15.0-65.0)		NS
Variable		N (%)	p-value
Gender	Male	14 (23)	NS
	Female	48 (77)	
Affected Hip	Right	30 (48)	NS
	Left	21 (34)	
	Bilateral	11 (18)	

LCEA=Lateral Center Edge Angle, AA=Alpha Angle.

Table 3. Pearson Correlation Coefficients (r) for Patient Reported Outcome Measures and Psychological Tests in Hip Preservation Patients

	VAS	PROMIS PF	PROMIS PI	PROMIS PB	HOOS	HOOS PF	HOOS PAIN	HOOS SPORT
PROMIS GMH	NS	r=0.297 p=0.03	r=-0.539 p<0.001	r=-0.588 p<0.001	r=-0.269 p=0.06	r=-0.378 p=0.007	r=-0.378 p=0.007	NS
Pain Catastrophizing (PCS)	r=0.30 p=0.037	r=-0.488 p=<0.001	r=0.648 p<0.001	r=0.630 p<0.001	r=0.547 p<0.001	r=0.502 p<0.001	r=0.534 p<0.001	r=0.404 p=0.004
Kinesiophobia (TSK)	NS	r=-0.619 p=<0.001	r=0.49 p<0.001	r=0.589 p<0.001	r=0.423 p=0.002	r=0.336 p=0.01	r=0.336 p=0.01	r=0.509 p<0.001
Grit (SGS)	NS	NS	NS	NS	NS	NS	NS	NS
Self-Efficacy (GSE)	NS	NS	NS	NS	NS	NS	NS	NS
Stress (DASS-S)	NS	r=-0.29 p=0.04	r=0.467 p<0.001	r=0.460 p<0.001	r=0.294 p=0.03	r=0.345 p=0.01	r=0.303 p=0.03	r=0.436 p=0.03
Anxiety (DASS-A)	NS	NS	r=0.412 p=0.003	r=0.413 p<0.003	NS	NS	NS	NS
Depression (DASS-D)	NS	NS	r=0.460 p<0.001	r=0.471 p<0.001	NS	r=0.279 p=0.05	r=0.596 p=0.002	r=0.538 p=0.008
Alcohol Use (AUDIT)	NS	NS	NS	NS	NS	NS	NS	NS
Resiliency (BRS)	NS	NS	r=0.405 p=0.02	r=-0.388 p=0.02	NS	r=0.333 p=0.06	r=0.445 p=0.05	NS

NS = not significant.

(table 2). Most participants had prior treatment consisting of physical therapy (46), followed by other forms of nonoperative treatment such as chiropractic care, activity modification (42) and corticosteroid injections (18). Eight participants had a history of prior surgery such as hip arthroscopy (5), periacetabular osteotomy (2), and total hip arthroplasty (1). Diagnosis of nonarthritic hip conditions such as femoroacetabular impingement and hip dysplasia were made in 11 and 7 participants, respectively. The majority of participants were found to have multiple diagnosis at presentation which included both nonarthritic hip conditions such as labral tear with femoroacetabular impingement and arthritic hip conditions such as osteoarthritis with labral tear.

The correlation between administered psychological tests and hip reported outcomes at both zero and eight weeks in our hip preservation population are reported in table 3. Higher PROMIS-Global Mental Health (GMH) scores correlated with lower pain perception scores such as Pain Interference (PI), Pain Behavior (PB), and HOOS-Pain (r= -0.54, -0.59, -0.38, all p<0.05). Higher Pain Catastrophizing (PCS) and Kinesiophobia (TSK) scores correlated with higher pain perception and lower physical function scores on hip PRO's. Patients who reported higher Stress, Anxiety, and Depression (DASS) also reported higher Pain Interference, Pain Behavior, and HOOS-Pain whereas higher Stress alone was correlated with lower PROMIS-Physical Function (r= -0.29, p<0.05). Depression and Low Resiliency (BRS) were also associated with elevated pain on pain-related patient-reported outcome tests (PI and PB) as well as on the HOOS Pain test. Alcohol use, self-efficacy, grit, age, gender, and BMI were not significant (all p>0.05) as they did not show a correlation between psychological tests and patient reported outcomes.

Baseline scores at week zero, week eight, and total change in scores for all participants are reported in the appendix as the median with interquartile range and range of completed scores. Although there was a moderately strong correlation between improvement in PROMIS PF from 0 to 8 weeks and subjects initial scores for kinesiophobia, anxiety, and stress (r= -0.45, -0.41, -0.44, all p<0.05), no such association existed when comparing the change in median value scores between psychological tests and patient reported outcomes.

DISCUSSION

It is well established that a patient's emotional health and coping skills significantly influence the outcome of many orthopedic surgeries.[20,23] A biopsychosocial model that recognizes these variables and includes intervention for those that are modifiable may be a future strategy to optimize outcome of treatment, however identifying which maladaptive traits may be most relevant and correlate best with pain and function in a given orthopedic population is a necessary first step to design and test future interventions.

Our primary study objectives were therefore to evaluate hip preservation patients for a wide variety of maladaptive psychosocial traits, to assess patient-reported outcomes (PROs), and to ascertain which specific maladaptive traits were associated with hip pain and dysfunction during evaluation and treatment of their hip condition at two separate time points eight weeks apart.

Our study results align with current published data supporting the presence and association of various maladaptive psychosocial traits with hip arthroscopy outcomes. Depression has been associated with worse function (iHOT-12) and pain (VAS) prior to and after hip arthroscopy.[20,21,22] Veterans RAND 12-Item Health Survey-Mental Component Score (VR-12 MCS), an overall measure of mental health disease burden, has also been associated with worse 1-year outcomes after hip arthroscopy.[19,23,24] To our knowledge the present study is the first to evaluate a much broader range of factors such as pain catastrophizing (PCS), kinesiophobia (TSK), resiliency (BRK), DASS-21 (anxiety, stress, and depression) and alcohol use (DASS-21). Our findings that several of these factors including pain catastrophizing, kinesiophobia, low resiliency, along with depression, anxiety, stress, and poor PROMIS-Global Mental Health (GMH) scores were correlated with poor physical function (PROMIS-Physical Function)[1] and high pain and dysfunction (HOOS-Pain, PROMIS-PI, PROMIS-PB)[1] are therefore unique. It is also the first to specifically evaluate the association between these traits and changes in pain and function in the nonoperative setting. Our additional findings that kinesiophobia, stress, and anxiety are associated with failure to improve pain or function during 8 weeks of nonoperative treatment in particular bears further investigation. We hypothesize these characteristics may be indicative of poor participation in rehabilitative therapies, potentially affecting both operative and nonoperative treatments, however this relationship is outside of the scope of this study.

Based on the findings of this study we recommend kinesiophobia, stress, and anxiety as more specific maladaptive traits that should be considered in the evaluation of hip preservation patients, instead of or in addition to broad mental health scores or depression scales which may not effectively capture the maladaptive coping strategies most relevant orthopedic provider. This data also supports the value of a holistic treatment approach in addition to the routine physical care provided to these orthopedic patients.[23,25]

LIMITATIONS

This study had several significant limitations. First, many of our participants did not complete follow-up testing at eight weeks (27) leading to attrition bias which may poses a threat to the internal validity of this study and its conclusion. Second, many of the psychosocial questionnaires employed in this study have been primarily tested on adults (>18 years of age) whereas our study included some participants 15-17 years of age. These tests may not be appropriate or accurate in this age group due to lack of consistent research on this subgroup utilizing these questionnaires. Third, some psychosocial tests such as kinesiophobia (TSK) do not have a strict cutoff to determine clinical importance or significance making results of those tests difficult to translate clinically. Finally, the broad inclusion of a variety of hip conditions including both impingement and dysplasia and multiple treatment protocols means we are unable to correlate changes in physical function or pain at eight weeks with a specific nonoperative treatment algorithm or therapy protocol.

CONCLUSION

Maladaptive psychosocial traits including pain catastrophizing, kinesiophobia, stress, depression, and low resiliency are associated with increased pain and disability in the hip preservation population. Kinesiophobia, anxiety, and stress may be predictors of failure to improve with nonoperative treatment, but further investigation is needed to understand association and should be investigated further as predictors of clinical outcomes.

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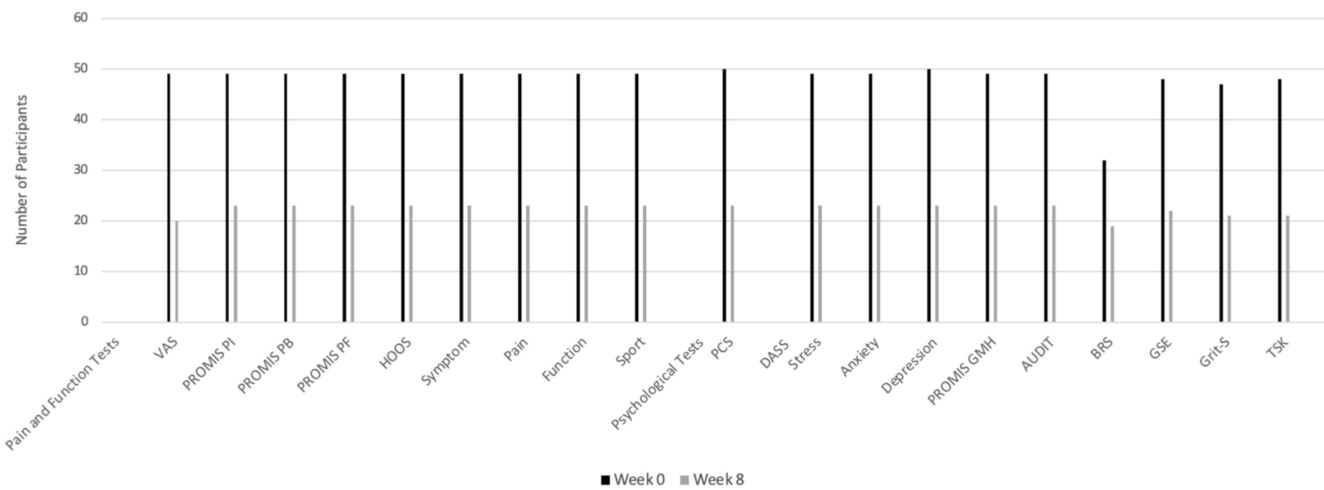
APPENDIX A. Baseline, Week 8, and Change in Score for Study Participants

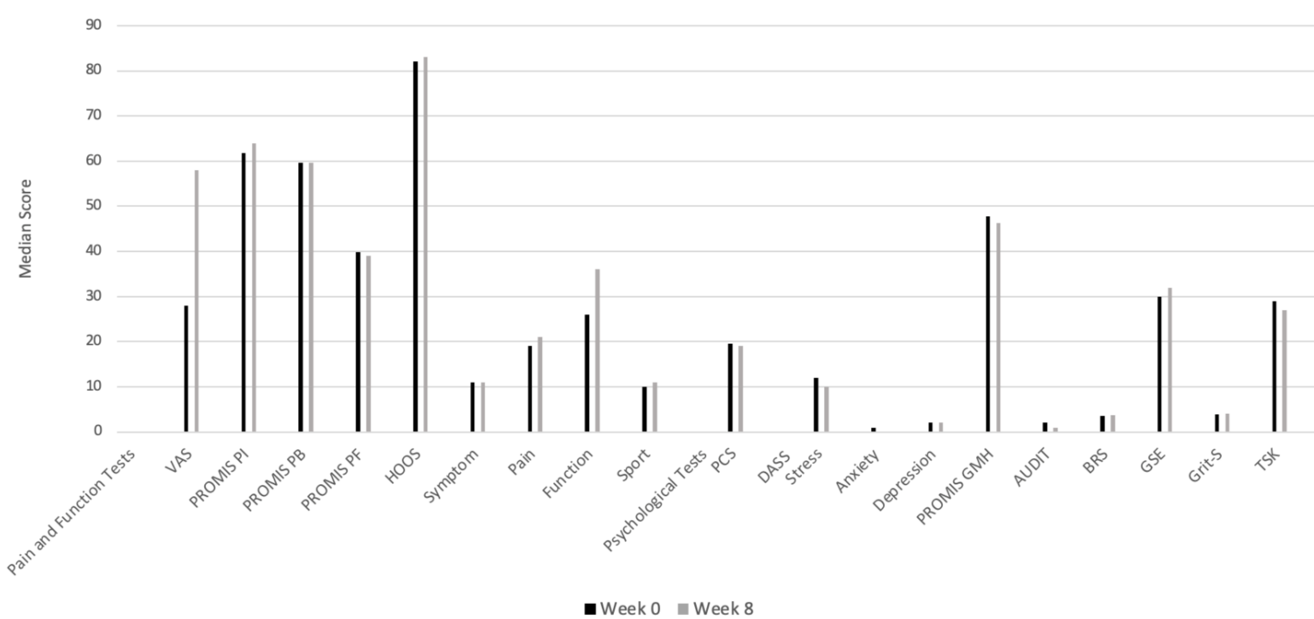
	Week 0		Week 8		Δ 0 to 8 weeks	
Pain and Function Tests	N	Median (IQR) range	N	Median (IQR) range	Median (IQR) range	p-value
VAS	49	28 (18-37) 15-49	20	58.0 (40.0-71.5) 0-80.0	-0.5 (-9-11) -28.0-60.0	NS
PROMIS PI	49	61.7 (59.1-66.9) 50.1-77.8	23	63.9 (57.7-68.2) 47.1-76.4	-1.3 (-4.7-5.2) -10.9-14.3	NS
PROMIS PB	49	59.6 (57.5-61.9) 51.2-67.6	23	59.6 (57.4-62.6) 49.7-66.9	0.0 (-2.0-2.9) -6.3-10.4	NS
PROMIS PF	49	39.9 (38.0-44.0) 27.2-73.3	23	39.0 (30.9-41.7) 22.2-50.1	3.4 (-1.8-9.0) -17.6-23.2	0.031
HOOS	49	82.0 (63.0-93.0) 16.0-160.0	23	83.0 (58.0-105.0) 16.0-155.0	-2.0 (-15.0-17.0) -63.0-51.0	NS
Symptom	49	11.0 (9.0-13.0) 4.0-20.0	23	11.0 (9.0-14.0) 3.0-19.0	-1.0 (-2.0-2.0) -6.0-6.0	NS
Pain	49	19.0 (15.0-24.0) 2.0-40.0	23	21.0 (14.0-27.0) 3.0-40.0	-2.0 (-4.0-3.0) -19.0-24.0	NS
Function	49	26.0 (20.0-34.0) 1.0-68.0	23	36.0 (19.0-42.0) 0-68.0	0.0 (-7.0-5.0) -33.0-14.0	NS
Sport	49	10.0 (8.0-12.0) 2.0-16.0	23	11.0 (7.0-15.0) 2.0-16.0	-1.0 (-3.0-2.0) -5.0-13.0	NS
Psychological Tests						
PCS	50	19.5 (13.0-28.0) 1-48.0	23	19.0 (9.0-24.0) 0-42.0	2.0 (-4.0-6.0) -23-26	NS
DASS						
Stress	49	12.0 (8.0-20.0) 0-40.0	23	10.0 (6.0-16.0) 0-40.0	2.0 (-4.0-4.0) -18.0-26.0	NS
Anxiety	49	1.0 (0.0-5.0) 0.0-51.0	23	0.0 (0.0-2.0) 0.0-22.0	0.0 (0.0-2.0) -12.0-33.0	NS
Depression	50	2.0 (0.0-10.0) (0.0-51.0)	23	2.0 (0.0-6.0) 0.0-26.0	0.0 (-1.0-4.0) -18.0-41.0	NS
PROMIS GMH	49	47.7 (44.1-52.7) 25.8-64.6	23	46.3 (36.0-52.7) 25.8-64.6	0.0 (-6.3-8.1) -14.6-14.9	NS
AUDIT	49	2.0 (0.0-5.0) 0.0-11.0	23	1.0 (0.0-4.0) 0.0-10.0	0.0 (0.0-1.0) -5.0-4.0	NS
BRS	32	3.6 (2.9-4.0) 1.8-5.0	19	3.8 (3.2-4.2) 2.0-5.0	-0.2 (-0.3-0.0) -1.8-0.7	NS
GSE	48	30 (29-36) 14 - 40	22	32 (30-38) 21-40	0 (-3-1) -12-6	NS
Grit-S	47	3.9 (3.4-4.3) 2.3-4.8	21	4.0 (3.6-4.1) 2.8-4.8	0.0 (-0.4-0.1) -2.0-0.6	NS
TSK	48	29.0 (26.5-31.5) 11.0-40.0	21	27.0 (24.0-33.0) 11.0-39.0	1.0 (-1.0-3.0) -8.0-17.0	NS

NS= not significant.

APPENDIX B. Number of Study Participants at Week 0 and Week 8



APPENDIX C. Median Scores of Participants at Week 0 and Week 8



SEX DIFFERENCES IN PATIENT-REPORTED OUTCOMES FOLLOWING SURGICAL HIP PRESERVATION INTERVENTIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Background: Female patients undergoing hip preservation surgery often have inferior patient-reported outcome scores (PROs), raising concerns about the clinical benefit of hip preservation surgery in women. Comparison of preoperative and postoperative PROs, and change in PROs, for female versus (vs.) male hip preservation patients was completed via systematic review.

Methods: In accordance with PRISMA guidelines, the MEDLINE, Cochrane Central, and Embase databases were searched. Level I-IV studies of patients undergoing surgical intervention for femoroacetabular impingement (FAI) and/or developmental dysplasia of the hip (DDH) with at least two years of postoperative follow-up were included. Sex-stratified PRO scores or outcome information had to be included.

Results: We identified 32 hip preservation studies evaluating sex-related PRO differences, and/or providing sex-specific PRO data. The quantitative analysis of 24 studies (1843 patients) was stratified by DDH status. The modified Harris Hip Score (mHHS), Hip Outcome Score-Activities of Daily Living subscale (HOS-ADL), and Hip Outcome Score-Sport-Specific subscale (HOS-SSS) were assessed.

Patients undergoing surgery for FAI only were 52.1% female (n= 806/1546). As predicted, women had lower preoperative PRO scores, however, they had significantly greater improvements in HOS-ADL (20.14±4.41 vs. 26.00±0.35, p<0.05) and HOS-SSS (33.21± 0.71 vs. 38.33± 0.46, p<0.05) compared to males. Similar results were found in the DDH cohort of 330 patients (72.1% female): females had lower preoperative PRO scores, but significantly greater improvement of mHHS (22.68±0.45 vs. 10.60±1.46, p<0.01).

Conclusion: The present review suggests that men undergoing surgery for FAI and/or DDH tend to have higher preoperative and postoperative PRO scores. However, it appears that women often have greater preoperative to postoperative improvement in PRO scores. This finding is strongest in surgical treatment of DDH.

Level of Evidence: III

Keywords: hip arthroscopy, femoroacetabular impingement syndrome, hip labral tears, patient-reported outcomes, patient-reported outcome scores, sex-based physiologic differences, clinical assessment/grading scales, medical aspects of sports

INTRODUCTION

Patient-reported outcome measures (PROs) are frequently utilized in hip preservation clinics to assess actual or perceived hip-related limitations.[1] PROs can also assist with tracking postoperative functional improvements following periacetabular osteotomy (PAO) for developmental dysplasia of the hip (DDH) and hip arthroscopy (HA) for femoroacetabular impingement (FAI) correction and possible repair of the acetabular labrum.[1-8] Postoperative PRO trends are a more nuanced data source on hip procedure efficacy; traditionally gauged by rates of reoperation, complication, return to sport, and return of pre-injury skill level.[9-14]

As with other sports medicine injuries such as anterior cruciate ligament (ACL) rupture, there are sex-specific differences in rate of injury, preoperative symptom burden, and postoperative recovery course among hip preservation patients.[12,13] Prior literature has noted significantly lower postoperative PROs in female patients undergoing PAO and/or HA, which has raised concerns regarding the magnitude of clinical benefit in women undergoing surgery.[13,15,16]

However, while PROs are superior to prior approaches for gauging the success of surgical procedures, they do not account for meaningful sex-specific differences.[17-19]

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Thus, any PRO-based conclusion that women have inferior postoperative outcomes may in fact have minimal validity.[18,19] Subsequently, it is important to elucidate if women truly have inferior hip intervention outcomes[20,21] or if lower postoperative PROs in women simply reflect sex-specific PRO trends.[18] Our current hypotheses are in accordance with the latter assumption; that PROs in women are lower because the scales do not account for sex-specific differences.

In the present review, we will evaluate the following hypotheses: (1) Compared to men, women's postoperative pain and function will improve to a greater extent (postoperative PRO minus preoperative PRO/ΔPRO) after hip preservation procedures; (2) Men and women will have different preoperative PRO "thresholds" for pursuing surgery; and (3) DDH patients of both sexes will have lower PRO scores overall, due to increased structural severity of their condition.

METHODS

Literature Search

Search strategies were developed by the authors, with the assistance of an orthopedic health sciences librarian with expertise in systematic reviews, in July 2020. Comprehensive strategies were devised for the following databases: PubMed (MEDLINE), Embase (Elsevier), and CENTRAL (Cochrane). Pre-established database filters other than the English language filter were not used. The following MEDLINE search strategy was adapted for the other databases; complete search strategies are available upon request. Supplementary searches included reviewing reference lists of the included studies.

MeSH terms and text words identifying patients with non-arthritic hip conditions (search #1) included "femoracetabular impingement"[MeSH Terms] OR "hip"[MeSH Terms] OR "hip joint"[MeSH Terms] OR "hip dislocation, congenital"[MeSH Terms] OR "cam lesion"[Title/Abstract] OR "pincer lesion"[Title/Abstract] OR "acetabular labrum"[Title/Abstract] OR "labral tear"[Title/Abstract] OR "hip impingement"[Title/Abstract] OR "hip dysplasia"[Title/Abstract] OR hip [Title] OR "femoroacetabular impingement*" [Title/Abstract] OR "femoracetabular impingement" [Title/Abstract] OR "femoro acetabular impingement*"[Title/Abstract].

MeSH terms and texts words identifying non-arthroplasty surgical hip interventions (search #2) included "arthroscopy"[MeSH Terms] OR "endoscopy"[MeSH Terms] OR "osteotomy"[MeSH Terms] OR "hip arthroscop*"[Title/Abstract] OR "labral repair"[Title/Abstract] OR "periacetabular osteotomy"[Title/Abstract] OR "PAO"[Title/Abstract] OR "hip preservation"[Title/Abstract] OR arthroscop* [Title/Abstract] OR endoscop* [Title/Abstract] OR osteotom*.

MeSH terms and text words identifying patient-reported outcome measures (search #3) included "patient reported outcome measures"[MeSH Terms] OR "patient outcome assessment"[MeSH Terms] OR "treatment outcome"[MeSH Terms] OR "harris hip score"[Title/Abstract] OR "PRO"[Title/Abstract] OR "PROM"[Title/Abstract] OR "PROMIS"[Title/Abstract] OR patient reported outcome* [Title/Abstract]. The search string for excluded literature types (search #4), was "Editorial" [Publication Type] OR "Comment" [Publication Type] OR "Letter" [Publication Type].

Combining these component searches ((#1 AND #2 AND #3) NOT #4), limited to English language results, resulted in 2114 papers. After similar searches in Embase and Cochrane CENTRAL, duplicates were removed via citation management software identification and manual review of records; yielding 3603 literature search results.

The search results were evaluated per our inclusion and exclusion criteria (Table 1) by two authors (EP and BP), with senior author oversight. Review of 290 full studies resulted in the inclusion of 32 final studies. Of these 32 final studies, 8 were appropriate only for qualitative analysis (Table 1), while the remaining 24 studies provided adequate data for statistical/quantitative analysis.

Statistical Analyses

Excel v.1808 (Microsoft Inc, Redmond, WA) was utilized for statistical analysis. Student's t-tests compared demographic data among all patients, specifically mean percent of female patients and mean patient age. Study outcome variables were also assessed by Student's T-tests. For each PRO, average preoperative PRO, average postoperative PRO, and average pre- to postoperative change in PRO were compared in males versus females. All PRO analyses were weighted by relative sample size.

Outcome Variables

The primary outcome variable of this study was the amount of change from preoperative PRO score to postoperative PRO score, also termed delta-PRO (ΔPRO), between male and female surgical hip preservation patients. Therefore, although discrete comparisons of preoperative PROs and postoperative PROs were completed, the evaluation of change in PRO scores is the principal study comparison. Therefore, we excluded of studies with only pre- or postoperative PRO values, and included studies with only ΔPRO values. Studies describing ΔPRO as the proportion of patients achieving minimal clinically important difference (MCID) were excluded because it was not possible to determine the values. Due to the limited number of mixed-sex studies which specifically provided sex-stratified PRO data, studies of single-sex cohorts were included.

Study Quality

Table 1. Literature Screen Inclusion and Exclusion Criteria

Inclusion	Exclusion
• Adults and children with FAI and/or DDH • Level I-IV, all dates • Pre- and postoperative PROs, or ΔPRO, stratified by sex • Minimum follow-up 2 years • Operative intervention for FAI and/or DDH (arthroscopy, PAO)	• Non-English • Non-human, non-operative • Level V; SR/MA, commentary, technique paper • PRO data not sex-stratified • Non-DDH congenital hip diseases • Non-FAI hip problems (SCFE, LCP)

Avg: Average
bDDH: borderline developmental hip dysplasia
DDH: developmental hip dysplasia
EQ-5D: Euroqual Five Dimensions
EQ-VAS: Euroqual Visual Analog Scale
FAI: femoroacetabular impingement
HA: hip arthroscopy
HOOS: Hip disability and Osteoarthritis Outcome Score
HOS: Hip Outcome Score
ADL: Activities of Daily Living
SSS: Sports-Specific Subscale
LO: labral ossification
MCID: Minimal Clinically Important Difference
mHHS: modified Harris Hip Score
NAHS: Non-Arthritic Hip Score
OHS: Oxford Hip Score
PAO: peri-acetabular osteotomy
Pre-Op: preoperative
Post-Op: postoperative
ΔPRO: absolute change from preoperative to postoperative PRO
PRO: Patient-Reported Outcome
SF-12: 12-item Short Form Survey
SHD: surgical hip dislocation
UCLA: University of California Los Angeles Hip Activity Score
WOMAC: Western Ontario and McMaster Universities Arthritis Index

Table 2a. ROBINS-E Results, Seven Domains of Bias

Domain 1 (Variant A) Response:	Some Concerns
Domain 2 (Variant A) Response:	Low Risk of Bias
Domain 3 Response:	Some Concerns
Domain 4 Response:	Low Risk of Bias
Domain 5 Response:	Low Risk of Bias
Domain 6 Response:	Some Concerns
Domain 7 Response:	Low Risk of Bias

Table 2b. ROBINS-E Results, Overall Risk of Bias per Algorithms

Overall Risk-of-Bias Rating:	Some Concerns
What is the predicted direction of bias?	N/A; all subjects had the same single-exposure event.
Does the overall risk of bias threaten conclusions about the exposure effecting the outcome?	No
Interpretation	There is some concern about bias in the result, although it is not clear that there is an important risk of bias

The quality of the included studies was assessed via the Modified Coleman Method Scores (MCMS), calculated independently by two authors (EP and BP). The average MCMS was 55.3±10.7, range 40 to 78. Among the 32 studies, 15 were poor quality (46.9%), 12 were fair quality (37.5%), and 5 were good quality (15.6%). The average MCMS of qualitatively-assessed studies (n=8) vs. quantitatively-assessed studies (n=24) was 56.3±11.7 vs. 55.0±10.6 (p=0.8); with no significant difference in average MCMS between the two subgroups, or between each subgroup and the average MCMS for all studies.

Risk of Bias Assessment

Per the most recent guidelines in the Cochrane Handbook for Systematic Reviews, Version 6.3 (2022), the ROBINS-E tool (Risk Of Bias In Non-randomized Studies - of Exposures) was utilized to assess the risk of bias in included studies for the present review.[22] For the seven domains of bias analyzed—confounding, selection of participants into the study, classification of exposures, departures from intended exposures, missing data, measurement of outcomes, and selection of the reported result—individual results are shown in Table 2a. Following the ROBINS-E algorithms, the determination of the overall risk of bias is shown in Table 2b. Higher bias risk was largely attributable to Domain 1; confounding. Two important potential confounds were subject age and preoperative activity level. The potential confounding effect of subject age was evaluated by using Student's t-tests to assess within-group and between-group heterogeneity of average patient age. Preoperative activity level was documented (Tables 3a and 3b), but it could not be meaningfully quantified for valid statistical subgroup analysis.

RESULTS

Our literature screen identified 32 hip preservation studies which met inclusion criteria (Table 3a,b).[1-16,3-38] Of these 32 studies, 8 were appropriate only for qualitative analysis, as their sex-specific information was presented in a manner non-compatible with statistical analysis. Quantitative assessment was possible for 24 studies (Table 3a,b). Three hip-specific PROs were analyzed: the Hip Outcome Score- Activities of Daily Living subscale (HOS-ADL), the Hip Outcome Score- Sport Specific subscale (HOS-SSS), and the modified Harris Hip Score (mHHS).

The 8 qualitatively-assessed studies included 2099 patients (64.4% female; n=1352). The condition being investigated in 5 of the studies was FAI (1546 total patients, 52.1% female; n=806). The remaining 3 studies were investigating DDH (330 total patients, 72.1% female; n=238). The average study size was 103 patients, and average patient age was 32.1±5.2 years (Table 3a).

Among these 8 studies, Byrd et al., Clohisy et al., and Nwachukwu et al. performed specific analyses related to patient sex and PROs.[1,23,24] Byrd et al. concluded that, after factoring in patient Tonnis Grade, sex was not a predictor of HA outcome.[23] Contrary to typical sex-PRO conclusions, Clohisy et al. found that male sex was actually an independent risk factor for lack of improvement in HOS ADL; Nwachukwu et al. found that female sex was a positive predictive factor for achieving MCID for mHHS.[1,24]

Among other qualitatively assessed studies, data reported by Byrd et al. showed no difference in average mHHS improvement by sex; female sex was not a risk factor for revision surgery per Domb et al.; and Impellizzeri et al. reported significantly lower baseline PROs among women, which improved by the 6-month postoperative mark to the extent that there was no longer a statistically significant difference between male and female scores. (Table 3a).[6,11,34]

The 24 studies which could be quantitatively assessed provided data for 1843 hip preservation patients (55.8% female; n=1028). Patients with FAI only were evaluated in 17 studies and patients with DDH only were evaluated in 2 studies, while 4 studies evaluated patients with both FAI and DDH. (Table 3b). The FAI-only studies included 1546 patients (52.1% female; n=806) and studies of DDH with or without concurrent FAI included 330 patients (72.1% female; n=238). Average study size was 56, and average patient age was 30.3±9.3 years (Table 3b).

Male FAI patients had higher average preoperative HOS-ADL scores (70.06±10.26 vs. 63.40±5.63, $p<0.05$) and HOS-SSS scores (48.29±7.82 vs. 40.79±3.72, $p<0.05$) compared to female FAI patients. There was no significant difference between male and female FAI patients for average preoperative mHHS (60.1±9.4 vs. 60.3±3.4, p=0.52) (Figures 1a-c). Male FAI patients had higher average postoperative HOS-ADL scores (90.20±5.48 vs. 89.40±5.87, $p<0.05$), HOS-SSS scores (81.50±7.92 vs. 79.12±6.70, $p<0.05$), and mHHS compared to female FAI patients (86.65±7.08 vs. 83.19±6.60, $p<0.05$) (Figures 1a-c). The degree of change from pre- to postoperative PRO scores showed that female FAI patients had significantly greater improvement of HOS-ADL scores (26.00±0.35 vs. 20.14±4.41, $p<0.05$) and HOS-SSS scores (38.33± 0.46 vs. 33.21± 0.71, $p<0.05$) compared to male FAI patients. Men had greater mHHS improvement (26.74±0.61 vs. 22.88±0.22, $p<0.05$) compared to women (Figure 1d).

Because a smaller pool of data was available for DDH patients, a sex-PRO comparison was only possible for mHHS. Men with DDH had higher average preoperative mHHS compared to women with DDH (72.25±10.90 vs. 66.29±8.55, $p<0.05$) (Figure 2a). However, women with DDH had higher average postoperative mHHS (88.97±6.50 vs. 82.85±3.39, $p<0.01$) and therefore a significantly greater improvement in mHHS compared to men (22.68±0.45 vs. 10.60±1.46, $p<0.01$) (Figures 2a-b).

DISCUSSION

In the present review, male FAI patients had significantly higher preoperative HOS-ADL and HOS-SSS scores, and significantly higher postoperative mHHS, HOS-ADL, and HOS-SSS. Male FAI patients also had significantly higher ΔmHHS, but female FAI patients had greater ΔHOS-ADL and ΔHOS-SSS. Among male versus female DDH patients, men had significantly higher preoperative mHHS, but women demonstrated higher postoperative mHHS and greater improvement in mHHS compared to men. Based on these findings, patient sex warrants discussion as a likely effect modifier in the analysis of postoperative outcomes among hip preservation patients.

The sex-specific differences in preoperative PROs, postoperative PROs, and change in PROs are likely attributable to multiple factors. Sex-specific variables of potential influence include: hip joint structure/biomechanics, pain coping, mechanism of injury/functional demands, and logistics of PRO administration.

Sex-Specific Structural and Biomechanical Differences of the Hip

Underlying structural, and subsequent biomechanical differences between male and female hips are an important factor when analyzing PRO differences. Generally, orthopaedic surgeons note that female patients have increased hip joint laxity, greater hip anteversion, less iliopsoas flexibility, and weaker hip abduction, translating to reduced ability of women to mitigate abnormal

Table 3a. Qualitative-Only Study Assessment

Author, Year	Patients (%F)	Avg Age (Range) (yrs)	Study Focus	PROs Assessed	Sex-PRO Analysis?	Study Summary Points	Sex-PRO Qualitative Assessment (N/A if analysis was a Study Summary Point)
Armand et al., 2005	12 (100%)	35 (20-50)	PAO for DDH	mHHS	No	Mechanical analysis can predict joint loading after PAO.	All female; one patient had a post-operative mHHS of 52, all others scores of 96+.
Byrd et al., 2018	100 (34%)	34.7 (13-76)	HA for FAI±LO	mHHS	Yes	Sex did not predict HA outcome after accounting for Tonnis Grade.	N/A
Byrd et al., 2016	104 (54.8%)	LO 45 (21-56), N 30 (19-53)	HA for FAI	mHHS	No	FAI improves symptoms in adolescent athletes, but only 87% return to sport.	No difference in average improvement of mHHS by sex.
Clohisy et al., 2017	391 (79%)	25.4 (10.2-53.6)	PAO for DDH	mHHS, UCLA, HOOS, SF-12	Yes	Male sex is an independent risk factor for less HOS ADL improvement.	N/A
Domb et al., 2018	19 (89.5%)	22.9 (15.5-39.3)	HA for FAI, bDDH	mHHS	No	HA can improve function in borderline dysplasia cases.	Sex was not a risk factor for revision surgery.
Impellizzeri et al., 2012	172 (50%)	F 37.7±12.2, M 33.7±10.3	HA for FAI	WOMAC, OHS, EQ-5D, EQ-VAS	No	PRO scores and improvements do not always correlate with patient satisfaction.	Women had lower baseline PROs but similar scores at 6 months, indicating greater improvement.
Nwachukwu et al., 2020	1103 (65%)	32.9±12.2	HA for FAI	mHHS, HOS-ADL, HOS-SSS	Yes	Female sex was a predictor of achieving mHHS MCID.	N/A
Rego et al., 2018	198 (43%)	33 (18-50)	HA or SHD for FAI	NAHS	No	Both HA and SHD improve FAI symptoms.	Males had higher preoperative NAHS score; females had more score variation.

Avg: Average
bDDH: borderline developmental hip dysplasia
DDH: developmental hip dysplasia
EQ-5D: Euroqual Five Dimensions
EQ-VAS: Euroqual Visual Analog Scale
FAI: femoroacetabular impingement
HA: hip arthroscopy
HOOS: Hip disability and Osteoarthritis Outcome Score
HOS: Hip Outcome Score
ADL: Activities of Daily Living
SSS: Sports-Specific Subscale
LO: labral ossification
MCID: Minimal Clinically Important Difference
mHHS: modified Harris Hip Score
NAHS: Non-Arthritic Hip Score
OHS: Oxford Hip Score
PAO: peri-acetabular osteotomy
Pre-Op: preoperative
Post-Op: postoperative
ΔPRO: absolute change from preoperative to postoperative PRO
PRO: Patient-Reported Outcome
SF-12: 12-item Short Form Survey
SHD: surgical hip dislocation
UCLA: University of California Los Angeles Hip Activity Score
WOMAC: Western Ontario and McMaster Universities Arthritis Index

Table 3b. Quantitative Study Assessment

Study Author, Year	Patients (%F)	Avg Age (Range) (yrs)	FAI or DDH, Procedure	FAI mHHS			FAI HOS ADL			FAI HOS SSS			DDH mHHS			Sex-Pro Study Analysis Results
				Pre	Post	Δ	Pre	Post	Δ	Pre	Post	Δ	Pre	Post	Δ	
Ahmad, 2018	6 (83.3%)	18.16 (13-25)	Both; Colonna interposition arthroplasty	54.0	84.2	30.2							50.0	84.0	34.0	Sex-PRO data non-contributory.
Amano, 2014	106 (68.0%)	M 35.8 (14-54), F 35.9 (13-58)	Both; eccentric rotational PAO	74.0	93.5	19.5							74.6	85.3	10.7	No significant differences between male and female mHHS.
T. Amenabar, 2013	27 (0%)	22.1 (16-30)	FAI; HA	83.6	98.0	14.4										Males only, mHHS and NAHS improved significantly.
Barastegui, 2018	21 (0%)	26.5 + 7.1	FAI; HA	72.5	88.8	16.3	67.7	96.7	29.0	37.6	86.7	49.1				Males only, all tests showed significant improvements in PROs.
Ben Tov, 2014	20 (70.0%)	58 (50-75)	FAI; HA	63.6	86.3	22.7	53.5	86.6	33.2							No significant differences in outcome measures when subdivided into sex groups.
Böhm, 2003	58 (74.1%)	22 (13-37)	Both; Salter's innominate PAO	63.4	78.7	15.3							70.9	79.7	8.8	Sex-PRO data non-contributory.
Boykin, 2013	21 (0%)	28 (19-41)	FAI; HA, labral reconstruction	67.0	84.0	17.0	77.0	85.0	8.0	56.0	77.0	21.0				Males only, mHHS and HOS improved for all patients.
Brooks, 2012	10 (100%)	23-36	FAI; HA	53.1	84.3	31.2										Females only, mHHS showed statistically significant improvement.
Brusalis, 2020	25 (100%)	27.3+6.9	Both; PAO	59.4	70.9	11.5										18/25 females achieved MCID in mHHS and iHOT-33
Byrd, 2015	41 (0%)	23 (18-34)	FAI; HA	81.0	96.0	15.0										Males only, mean improvement was statistically significant.
Byrd, 2016	2 (0%)	34.7 (13-76)	FAI; HA	55.5	85.9	30.4										The LO group (F>M) mHHS improved significantly, but the group had lower preop and postop mHHS and HOS.
Chaharbakhshi, 2019	12 (100%)	29.4 (14.5-54.4)	Both; HA	63.1	85.9	22.8				46.1	78.4	32.3	57.3	76.1	18.8	Females only, significant improvements were found in mHHS, NAHS, HOS-SSS, and VAS scores.

Table 3b. Quantitative Study Assessment (Continued)

Costa Rocha, 2013	4 (75%)	32.5 (20-47)	FAI; SHD, labrum recon-struction	54.2	80.4	26.2	63.0	89.1	26.1	42.3	76.0	33.7	67.6	78.2	10.6	Sex-PRO data non-contributory
Cveta-novich, 2017	36 (75.0%)	Nml 32.9 + 12; BD 31.5 + 11.8	Both; HA										60.1	93.0	32.9	BD females had lower preop mHHS scores, greater improve-ments in HOS-ADL and mHHS.
Degen, 2016	70 (0%)	22.5 (14-35)	FAI; HA	63.0	82.6	19.6										Males only, significant im-provements in all outcome scores.
Dierck-man , 2017	739 (64%)	36.6 (13-76)	FAI; HA	58.2	88.2	30.0	64.1	92.7	28.6	41.0	83.1	42.1				Sex was not a significant predictor of out-come scores.
Frank, 2019	330 (100%)	A 29.1 + 11.1, NA (39.3 + 11.4)	FAI; HA				68.2	91.2	23.0	47.5	88.7	41.2				Females only, significant improvements were found in HOS-ADL, HOS-SSS, mHHS, and VAS.
Krych, 2013	36 (100%)	R 38 (20-59), D 39 (19-55)	FAI; HA, repair or resect labrum	66.8	86.3	19.5	60.2 74.4	80.9 89.8	20.7 15.4	40.6 54.3	76.3 77.3	35.7 23.0				Females only, significant im-provement of all outcome scores.
Novais, 2018	33 (100%)	20.3 + 5.6	Both; PAO										58.0	95.0	37.0	Females only, significant im-provement of all outcome scores.
Rathi, 2017	10 (0%)	35 (26-44)	FAI; HA										58.0	86.0	28.0	Males only, sig-nificant improve-ment in mHHS.
Ric-ciardi, 2017	27 (100%)	25 (15-43)	Both; PAO	80.1	95.4	15.3										Sex-PRO data non-contributory.
Saka-moto, 2015	27 (100%)	17 (14-19)	Both; PAO	63.1	92.0	28.9							57.8	82.3	24.5	mHHS improved significantly among female population.
Sood, 2007	5 (0%)	38.5 (27-51)	FAI; HA	60.2	88.7	28.5										Sex-PRO data non-contributory
Yama-guchi, 2009	210 (100%)	OF 53 + 10.3, UF 36.7 + 2.7	FAI; HA	54.0	84.2	30.2							50.0	84.0	34.0	Sex-PRO data non-contributory.
Mean 55.8 StDev 45.2		30.3 9.3		64.2 8.8	87.1 6.8	22.8 7.3	66.9 7.2	89.4 5.4	22.6 7.6	46.4 6.5	81.4 6.5	34.6 9.7	61.3 9.4	81.8 3.9	20.6 9.8	

Avg: Average
bDDH: borderline developmental hip dysplasia
DDH: developmental hip dysplasia
EQ-5D: Euroqual Five Dimensions
EQ-VAS: Euroqual Visual Analog Scale
FAI: femoroacetabular impingement
HA: hip arthroscopy
HOOS: Hip disability and Osteoarthritis Outcome Score
HOS: Hip Outcome Score
  ADL: Activities of Daily Living
  SSS: Sports-Specific Subscale
LO: labral ossification
MCID: Minimal Clinically Important Difference
mHHS: modified Harris Hip Score
NAHS: Non-Arthritic Hip Score
OHS: Oxford Hip Score
PAO: peri-acetabular osteotomy
Pre-Op: preoperative
Post-Op: postoperative
ΔPRO: absolute change from preoperative to postoperative PRO
PRO: Patient-Reported Outcome
SF-12: 12-item Short Form Survey
SHD: surgical hip dislocation
UCLA: University of California Los Angeles Hip Activity Score
WOMAC: Western Ontario and McMaster Universities Arthritis Index

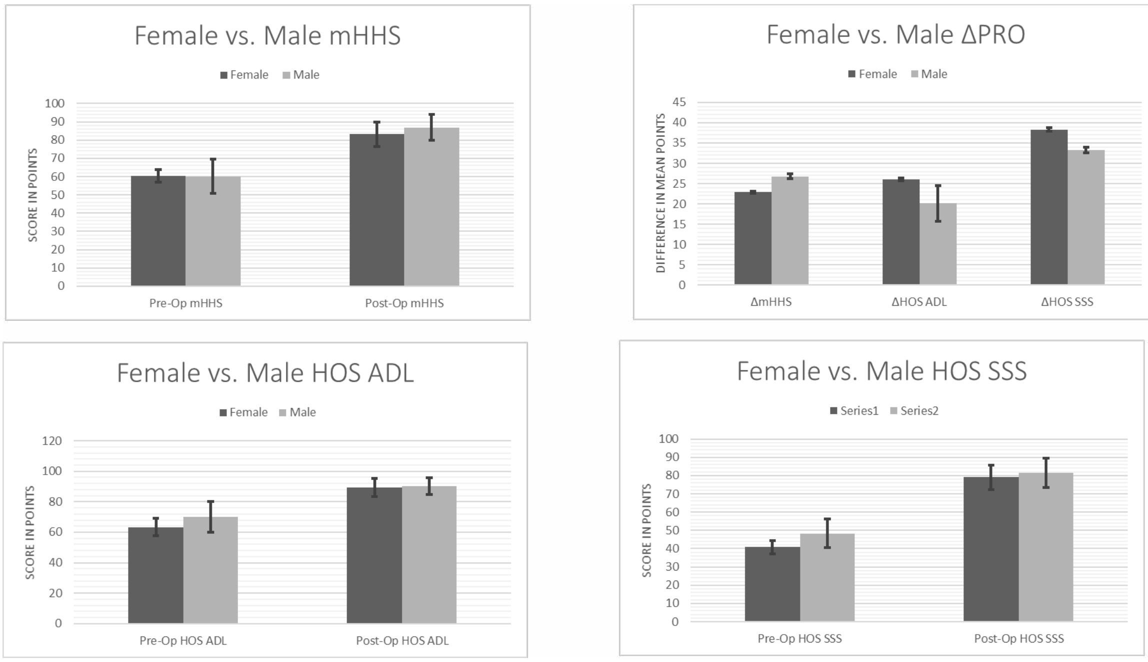

Figure 1A to 1B. FAI Male vs. Female Pre- and Postoperative PROs; Male vs. Female ∆PRO. HOS: Hip Outcome Score, ADL: Activities of Daily Living, SSS: Sports-Specific Subscale, mHHS: modified Harris Hip Score, Pre-Op: preoperative, Post-Op: postoperative, ∆PRO: absolute change from preoperative to postoperative PRO.

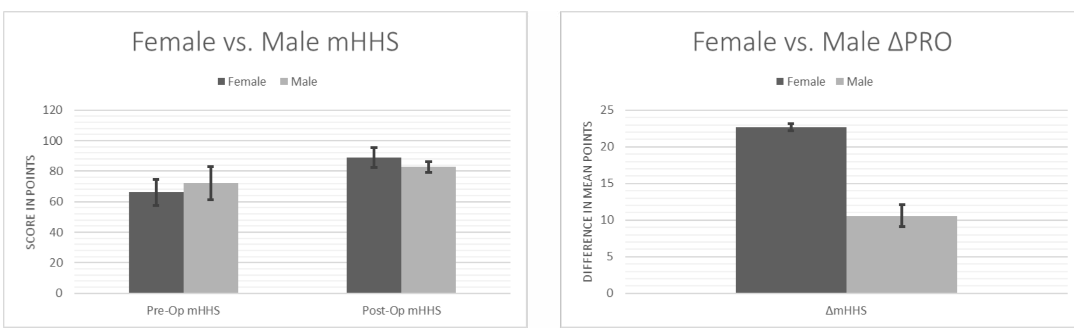

Figure 2A to 2B. DDH Male vs. Female Pre- and Postoperative, ∆mHHS. HOS: Hip Outcome Score, ADL: Activities of Daily Living, SSS: Sports-Specific Subscale, mHHS: modified Harris Hip Score, Pre-Op: preoperative, Post-Op: postoperative, ∆PRO: absolute change from preoperative to postoperative PRO.

forces on the hip joint.[11] This results in women being more susceptible to hip injuries, and more likely to suffer severe injury, with an increased symptom burden and likelihood of failing conservative care.[39,40] These differences are present even among elite athletes suggesting that differences in activity levels between males and females are not responsible for these findings.[21]

Subsequently, women presenting for a surgical evaluation are more likely to have severe pathology, contributing to low preoperative PROs.[21,40] These findings are also relevant to lower female post-operative PROs: the underlying structural/biomechanical differences which led to injury may require more intensive surgical interventions, or may not be completely addressed by surgery.[21,40] The impact of sex-based structural susceptibility to injury is demonstrated by Byrd et al.[23] in a comparative analysis of postoperative FAI patients who showed no sex-specific difference in outcomes; only if they were first stratified by Tönnis grade. This is also in agreement with the analysis by Mygind-Klavsen et al. showing that age and severity of hip cartilage injury negatively impacted the postoperative outcome of hip procedures, but sex did not. Additionally, Vesey et al. concluded that pre-existing OA correlated with conversion to hip arthroplasty, but sex did not.[41,42]

Finally, structural differences can help to explain the greater improvement in PROs of female patients. At their pre-injury baseline, women have biomechanical differences which not only make them more susceptible to hip injury, but also make them more susceptible to non-traumatic hip conditions such as greater trochanteric pain syndrome.[39,40,43] Therefore, surgical stabilization of the hip may in fact improve their hip biomechanics above their pre-injury baseline. Additionally, women having low preoperative PROs allows for "more room" to improve.[39,40,43]

Sex-Specific Approach to Coping with Pain

Another PRO-relevant consideration is sex-specific approaches to pain coping. Literature tends to ubiquitously cite lower pain tolerance of women as causing lower PROs.[44,45] Interestingly, while women do have a lower tolerance for acute experimental pain (i.e., withdrawing their hands from ice water more quickly), they do not rate the pain severity of set stimulus levels higher than their male counterparts (i.e., both sexes would rate the pain of an identical electric stimulus as '4 out of 10').[44] Among chronic pain patients, women have significantly greater "pain acceptance" and higher activity levels compared to men, who have significantly more kinesiophobia.[45] These studies suggest that when women are living with chronic pain, their approach is to "accept and move".[45]

Therefore, women with longer-term hip pain may have remained active until the severity of their condition worsened significantly relative to injuries in men, causing their preoperative PROs to be lower.

Similarly, during the postoperative period, women may remain more active causing a more symptomatic recovery and resulting lower pain-centric postoperative PROs at follow-up visits. Study findings by Clohisy et al.[1] and Flores et al.,[46] showed that after hip procedures, women are likely to have significantly higher postoperative HOS-ADL scores compared to men.

Mechanism of Injury and Functional Demands

Patient lifestyle and circumstances are important variables for any orthopedic procedure, as is the ability of survey tools to collect this information. Specifically, for the present study, are commonly utilized hip preservation PROs appropriate for the studied populations, and do PRO scores account for patient postoperative priorities?

This is an important consideration for preoperative PRO differences among FAI patients. Because females have a morphological predisposition to hip injuries, male patients with hip injuries are more likely to have sustained the injury via high-impact mechanisms. One example is forceful collisions during contact sports, which exacerbate what may be, at baseline, mildly abnormal hip morphology. At a tertiary care hip preservation clinic, Palsson et al. noted that male patients tended to report high pre-injury activity levels, consistent with elite or professional athletics participation, coupled with poor perceived hip-related function after their injuries.[47] Many studies of male hip arthroscopy patients are studies of high-level athletes– rather than patients with congenital/morphological susceptibility to injury– suggesting that their self-assessment of hip-related function is dependent upon the ability to continue participation in high-level athletics.[2,12] It is a reasonable assumption that among these elite male athletes, particularly career athletes, athletic function is a paramount priority. This may explain why men in the present study tolerated significantly less decrease in HOS-SSS before electing to proceed with surgery. Additionally, studies of women more often involve both athletes and non-athletes, so HOS-SSS questions such as "Because of your hip, how much difficulty do you have with running one mile?" are more likely to receive an answer and score of "+0, unable to do" from non-athletes, which may skew the preoperative scores lower in studies of women.

This difference in mechanism of injury and postoperative functional hip demands among male versus female hip preservation patient populations is also relevant for postoperative PRO differences. Different patient populations will vary in the degree that they value being able to resume specific tasks. Thus, the questions specific to activities of daily living (HOS-ADL) versus sports-specific abilities (HOS-SSS) will vary in relevance among patients groups.

These influences may limit the trajectory of postoperative PRO improvement in male vs. female patients. Even with accelerated rehabilitation protocols, recovery from a hip preservation procedure involves longitudinal participation in physical therapy. As therapy progresses, many of the movements reflect modified versions of activities commonly included in traditional workouts; squatting, stationary bicycling, and leg presses. Therefore, among the non-athlete population, with heavier female representation in the present study, participation in advanced physical therapy phases may actually improve their physical function beyond their baseline pre-injury level. Conversely, for high-level male athletes, returning to activity with normal technique and endurance (HOS-SSS questions) may require a longer rehabilitation period.

PRO Administration Logistics and Data Extrapolation

In addition to the variables discussed above, completion rates for PROs should also be considered. Approximately 76% of patients complete preoperative PRO questionnaires; this number drops to 57% of patients 6 months postoperatively and 45% of patients at 12 months postoperatively. Therefore, although the isolated postoperative PROs analyzed in the present study may suggest an inferior outcome for female FAI patients, the collective postoperative population is not fully representated in this data. Even with completed PRO scores, as discussed above, these instruments are susceptible to being impacted by sex-specific differences which are not factored into the design of the PRO measures. Information in the present review highlights the importance of utilizing PROs as a metric to evaluate postoperative progress for individual patients, rather than a predictive tool for postoperative success amongst or between groups of patients. Making sex-specific changes to the MCID of hip-preservation PROs, and adjusting PRO instruments to account for sex-specific differences may be appropriate considerations to facilitate more accurate data collection among this patient population.

LIMITATIONS

It proved difficult to find studies which qualitatively and quantitatively assessed sex-based PRO data. Of the 32 quantitatively evaluated studies, only 4 (12.5%) performed a sex-specific analysis of PROs. Even among the 8 studies assessed by qualitative methods only, just 3 studies (37.5%) specifically made conclusions regarding sex-specific PRO factors. Additionally, there was a lack of mixed-sex studies that provided PRO data with the necessary sex-stratification. As a result, the majority of the quantitatively assessed studies are single-sex studies. On quality assessment of the included studies via MCMS, approximately 50% received quality rankings of “poor”. However, the range of scores was reasonable (40-78) and the overall average score was “fair”. Additionally, both the average MCMS and the ratio of poor:fair:good studies were similar between the qualitative-only and quantitative assessment groups, and similar when compared to whole-study numbers. Of note, studies achieving fair quality scores appeared to do so chiefly because of large population sizes; studies achieving good quality scores had both large population sizes and higher quality study designs (prospective cohort, randomized controlled trial).

CONCLUSION

The present review suggests that men undergoing surgery for FAI and/or DDH tend to have higher preoperative and postoperative PRO scores. However, it appears that women often have greater preoperative to postoperative improvement in PRO scores. This finding is strongest in surgical treatment of DDH.

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APPENDIX A. List of Abbreviations

Avg: Average
bDDH: borderline developmental hip dysplasia
DDH: developmental hip dysplasia
EQ-5D: Euroqual Five Dimensions
EQ-VAS: Euroqual Visual Analog Scale
FAI: femoroacetabular impingement
HA: hip arthroscopy
HOOS: Hip disability and Osteoarthritis Outcome Score
HOS: Hip Outcome Score
ADL: Activities of Daily Living
SSS: Sports-Specific Subscale
LO: labral ossification
MCID: Minimal Clinically Important Difference
mHHS: modified Harris Hip Score
NAHS: Non-Arthritic Hip Score
OHS: Oxford Hip Score
PAO: peri-acetabular osteotomy
Pre-Op: preoperative
Post-Op: postoperative
ΔPRO: absolute change from preoperative to postoperative PRO
PRO: Patient-Reported Outcome
SF-12: 12-item Short Form Survey
SHD: surgical hip dislocation
UCLA: University of California Los Angeles Hip Activity Score
WOMAC: Western Ontario and McMaster Universities Arthritis Index

THE INCIDENCE AND OUTCOMES FOLLOWING TREATMENT OF CAPSULOLABRAL ADHESIONS IN HIP ARTHROSCOPY: A SYSTEMATIC REVIEW

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ABSTRACT

Background: To perform a systematic review to evaluate the incidence of capsulolabral adhesions following hip arthroscopy (HA) for femoroacetabular impingement (FAI); including risk factors and post-treatment outcomes.

Methods: Using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, we queried PubMed, EMBASE, and Cochrane Central Register of Controlled Trials for English-language studies with minimum 6-month follow-up after primary or revision HA for FAI, which reported the incidence of capsulolabral adhesions. Potential adhesion risk factors, such as anchor type used and protocol for capsule closure, were assessed. Pre-operative and post-operative modified Harris Hip Score (mHHS) values were compared in studies that reported them.

Results: Thirty-seven articles were included (24 primary HA; 13 revision HA). There were 6747 patients who underwent primary HA (6874 hips; 3005 female, 44%). The incidence of capsulolabral adhesions, confirmed surgically during revision HA, was low. Patients undergoing surgical treatment reported postoperative improvement per modified Harris Hip Scores. Data for 746 patients undergoing second revision HA (761 hips; 449 female, 60%), showed an incidence of adhesions greater than that of primary HA patients.

Conclusion: While the incidence of symptomatic capsulolabral adhesions after primary hip arthroscopy is low; revision hip arthroscopy is strongly associated with adhesion development. Lysis of adhesions in primary hip arthroscopy patients reliably improved patient-reported outcomes.

Level of Evidence: IV

Keywords: Hip preservation, femoroacetabular impingement syndrome, outcome studies, patient-report outcome scores, postoperative recoverye

INTRODUCTION

Hip arthroscopy (HA) has exponentially gained popularity in the last two decades as a means of treating femoroacetabular impingement (FAI) with an 18-fold increase from 1999 to 2009; and a nearly 4-fold increase from 2004 to 2009 alone.[1,2] As with any new procedure, greater utilization has highlighted pearls, pitfalls, outcome ratios, and success rates of the intervention.

The etiology of persistent pain following hip arthroscopy can be elusive. Residual impingement, failure of labral repair, new tears of the labrum, chondral defects, previously unaddressed or iatrogenic instability, femoral and/or acetabular version, and development adhesions are among possible differential diagnoses.[3] In all patients, some degree of scar tissue formation between the hip joint capsule and labrum occurs during postoperative healing. However, the development of tough, fibrous bands of scar tissue—capsulolabral adhesions—can pathologically adhere the hip joint capsule to the acetabular labrum. These adhesions impact range of motion and disrupt the fluid seal of the hip joint, increasing friction forces on the chondral cartilage. Despite evidence that adhesions are a frequent generator of postoperative hip pain, they remain poorly understood and sparingly researched.[4,5]

This paucity of knowledge includes precipitating factors, diagnostic strategies, preventive approaches, and treatment options.[3,4,6] Greater emphasis should be placed on exploring these factors, given the prevalent role of adhesions in cases of failed primary hip arthroscopy. This can significantly improve primary HA outcomes and decrease the need for revision HA. Therefore, this study aimed to perform a systematic review of capsulolabral adhesion incidence, precipitating intra-operative factors, and patient outcomes after current treatment approaches.

METHODS

Literature Search

Search strategies were developed with the assistance of an orthopedic health sciences librarian with expertise in systematic reviews. Searches were developed by the

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authors and the librarian beginning in July 2019 using an iterative process of gathering and evaluating terms. The final literature search was performed and completed in December 2020. Comprehensive strategies, including both index and keyword terms, were devised for the following databases: PubMed (including MEDLINE), Embase (Elsevier platform), and Cochrane Central (Wiley platform). To maximize sensitivity, pre-established database filters other than the English language filter were not used. The full PubMed search strategy below was adapted for use with the other electronic databases. Complete search strategies are available upon request. Supplementary approaches for searching included reviewing reference lists of the included studies. Please see Appendix I for MESH terms.

Our aggregate PubMed search combined these component searches as follows: (#1 OR #2) AND #3 NOT (#4 OR #5). When limited to English language results, 722 papers were found. After performing a similarly focused search via Embase and Cochrane, duplicates were removed using an approach to ensure accuracy and prevent accidental loss of records. This process was facilitated by citation management software and supplemented by manual review of records. Our initial search yielded 1481 results that were evaluated according to our inclusion and exclusion criteria (Table I). Two authors, with oversight from the senior authors, reviewed 198 full papers and screened-in 37 final studies for qualitative analysis (Figure I).

Statistical Analyses

Excel v.1808 (Microsoft Inc, Redmond, WA) was utilized to perform basic demographic calculations and all Student t-tests. Student t-tests evaluated demographic data among all patients including mean age, mean percent of female patients, and mean length of follow-up; these values were calculated for multiple population subgroups to ensure appropriate between-groups demographic homogeneity.

Outcome Variables

For patients undergoing primary hip arthroscopy, the principal outcome variable was the number of patients (count or percent) with capsulolabral adhesions subsequently confirmed on revision HA indicated for persistent hip symptoms. For studies with no incidence of revision HA for adhesions, it was also acceptable for data to be presented in unambiguous text format. If the studies mentioned specific postoperative interventions aiming to prevent adhesions after primary HA, such as use of continuous passive motion machines or prescribed circumduction exercises, this data was recorded as well.

In studies of patients undergoing revision hip arthroscopy, the principal outcome variable was number of patients (count or percent) with intra-operative confirmation of capsulolabral adhesions. Similar to the analysis of the primary HA studies, if revision HA studies mentioned specific postoperative interventions designed to prevent

Table I. Review Criteria

Inclusion Criteria	Exclusion Criteria
Articles describing primary or revision hip preservation surgery for FAI	Review articles
Assessment of incidence of capsulolabral adhesions and arthroscopic lysis of adhesions	Case reports
Evaluation of patient characteristics related to capsulolabral adhesions	Technique articles
Evaluation of strategies to prevent adhesion development	Non-english language articles
Evaluation of objective or subjective outcomes of patients after lysis of adhesions	
Minmum mean follow-up of 6 months for reported outcomes	

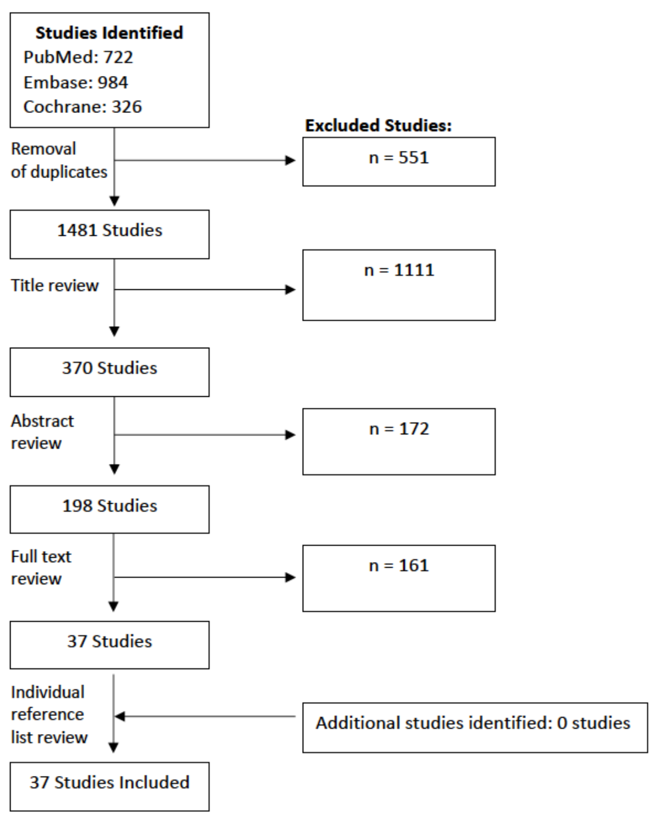

Figure I. Flow diagram of systematic search performed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.

adhesions, this data was recorded with other study information. To approximate success of the revision HA procedures, pre- and postoperative modified Harris Hip Scores (mHHS) were recorded if included in the study; however, mHHS was not a requirement for study inclusion during the screening process.

Two subgroup analyses of primary and revision HA patients were performed to evaluate potential intra-operative precipitants of symptomatic postoperative adhesions: suture anchor composition and hip joint capsule closure protocol. Hip arthroscopy patients noted to undergo labral repair with knotted or knotless sutures were identified, and incidence rates of postoperative capsulolabral adhesions compared. Similarly, patients undergoing procedures where capsular closure or non-closure was documented were identified, to compare development of capsulolabral adhesions. For both subgroup analyses, adequate data was only present among primary HA studies.

Study Quality

The mean Modified Coleman Methodology Score (MCMS) was assessed for each included study by two authors, individually, before consensus scores were determined. The mean MCMS score for the included studies was 70.11 ± 8.58 (Table II), considered "good" per MCMS standards. The mean MCMS of the primary HA cohort was significantly greater than the revision HA cohort (75.3 ± 5.2 vs. 70.5 ± 3.5, p=0.002), likely due to the weight MCMS assigns to study size, and size differences between the primary and revision study cohorts (Primary 8.6 ± 2.3 vs. Revision 4.8 ± 2.8, p=0.0067). Please see Appendix II for full MCMS for each study.

Study Heterogeneity

Due to the paucity of literature on this topic, a systematic review of heterogenous studies was indicated. To better explore this heterogeneity and potential impacts on study findings, Table III and Figure II can be referenced. Table III details design characteristics and properties of included studies. Figure II is an index random effects model for the review, focused on one of the subgroup analyses—use of knotted versus knotless sutures. The resulting I2 heterogeneity, 86%, reinforces the need for high-level homogenous studies on the topic.

RESULTS

Eligibility and Patient Characteristics

Our literature screen identified 37 qualifying studies, 24 of which addressed primary hip arthroscopy (Table III). There were 6747 patients (3005 female, 44%) in the primary HA cohort. One hundred fifteen patients in this group underwent bilateral HA (1.9%) for a total of 6874 operative hips. The mean age was 30.2 ± 9.8 years and mean follow-up was 39.0 ± 29.3 months. Body mass index (BMI) was reported in 12 of 24 articles for an attenuated mean of 24.48 ± 2.3 kg/m^2. The operative side was not consistently reported.

The revision HA cohort consisted of 737 patients, with 14 patients (1.9%) undergoing bilateral revision HA, for a total of 751 operative hips. There were 303 males (40%) and 445 females (60%). The mean age of patients was 32.9 ± 3.4 years and mean follow-up was 30.3 ± 9.7 months. The mean BMI was only reported in 3 of 13 articles and thus was negligible statistically. The operative side was not reported consistently.

Table II. Summary of Article Methodology Assessment According to the Modified Coleman Methodology Score

Primary HA		Revision HA	
Author & Year	Total Score (100)	Author & Year	Total Score (100)
Buchler et al. 2013	67	Philippon 2008	56
Arashi et al. 2019	73	Karthikeyan et al. 2012	64
Bolia et al. 2019	85	Aprato et al. 2014	66
Philippon 2012	66	Larson 2013	73
Domb et al. 2013	73	Ross et al. 2015	50
Matsuda et al. 2013	70	Gupta et al. 2016	71
Willimon et al. 2014	74	Gwathmey et al. 2017	71
Byrd et al. 2014	70	Philippon 2018	76
Fukui et al. 2015	82	Locks 2018	71
Gupta et al. 2016	79	Nwachuku et al. 2018	60
Sawyer et al. 2015	74	Fagottia et al. 2019	73
Byrd et al. 2016	74	Arriaza et al. 2020	51
Nawabi et al. 2016	68	Cancienne et al. 2020	73
Degen 2017	60		
Weber 2017	64		
Nho et al. 2019	69		
Webb 2019	53		
Brick et al. 2020	85		
Filan et al. 2020	71		
Hwang et al. 2020	82		
Makovicka et al. 2020	70		
Menge et al. 2020	77		
Philippon 2020	77		
Philippon 2012	76		

Mean	70.11
SD	8.58

Table III. Characteristics of Included Articles

Authors	Study Type	Level of Evidence	Total Patients	Total Hips	Male	Female	Mean Age (Range or ±SD)	Mean Follow-up (Months, Range or ±SD)
Primary HA								
Buchler et al.	Retrospective Cohort	III	66	66	17	49	33.8	11.3 (1.5-55)
Arashi et al.	Retrospective Cohort	III	33	36	22	11	16.7	24 (15-32)
Bolia et al.	Retrospective Comparative	III	126	126	72	54	38	82.2
Philippon	Case Series	IV	153	153	72	81	57 (50-77)	35.7 (12-52)
Domb et al.	Case Series	IV	22	22	4	18	20 (14-39)	27.5
Matsuda et al.	Retrospective Cohort	III	54	54	32	22	37.08 ± 18.24	30 (24-27)
Willimon et al.	Retrospective Cohort	III	1264	1264	752	512	32 ± 11	12
Byrd et al.	Case Series	IV	37	38	26	11	26	24
Fukui et al.	Case Series	IV	100	102	50	50	35 (18-69)	40 (24-97)
Gupta et al.	Case Series	IV	546	546	228	318	38 (13.2-76.4)	28.98 (24-66.1)
Sawyer et al.	Retrospective Cohort	III	326	326	162	164	34.6 (18-64)	37.4 (24-61.2)
Byrd et al.	Case Series	IV	104	116	47	57	16 (12-17)	38 (24-120)
Nawabi et al.	Retrospective Cohort	III	177	207	82	95	29.7 ± 10	31.3 ± 7.6
Degen	Retrospective Comparative	III	34	38	18	16	16 (13-17)	36.1
Weber	Case Series	IV	59	59	23	16	31.7 ± 11.4	12.5 ± 6.8
Nho et al.	Retrospective Case-Control	III	935	935	347	588	33 ± 12.3	27.8
Webb	Retrospective Cohort	III	950	1010	591	419	36 (14-72)	18
Brick et al.	Retrospective Cohort	III	228	228	120	108	34.5	60.95
Filan et al.	Retrospective Comparative	III	966	966	829	137	28.05	28.8
Hwang et al.	Retrospective Cohort	III	162	162	89	73	35.1 (15-69)	87.4 (60-244)
Makovicka et al.	Retrospective Cohort	III	85	85	53	32	29.7	29.1
Menge et al.	Case Series	IV	60	70	21	49	16 ± 1.2	144 (120-168)
Philippon	Case Series	IV	200	200	118	82	35.3	43.8
Philippon	Case series	IV	60	65	17	43	15	24 (12-38)
Revision HA								
Philippon	Case Series	IV	9	9	5	4	37.2 (21-49)	20 (10-36)
Karthikeyan et al.	Case Series	IV	20	20	16	4	37 (17-54)	17
Aprato et al.	Case Series	IV	63	63	27	36	37 ± 10.7	36
Larson	Retrospective Cohort	III	79	85	35	44	29.5 (16-59)	26 (12-72)
Ross et al.	Retrospective Cohort	III	50	50	33	27	29 (16-52)	-

Table III. Characteristics of Included Articles (Continued)

Gupta et al.	Case Series	IV	70	70	31	39	36.3 (16.8-70.2)	27.99
Gwathmey et al.	Case Series	IV	186	190	69	117	32.7 (14-64)	46.9 (24-60)
Philippon	Case Series	III	99	99	36	63	29 ± 10	40
Locks	Retrospective Comparative	III	26	28	8	18	33 ± 14	43.2 ± 12
Nwachuku et al.	Case Series	IV	49	49	22	27	29.7 ± 8.6	12
Fagottia et al.	Retrospective Cohort	III	36	36	9	27	30.4	25 (18-38)
Arriaza et al.	Case Series	IV	10	13	6	4	36.3 ± 15.5	26.3 ± 13.85
Cancienne et al.	Retrospective Comparative	III	49	49	10	39	30 ± 10.5	25 ± 3.5

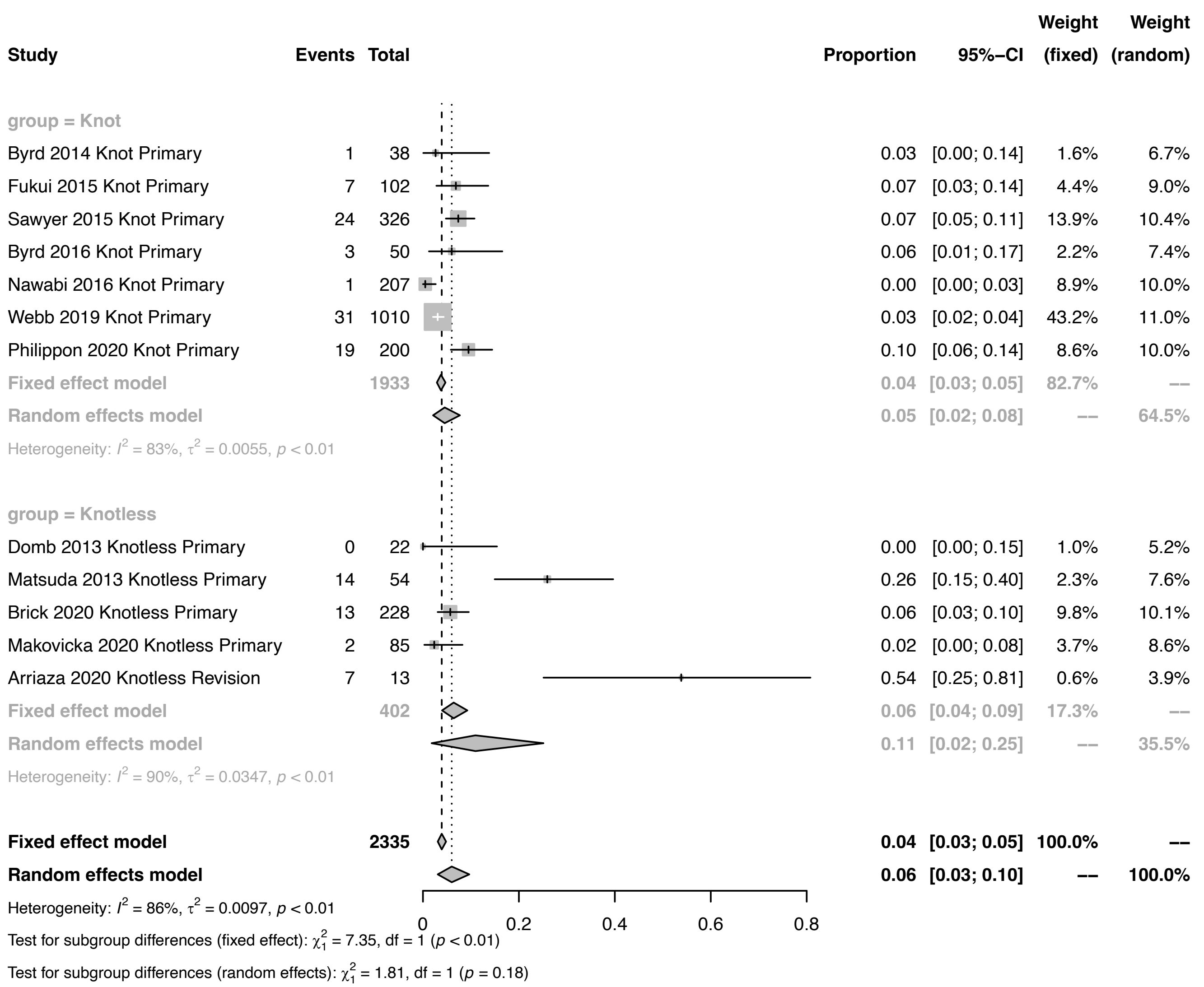

Figure II. Random effect model comparing the pooled prevalence of adhesions in labral repairs with knotted versus knotless suture anchors. There was no difference in adhesion incidence between anchor types (p=0.18).

Indications and Procedures

Of the 24 studies in the primary HA group, patients in 20 studies were indicated for surgery for FAI, while patients in four studies (493 hips; 7% of primary HA cohort) had a dual surgical indication of FAI and borderline hip dysplasia (lateral center edge angle 18-25°[7,8] or 20-25°.)[9,10] Among all 24 primary HA studies (6874 hips), 77% (5263 hips) underwent labral repair, 59% (4034 hips) underwent femoral osteochondroplasty, 52% (3568 hips) underwent acetabular rim trimming, 8% (572 hips) underwent acetabular or femoral microfracture, and 3% (223 hips) underwent labral reconstruction. It is important to note that patients likely underwent two or more of the above interventions during surgery. Five studies[11-15] (325 hips; 5% of group total) evaluated postoperative outcomes; all patients were adolescents.

The 13 revision HA study patients were indicated for surgery for various diagnoses: all including FAI. Among the 750 operative hips, 21% (160 hips) underwent labral repair,15% (115 hips) underwent labral reconstruction, 61% (465 hips) underwent femoral osteochondroplasty, 38% (287 hips) underwent acetabular rim trimming, and 9% (65 hips) underwent acetabular or femoral microfracture.

In the subgroup analysis of capsule closure vs. nonclosure, 18 of 24 primary HA studies reported capsule closure (14 studies;[7-9,11,13-22] 3055 hips) or non-closure (4 studies,[10,12,16,23] 842 hips), while two of thirteen revision HA studies mentioned capsule management: Philippon et al.[24] (99 hips) performed capsule repair, and Locks et al.[25] performed capsule reconstruction with iliotibial band autograft.

For the subgroup analysis of suture anchor type, 11 of 24 primary HA studies reported use of knotted suture anchors (7 studies;[8,9,12,22,26-28] 1933 hips) versus knotless suture anchors (4 studies; 389 hips), and one revision HA study (13 hips) reported use of knotless suture anchors Among the eleven primary HA studies with this data, two studies (222 hips) were specifically involving patients treated with labral reconstruction.[22,29]

Incidence of Capsulolabral Adhesions

The incidence of capsulolabral adhesions after primary HA was globally low but not negligible, with incidence rate among studies ranging from 0% to 25.9%. Almost all the primary HA patients suspected of having capsulolabral adhesions were treated with revision HA for lysis of adhesions in addition to correction of any residual pathology, if needed. In the four primary HA studies where patients had both FAI and borderline dysplasia, the incidence of capsulolabral adhesions confirmed during revision HA was lower than collective incidence rates among studies of FAI-only patients, with rates ranging from 0% to just 6.86%.

Demographic Variables of Patients with Capsulolabral Adhesions

Patient demographics including age, sex, and BMI were not regularly reported in the included studies, limiting availability of this data for specifically adhesion patients. Thus, index studies providing comprehensive data were examined as a proxy. The primary HA study by Matsuda et al. identified 57 patients with adhesions (29 females, 50.9%), who had a mean age of 32 ± 11 years and mean BMI of 24 ± 4 kg/m^2.[29] Another primary HA study identified 3 patients with adhesions (2 females, 66.7%) with a mean age of 16 years[30] and a third primary HA study reported adhesions in 2 females (100%) with no specified age.[11]

One revision HA study reported 15 cases of adhesions (9 female; 60%) with a mean age of 23.2 ± 8 years[24] while another revision HA study noted 36 cases of adhesions (9 female; 75%)with a mean age of 30 years and mean BMI of 22.8 kg/m^2.[31] A third revision HA study identified 13 patients with adhesions, with a mean age of 27.9 ± 8.5 years. No other studies in the primary or revision HA cohorts reported demographics of patients treated for capsulolabral adhesions.

The limited number of studies reporting demographics of adhesion patients precluded any generalizable conclusions, but the three studies each from the primary and revision cohorts did allow for limited assessment of trends. For example, five studies provided mean patient ages—32, 16, 23.2, 30, and 27.9—indicating that symptomatic adhesions may be less likely among adolescent patients. One study each from the primary and revision HA groups reported a mean healthy BMI in adhesion patients; too small of a data pool for use beyond forming future research hypotheses.

Capsulolabral Adhesion Subgroup Analyses

Adhesions occurred in 86 of the 1933 hips reported to use knotted suture anchors (4.45%), and in 38 of the 402 hips reported to use knotless suture anchors (9.45%), demonstrating no substantial impact of suture anchor type on development of adhesions. Number of anchors used at index procedure was not regularly reported. When evaluating capsule management, adhesions occurred in 152 of 3055 hips that underwent capsule closure (4.37%) and, in almost identical proportion, in 11 of 842 hips with no capsule closure (4.33%). The subgroup analyses indicated that these specific intra-operative variables did not have a significant impact on development of postoperative adhesions.

Patient Outcome After Treatment of Adhesions

Overall, 811 hips in the present review had revision HA which surgically confirmed capsulolabral adhesions and treated them with lysis. A limited analysis of postoperative patient-reported outcomes—the modified Harris Hip Score (mHHS)— following this intervention for adhesions was performed. Eight of 14 studies (560 hips, 69%) reported improvement in modified Harris Hip scores (mHHS) after undergoing revision HA with lysis of adhesions, indicating the lysis of adhesions is a reasonable early treatment consideration for this condition.

Prevention of Adhesions

Thirteen studies reported trial protocols for postoperative capsulolabral adhesion prophylaxis. All 13 studies emphasized the potential benefit of early postoperative passive range of motion activities, specifically use of continuous passive motion (CPM) machines or regular performance of hip circumduction exercises. Willimon et al. and Menge et al. provide practice-level support for these recommendations.[14,38] Both authors noted decreased development of postoperative capsulolabral adhesions in their hip preservation patients after implementation of a rehabilitation protocol which included early use of CPM and performance of circumduction exercises.

DISCUSSION

When analyzing study data from 6747 patients undergoing primary hip arthroscopy (HA), a low but not inconsequential number had capsulolabral adhesions confirmed on revision hip arthroscopy (range: 0% to 25%). With a mean follow-up of 39.6 months, many of these cases of adhesions requiring surgical intervention occurred within the first three postoperative years. However, intraoperative findings from 737 revision hip arthroscopy patients revealed that capsulolabral adhesion incidence rates may in fact be much higher, with the adhesions either not rising to the level of clinical significance for the patient or being misdiagnosed as one of the many other potential post-arthroscopy problems. Among all 13 revision HA studies, the main surgical indication was FAI syndrome and associated osteochondral procedures. Despite this, nearly one in three patients (224/737, 30.0%) were found to have capsulolabral adhesions requiring lysis during their procedures. In the subgroup analysis, neither suture anchor type nor capsule closure protocol appeared to influence rate of adhesions.

It cannot be concluded in isolation that capsulolabral adhesions alone caused the symptomatology of the revision HA patients, particularly when so many were indicated for surgery for objectively confirmed pathology, such as FAI detected on imaging. However, treatment of the adhesions with lysis did not appear to have a detrimental impact in any patients, with 8 of the 14 studies recording mHHS showing improved scores after revision HA with lysis of adhesions.

Recovery from hip arthroscopy requires maintaining ”homeostasis” of soft tissue and osseous healing within an optimal range.[32,33] Failure of a repaired labrum to heal translates to failure of the procedure, and failure of appropriate healing at osteochondral sites in the pelvis could put the patient at serious risk given the continual weightbearing demands on the pelvis. Appropriate osseous healing after hip arthroscopy involving offset correction is the development of bony callus over resection sites, followed by coverage with mature bone.[32,34-36] However, excessive osseous healing has been shown to cause heterotopic ossification in post-hip arthroscopy patients; where extra-articular bone formation along portal tracks can cause pain and debility, and require further surgical intervention.[32-36] Similarly, inappropriate healing of incised/repaired soft tissue after hip arthroscopy, forming fibrotic tissue, can, cause symptomatic and functional setbacks, requiring revision HA.[3,37]

Capsulolabral adhesions can cause painful pathologic mechanisms of movement in the hip joint.[3,4,37] Adhesions to the labrum can prevent it from maintaining an adequate seal with the femoral head throughout various ranges of motion.[4,38] Loss of this seal can result in loss of fluid tension within the joint, thus increasing frictional stresses between joint components.[4,5] This friction can cause pain and mechanical symptoms, which may necessitate revision HA for lysis of adhesions; even if symptoms are not severe enough to require revision HA, there remains a risk of increased rate of chondral degeneration.[3,5]

Because hip arthroscopy is a relatively young field, work is ongoing to determine optimal treatment for postoperative complications, and to elucidate possible prevention strategies.[33,37] A relevant example is the earlier treatment of HO with revision surgery, followed by the development of strategies such as HO prophylaxis with naproxen or celecoxib (NSAIDs), with a goal of superseding the need for revision HA.[34,39] Current literature lacks a consensus opinion on the use of NSAIDs for adhesion prophylaxis. Currently, revision HA for lysis of adhesions is the only effective treatment for symptomatic capsulolabral adhesions.[3,37] However, the procedure and its efficacy are not a flawless solution. As shown in the present review, adhesions can be a significant source of continued pain and functional impairment in HA patients; one in four revision HA patients required this additional surgery due to adhesions. While this review shows improvement in hip-relevant patient-reported outcomes after lysis of adhesions, it is important to consider the number of patients with adhesions who are not able to or willing to undergo revision HA, and continue to suffer from pain and reduced functional status.[3,37]

Just as revision HA was not an optimal solution for HO, it is similarly not an optimal solution for capsulolabral adhesions.[4] Intra-operative and postoperative prevention strategies are being investigated. One modifiable intra-operative consideration is the use of knotted versus knotless suture anchors.[40] Preliminary research shows no significant difference in incidence of adhesions with use of knotted versus knotless suture anchors;[40] similar to the findings of the present study. However, knotless sutures had a higher rate of adhesions that did not reach significance, and sporadic reporting of suture anchor type consequently made the analysis low power. A dedicated, higher power investigation may clarify these findings. Postoperative prevention strategies range from chemoprophylaxis with anti-fibrotic medications such as losartan, to mechanical prophylaxis using continuous passive motion or scheduled circumduction exercises.[4,38,41] There is currently no high-quality literature demonstrating consistent success with any of these methods.

LIMITATIONS

The present review has several limitations. First, the results of the review are limited by the quality of evidence of each individual study included. All articles were Levell III or IV evidence and mostly single surgeon series. FAI syndrome encompasses several potential sites of pain generation, and operative treatment often requires many concomitant procedures to address intra- and extra-articular sites of impingement. Operative management also differs between primary and revision HA. There were indeed differences in procedures performed between the primary and revision HA cohorts, which likely explains the differences in the incidence rates of capsulolabral adhesions. However, studies did not address which specific pathologies are potentially risk factors for adhesion development. In addition, procedural information is limited by data available in each study. Not every study reported the number of patients who received a specific procedure during hip arthroscopy and as such, we were unable to stratify by bony versus non-bony procedures performed. This could be a focus for future investigations.

CONCLUSION

While the incidence of symptomatic capsulolabral adhesions after primary hip arthroscopy is low; revision hip arthroscopy is strongly associated with adhesion development. Lysis of adhesions in primary hip arthroscopy patients reliably improved patient-reported outcomes.

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TRAUMATIC IRREDUCIBLE PEDIATRIC RADIAL HEAD DISLOCATIONS: A UNIQUE CASE AND REVIEW OF THE LITERATURE

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ABSTRACT

Background: Irreducible radial head dislocations are uncommon injuries and blocks to reduction typically result from interposed soft tissue. We report the case of a pediatric patient who sustained an irreducible radial head dislocation with a concomitant posterior elbow dislocation and coronoid process fracture. To the author's knowledge, irreducible radial head dislocations presenting as part of a terrible triad like constellation of injuries have not been previously reported. A case-based review of the literature was also performed.

Case Description: A 7-year-old male presents to our pediatric hospital as a transfer from an outside hospital after sustaining a posterolateral radial head and posterior elbow dislocation secondary to a fall. CT imaging and 3D reconstruction revealed a Type 1 coronoid process fracture. At our institution, closed attempts at reduction in the operating room under fluoroscopy with general anesthesia were also unsuccessful. Open reduction of the radial head and repair of the soft tissue structures was ultimately required to stabilize the patient's elbow injury.

Conclusion: Irreducible pediatric radial head dislocations are rare and inherently unstable injuries. To the authors' knowledge, there are no prior reports of irreducible radial head dislocations that present in a terrible triad like fashion with a coronoid process fracture and posterior elbow dislocation. In the present report, successful treatment of this injury required open reduction and soft tissue repair.

Level of Evidence: IV

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INTRODUCTION

Elbow injuries are frequently seen in pediatric emergency departments (ED). The peak incidence of acute elbow fractures and dislocations in the general population occur in children 5-8 years old, often while engaging in activities such as hanging from monkey bars. These activities can lead to unintentional falls that are more likely to result in elbow injuries.[1] Elbow dislocations are one of the more urgent types of elbow injuries due to the potential for neurovascular compromise. Elbow dislocations can be isolated or can also be associated with ligamentous injury or concomitant fractures. In the pediatric population, elbow dislocations are the most common large joint dislocation, with the incidence of 5.21 per 100,000.[2] Among these, posterior dislocations are the most common type of dislocations reported.[3]

The elbow joint is comprised of a combination of three articulations – the radiocapitellar joint, the ulnohumeral joint, and the proximal radioulnar joint. Complete radial head dislocations are rare, as most present either as subluxation or partial dislocations.[4] Typically, complete radial head dislocations are a result of high energy mechanisms and are therefore associated with forearm fractures or dislocations.[4] Fractures associated with traumatic elbow dislocations account for approximately 10-12% of all pediatric fractures.[5] Various fractures can be seen in both posterior elbow dislocations and radial head dislocations. For example, posterior elbow dislocations can occur with coronoid process fractures and/or radial head/neck fractures. This particular constellation of injuries is known as a terrible triad injury.[6] While well described in the adult population, pediatric 'terrible triad' injuries are very rare.[7] While some studies have described radial head dislocations to be isolated injuries, some authors suggest that these are really accompanied with ulnar shaft injuries that are missed.[8] In this constellation, they are identified to be variants of Monteggia injuries. Rapid management of 'terrible triad' and Monteggia injuries is essential as these dislocations can cause neurovascular compromise.[9]

The initial management of all joint dislocations is timely reduction to preserve joint function and prevent further neurovascular injury. Elbow joint dislocations can often be close reduced and immobilized for a period of time until adequate stability is achieved. However, surgical intervention or open reduction may be required in certain cases. Indications for operative intervention in acute pediatric elbow dislocations include associated unstable fracture injuries, instability of the elbow joint, and finally, if closed reduction is not feasible.[2] Although there have been various reports of irreducible radial head dislocations in the pediatric population, these injuries are uncommon.[10-24] To the author's knowledge, there are no reports of an irreducible head dislocation in the setting of an ipsilateral posterior elbow dislocation and coronoid process fracture. We present a case of a pediatric patient who sustained a terrible triad variant. In lieu of a radial head/neck fracture, our patient presented with an irreducible radial head dislocation with an ipsilateral coronoid process fracture and posterior elbow dislocation.

CASE DESCRIPTION

Initial Presentation

A 7-year-old right hand dominant male with no significant past medical history initially presents to an outside hospital after sustaining an injury to his right elbow after falling from monkey bars (~5 feet). He complained of pain in his right elbow and held his elbow in a fixed extended position. Right elbow antero-posterior, oblique, and lateral radiographs obtained demonstrated a posterolateral radial head dislocation with a concomitant posterior elbow dislocation. An attempt at closed reduction was made under conscious sedation in the emergency department by a community emergency medicine provider. After an unsuccessful closed reduction, the right upper extremity was placed into a provisional splint and the patient was transferred to the emergency department at our pediatric hospital for further care. Upon initial evaluation by the orthopaedics team, the patient had a right elbow effusion and globally tender to palpation along the medial, lateral, and posterior aspects – the forearm was held in a supinated position with the elbow extended. Mild ecchymoses without abrasions or open wounds noted about the skin. Of note, there was an area of skin tenting with mild skin blanching noted on the posterolateral aspect of the proximal forearm – palpation revealed a hard bony prominence placing pressure on the skin. The patient was unable to supinate, pronate, flex, or extend the right elbow due to extreme pain and restriction in movement both actively and passively. The patient had no distal motor deficits and sensory exam was intact without paresthesias in the median, ulnar, and radial nerve distributions.

Anteroposterior, oblique, and lateral radiographs of the right elbow were obtained in the emergency department (Figure 1). Initial radiographs demonstrated the previously reported divergent elbow dislocation with the posterolateral radial head and posterior elbow dislocation. The bony prominence palpated on exam correlated with the radial head seen on radiographs. No obvious fractures were identified on these films. A CT scan with 3D reconstruction was completed to further evaluate the injury demonstrating a Type 1 coronoid process fracture as well. (Figure 2)

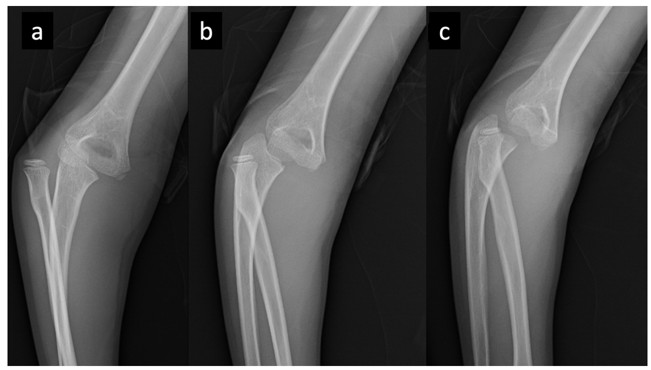

Figure 1A to 1C. Anteroposterior (1A), oblique (1B), and lateral (1C) views of the right elbow demonstrating posterolateral radial head dislocation and posterior elbow dislocation.

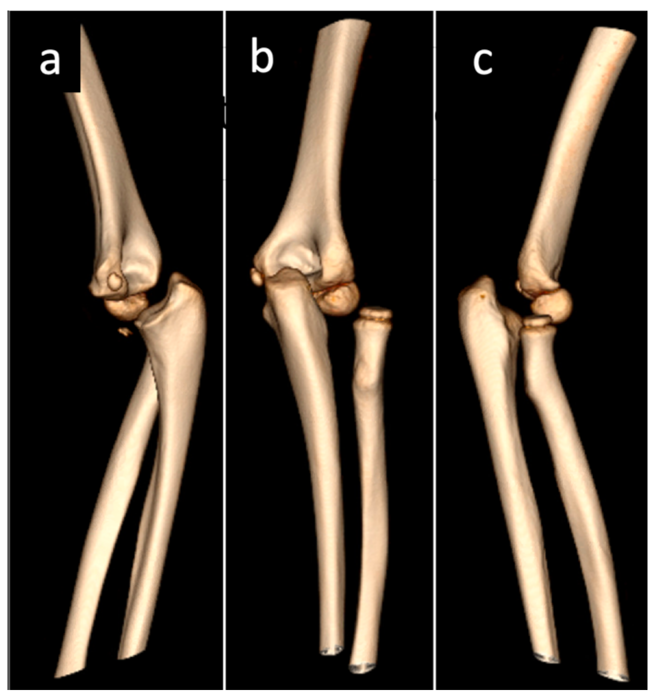

Figure 2A to 2C. Lateral (2A), Anteroposterior (2B), and Oblique (2C) views of the 3D reconstruction from computed tomography demonstrating divergent elbow injury with posterolateral radial head dislocation, posterior elbow dislocation, and Type 1 coronoid process fracture.

Intervention

A mutual decision with the patient's family and the orthopaedics team was made at operative intervention given the concern for potential soft tissue interposition blocking closed reduction. Once in the operating room, an attempt at closed reduction was done with initial fluoroscopic images demonstrating the divergent elbow injury (Figure 3). The posterior elbow dislocation was easily close reduced under fluoroscopy with flexion of the elbow in the supinated position (Figure 4). The elbow was noted to be very unstable as minimal extension (about 5 degrees) from the flexed position would cause the elbow to dislocate posteriorly. An attempt at closed reduction of the posterolateral radial head dislocation was performed with an anteromedial force with pronation – however, there was significant resistance to reduction.

A decision was therefore made to openly reduce the radial head dislocation. A standard lateral approach to the elbow was utilized with the incision going directly over the dislocated radial head. Elbow was placed at 90 degrees with a gentle curved skin incision directly over the middle of the lateral condyle approximately 5 cm in length. Subcutaneous skin flaps were raised to expose the fascia over the muscles with care taken not to expose distally protecting the posterior interosseous nerve. The Kocher interval between the extensor carpi ulnaris and anconeus was then noted. Portions of the dorsal extensor mechanism could be seen buttonholing through the superficial fascial layer. In addition, the radial head was noted to be extruded through both the superficial fascial layer and extensor mechanisms as well (Figure 5). Extensor mechanism soft tissue was noted around the radial neck. After incising the joint capsule, a large hematoma was evacuated. The soft tissues incarcerating the radial neck were removed to allow mobilization of the radial head. Deeper inspection revealed the annular ligament to have been displaced anterior to the radiocapitellar joint. The annular ligament was able to be pulled over the radial head while an anteromedial force was applied on the radial head with gentle pronation. Reduction was confirmed with fluoroscopic imaging. Once the radial head dislocation was reduced, the posterior elbow

Figure 3. Fluoroscopic imaging demonstrating divergent elbow injury.

Figure 4. Initial lateral fluoroscopic imaging demonstrating successful, but unstable, posterior elbow dislocation closed reduction. The elbow, however, was unstable with minimal extension and dislocated posteriorly.

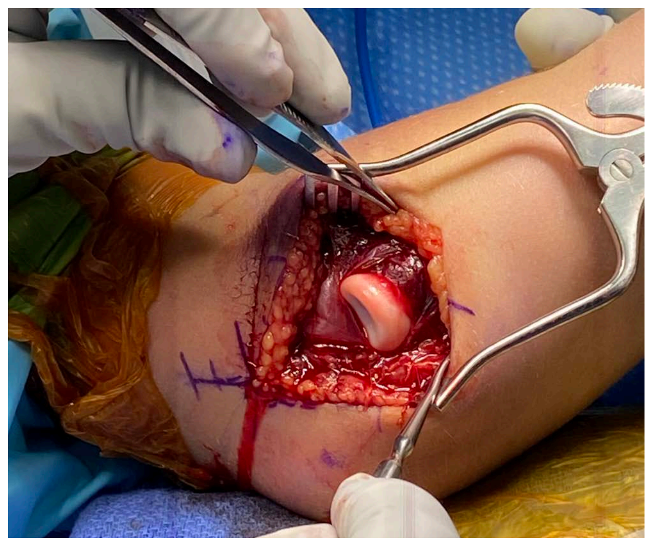

Figure 5. Upon dissection down to the level of the muscle layer, the radial head was noted to be violating the extensor mechanism and buttonholing through.

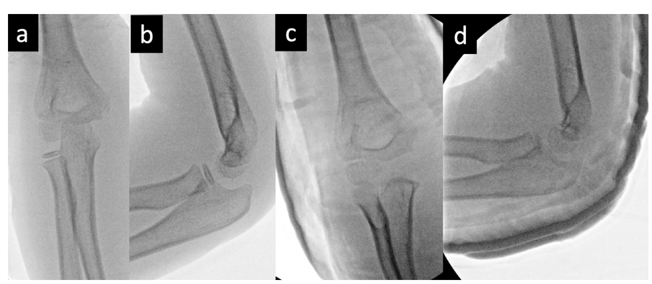

Figure 6A to 6D. Anteroposterior (6A) and lateral (6B) views of the right elbow immediately after successful open reduction of the radial head and posterior elbow dislocation reduction. Anteroposterior (6C) and lateral (6D) views in the double sugar tong splint at the end of the case demonstrate maintained reductions.

instability vastly improved and stayed reduced. Care was taken to repair the soft tissue defects in the extensor mechanisms and fascial layers to help ensure soft tissue stabilization and reduce the risk of re-dislocation.

After repair of the soft tissues, the patient's elbow was gently ranged and had no restriction in pronation/supination or flexion/extension. No excessive instability was noted. The patient was then splinted in a double sugar tong splint to the right upper extremity to allow for swelling as the patient was returning to his home country via flight the following day for further follow up care and rehabilitation. Final fluoroscopic imaging confirmed successful reduction of the divergent, terrible triad variant injury. (Figure 6) Upon discharge, the patient's pain was well controlled on oral medications and no sensory or motor deficits were observed in the right upper extremity. The patient returned with his parents to their home in another country the following day. Communication via mail 3 months after injury revealed the patient's condition to be stable after discontinuation of immobilization and range of motion to be recovered. No residual feelings of instability or sequelae of neurovascular compromise were reported.

DISCUSSION

Pediatric elbow trauma and fractures account for a third of all limb fractures, but can be easily misdiagnosed due to the complicated anatomy seen in children. Hanlon et al. estimated that upper extremity injuries account for 65% of all fractures and dislocations in children. Moreover, radial head subluxation has been estimated to occur in up to 25% of all elbow injuries in children younger than 10 years old.[17] Dislocations of the radius can be seen in isolation or in combination with an ulnar or humeral fracture, but the dislocation can be much more subtle than the occult fractures that may accompany it. Not identifying and properly addressing these dislocations can lead to a plethora of complications including impairment of elbow function.[25]

There are three main types of radial head dislocations: traumatic, congenital, and idiopathic. Acute traumatic radial head dislocation injuries are rare, as the annular ligament and anterior capsule must be torn for the anterior dislocation to occur. These injuries are usually the result of a direct blow to the elbow. Children with congenital radial head dislocations are often asymptomatic and can have bilateral dislocations or dislocations associated with syndromes of ligamentous laxity, such as Ehlers-Danlos syndrome. Idiopathic dislocations have been reported, however a trauma history is typically present.[11] For the purposes of the present report and review, only acute traumatic irreducible radial head dislocations were included, whereas idiopathic and congenital forms of radial head dislocations were excluded.

Although irreducible radial head dislocations are rare injuries, there are prior reports of these types of injuries.[10-24] In cases of acute traumatic irreducible radial head dislocations, various blocks to closed reduction have been previously described. Irreducible radial head dislocation secondary to anterior annular ligament interposition has been documented in some of these cases and its detection and management are crucial to prevent future complications in the pediatric population. The limited cases available suggest the two most common anatomic factors limiting reducibility of the radial head are the anterior capsule and annular ligaments. Other potential causes of irreducibility in these cases include entrapment of the biceps tendon, brachialis, and posterior interosseous nerve. Table 1 reviews the injury, amount of attempted closed reductions, type of radial displacement, interposition, and treatment of the various case reports cited. Similar to other reported cases, capsular tissue and annular ligament interposition were primarily responsible for blocked reduction in the present report. (Table 1)

Despite these prior reports, the present case is a unique example of an irreducible radial head dislocation for several reasons. To the author's knowledge, no other reports have been described of an irreducible radial head dislocation in the setting of both a posterior elbow dislocation and coronoid process fracture. Irreducible radial head dislocations, however, have been reported in the setting of Monteggia injuries. Defined primarily as a proximal ulnar shaft fracture with an associated radial head dislocation, Monteggia injuries themselves are rare, only accounting for 0.6-2.0% of fractures in children.[24] Therefore, the association of a potentially irreducible radial head dislocation in Monteggia injuries is intuitive. With enough force to break the proximal ulna, the same force can very well allow for radial head dislocation with soft tissue interposition blocking reduction. Our case, however, is unique in that the irreducible radial head dislocation occurred in a terrible triad like setting – with a simultaneous coronoid process fracture and posterior elbow dislocation.

Most cases of irreducible radial head dislocations report anterior dislocations. Our case is also unique in that the radial head was dislocated in a postero-lateral direction. This is best explained by the overall posterior translation of the olecranon as well. In a terrible triad injury, a posterior elbow dislocation causes fractures to the coronoid process and radial head/neck when they impact into the distal humerus. In our case, though not a true terrible triad given the lack of radial neck/head fracture, this same mechanism appears to have dislocated the radial head rather than fracturing it. As the distal humerus impacted into the radial head, the annular ligament in our case displaced from around the radial neck (not unlike a nursemaid's elbow). This ultimately allows the radial head to travel in a divergent trajectory, with respect to the proximal ulna, and buttonhole in the extensor mechanism of the forearm.

In addition to repairing the disrupted joint capsule and extensor mechanisms, the integrity of the annular ligament must be assessed. Tears in the annular ligament may need to be repaired. When present, these tears can be managed based on size. In small annular ligament tears, the radial head can sublux through the ligament, however < 50% of the radial head will be exposed.[17] The ligament can be reduced through maneuvers like longitudinal traction, extension, and supination followed by flexion.[17] Maintaining correct placement of the annular ligament around the radial head can be achieved via immobilization in flexion.[17] In large tears, the radial head can buttonhole distally and cause the annular ligament to flip proximally. This occurs when > 50% of the radial head is through the membrane, making closed reduction difficult.[17] During reduction attempts, the annular ligament can become locked between the radius and capitellum as well.[11] In our case, complete subannular tear was observed given the complete dislocation of the radial head. However, complete circumferential integrity was observed in our case and the annular ligament was reduced around the radial neck. This ultimately aided in overall stability following reduction.

Table 1. Previous Reported Cases of Traumatic Pediatric Irreducible Radial Head Dislocations

Author	Year	Injury	Closed Attempts	Radial Displacement	Block to Reduction
Nevaiser[10]	1971	Radial head dislocation	1	Anterior	Anterior Capsule
Morris[11]	1974	Radial head dislocation with a Monteggia fracture	0	Anterior	Posterior interosseous nerve
Spur[12]	1977	Radius dislocation with proximal ulna fracture	2	Anterolateral	Posterior interosseous nerve
Manske[13]	1982	Isolated traumatic dislocation of the radial head	1	Anterior	Annular Ligament
Armstrong[14]	1987	Isolated radial head dislocation	1	Anteromedial	Biceps Tendon
Veenstra[15]	1993	Radius dislocation with a radial head dubious fissure	>1	Anteromedial	Biceps Tendon
Yoshihara[16]	2002	Radial head fracture dislocation	1	Anteromedial	Biceps Tendon
Bradley[17]	2007	Radial head dislocation	4	Anteromedial	Annular Ligament
Aversano[18]	2011	Radial head dislocation	>1	Anterior	Anterior Capsule
Aversano[18]	2011	Left lateral humerus fracture with Monteggia fracture	1	Anterior	Anterior Capsule
Aversano[18]	2011	Radial head dislocation with ulnar plastic deformation and Monteggia fracture	>1	Anterior	Anterior Capsule
Takase[19]	2011	Isolated radial head dislocation with non-displaced olecranon fracture	1	Anteromedial	Anterior Capsule
Li[20]	2013	Monteggia fracture dislocation	1	Anterolateral	Posterior interosseous nerve
Ha[21]	2014	Monteggia fracture dislocation	>1	Anterior	Anterior Capsule
Camp[22]	2015	Isolated radial head dislocation	1	Anterior	Brachialis Tendon
Tarallo[23]	2020	Isolated radial head dislocation	2	Anterior	Anterior Capsule
Tran[24]	2021	Dislocation of radial head with plastic bowing of the ulna	2	Anterior	Annular Ligament

CONCLUSION

Irreducible radial head dislocations are documented, but extremely rare in the pediatric population. This is in part due to the high amount of force needed to cause such an injury pattern. Additionally, given how rare this type of injury is, it is often easily missed, and delays in treatment contribute to a multitude of complications. Given that the annular ligament is the main stabilizer of the radial head, prompt attention should be given to reconstruction or repositioning of this structure to maintain the elbow joint articulations. In our case and many similar to it, the rapid time to visualization and stabilization of the radial head continues to be essential in preventing further injury and providing the best opportunity for regaining full range of motion in the joint.

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UTILIZATION TRENDS, PATIENT-DEMOGRAPHICS, AND COMPARISON OF MEDICAL COMPLICATIONS OF SLIDING HIP SCREW OR INTRAMEDULLARY NAIL FOR INTERTROCHANTERIC FRACTURES: A NATIONWIDE ANALYSIS FROM 2005 TO 2014 OF THE MEDICARE POPULATION

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ABSTRACT

Background: Studies demonstrate an increase incidence of intertrochanteric fractures within the United States. Matched studies evaluating intertrochanteric fractures managed with either sliding hip screw (SHS) or intramedullary nail (IMN) within the Medicare population are limited. The purpose of this study was to investigate: 1) annual utilization trends; 2) patient demographics; and 3) complications including mortality.

Methods: A retrospective query using a nationwide database was performed. Patients undergoing SHS or IMN for intertrochanteric fractures were identified. The query yielded a total of 37,929 patients utilizing SHS (n = 11,665) or IMN (n = 26,264). Patients were matched 1:1 based on comorbidities. Primary outcomes included: utilization trends, patient demographics, 90-day complications, and 90-day readmission rates. Linear regression analyses were used to compare utilization trends. Pearson's c^2 analyses were used to compare patient-demographics, medical complications, and 90-day readmission rates. A p-value less than 0.05 was considered statistically significant.

Results: Linear regression analysis demonstrated a statistically significant decrease in utilization of SHS for IT fractures (p<0.0001); whereas utilization for IMN stayed consistent (p=0.36). IMN had significantly higher prevalence of comorbidities compared to SHS, notably, hyperlipidemia (70.6 vs. 62.6%; p<0.0001). Based on 1:1 match, IMN patients had significantly higher rates of 90-day medical complications, such as respiratory failure (11.0 vs. 8.1%; p<0.0001) and VTE (4.2 vs. 3.2%; p<0.001; however, there was not a statistical difference in postoperative infection (1.4 vs. 1.5%, p=0.06). There was no statistical difference in 90-day mortality between IMN and SHS cohorts (0.19 vs .13%, p = 0.249).

Conclusion: This analysis demonstrates a difference in utilization of SHS and IMN for patients with IT fractures. Patients with IMN had significantly higher prevalence of comorbid conditions and incidence of 90-day postoperative complications compared to SHS patients. The study can be utilized by orthopaedic surgeons to potentially anticipate healthcare utilization depending on implant selection.

Level of Evidence: III

Keywords: intertrochanteric fractures, SHS, intramedullary nail, national trends

INTRODUCTION

Intertrochanteric femur fractures are a common injury pattern in the United States as we observe a growing elderly population with subsequent age-related bone changes, drawing attention to surgical management, cost trends, patient specific factors, morbidity, and mortality. Annual incidence of 150,000 has been reported.[1,2] Furthermore, the incidence of elderly hip fractures and cost are modeled to increase from 2005 to 2025 by 51% and 49%, respectively.[3] Conversely, some studies have reported a decrease in incidence of hip fractures and subsequent mortality with an increase in comorbidities between 1995 and 2005, which has coincided with increasing use of bisphosphonate therapy in this patient population.[1,4-9]

The possibility of increasing incidence has raised concern over the burden of cost of management as hip fractures contribute disproportionately to annual expenditure compared to other osteoporotic fractures, $6 billion USD per year.[7,10-16] It has been reported that patients typically require $40,000 in medical resources in the first year after injury and around $5000 in the following years.[3,17,18] The preferred treatment for these fractures remains surgical with the choice of modality

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primarily based on fracture pattern and surgeon preference. Currently, the two mainstay implant options in treating intertrochanteric femur fractures are the sliding hip screw (SHS) with side plate, introduced in the 1950s, and the intramedullary nail (IMN) with an SHS component, also referred to as the cephallomedullary nail (CMN), which came into common practice in the 1990s.[10,19-21]

A national trend exists for younger surgeons preferring IMN over SHS despite lacking a strong body of evidence supporting the benefit of this transition.[2,9,10,22] It has been recently reported that 92.4% of IT fractures have been estimated to be managed with IMN, representing a 49.1% increase in the study period.[22] Advantages of the IMN are thought to provide an internal buttress effect against fracture collapse and medialization of the distal fracture component, especially in unstable fracture patterns. Additionally, IMN offers limited soft tissue insult by percutaneous insertion in an era of minimally invasive focus. However, use of IMN traditionally have posed the risk of intraoperative and postoperative femur fracture, which may have been improved by the development of more anatomically conforming implant designs and increased surgeon familiarity with technique.[23-31] Despite these proposed advantages, there is limited literature to prove the superiority of this implant. In fact, randomized trials have described similar outcomes in treatment with IMN when compared to SHS.[25-29,31-37]

Current American Academy of Orthopedic Surgeons (AAOS) recommendations include both SHS and IMN as suitable implants for treating stable IT fractures, and IMN as superior in managing unstable fracture patterns due to the aforementioned biomechanical advantages.[20,28,38-40] However, the implant cost of IMN remains approximately 2-3 times higher than SHS, when both devices are appropriate options for management of stable fractures, information that may not be common knowledge of the operating surgeon.[30,38,41,42]

Given current implant trends, cost considerations, and changing patient population factors, it is prudent to continue to further investigate outcomes surrounding the two treatment options. Therefore, the purpose of this study was to analyze a comprehensive administrative database and investigate patients undergoing SHS or IMN for intertrochanteric fractures. Specifically, we evaluated: 1) annual utilization trends; 2) patient-demographics; and 3) complications including mortality.

METHODS

Database

A query from January 1st, 2005 to March 31st, 2014 was performed using the Medicare Standard Analytical Files from the PearlDiver (PearlDiver Technologies, Fort Wayne, Indiana) supercomputer. PearlDiver is a commercially available database which has been used extensively for orthopedic-related research as it contains the records of over 100 million patients from the Humana and Medicare claims databases. The database relies on International Classification of Disease, ninth revision (ICD-9), ICD-10, and Current Procedural Terminology (CPT) coding to query complications, diagnoses, reimbursements, discharge dispositions, in addition to other metrics. Since the database provides anonymous patient information the study was exempt from the institution's Institutional Review Board (IRB) approvals.

Study Group

The database was first queried for all patients who sustained closed intertrochanteric fractures and were queried using ICD-9 diagnosis code 801.20 to 801.22. The database was then queried for all patients having undergone SHS or IMN fixation using CPT codes 27244 and 27245, respectively. The query yielded a total of 37,929 patients utilizing SHS (n = 11,665) or IMN (n = 26,264) for intertrochanteric fractures during the study interval. Patients were then matched on a 1:1 basis based on medical comorbidities, which included age, sex, tobacco use, hypertension, chronic obstructive pulmonary disease, body mass index, hyperlipidemia and major depressive disorder. After 1:1 matching, the query yielded 23,236 total patients with an equal number in each group (n=11,618).

Outcomes Assessed

Outcomes analyzed in this study included annual utilization trends, patient demographics, 90-day medical complications, and 90-day readmission rates between the two cohorts. Patient demographics analyzed and compared included: age, sex, and medical comorbidities – body mass index (BMI), congestive heart failure, chronic obstructive pulmonary disease, coagulopathies, depression, diabetes mellitus, electrolyte/fluid imbalance, hyperlipidemia, hypothyroidism, peptic ulcer disease, peripheral vascular disease, opioid use disorder, renal failure, rheumatoid arthritis, sleep apnea, and tobacco use between the two cohorts.

Ninety-day medical complications analyzed and compared included post-operative infections, irrigation and debridement, myocardial infarction, respiratory failure, urinary tract infections, pneumonia, cholecystitis, cerebrovascular accidents, and transfusions of blood products. Ninety-day medical post-operative complications were also analyzed for patients that were matched 1:1, which also included the same variables discussed above in addition to 90-day mortality.

Data Analyses

Statistical analyses were performed using the open programming language R (R Foundation for Statistical Computation, Vienna, Austria). Linear regression analyses were used to compare changes in rates of the two procedures for intertrochanteric fractures through the study interval. Patient demographics of age, sex, and medical comorbidities were analyzed and compared using Pearson's c^2 analyses. Medical complications and 90-day readmission rates were also analyzed utilizing Pearson's c^2 analyses. A p-value less than 0.05 was considered statistically significant.

RESULTS

Patient Demographics

Intramedullary nail for intertrochanteric fractures were utilized more often across all age groups compared to sliding hip screw in a statistically significant manner ($p<0.0001$), however distribution of intramedullary nail and sliding hip screw were similar with respect to sex ($p=0.316$). Patients with intramedullary nail for intertrochanteric fractures were found to have significantly higher frequency of comorbid conditions compared to SHS, except for congestive heart failure and renal failure; however, the frequency of the latter comorbid conditions did not reach statistical significance. Comorbid conditions with the greatest prevalence in the IMN cohort included hypertension (95.0%), electrolyte/fluid imbalance (81.4%), and hyperlipidemia (70.6%); whereas the greatest comorbid conditions seen in the SHS cohort were hypertension (94.4%), electrolyte/fluid imbalance (80.5%), and peripheral vascular disease (65.9%) (Table 1).

Annual Utilization

The number of intertrochanteric fractures decreased through the study interval from 122,481 in 2005 to 99,607 by first quarter of 2014 ($p<0.0001$). During this same time, annual utilization rates of intramedullary nail for intertrochanteric fractures increased 21.19% through the study interval (2005 = 2,137; 2014 = 2,590; $p=0.59$), but failed to reach statistical significance. Annual utilization rates of SHS for intertrochanteric fractures decreased 80.81% during the study interval (2005 = 2,544; 2014 = 488; $p<0.0001$) (Figure 1).

90-Day Complications

Patients in the IMN cohort were found to have significantly higher incidence of medical complications compared to patients within the SHS cohort. IMN cohort patients were found to have significantly higher incidences of cerebrovascular accidents (6.4 vs. 5.3%, $p<0.0001$), cholecystitis (0.2 vs. 0.2%; $p=0.005$), deep

Table 1. Patient Demographics

	Intramedullary Nail		Sliding Hip Screw		
Demographics	n	%	n	%	p-value[D]
Age (Years)					<0.0001
<64	1,071	4.1	514	4.4	
65 – 69	1,484	5.7	615	5.3	
70 – 74	2,200	8.4	886	7.6	
75 – 79	3,486	13.3	1,633	14.0	
80 – 84	5,616	21.4	2,554	21.9	
85>	12,337	47.0	5,422	46.5	
Unknown	70	0.3	41	0.4	
Sex					0.316
Female	19,142	72.9	8,463	72.6	
Male	7,052	26.9	3,161	27.1	
Unknown	70	0.3	41	0.4	
Comorbidities					
Alcohol Abuse	1,612	6.1	705	6.0	0.741
BMI <19kg/m^2	1,703	6.5	617	5.3	<0.0001
BMI 19 – 24kg/m^2	1,206	4.6	367	3.1	<0.0001
BMI 25 – 29kg/m^2	778	3.0	214	1.8	<0.0001
BMI 30 – 39kg/m^2	776	3.0	257	2.2	<0.0001
BMI 40 – 70kg/m^2	254	1.0	87	0.7	0.04
CHF	15,745	59.9	7,099	60.9	0.09
Coagulopathies	7,933	30.2	3,263	28.0	<0.0001
COPD	1,444	5.5	556	4.8	0.003
Depression	13,428	51.1	5,699	48.9	<0.0001
Diabetes Mellitus	13,350	50.8	5,625	48.2	<0.0001
Electrolyte/Fluid Imbalance	21,380	81.4	9,389	80.5	0.03
Hyperlipidemia	18,532	70.6	7,308	62.6	<0.0001
Hypertension	24,950	95.0	11,007	94.4	0.01
Hypothyroidism	12,756	48.6	5,336	45.7	<0.0001
Opioid Use Disorder	461	1.8	189	1.6	0.37
Peptic Ulcer Disease	3,219	12.3	1,329	11.4	0.01
Peripheral Vascular Disease	17,830	67.9	7,683	65.9	<0.0001
Renal Failure	5,334	20.3	2,400	20.6	0.56
Rheumatoid Arthritis	5,159	19.6	2,000	17.1	<0.0001
Sleep Apnea	2,139	8.1	793	6.8	<0.0001
Tobacco Use	4,471	17.0	1,736	14.9	<0.0001

Demographics of Patients Utilizing Either Intramedullary Nail or Sliding Hip Screw for Intertrochanteric Fractures within the Medicare Population from 2005 to 2014. BMI = Body Mass Index; CHF = Congestive Heart Failure; COPD = Chronic Obstructive Pulmonary Disease; D = Assessed by Pearson's c^2; * = <11 Patients.

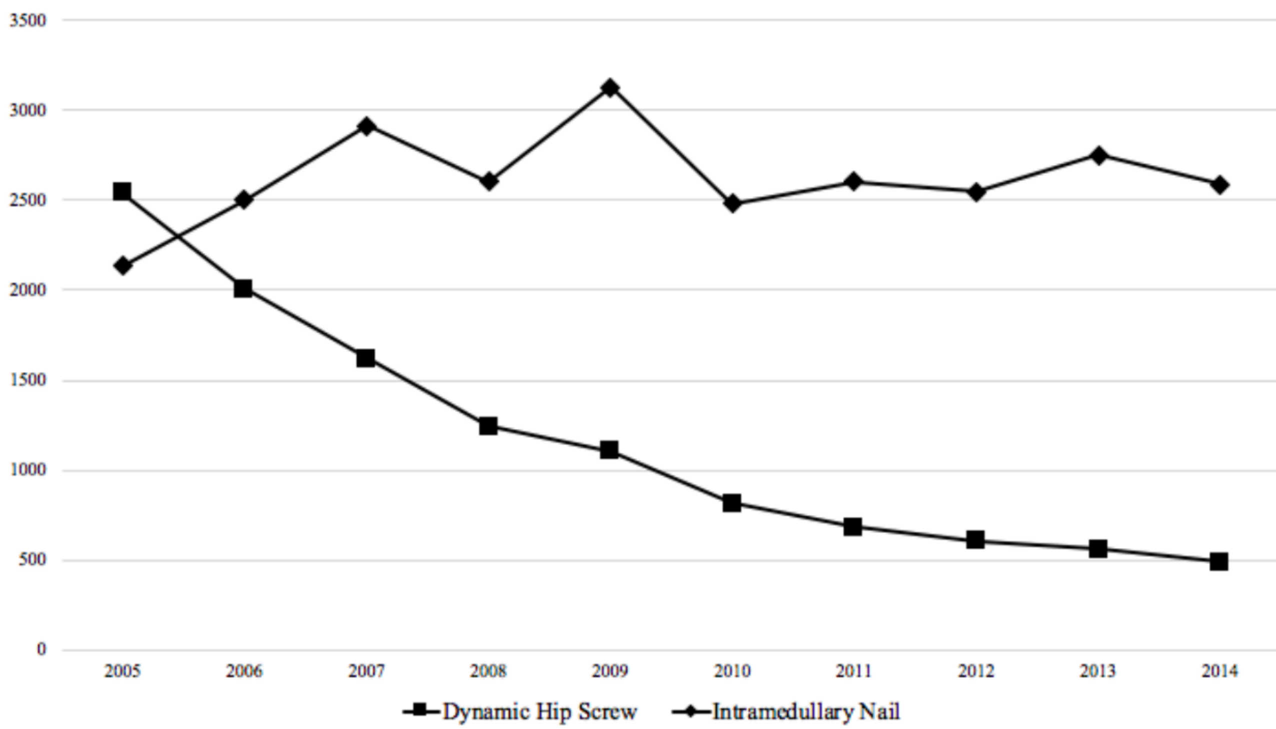

Figure 1. Annual Utilization Trends of Intramedullary Nails vs Sliding Hip Screws. Linear representation of the annual utilization rates (2005-2014)0of intramedullary nail or sliding hip screw for treated patients with intertrochanteric fractures within the sampled Medicare population.

vein thromboses (3.8 vs. 2.8%; p<0.0001), myocardial infarctions (3.0 vs. 2.3%; p<0.0001), pneumonias (3.1 vs. 2.5%; p<0.0001), pulmonary embolisms (1.0 vs. 0.8%, p<0.0001), requiring transfusion of blood products (7.0 vs. 5.9%; p<0.0001) and urinary tract infections (27.5 vs. 23.3%, p<0.0001) within 90-days following the index procedure (Table 2).

Patients undergoing IMN for stable IT fractures were found to have higher incidence of cerebrovascular accidents (6.4 vs 5.3%, p<0.0001), DVT (3.8 vs 2.8% p<0.0001), MI (3.0 vs 2.3%, p<0.0001), pneumonia (3.1 vs 2.5%, p<0.0001), post-operative infection (1.5 vs 1.5%, p<0.0001), PE (1.0 vs 0.8%, p<0.0001), respiratory insufficiencies (11.8 vs 8.3%, p<0.0001), transfusions (7.0 vs 5.9%, p<0.0001), and UTI (27.5 vs 23.3%, p<0.0001). However, patients undergoing SHS had significantly higher incidence of irrigation and debridement (0.5 vs 0.4%, p<0.0001).

90-day medical complications and 90-day mortality was also identified after 1:1 matching based on medical comorbidities. Patients undergoing IMN had statistically higher incidence of DVT (3.20 vs 2.33%, p<0.0001), MI (2.82 vs 2.27%, p=0.007), VTE (4.18 vs 3.24%, p<0.0001), respiratory insufficiencies (11.02 vs 8.14%, p<0.0001), and UTIs (26.8 vs 22.3%, p<0.0001). Overall, patients in the IMN cohort had significantly greater incidence of 90-day complications (60.71 vs 50.56%, p<0.0001) (Table 3). There was no significant difference in 90-day mortality between the two groups (0.19 vs 0.13%, p=0.249) (Table 3).

DISCUSSION

Intertrochanteric femur fractures are commonly encountered by orthopedic surgeons in all subspecialties with an annual incidence of 150,000 in the United States alone1. With an aging population and increased rates of osteoporosis, it is projected that the incidence of IT fractures continues to grow, though these projections have not fully been realized as recent studies have conflicting evidence for increased incidence of IT fractures.[2,3,9,22] Treatment for these fractures remains operative, with surgeon choice of sliding hip screw versus intramedullary nail.[20] The main difference between implant choices remains theoretic superiority of IMN in unstable patterns as well as cost, with IMN costing roughly 2-3 times that of SHS.[30,38,41] Despite this cost difference and lack of clinical evidence of superiority, the rates of IMN usage continue to increase.[10,25,28,37] The current study demonstrates the continued preference of orthopedic surgeons for use of intramedullary nail for treatment of intertrochanteric femur fractures over sliding hip screws. Additionally, when accounting for underlying comorbid conditions,

Table 2. Medical Complications at 90-Days

	Intramedullary Nail		Sliding Hip Screw		
Medical Complications	n	%	n	%	p-value[D]
Cerebrovascular Accidents	1,679	6.4	613	5.3	<0.0001
Cholecystitis	64	0.2	26	0.2	0.005
Deep Vein Thromboses	1,011	3.8	325	2.8	<0.0001
Irrigation and Debridement	102	0.4	58	0.5	<0.0001
Myocardial Infarction	780	3.0	268	2.3	<0.0001
Pneumonias	803	3.1	286	2.5	<0.0001
Post-operative Infections	392	1.5	177	1.5	<0.0001
Pulmonary Embolisms	266	1.0	93	0.8	<0.0001
Respiratory Insufficiencies	3,093	11.8	964	8.3	<0.0001
Transfusions	1,839	7.0	693	5.9	<0.0001
Urinary Tract Infections	7,225	27.5	2,722	23.3	<0.0001

Comparison of 90-Day Medical Complications in Patients Undergoing Intramedullary Nail or Sliding Hip Screw for Intertrochanteric Fractures within the Medicare Population. D = Assessed by Pearson's c^2.

this study found patients treated with IMN had higher 90 day complication rates as compared to those treated with SHS; however, there was no significant difference in 90-day mortality rates between the two groups. To our knowledge, this is the first study to compare outcomes in matched patients undergoing IMN compared to SHS for stable IT fractures in the Medicare population with a large sample size in each group (n=11,618).

The trend toward use of IMN for IT fractures was first identified by Anglen et al. who identified a dramatic increase of IMN usage from 3% in 1999 to 67% in 2006 using the ABOS Part II database.[10] Smith et al. confirmed the continuation of this trend in young orthopedic surgeons through 2017, at which time 92.4% of IT femur fractures were treated with IMN.[22] This trend has not only been observed in young orthopedic surgeons. Studies by Radcliff et al. and Werner et al. demonstrated a very similar trend in patients at Veteran's Affairs hospitals as well as the Medicare patient population.[9,43] The study presented here serves to demonstrate the continuation of the trend in Medicare patients as first demonstrated by Werner et al. The final five years of study seem to indicate a plateau reached in the use of IMN, which may be the result of hitting a "floor" in the use of SHS as suggested by Smith et al.

Table 3. Medical Complications at 90-Days (Matched)

	Intramedullary Nail		Sliding Hip Screw		
Medical Complications	n	%	n	%	p-value[D]
Post-Operative Infection	164	1.41	173	1.49	0.0621
Irrigation and Debridement	45	0.39	56	0.48	0.272
Deep Vein Thromboses	372	3.20	271	2.33	<0.0001
Cerebrovascular Accidents	720	6.20	633	5.45	0.0148
Myocardial Infarction	328	2.82	264	2.27	0.007
Pneumonias	333	2.87	279	2.40	0.026
Venous Thrombus Embolism	486	4.18	376	3.24	<0.0001
Pulmonary Embolisms	117	1.01	97	0.83	0.169
Respiratory Insufficiencies	1280	11.02	946	8.14	<0.0001
Transfusions	90	0.77	69	0.59	0.094
Urinary Tract Infections	3118	26.8	2710	22.3	<0.0001
Mortality	22	0.19	15	0.13	0.249
Total	7053	60.71	5478	50.56	<0.0001

Comparison of 90-Day Medical Complications in patients matched 1:1 for comorbidities undergoing Intramedullary Nail or Sliding Hip Screw for Intertrochanteric Fractures within the Medicare Population. D = Assessed by Pearson's c^2.

There are several hypothesized reasons for the increased incidence in the use of IMN. Forte et al. demonstrated younger surgeons and those that work at teaching hospitals were more likely to opt for IMN.[44] Further studies have shown that surgeons who worked at their institution for shorter periods, specialties outside of lower limb trauma, and those who had exposure to IMN in training were more likely to use IMN.[45,46] Given these findings, it is not surprising that young surgeons coming out of training are more likely to use intramedullary devices as this is a familiar device. This may explain the trend noted in the ABOS part II.[10,22] No current study is available that reviews current orthopedic surgery resident case numbers when comparing these treatment options, but may be an interesting area of future study.

This study identified that 90 day medical complication rates are increased in the IMN group. This is in agreement with the previous studies by Smith et al. and Werner et al.[9,22] In addition to medical complications, some studies have also shown increases in 30 day mortality for patients treated with IMN.[47] These findings may be multifactorial and could be related to patient selection, as this study demonstrated increased co-morbidities among the IMN group. Although, when controlling for these variables, complication rates remained significantly elevated. There may be characteristics inherent to the device that contribute to this as well. Reaming of the intramedullary canal introduces increased intramedullary pressure that has been demonstrated to increase fat intravasation which may lead to pulmonary emboli.[48,49] This may explain the higher rates of pulmonary emboli and cerebrovascular accidents, but does not fully explain the remainder of the medical complications. Increased operative time and blood loss have also been implicated as a reason for the increase in medical complications9. However, the current literature does not seem to demonstrate a clear increase in blood loss or operative time when comparing these two treatment options.[50,51]

The 90-mortality rate between the IMN and SHS cohorts were also compared in this study. The findings in this study were consistent with Werner et al., where there was no statistical difference in the 90-day mortality.[52] However, there does not appear to be a consensus in the literature regarding mortality rates in patients undergoing IMN vs SHS for IT fractures. Whitehouse et al. analyzed the 82,990 patients from the National Hip Fracture database and found a 12.5% increase in 30 day mortality for patients undergoing IMN compared to SHS.[47] On the other hand, Grønhaug et al. demonstrated significantly lower one year mortality rates in patients undergoing treatment of unstable and stable IT fractures with IMN using the Norwegian Hip Fracture Register.[53]

While the large number of patients ensures the study was well-powered, the current study is not without limitations; most of which are inherent to the use of an administrative database. We analyzed only a single insurance database, and the results of the study might not be a true cross-sectional representation on the trends of treating intertrochanteric fractures in the United States. Additionally, the study is reliant on accurate diagnostic and procedural coding, and it is currently estimated that there are up to 1.3% of coding errors within the Medicare database. Furthermore, the database was unable to provide additional granular detail such as radiographic imaging to determine whether patients had stable or unstable intertrochanteric fractures, as the fracture classification is vital in driving management on treating these fracture patterns. Finally, clinical outcome data is not available through the database that was utilized, which limits the ability to comment on outcomes.

CONCLUSION

There remains a trend toward the use of IMN over SHS for the treatment of intertrochanteric femur fractures despite evidence to support superiority of the implant. Given the increased cost associated with the implant and increased rates of 90 day medical complications, this study can assist surgeons and consoling patients on possible outcomes depending on treatment modality of stable intertrochanteric femur fractures.

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WHAT ARE THE BARRIERS TO INCORPORATING NUTRITION INTERVENTIONS INTO CARE OF OLDER ADULTS WITH FEMORAL FRAGILITY FRACTURES?

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ABSTRACT

Femoral fragility fractures cause substantial morbidity and mortality in older adults. Mortality has generally been approximated between 10-20% in the first year after fracture and among those who do survive, another 20-60% require assistance with basic activities within 1-2 years following fracture.[1] Malnutrition is common and perpetuates these poor outcomes. Nutrition supplementation has potential to prevent post-injury malnutrition, preserve functional muscle mass, and improve outcomes in older adults with femoral fragility fractures, however high-quality evidence is lacking, thus limiting translation of interventions into clinical practice. This review article is designed to highlight gaps in the evidence investigating nutrition interventions in this population and identify barriers for translation to clinical practice. Our goal is to guide future nutrition intervention research in older adults with femoral fragility fractures.

Level of Evidence: V

Keywords: femoral fragility fracture, nutrition, malnutrition, protein, muscle, physical function, osteoporosis, sarcopenia, osteosarcopenia, hip fracture, nutrition supplementation

INTRODUCTION

Femoral fragility fractures, which include hip and distal femur fractures, are devastating complications of osteoporotic disease in the elderly. Over 75% of fragility fractures occur in people aged 75 years or older, resulting in dramatic loss of independence, physical function, and mortality in an already frail population.[2,3] Many of these complications are associated with loss of muscle mass and progression to sarcopenia. Significant loss of muscle mass occurs during the first six weeks after injury and is directly due to disuse and nutritional deficiencies.[4] Postoperative nutritional supplementation provides an opportunity to preserve muscle mass and accelerate return to functional status, as well as reduce surgical complications and mortality.[5-6]

Various modalities of postoperative nutrition interventions have been explored in the context of fragility fracture. Protein supplementation has shown promise in reducing surgical complications in addition to enhancing walking recovery and body weight maintenance in the acute phase of recovery.[7-10] Formal dietician evaluation, in conjunction with diet modification and supplementation, is also utilized to provide multimodal, individualized care to patients. Evidence suggests that these interventions have the potential to improve postoperative nutritional status, blunt reduction in quality-of-life, and shorten length of hospital stay.[11-13] Select previous clinical trials of nutrition interventions in older adults with femoral fragility fractures are summarized in Table 1.

Inconsistent interventions in the current literature limit ability to draw definitive conclusions about the efficacy and feasibility of nutritional interventions following fracture fixation. Low enrollment, varying supplement type, composition, and duration, and lack of clinically significant outcomes make it difficult to establish widespread practice guidelines. The 2021 American Academy of Orthopedic Surgeons guidelines strongly recommended that nutrition assessment should be a part of the inter-disciplinary team, however the two studies cited are dated and do not recommend specific nutrition supplementation.[14] Additionally, a relative dearth of basic science evidence supporting benefits of nutritional interventions, exploration into the cost-effectiveness of these modalities, and inconsistent patient compliance in trials further serve as roadblocks toward future use of nutritional interventions in the context of orthopedic trauma such as fragility fractures.

The objectives of this literature review are to summarize the current evidence for postoperative nutritional interventions in patients with femoral fragility fracture, critically evaluate limitations, and provide guidance for establishing a more complete and uniform knowledge base for future research. We highlight areas of contro-

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Table 1. Summary of Randomized Clinical Trials Evaluating the Impact of Protein/Amino Acid Supplementation in Patients with Femur Fractures

First Author	Injury Treated	Age Criteria	Number Enrolled	Randomization	Intervention	Duration	Primary Outcome(s)	Secondary Outcome(s)
Anbar[16]	Hip Fracture	≥65 years	50	1:1.3	Ensure Plus® or Glucarna®	14d or until hospital discharge	Postoperative complications and hospital LOS	Energy intake and calculated energy balance
Botella-Carretero[54]	Hip Fracture	≥65 years	60	1:1	Oral nutritional supplement (ONS) 40 g protein and 400 kcal of energy daily	Duration of hospital stay	Change in serum albumin, prealbumin, and RBP	Tolerance to supplementation, LOS, postoperative complications, time to start of mobilization
Botella-Carretero[21]	Hip Fracture	≥65 years	90	1:1:1	Protein group: ONS of 36g protein daily Protein-energy group: ONS of 37.6g protein and 500kcal energy daily	Duration of hospital stay	Change in serum albumin, prealbumin, and RBP	Tolerance to supplementation, LOS, postoperative complications, time to start of mobilization
Bruce[49]	Hip Fracture	All	109	1:1.2	235 mL daily ONS of 352 kcal energy, 17.6 g protein, 11.8 g fat, 44.2 g carbohydrate, vitamins, and minerals	28d	Weight change	Mortality rate, discharge destination, ADL, LOS
Delmi[15]	Femoral Neck Fracture	≥60 years	59	1:1.2	250 mL ONS of 20 g protein and 254 kcal energy daily	Mean = 32d	Postoperative complications, mortality	LOS, anthropometric measures (triceps skinfold, upper arm circumference), Biochemical measures (e.g. albumin, 25(OH) D, prealbumin, alkaline phosphatase)
Ekinci[28]	Hip Fracture	≥65 years	75	1:1	Enteral 3 g calcium β-hydroxy-β-methylbutyrate, 1000 IU vitamin D, and 36 g protein twice daily	30d	Weight and BMI	Wound healing time, LOS, arm circumference, calf circumference, muscle strength, CRP
Espaulella[55]	Proximal Femur Fracture	≥70 years	171	1:1	20 g protein, 800 mg calcium, 25 IU vitamin D3, 149 calorie ONS daily	60d	Functional recovery, fracture-related mortality	Postoperative complications, discharge outcome, compliance, LOS
Houwing[19]	Hip Fracture	All	103	1:1	400 mL daily ONS of 125 kcal, 10 g protein, 1.5 mg l-arginine, 5 mg zinc, 125 mg vitamin C, 50 mg vitamin E, 1 mg carotenoids	4 weeks or until discharge	Incidence of pressure ulcers	Severity of pressure ulcers, time of ulcer onset
Invernizzi[56]	Hip Fracture	≥65 years	32	1:1	Aminotrofic® 4 g daily in conjunction with physical exercise rehabilitation program (performed in both groups)	2 months	Hand grip strength, Timed Up and Go Test, Iowa Level of Assistance scale	Daily caloric and protein intake, health-related quality-of-life
Malafarina[5]	Hip Fracture	≥65 years	107	1.1:1	Ensure Plus® enriched with 0.7 g/100 mL CaHMB, 227 IU/100 mL 25(OH)D, and 227 mg/100 mL of calcium twice daily	Duration of hospital stay	Body composition measures (e.g. BMI, appendicular lean mass) and nutritional markers (e.g. albumin, triglycerides, 25(OH)D)	Postoperative complications, functional status, inflammatory markers (e.g. CRP, IL-1, IL-6)

Table 1. Summary of Randomized Clinical Trials Evaluating the Impact of Protein/Amino Acid Supplementation in Patients with Femur Fractures (Continued)

Olofsson[57]	Femoral Neck Fracture	≥70 years	199	1.1:1	Multidisciplinary program on orthopedic-geriatric unit consisting of dietician consult, systematic food and liquid intake, nutritional and protein drinks twice daily, and protein-enriched meals as necessary.	≥4d postoperatively	Postoperative complications and nutritional status	None noted
Schürch[42]	Hip Fracture	≥60 years	82	1:1	ONS of 250 kcal energy, 20 g proteins, 3.1 g lipids, 35.7 g carbohydrates, 1000 IU vitamin A, 30 μg vitamin K1, 20 mg vitamin C, 550 mg calcium, 91 mg magnesium, 429 mg phosphorus, and 228 mg sodium 5 days per week	6 months	Function and LOS	Nutrition (e.g. albumin, prealbumin, IGF-1) and immunologic (e.g. IgG, IgM) status, bone mass and remodeling
Tidermark[53]	Femoral Neck Fracture	≥70 years	60	1:1:1	Protein group: 20 g/day Protein-steroid group: 20 g/day protein and 25 mg/3 weeks nandrolone All groups received 400 IU vitamin D and 1 g calcium daily	6 months	Nutritional Status (body composition), Function, Quality-of-life	Postoperative complications
Van Stijn[58]	Hip Fracture	≥75 years	236	1:1.1	≥31.2 g taurine	6d postoperatively	Mortality and morbidity (e.g. infectious, cardiovascular event)	LOS, ADL index, oxidative stress
Wyers[25]	Hip Fracture	≥55 years	152	1:1.1	400 mL Cubitan® daily	3 months	LOS in hospital and rehabilitation units, readmissions within 6 months	Nutritional status, functional status, cognition, quality of life, postoperative complications, subsequent fracture, all-cause mortality

ONS= oral nutritional supplement, LOS=length of stay, RBP=retinol binding globulin, BMI=body mass index, ADL=activities of daily living, CRP=C-reactive protein.

versy in nutrition interventions and opportunities to fill gaps in the clinical and mechanistic evidence that, once addressed, may accelerate translation to clinical practice.

LIMITATIONS OF PREVIOUS CLINICAL TRIALS

Sample Size

Limited enrollment in clinical trials can lead to type II error and inability to apply findings to a general population. Previous clinical trials demonstrate promising benefits but were not sufficiently powered for general application. A multicenter trial performed by Delmi et al. randomized 59 older adults with femoral neck fractures to standard diet or an intervention with 20 g protein supplement twice daily for a mean 32 days postoperatively.[15] Compared to controls, patients that received supplementation had lower rates of malnutrition (as determined by serum albumin levels) and lower rates of bedsores, severe anemia, and surgical-site infections. Six-month mortality was also greater in patients that did not receive supplementation. No power analysis was performed.

Another prospective cohort study of 50 patients showed promising benefits of Ensure plus® and Glucarna® supplementation on energy balance, hospital course, and infection rate in patients over 65 admitted for hip fracture.[16] Supplementation and follow-up was limited to the duration of the hospital stay, and slow recruitment led to failure to reach the enrollment required to provide definitive conclusions. Similarly, Hitz et al. suffered from insufficient power due to small sample size in their trial examining the effect of one year of daily 3000 mg calcium carbonate along with 1400 IU cholecalciferol on bone mineral density in patients with low-energy hip fractures.[17] Hip bone mineral density was similar at 12-month follow-up, but differences were observed in spine bone mineral density in patients ≤70. Their trial included only 29 hip fracture patients, leading to a poststudy power calculation of 73.2% for their lumbar spine measurements and 29.9% for hip bone mineral density calculations.

In another example, a randomized, double-parallel trial by Neumann et al. enrolled hip fracture patients aged over 60 years, randomizing them to either two eight-ounce cans daily of Ensure® or Boost HP® postoperatively for a 28-day period.[18] Once again, recruitment goals were not reached due to lower-than-expected rates of eligible subjects in addition to high refusal rates, leading to inclusion of 46 patients. No significant differences were found between functional independence measures up to three months post-discharge in addition to length of stay on the rehabilitation unit. The underpowered nature of the study, in addition to the lack of a true control arm, increases the probability of type II error, as greater recruitment may have revealed significant differences in functional outcomes between the two groups. Low recruitment in these trials highlights the challenges of enrolling older adults with femoral fragility fractures in nutrition intervention trials and limits the reliability of conclusions. Future clinical trials of nutrition interventions should be multi-center to increase enrollment and diversity of the patient population, so that definitive conclusions can be applied to clinical practice.

Clinically Meaningful Outcomes

Another obstacle to demonstrating clinical benefit of nutritional interventions is the lack of clinically meaningful outcomes in previous trials. Houwing et al. investigated the effect of supplementing a standard hospital diet with 400 mL daily of 500 kcal energy, 40 g protein, along with arginine, zinc, vitamin C and E, and carotenoids on the incidence and severity of pressure ulcers in the acute phase of recovery from hip fracture patients.[19] Significant differences were found in relative severity, but not incidence, of pressure ulcers between the control (n=52) and intervention (n=51) arms, but there were no other clinical or functional outcomes reported to clarify the somewhat mixed results.

Wyers et al. assessed the efficacy in improving nutritional status and reducing postoperative complications of 400 mL daily of Cubitan® (500 kcal energy, 40g protein) in conjunction with scheduled dietetic counseling for three months after surgery for a low-energy hip fracture.[11] Although significant improvements in nutritional status and fewer surgical complications were found in the intervention arm (n=73) when compared to the control arm (n=79), these improvements did not translate to reduced postoperative complications, including infections, cardiovascular events, pressure ulcers, delirium, and anemia. Additionally, fracture incidence and all-cause mortality did not differ between the two groups at one- and five-year follow-up.

A single-blinded randomized control trial conducted by Torbergsen et al. found that supplementation of a regular orthogeriatric unit diet with 150 µg vitamin A, 10 mg vitamin E, 1.2 g ω-3 fatty acids, as well as calcium, vitamin D3, and vitamin K1 fortification improved 25(OH)D and vitamin K1 levels at four month follow-up, but once again the improved nutritional profile in the 31 experimental patients did not translate to improved profiles of other vitamins or bone turnover markers when compared to controls.[20] Functional and clinical outcome measures were not compared between the two groups.

Last, a parallel, three-arm trial led by Botella-Carretero and Vázquez investigated biochemical and anthropometric changes in three groups of moderate-to-severely malnourished patients, one taking 36 g of supplemental protein daily, one taking 37.6 g of supplemental protein in conjunction with 500 kcal of energy supplement per day, and the other receiving no nutrition intervention (n=30 in all groups).[21] There was a significant increase in serum albumin from admission to discharge, but the extent of this increase did not differ between any of the three groups. Additionally, there were no statistically significant differences in hospital time and postoperative complication rates between the groups, leading to inconclusive findings on the impact of the regimen on clinical outcomes. Future clinical trials should focus on outcomes important to older adults that sustain hip fractures including improved physical function and independence with reduced medical and surgical complication.[22]

Variability in Type and Composition of Nutritional Intervention

A significant roadblock to translating nutritional interventions into clinical practice is the widespread variability in type and composition of intervention studied. While EAAs have shown promise in improving functional outcomes and reducing complications, there are significant differences in the composition of EAAs administered. For example, Hendrickson et al. provided twice daily supplementation of 7 g arginine, 7 g glutamine, and 1.5 g of beta-hydroxymethylbutyrate (HMB), demonstrating reductions in postoperative complications, nonunion, and mortality in acute fracture patients randomized to standard diet and EAA supplementation (n=200) versus placebo.[7] Rondanelli et al. administered a supplement consisting of 1500 mg leucine, 1000 mg lysine, 750 mg glutamine, 550 mg valine, 450 mg threonine, 250 mg phenylalanine, 350 mg tyrosine, 350 mg histidine, 200 mg cysteine, 125 mg methionine, and 75 mg tryptophan twice daily for four weeks in randomized groups of 19 hip fracture patients.[9] This small study demonstrated a reduction in post-operative pain and increase in time spent in physiotherapy up to 45 days post-operatively, but there were no statistically significant improvements in mental or physical health measures.

A single-center trial by Eneroth et al. found that the commercially available Fortimel® (protein, vitamins, minerals) along with Vitrimix® (EAAs, minerals) infusions reduced postoperative infectious complications at 10, 30, and 120-day timepoints, largely due to reduced incidence of pneumonia and wound infections in the intervention group.[23] Subjects were given 1000 mL of IV Vitrimix® daily for three days postoperatively, then 400 mL of enteral Fortimel® daily for seven days. This protocol also attenuated mortality in the intervention group (n=40) at four-month follow-up.

Boost HP®, a commercially available drink with 20 g of protein per serving, was also explored in an underpowered trial that did not yield any statistically significant improvement in functional recovery or shortening of hospital stay when compared to Ensure® supplementation.[18] This trial brings to light an additional concern not sufficiently addressed: added sugar content in commercially available oral protein supplements. Both Boost HP® and Ensure® contain glucose, sugar, and/or maltodextrin, in the first three ingredients. Yet, a clinical assessment of blood glucose or hemoglobin A1c levels were not included, which is an important clinical outcome to monitor when supplementing a product containing more than 10 g of added sugar per serving.

Nutrition interventions have been frequently paired with participant engagement with a registered dietician, which leaves it difficult to discern improvement attributed to supplementation alone. In isolation, registered dietician intervention can positively affect postoperative nutritional and functional outcomes. Duncan et al. investigated dietician evaluation in women over 65 years old with non-pathologic hip fracture.[24] Patients who received dietetic care in addition to their standard care had lower mortality in both the trauma unit and at four-month follow-up compared to controls. There were also improvements in energy intake, handgrip strength, anthropometric measurements, weight, and biochemical values such as albumin, hemoglobin, and lymphocyte count in the experimental group. There were no significant differences in length-of-stay or complications in any of the settings studied.

A series of studies describe the outcomes of multimodal approaches. Wyers et al. utilized an oral regimen of a milk-protein based, yogurt, or juice style supplement (Cubitan®, Nutridrink Yogurt®, Nutridrink® Juice) combined with five dietetic visits over a three month span.[25] Hoekstra et al. assessed the impact of implementing a multidisciplinary nutritional program on nutritional status, body cell mass, and quality-of-life in patients with low-energy hip fracture at a single hospital.[26] Patients whose care followed the multidisciplinary protocol (n=61) had improved energy and nutritional intake, attenuated reduction in quality-of-life scores, lower risk of malnutrition, and reduced VAS pain scores three months post-operatively when compared to patients receiving standard care.

High-dose vitamin D and calcium regimens have been explored both in isolation and in conjunction with other interventional modalities for recovering hip fracture patients. As previously mentioned, Hitz et al. found no differences in hip bone mineral density at one-year follow-up in patients given 1400 IU cholecalciferol and 3000 mg calcium carbonate when compared to controls.[17] In a four-arm randomized control trial that was part of the Nottingham Neck of Femur (NoNof) study, patients within seven days of surgery for hip fracture received either a single injection of 30000 units vitamin D2 (n=25), 30000 units of vitamin D2 with one gram daily calcium (n=20), 800 units of daily vitamin D3 with one gram daily calcium (n=26), or no treatment (n=32).[27] The NoNof study group found that all modalities of vitamin D supplementation improved neck of femur, trochanter, and total hip bone mineral density while also reducing falls when compared to the placebo arm, with oral vitamin D and calcium supplementation showing the most drastic increases in total hip bone mineral density of the three treatment modalities.

Ekinci et al. supplemented 1000 IU vitamin D alongside 3 g calcium beta-hydroxy-beta-methylbutyrate (CaHMB) and 36 g protein twice daily.[28] Their formulation shortened wound healing, increased patient mobility, and reduced postoperative complications within 30 days of surgery. Malafarina et al. used a similar formulation of Ensure Plus® enriched with 0.7 g/100 mL CaHMB, 227 IU/100 mL 25(OH)D, and 227 mg/100 mL of calcium to assess impact on anthropometric measures, inflammatory markers, and functional recovery.[29] From admission to discharge in two rehabilitation facilities (mean=42.3 days), patients in the intervention group (n=49) had stable body mass index, appendicular lean mass, and muscle mass, all of which decreased significantly in controls. Activities of daily living recovery trended toward positive association with the intervention but did not reach statistical significance. The CaHMB, vitamin D, and calcium enriched Ensure Plus® reduced sarcopenic markers in patients while on the rehabilitation unit. Based on our review, future clinical trials should continue to focus on outcomes specific for the intervention chosen in the trial. For example, EAA supplementation has a known positive impact on body composition and muscle mass. Clinical trials focusing on EAA supplementation should focus on outcomes related to muscle mass, physiology, and function.

LACK OF MECHANISTIC EVIDENCE

A limiting factor in the clinical application of nutrition interventions in fragility fracture patients is the lack of mechanistic evidence to serve as a basis explaining how supplementation affects physiologic and metabolic processes. Much of the mechanistic data for supplementation and bone health or healing outcomes have been performed in rodent models, which can be difficult to use as the basis for translation to patient populations. In a study by Yoneme et al., mice that received water supplemented with milk-based proteins experienced higher expression levels of genes associated with chondrogenesis and osteogenesis up to 56 days after fracture when compared to controls.[30] Meesters et al. found that supplementation with citrulline, a non-essential amino acid, enhanced post-operative maintenance of body weight and expedited callus formation in mice after a controlled femoral osteotomy.[31] Roberts et al. investigated probiotic supplementation of the bacterium bifidobacterium adolescentis in mice healing from bone fracture.[32] Their results indicated that probiotics with bifidobacterium adolescentis decreased systemic inflammation after bone fracture and increased the rate of bone healing while also protecting the intact skeleton. A final example by Küçükalp et al. found no statistically significant difference in fibular fracture healing in rabbits after giving the experimental group 2 mL/kg/day of 20% L-arginine L-glutamine solution, but this may have been due to an underpowered sample, as positive radiographic, histopathologic, and clinical outcomes trends were noted.[33]

While few human studies have sought to explain the mechanisms by which nutritional interventions affect clinical and functional outcomes following femoral fragility fractures, much of the rationale supporting nutritional supplementation originates from the current understanding of underlying physiology of bone growth and healing. Vitamin D, calcium, and phosphorous supplementation have been frequently investigated in the pre-clinical setting due to their important role in bone growth. Vitamin D supplementation has been investigated in numerous basic science research studies with positive results suggesting bone healing benefits, but direct translation of these results to clinical practice is limited due to the necessary inclusion of calcium supplementation to assist absorption.[34-36] Zinc's role in osteoblast and osteoclast differentiation may allow it to serve as a promoter of fracture healing by increasing alkaline phosphatase activity and osteocalcin.[37-38] Additionally, antioxidants have been suggested as potential accelerators of bone healing in the setting of fracture.[37,39] Investigation of these compounds, amongst others, is warranted for improvements to translational research.

Populations at highest risk for femoral fragility fractures, particularly osteopenic and osteoporotic patients, commonly have nutritional deficiencies present before injury occurs, giving rise to another theoretical source of support for nutritional intervention – identifying existing nutritional deficiencies present in patients at higher risk for poor clinical and functional outcomes. Insulin-like growth factor 1 (IGF-1) represents an example of such theories. Implicated in early satellite cell activation and proliferation, increased IGF-1 levels could theoretically improve recovery and rehabilitation outcomes for patients following femoral fragility fracture.[40] The importance of differences in IGF-1 is well-outlined by Ohlsson et al., who established increased risk for fractures, especially hip fractures, in elderly men with low IGF-1 levels.[41] Protein supplementation in patients with osteoporotic hip fractures was associated with increased serum levels of IGF-1 compared to controls.[42] Patients that received protein supplementation had significantly less loss of proximal femur bone mineral density at 12 months, as well as fewer new vertebral deformities and shorter rehabilitation ward stays (although not statistically significant). Although these studies suggested a mechanistic contribution for which nutritional supplementation impacts outcomes following femoral fragility fractures, the precise mechanisms are unclear and future investigation is warranted.

COST OF INTERVENTIONS

Compared to the efficacy and safety of interventions, cost-effectiveness remains a poorly explored dimension of post-operative nutrition programs in orthopedics, and even moreso in the context of fragility fracture. Shafrin et al. explored the cost-effectiveness of conditionally essential amino acids after in adults ≥18 after fracture fixation of the lower extremity, upper extremity, or pelvis.[43] Their model indicated that a two-week, twice daily regimen would provide a net incremental cost savings per patient of $4,902, largely due to reduced postoperative complications. Application to the US population yielded an expected annual savings of $316 million with 813 quality-of-life-years added. In a retrospective cohort study by Williams et al., malnourished patients who underwent either a hip or femur fracture repair during a ten-year period were grouped by exposure to oral nutrition supplements, tube feed formulas, or modular nutritional supplements within one day postoperatively.[44] Early supplement exposure was associated with significantly reduced length of hospital stay without a statistically significant difference in hospital cost. There were no reported differences in infection rates, intensive care unit admission, or hospital mortality.

There is limited evidence regarding cost-effectiveness of nutritional care in this setting, including registered dietician referral and use. This article has highlighted the efficacy and outcomes of various explored nutritional supplements, of which multiple have shown promise in reducing complications, shortening length-of-stay, and reducing disability within various follow-up periods. These outcomes likely translate to less cost both for patients and healthcare systems. Future work should prioritize inclusion of cost metrics and health-related quality of life assessments that allow for assessment of incremental cost effectiveness ratios alongside clinical and functional outcomes.

VARIABILITY IN DOSE AND DURATION OF NUTRITION INTERVENTIONS

Among fragility fracture patients, malnutrition frequently underlies the presenting clinical problem and complicates physicians' ability to optimize clinical outcomes.[45] While interventions like nutritional supplementation and dietician consultation have produced positive results, best practices for dosing and duration of these interventions remain unclear. To find a solution to the question of "how long is long enough" for nutritional interventions in this population, one must first consider how long significant complications of hip fragility fracture may occur. Some of the most severe complications include acute loss of skeletal muscle due to disuse, decreased physical function, pain, and resulting loss of independence and quality of life. Mortality is also a reported complication among this population, for which risk is as high as 10% within the first 30 days postoperatively.[46]

Outcomes also greatly improve with intervention beyond the time they are admitted to the hospital, yet many studies limit intervention and follow-up to the acute phase of recovery due to logistical barriers. The greatest amount of recovery occurs within the first six months postoperatively, but patients continue to improve their pain status and functional ability out to one year.[47] Because many fragility hip fracture patients are malnourished prior to injury, it is reasonable to conclude that most would benefit from lifelong nutritional supplementation.[5-6] This should certainly be considered, but may not be feasible considering the cost of nutritional interventions and low compliance in long-term studies. Trials cited throughout this review have found variable success in extending intervention beyond hospital stay due to compliance concerns. As addressed later, coupling successful tools used by prior trials to increase compliance with extension of supplementation length would provide more impactful assessment of the long-term efficacy of interventions.

Supplement dosing is highly heterogenous, making it difficult to compare trials. Rarely has a clinical trial evaluating a nutritional supplement addressed potential differences in body weight, sex, or even pre-nutritional status by altering supplement dose. Gunnarsson et al. tailored preoperative and postoperative supplementation to reach 30 kcal/kg of energy intake for hip fracture patients.[48] Nasogastric and tube feeds, in addition to glucose infusions, were given if patients did not reach their energy intake goal. Their regimen reduced incidence of pressure ulcers and nosocomial infections within five days postoperatively in the experimental group, while also serving as a potential guide for future interventions in terms of individualized dosing.

COMPLIANCE WITH NUTRITIONAL INTERVENTIONS

Reported Compliance in Randomized Clinical Trials

Compliance with nutrition supplementation regimen remains a significant challenge and is highly variable depending on duration and mode of supplementation. A trial by Bruce et al. illustrates this concept, as their results showed significantly increased postoperative weight loss with decreased compliance to nutritional supplementation.[49] Flodin et al. provided 200 mL of twice daily protein and energy supplement for six months.[50] Of the 18 patients in the intervention group, only seven reported taking the full supplement as prescribed, with the remaining 11 taking half of their prescribed doses, a compliance rate of 39%.

Adherence to intervention is highly variable depending on length and mode of supplementation. Myint et al. finished their trial with a 78% compliance rate with twice daily oral nutritional supplementation for four weeks.[51] Many trials with similar length of intervention have comparable compliance rates. A four-week trial by Chevalley et al. had a compliance rate of 73% in the intervention arm, and Houwing et al. had 75% of subjects consume 75% or more of their prescribed supplementation.[19]

Nutritional supplementation has the potential to enhance clinical outcomes in older adults with fragility fracture. However, trials provide evidence of persistent difficulties with prescribed compliance. To realize translation to clinical practice, it is necessary that investigators improve approaches to measuring and assuring consistent adherence to the intervention.

Measures to Improve Oral Nutrition Supplementation Compliance

Higher compliance rates have been achieved in prior trials through shorter duration of prescription, scheduled days off from treatment, and home nurse visits. Tidermark et al. reported 100% compliance in their trial investigating anabolic steroid injections and oral protein supplement in patients after fixation of femoral neck fractures.[53] In their trial, a research nurse was assigned to visit subjects at home to administer the nandrolone injections. Schurch et al. investigated protein supplementation over a six-month period.[42] However, they required their subjects to only take prescribed supplements for five days per week. Compliance was 73% in the intervention group and 80% in the control group.

CONCLUSION

Postoperative nutritional interventions show promise for improving outcomes after fragility fracture in older adults. Implementation into clinical practice has been complicated by an inconsistent literature supporting supplement composition, dose, and duration. Future trials should aim to achieve consistency in the characteristics of interventions studied through dose standardization and use of widely available products. In addition, issues with compliance and small sample size limit reliability of findings. Investigators should adopt tools from past research to increase compliance and strengthen approaches for improving subject recruitment and retention. Further, clinical trials aiming to demonstrate the impact of nutrition interventions on the clinical and functional outcomes in patients with femoral fragility fractures should also include key economic indicators that will allow clinicians, hospitals, and policy makers to better evaluate and compare cost-effectiveness. Last, there is a great need for basic science research into the mechanisms by which supplementation may improve clinical and functional outcomes. Without basic science and mechanistic literature as a foundation, it will be difficult to fully understand and explain the efficacy, safety, and cost-effectiveness of nutritional interventions.

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