University of California,
Irvine

Management of Massive Rotator Cuff Tears in the Wheelchair Bound, Spinal Cord Injury Population: Study Proposal toward the Establishment of Higher Level of Evidence Care

THESIS

submitted in partial satisfaction of the requirements for the degree of

MASTER OF SCIENCE

in Biomedical and Translational Science

by

Hansel E. Ihn

Thesis Committee:
Professor Thay Q. Lee, PhD, Chair
Professor Sheldon Greenfield, MD
Professor Sherrie H. Kaplan, PhD

2017

Table of Contents

List of Abbreviations

AAOS = American Academy of Orthopaedic Surgeons

ASES = American Shoulder and Elbow Surgeon score

CLEAR- NPT = The Checklist to Evaluate a Report of a Nonpharmacological Trial

IOM = Institute of Medicine

MeSH = Medical Subject Headings

NIH = National Institutes of Health

NSCISC = National Spinal Cord Injury Statistical Center

PICO = (P) population of interest, (I) intervention of interest, (C) comparisons of interest, and (O) patient- oriented outcomes of interest

PRISMA = Preferred Reporting Items for Systematic reviews and Meta- Analyses

RCT = Randomized Controlled Trial

SAD = Subacromial Decompression

SCI = Spinal Cord Injury

SPORT = Spine Patient Outcome Research Trial

SST = Simple Shoulder Test

WUSPI = Wheelchair Users Shoulder Pain Index

List of Figures

List of Tables

ABSTRACT OF THE THESIS

Management of Massive Rotator Cuff Tears in the Wheelchair Bound, Spinal Cord Injury Population: Study Proposal toward the Establishment of Higher Level of Evidence Care

By

Hansel E. Ihn

Master of Science in Biomedical and Translational Science

University of California, Irvine 2017

Professor Thay Q. Lee, Chair

Background: The wheelchair bound, paraplegic population are heavily reliant on their upper extremities for independence. As a result, there is a high prevalence of rotator cuff tears within this population. However, there is no established clinical practice guideline to help guide the care of this problem.

Aims: The original goal of this thesis was to conduct a systematic review and meta- analysis of the available literature in the hopes of take a step toward establishment of a clinical practice guideline. Once a preliminary evidence- mapping procedure was done, it was decided there was not enough evidence available to warrant a meta- analysis. Consequently, the aim of this thesis then shifted toward the proposal of a potential clinical trial that would provide a high level of evidence.

Methods: The evidence mapping procedure simulated the process ordinarily taken for systematic reviews as outlined in the Preferred Reporting Items for Systematic reviews and Meta- Analyses (PRISMA) guidelines. PubMed, Web of Science, and the Cochrane Library

databases were searched using pre-determined search strategies with keywords. The clinical trial proposal process that then followed utilized the evidence gained from the evidence mapping procedure as well as that attained from a literature review of high level of evidence studies in orthopaedic surgery.

Results: The evidence mapping procedure netted a total of 191 studies of which only 6 studies were fully reviewed. Upon review, these six studies were found to be all of level IV evidence. These studies represented a heterogeneous use of surgical techniques and outcome measures. Consequently, they did not meet the inclusion criteria to perform a meta- analysis.

Discussion: The data extraction process made it apparent that the evidence available has multiple methodologic flaws precluding meaningful synthesis. Even by case series standards as outlined by Obremskey et al., these six studies did not meet many of the criteria necessary to provide evidence that would be deemed useful for clinical judgement. To that end, the thesis concludes with a proposal of a clinical trial that would provide a higher level of evidence for clinical management. Specifically, the proposal addresses massive rotator cuff tears in the wheelchair bound, paraplegic population. The interventions compared in the study will be rotator cuff repair with subacromial decompression or subacromial decompression alone. The potential pitfalls and ethical dilemmas that may present during the study are also discussed.

Introduction

Population of Interest

There is an estimated 1.6 million manual wheelchair users in the United States.[1] At a reported 3.3% of that figure, spinal cord injury patients account for only a small proportion of those users. However, the National Spinal Cord Injury Statistical Center estimates that the prevalence of spinal cord injury in the US is approximately 276,000 with an annual incidence of about 12,500 cases. [2] Consequently, the disproportionate prevalence of shoulder pain and rotator cuff pathology in this population is a significant health issue, especially since these patients rely so heavily on their upper extremities for independent functionality.

There is a high prevalence of shoulder pain in the wheelchair bound, paraplegic population. The prevalence of shoulder pain in paraplegic manual wheelchair users in the literature ranges from 30% to 73%. [3, 4] [5] In comparison, the prevalence of shoulder pain in the able-bodied population has been reported to be between 7% and 26%. [3, 4] [5] Several studies have examined the association between shoulder pain and the wheelchair bound, paraplegic population. [6-10] It is thought that the high prevalence of shoulder pain in this population is due to the fact that paraplegic wheelchair users not only subject their shoulders to stress from wheelchair propulsion but also from other activities of daily living. [10] Activities like transfers and weight-relief raises may trigger shoulder pain, and repetition of these activities may exacerbate the pain. [11, 12]

Paraplegic patients rely heavily on their upper extremities in order to be independent. As a result, any condition that limits upper extremity function will burden both the individual and their caretakers.[13-15] The upper extremities receive increased biomechanical stress in this

patient population because of the absence of trunk musculature innervation. [16] Consequently, a painful shoulder may be severely debilitating. The issue is compounded by the fact that paraplegic patients are unable to give their painful shoulders the same level of rest that their able-bodied counterparts are able to. The most common pathology that has been associated with shoulder pain in paraplegic manual wheelchair users is reported to be shoulder impingement syndrome.[11, 16] Tendon degeneration has also been implicated in chronic shoulder pain within this population. [17] The reported prevalence of rotator cuff tears amongst wheelchair users who have painful shoulders is 65 – 73%. [11, 18]

Gap in Care

Medical decision making in all fields of medicine has largely shifted toward evidence-based practice from the more traditional eminence- based practice.[19] The latter describes medical decision making based on opinion and experience while the former also takes into consideration the best available scientific evidence.[19] Clinical practice guidelines are one of the tools that have resulted from this trend toward evidence- based practice. The American Academy of Orthopaedic Surgeons (AAOS) has published seventeen clinical practice guidelines on varying orthopaedic health issues.[20] These guidelines were established according to the Institute of Medicine (IOM) standards. However, the guideline for "Optimizing the Management of Rotator Cuff Problems" explicitly states that it does not address "patients with wheelchair/ weight bearing shoulders (i.e., polio patients, paraplegics, crutches)". [20]

Consequently, the most up – to – date guideline addressing rotator cuff management in our patient population of concern is the "Preservation of Upper Limb Function Following Spinal Cord Injury". This guideline was developed by the Consortium for Spinal Cord Medicine in

2005 to address the high prevalence of upper extremity complaints amongst the spinal cord injury (SCI) population. [21, 22] Within the guideline, the recommendation concerning surgical management of rotator cuff tears was based on two case series studies. To our knowledge, no further updates to this guideline have been made since this initial publication. Given the significance of rotator cuff tears in this patient population and with the ten- year anniversary of the guideline well past, an update with the most current available evidence is necessary.

Purpose

With this in mind, we performed an evidence mapping of the currently available literature for the management of rotator cuff tears in the paraplegic, wheelchair- bound population. The original purpose of this thesis was to perform a systematic review and meta-analysis of the highest level studies currently available and formulate a recommendation to be included in a clinical practice guideline based on the findings. However, we only managed to find six level 4 studies, which would only amount to a guideline with "limited" recommendation per current AAOS guidelines for a clinical practice guideline. Consequently, what is found herein is a critical review of the available literature and a proposal for a high level of evidence clinical study that would allow a guideline to provide a stronger recommendation for the management of rotator cuff tears in this patient population.

Research Questions

The primary objective of this study was to determine the effectiveness of rotator cuff repairs in the paraplegic, wheel-chair bound population. The review would have ideally compared outcomes between rotator cuff repairs and conservative management (i.e., physical therapy). The specific questions that guided the systematic search were:

1. What are the characteristics of rotator cuff tears in the paraplegic, wheelchair bound population?
2. How effective is surgical management of rotator cuff tears in this patient population?

Once it was determined that the yield from the systematic review was too low to perform a valuable meta- analysis, the focus turned to what steps would be needed to perform one in the future.

Methodology Overview

Systematic review and meta- analysis often work hand-in- hand and both are important parts of evidence- based medicine. A systematic review is conducted first to determine the propriety of a meta- analysis. Generally, a systematic review consists of five basic steps: (1) Framing questions for a review, (2) Identifying relevant work, (3) Assessing the quality of studies, (4) Summarizing the evidence, and (5) Interpreting the findings.[23] The first part of our review utilized this basic framework to gather studies to conduct an evidence mapping, which simulates the systematic review process. In critically analyzing the available literature, one goal of this thesis was to highlight the limitations presented by the available literature and areas that will require future research.

The second part of the thesis defines the level of evidence in the orthopaedic literature. Based on these definitions, a proposal is made for a study that would potentially have a higher level of evidence. Thereby, the proposed study would allow a guideline addressing rotator cuff surgical management be made with a stronger recommendation.

Chapter 1

Background

Rotator Cuff

Anatomy/ Biomechanics

There are four rotator cuff muscles: subscapularis, supraspinatus, infraspinatus, and teres minor. These four muscles originate on the scapula and their tendons insert onto the greater and lesser tuberosities of the proximal humerus. While individually, each has a specific function, as a group their role is to provide glenoid concavity compression of the humeral head; thereby, centering and stabilizing the head in the glenoid. This allows the periscapular muscles to act on the humerus producing coordinated shoulder motions.

The glenohumeral joint is the most mobile joint in the body as a result of its lack of osseous constraint. The main stabilizers consist of a system of active and passive stabilizers. The rotator cuff muscles mentioned above act as active stabilizers while the various ligaments that span the joint and the bony anatomy act as passive stabilizers. As a direct consequence of these anatomical features, the main role of the glenohumeral joint is in prehension and mobility. However, in the paraplegic, wheelchair bound patient, the joint takes on a weight-bearing function as a result of continuous, repetitive use through transfers, weight- relief raises, and wheelchair propulsion. Wheelchair propulsion has been shown to increase the vertical force across the shoulder joint by greater than 360%. [24] Several studies have demonstrated that these repetitive, unnatural stresses placed on the glenohumeral joint may clinically manifest in a higher prevalence of shoulder joint pathologies.[11, 25, 26]

Rotator Cuff Tears

Rotator cuff disease is the most common cause of shoulder pain, and encompasses a spectrum of disorders involving the rotator cuff muscles. This includes subacromial/subcoracoid impingement, calcific tendinitis, rotator cuff tear, and rotator cuff arthropathy. By some estimates, up to 17 million individuals are at risk for rotator cuff disease in the United States, and the disease's annual incidence is approximately 4 million.[27-29] Rotator cuff tear etiology is multifactorial and is most likely due to an interplay between extrinsic and intrinsic factors. [28, 30, 31] Extrinsic factors include coracoacromial arch anatomy, load on the tendon(s), and repetitive use phenomena. [28, 31] Intrinsic factors include age- related degeneration, vascular supply, tendon regional material property variation, and collagen orientation resulting in structural abnormalities.[28, 31]

In the able- bodied population, age related tendon degeneration has been thought to be the primary impetus for the generation of a cuff tear.[28, 29, 32] A recent systematic review, also found that the etiology of a cuff tear in younger patients (those less than 40 years of age) is more likely to be a result of an acute traumatic event. [33] This is in stark contrast to that in an older patient population, where the etiology is more likely to be degenerative and atraumatic in nature.[34-36]

In the paraplegic- wheelchair bound population, the generation of rotator cuff disease has been attributed to a mechanical etiology.[25, 37] As outlined previously, the wheelchair bound shoulder undergoes unnaturally high loads of stress and essentially functions as a weight bearing joint.[24] As a result, the subacromial and subcoracoid structures may repetitively impinge on the undersurface of the acromion and coracoid, eventually leading to a cuff tear. Akbar et al. conducted a case- control study in 200 patients (100 able- bodied and 100 wheelchair bound

paraplegic patients).[25] This study found that the prevalence of rotator cuff tears in the able-bodied versus the wheelchair- bound population was 15% and 63%, respectively; which, translated to a 10 fold increased risk for rotator cuff tears in the paraplegic group.[25] Furthermore, there seems to be a positive correlation between not only age and rotator cuff tear in this population but also with time since injury.[25, 38] In other words, the longer period of time a patient has been a paraplegic, the more likely a rotator cuff tear is present. [25, 38]

The natural progression of rotator cuff tears both in terms of symptomatology and in size is also a topic of debate.[31, 39, 40] The overall consensus seems to be that there is a correlation between an increase in tear size and onset of symptoms (i.e. pain).[31, 40] Yamaguchi et al.'s study demonstrated that 51% of patients with bilateral rotator cuff tears where only one side is symptomatic will become symptomatic on the asymptomatic side over an average of 2.8 years.[31] 50% of these newly symptomatic tears will have progressed in size while only 20% of those remaining asymptomatic will have progressed in size. However, as Moosmayer et al. pointed out, this association is not always straightforward.[39] In a prospective study of 50 patients with asymptomatic rotator cuff tears followed for three years, 18 (36%) became symptomatic. While a majority of those that became symptomatic were associated with an increase in tear size, there were some that had this progression yet still did not become symptomatic. Consequently, in able- bodied individuals, factors other than tear size progression is most likely involved in onset of symptoms. While a similar relation may also apply to the wheelchair- bound, paraplegic population, Escobedo et al. demonstrated that a higher percentage of symptomatic, paraplegic individuals have rotator cuff tears (73%) than symptomatic, able-bodied individuals (59%).[38] Given this study's results and with the daily mechanical stress that a paraplegic patient's shoulder is placed under, it stands to reason to state that rotator cuff

disease may have a much closer association with symptoms in the paraplegic population than in the able- bodied population.

Rotator Cuff Tear Treatment: Conservative versus Operative

The decision to treat a patient operatively should be made after first thoroughly weighing the respective benefits against the risks of treating nonoperatively versus operative repair. Nonoperative treatment include exercises, steroid injections, and avoidance of repetitive motion. The benefits of nonoperative treatment include financial savings and the avoidance of the risks associated with undergoing an operation (i.e., infection, pain, etc.). Unfortunately, the risks associated with taking this route may undermine any operative efforts down the line. As previously mentioned, tears that are treated conservatively are at risk for progression in size.[31] Additionally, chronic tears are at risk for fatty infiltration and muscular atrophy.[41, 42] When these factors are taken together, they equate to poorer outcomes and a higher potential for re-tear postoperatively.[41-43] Consequently, it may be in the best interest of the patient to repair the tear prior to the onset of tear progression or fatty infiltration.

Reparability of the tear will ultimately determine the potential benefits of a repair. In terms of risk of a repair procedure, consideration should be given to potential for repair failure, iatrogenic injury, and surgical site infection among other potential risks. Reparability is determined by two factors: potential for apposition and for healing. Apposition refers to the ability to bring a tendon in direct contact with bone. It is important to understand that just because a tendon is brought into contact with bone, it does not necessarily indicate a good potential for healing. Given all of this information, the decision of whether to pursue a conservative versus an operative approach, and which operative approaches to consider, can be simplified by the classification of the tear in question.

Classification of Full Thickness Rotator Cuff Tears

A classification system is a useful tool when attempting to understand the natural history and apply the best treatment to musculoskeletal disorders. Unfortunately, rotator cuff tears have a myriad of classification systems to choose from.[44] The most commonly used system for full-thickness tears is the one developed by DeOrio and Cofield, based purely on the size of the tear: [45]

Classification	**Size**
small	< 1 cm
medium	1-3 cm
large	3-5 cm
massive	> 5 cm

Table 1. DeOrio and Cofield Tear Size Classification

However, the size of the tear is only one of many characteristics to consider when deciding the proper treatment. Other important components include the natural history of the tear, reparability of the tear, and functional outcome prognostic factors. Based on all these components, patients can generally be divided into three overall groups. [46]

Group I	Minimal risk for chronic changes in the near future
Group II	Significant risk for chronic, irreversible changes with conservative care
Group III	Chronic changes already present

Table 2. Tear Size Classification Based on History, Reparability, and Outcome

Patients in Group I are associated with rotator cuff tendinitis or a partial thickness tear. These entities of rotator cuff disease usually do not experience chronic changes and may be treated nonoperatively. Group II patients encompass those with a full thickness, small or medium sized tear and is less than 65 years old; with acute tears of any size; with overhead throwing associated tears and is a highly competitive athlete; with tears that are nonresponsive to conservative management; or tears associated with a loss of function. All group II patients are indicated for surgical intervention to avoid any irreversible changes in their rotator cuffs. Finally, Group III patients include those who already have chronic, irreversible changes present and also include the elderly (over 70 years of age) with full thickness tears. This final group essentially consists of those patients who would most likely find minimal benefit in undergoing an operative rotator cuff repair.

A wheelchair, bound paraplegic patient will likely fall into either of the latter two groups. However, to our knowledge, no study has determined the prevalence of different size tears within the wheelchair, bound paraplegic population. A recent observational study involving ten manual wheelchair users with paraplegia found that supraspinatus tears were more common than tears involving the infraspinatus, subscapularis or long head of the biceps.[47] While this is a similar pattern as seen in studies involving able- bodied individuals, the sample size of the study was too small to make any meaningful conclusions on potential rotator cuff tear patterns in this patient population.

Outcomes

The outcome of a repair has been attributed to multiple factors. Chief among these, however, may be age of the patient and tear size. Additionally, there appears to be a discrepancy between surgical repair outcome and clinical outcome.[48, 49] Large and massive rotator cuff

tears generally are associated with poorer surgical outcomes and repair failure rates are reportedly between 57 and 94%.[48-50] However, the clinical outcomes in these same patients are significantly improved relative to their preoperative pain and function scores. Paxton et al.'s study included thirteen patients who, after a minimum follow- up of 10 years, demonstrated maintenance of the improved functional and pain scores after first receiving the procedure.[49] Similarly, Zumstein et al.'s study of twenty-three patients who, after an average follow- up of 9.9 years, demonstrated maintenance of the improved functional scores after first receiving the procedure.[48] The lack of correlation between clinical outcomes and structural integrity of the repairs in these studies has been interpreted to indicate that healing is not necessary to achieve satisfactory clinical outcomes. However, it is worth noting that both mentioned studies consisted of patients whose average age was 74.6 years (Paxton et al.) and 54 years (Zumstein et al.). While the latter study's participants were on average 20 years younger than the former, a recent systematic review has demonstrated that there is a difference in etiology of rotator cuff tears in patients who are under forty years of age.[33] Consequently, the results of these studies may only be applicable to the elderly population. Furthermore, the functional scores being used to assess clinical outcome may be an incorrect *surrogate marker*. In Paxton et al., a majority of the patients displayed radiographic evidence of chronic changes in the glenohumeral joint.[49]

The generalizability of these findings may become an even greater issue when wheelchair – bound, paraplegic patients are considered. Repairs of large to massive rotator cuff tears in the elderly population are generally indicated for the active, high energy demand patients.[51] Nevertheless, the stress that the glenohumeral joint is placed under in these patients is not comparable to that placed under a patient who uses the joint for weightbearing purposes. As mentioned already, Kulig et al.'s study has demonstrated that wheelchair propulsion may

increase vertical shear forces in the glenohumeral joint by as much as 360%.[24] Therefore, it stands to reason that the clinical outcomes may not be as promising in this patient population should a repair suffer from a structural failure.

Hypothesis as to why these techniques are so poor in outcome

A potential reason why massive rotator cuff tears have historically had poor structural outcomes is most likely because the repair methods have failed to account for all components of a rotator cuff tear. All rotator cuff repair techniques address the cuff deficiency. However, larger rotator cuff tears tend to be associated with a capsule deficiency as well. The glenohumeral capsule and its thickened components (i.e. ligaments) are important passive stabilizers of the glenohumeral joint especially at end ranges of motion. Consequently, when a repair is done without consideration of the capsule, the repair construct may be vulnerable to increased stresses at end ranges of motion thereby accounting for the high rates of failure seen in massive rotator cuff repairs.

Evidence – Based Medicine

Evidence- Based Medicine

Sackett et al. described evidence- based medicine as "the conscientious, explicit, and judicious use of current best evidence in making [clinical] decisions..." [52] The challenge of incorporating the best evidence is the overwhelming volume of information physicians currently face due to the exponential growth of scientific publications in the 20th and early 21st centuries. [53] The hierarchical system of ranking a study based on "level of evidence" has been adopted by the medical field and by orthopaedic surgery to help place studies in context. In 2003, The Journal of Bone and Joint Surgery: American version began implementing this rating system and many other orthopaedic journals have followed suit.[54] Wright et al. described the

implementation of the rating system as comprising of three main steps: (1) determine study's primary research question, (2) establish the study type, and (3) assign a level of evidence.[55] Specific details of each level of evidence is covered in Chapter 3.

Clinical Practice Guidelines

Systematic reviews and clinical practice guidelines are essential tools in the practice of evidence- based medicine. The Committee on Standards for Developing Trustworthy Clinical Practice Guidelines define clinical practice guidelines as such: "…statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options."[56] This same committee came up with eight standards for developing clinical practice guidelines that can be deemed "trustworthy", which includes the following [56]:

1. Establish Transparency
2. Manage Conflict of Interests
3. Guideline Development Group Composition
4. Systematic Review Intersection
5. Establish Evidence Foundations/ Rating Strength of Evidence
6. Articulation of Recommendations
7. External Review
8. Updating

The goal of all eight standards was to establish criteria by which clinical practice guidelines could be consistently developed with the best available evidence. While the specific details of some of these standards will be covered in chapter three, the specific details of each standard is beyond the scope of this thesis.

Systematic Reviews and Evidence Mapping

The Committee on Standards for Systematic Reviews of Comparative Effectiveness Research describe four main steps in the systematic review process: (1) Initiating a Systematic Review, (2) Finding and Assessing Individual Studies, (3) Synthesizing the Body of Evidence, and (4) Reporting Systematic Reviews. [57] Systematic reviews are labor intensive ventures that require a significant allocation of resources if done properly. Evidence mapping is a cost-effective method used prior to conducting a systematic review that allows researchers to get a grasp of the currently available evidence and identify research gaps.[58] Thereby, evidence maps provide researchers with a quick overview of the available evidence without undergoing an extensive systematic review of evidence that may not be there to begin with.[58]

Chapter 2

While the body of evidence surrounding the treatment of rotator cuff tears in the wheelchair bound, paraplegic population continues to grow, there has yet to be a study, to our knowledge, that systematically reviewed the available literature. Shoulder pain caused by rotator cuff tears can be particularly debilitating within this patient population due to the high reliance on the shoulder joints for independent functionality. Operative treatment within this patient population is an attractive option in the long-term; however, the short term consequences of postoperative immobilization are certainly factors that should be weighed against the potential benefits of an operation. Consequently, it is important to examine the effectiveness of operative treatment of rotator cuff tears within this particular patient population. A systematic review of the available evidence will potentially guide better care practice and highlight areas of future research that is required. This chapter details the process and results of our attempt.

Evidence Mapping

To assess whether a systematic review and meta- analysis was possible, evidence mapping was undertaken for the question. Since evidence- mapping is thought of as an equivalent process of the systematic review undertaken with relatively limited resources, the process of evidence mapping presented here mirrors that of a systematic review. The utility of systematic reviews in evidence based practice is perhaps most evident in areas of clinical practice where the outcome of an intervention is uncertain. In hopes of addressing an example of such an area, a review of the available literature was carried out according to the standards set forth by The Committee on Standards for Systematic Reviews of Comparative Effectiveness Research. There are six key standards for “finding and assessing individual studies”: (1) Conduct a comprehensive systematic search for evidence, (2) Take action to address potentially biased

reporting of research results, (3) Screen and select studies, (4) Document the search, (5) Manage data collection, and (6) Critically appraise each study. [57]

This evidence mapping was carried out in accordance with the protocol established by the Preferred Reporting Items for Systematic reviews and Meta- Analyses (PRISMA) as closely as our available resources allowed. The PRISMA protocol is one of the most widely- used protocols for systematic reviews in the medical science literature. Figure 1 displays the itemized PRISMA checklist.

Checklist of Items to Include When Reporting a Systematic Review or Meta-Analysis

Section or Topic	Item No.	Checklist Item
Title	1	Identify the report as a systematic review, meta-analysis, or both.
Abstract	2	Provide a structured summary, including, as applicable, background, objectives, data sources, study eligibility criteria, participants, interventions, study appraisal and synthesis methods, results, limitations, conclusions and implications of key findings, and systematic review registration number.
Introduction		
Rationale	3	Describe the rationale for the review in the context of what is already known.
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).
Methods		
Protocol and registration	5	Indicate whether a review protocol exists and whether and where it can be accessed (e.g., Web address) and, if available, provide registration information, including registration number.
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.
Study selection	9	State the process for selecting studies (e.g., screening, eligibility) included in systematic review, and, if applicable, included in the meta-analysis.
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of if this was done at the study or outcome level) and how this information is to be used in any data synthesis.
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2 statistic) for each meta-analysis.
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, metaregression), if done, indicating which were prespecified.
Results		
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review with reasons for exclusions at each stage, ideally with a flow diagram.
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome-level assessment.
Results of individual studies	20	For all outcomes considered (benefits or harms), present for each study simple summary data for each intervention group and effect estimates and confidence intervals, ideally with a forest plot.
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies.
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, metaregression).
Discussion		
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policymakers).
Limitations	25	Discuss limitations at the study and outcome levels (e.g., risk of bias) and at the review level (e.g., incomplete retrieval of identified research, reporting bias).
Conclusions	26	Provide a general interpretation of the results in the context of other evidence and implications for future research.
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data) and roles of funders for the systematic review.

Figure 1: PRISMA checklist [59]

Formulating the Question

In formulating the main question for the systematic review, we used a set of PICO questions. These set of questions addresses the (P) population of interest, (I) intervention of interest, (C) comparisons of interest, and (O) patient- oriented outcomes of interest.

Population: Wheelchair bound, paraplegic patients

Intervention: Rotator cuff repair

Comparison: Nonoperative/ Conservative Therapy

Outcomes: Shoulder function scores

Consequently, the guiding question for this review was: **How effective are rotator cuff repairs in wheelchair bound, paraplegic patients with rotator cuff tears?**

Inclusion and Exclusion Criteria

The following criteria was used to determine whether a study was included for review purposes.

1. Study type: the review sought to include randomized controlled trials (RCT), meta-analysis of RCTs, prospective comparative studies, retrospective cohort studies, and case-control studies.
2. Participant type: Wheelchair bound, paraplegic patients with no restrictions on age or duration of time since injury. The cause of the shoulder pain in the patients included in the studies had to be musculoskeletal in origin and not from a pathologic or neuropathic process.
3. Intervention type: The review included studies of rotator cuff repair both arthroscopic and open.
4. Outcome measure type: American Shoulder and Elbow Surgeons (ASES), Constant and Murley shoulder function score, and functional independence measure score were the shoulder function scores the included studies used.
5. Geography: No studies were excluded based on which country the study took place.
6. Language: All studies published in non- English languages were excluded from the study.

7. Timeframe: Studies published up until May 10, 2016 were included.

Search Strategy for Identification of Relevant Studies

PubMed, Web of Science, and Cochrane databases were used to conduct the search. The literature search was performed systematically to exhaust the available databases for relevant studies. The following combinations of keywords and Medical Subject Headings (MeSH) were used to carry out the search: "shoulder pain OR shoulder pains OR shoulder OR shoulders", "paraplegia OR paraplegic OR spinal cord injury OR spinal cord injuries OR wheelchair", "rotator cuff OR rotator cuff repair OR rotator cuff surgery OR arthroplasy OR arthroplasties OR decompression." Additionally, the reference lists of relevant studies found via database searches were examined for further studies that may have been missed by the original search. The search strategy used for PubMed and Web of Science can be found in the appendix section. Each study was analyzed by one investigator.

Documenation of the Search and Selection Process

A detailed account of the search process was maintained to keep track of progress made from the start of the study. The following were accounted in detail: (1) databases utilized, (2) search engines utilized, (3) number of hits, (4) key words used, (5) inclusionary decisions, (6) exclusionary decisions, and (7) study level of evidence. Studies were located through the University of California, Irvine library system. The results and documenation were saved in electronic files.

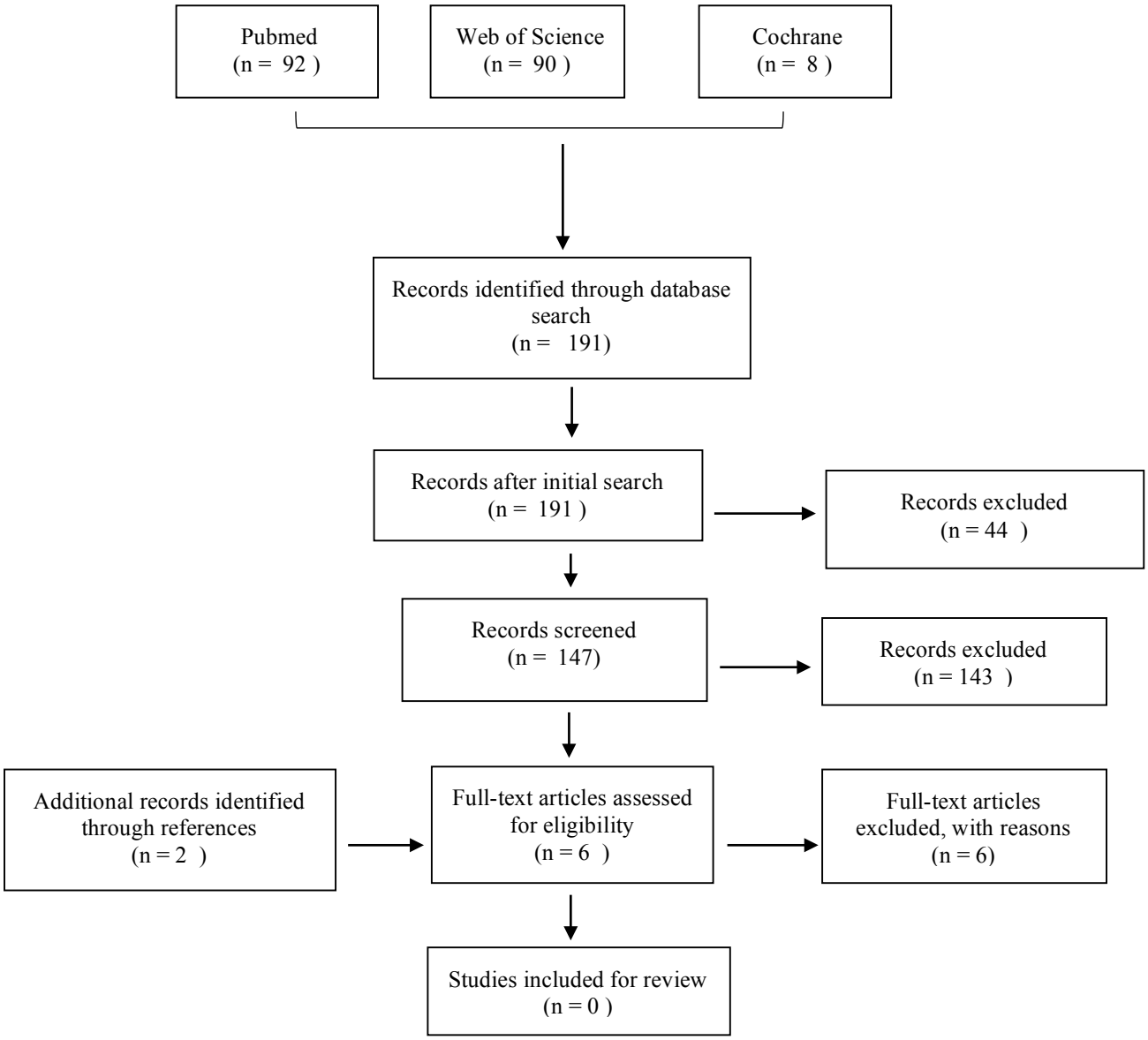

Figure 2. Flow diagram

Results

Figure 2 displays an illustration of the evidence mapping process. Table 3 summarizes the study demographics. A more detailed description of each study is available in the Appendix. The PubMed, Web of Science, and Cochrane Library databases produced an overall total of one hundred and ninety- one publications. After excluding duplicates and nonrelevant studies, only four out of one hundred and ninety-one studies met initial screening criteria by title. The full text of all four were reviewed by one reviewer. A reference search in these four studies yielded two additional unique studies for a total of six studies. All six studies were published in English and in professional journals. All were identified to be case series with Level IV evidence. There were no RCTs, meta- analysis of RCTs, prospective comparative studies, retrospective cohort studies, and case- control studies. Consequently, no studies met the inclusion criteria.

If the inclusion criteria was expanded to include case series, only six studies would be available. Only one out of the six studies was designed in a prospective manner. Four out of the six studies looked at less than 20 subjects. However, these six studies used heterogenous outcome measures and heterogenous surgical techniques, so a meta- analysis was believed to be inapproriate. Five studies looked at postoperative pain. However, the assessment of function in each study differed. Three studies utilized the American Shoulder and Elbow Surgeons score and range of motion to assess function. Additionally, even within studies, the diagnosis varied widely.

The overall outcomes reported were fairly homogeneous with only one study reporting no change in functional scores after intervention.[60] The remaining five all reported postoperative improvements in pain, range of motion, and function.

Study	Surgery	Shoulder #	Level of SCI	Follow- up	Outcome
Robinson et al.[61]	Repair & SAD	6	C5- T12	Unavailable	ROM, Function, Pain
Goldstein et al.[60]	Repair & SAD	6	T3- L1	Unclear	ROM, Function, Pain
Popowitz et al.[62]	Repair & SAD	8	C5- T10	12-72 months	ASES,Shoulder Score
Fattal et al. [63]	Repair & SAD	38	C5- L4	0.2- 2.9 years	ROM, FIM, pain
Kerr et al.[37]	Repair & SAD	46	C5- L3	24- 82 months	ASES, Constant, Subjective Shoulder
Jung et al.[64]	Repair & SAD	16	C5- T10	Avg 31.2 months	ASES, Constant

Table 3. Study demographics

Discussion

Though case series generally are considered lower level studies, a well designed case series has the potential to provide great information and guidance for patient care.[65] Obremskey et al. described the characteristics of a well executed case series study as consisting of: all patients have the same diagnosis, strict inclusion and exclusion criteria, a standard treatment protocol, patient follow- up at specified time intervals, well- defined outcome measures that include clinical parameters and validated patient- derived instruments for functional assessment.[65].

The Cochrane Library published a data collection form to help expedite the data extraction process in systematic review/ meta- analysis.[66] However, this form was designed for randomized control trials and other higher level of evidence studies. Consequently, to assess the value of the evidence presented by all the studies this review netted, an adaptation of

qualifications for a well- designed, well- executed Level – IV study as presented by Obremskey et al. was used. [65] Results of this analysis is available in the Appendix. Out of a possible nine criteria that Obremskey et al. specified, one study met five of the criteria. Three studies met just three out of nine. Two studies met only one of nine. The one study that met five of the criteria was the only prospective study.[63] This study even had a comparator group that was treated with nonoperative interventions, which begged the question of why this study did not deserve a higher level of evidence rating. The comparator group used was the group that did not meet inclusion criteria for surgery, so most likely had less severe symptoms. Consequently, a valid comparison between these two groups to assess the effect of the surgical intervention would not be appropriate.

In all six studies, the authors discuss the dearth of information available for the managmeent of rotator cuff disease in the wheelchair bound, paraplegic population. The publication dates for these studies range from 1993- 2015. Unfortunately, even after more than twenty years after the earliest publication, the scientific community still has only level IV evidence studies to refer to. More studies are necessary to answer the question posed by this evidence mapping; however, these studies must also be of higher level of evidence.

Chapter 3

Eminence based medicine was the traditional method of practicing medicine, where the standard for clinical practice was established by physicians who were widely regarded as the best in the field. In the latter half of the 20th century, evidence- based medicine came into vogue; however, the vestiges of the traditional method of practice are present even to this day, especially in the field of orthopaedic surgery. Historically, much of the evidence used in orthopaedic practice was drawn from case- series. These studies were conducted by a single surgeon whose new technique was used in a small number of patients. Overtime, the proliferation of such studies contributed to the wide variations in regional practice as the apprentices of said surgeon went on to teach their own group of apprentices. This discrepancy is one of the major challenges that evidence- based practice of orthopaedic surgery faces today.[67]

In this chapter, we will describe the need for higher level of evidence studies in orthopaedic surgery scientific literature. First, we define the specific levels of evidence as adapted by the first orthopaedic journal to adapt this hierarchical system. Second, we highlight some of the challenges of carrying out studies of high level of evidence within orthopaedic surgery. Third, this chapter ends with a review of a successful evidence- based study. In the subsequent chapter, a study will be proposed based on what is discussed in the present chapter.

Level of Evidence

As previously mentioned, The Journal of Bone and Joint Surgery American version adopted the level of evidence hierarchical system to classify studies that were submitted for review.[54] In the face of exponentially increasing volume of studies being conducted and published, the system was put in place to help clinicians navigate this sea of information and

contextualize any given study. Four different five tiered systems were introduced, one for each different type of study. The four different types of studies were defined as therapeutic, prognostic, diagnostic, and economic/ decision analysis. The five ratings of levels I – V have slight nuances across the four different types of studies; however, the requirements for a given rating is generally the same. This thesis' descriptions of the five ratings focuses on that described for *therapeutic studies* because the other three types of studies are beyond the scope of this thesis.

The highest level of evidence rating, level I, is reserved for randomized control trials or a systematic review of randomized control trials. The randomized control trials included in the systematic review must all have homogenous results. These trials must also be high quality studies as demonstrated by a rigorous study design and greater than 80% of the patients must have been included in the follow- up analysis. If the study is deemed to be of poor quality, this constitutes a lower rating of level II.

Other studies that are considered level II include prospective cohort studies and systematic reviews of either level II studies or non-homogenous level I studies. Level III studies encompass case- control studies, retrospective cohort studies, and systematic review of level III studies. Level IV studies are case- series where no control group was used. Finally, level V studies are publications that detail expert opinion.

Challenges of Carrying Out High Level of Evidence Studies

Case series was the foundation of much of orthopaedic scientific literature for many years. In 1978, the percentage of available orthopaedic literature considered to be of level I and level IV evidence was estimated to be 4% and 81%, respectively.[68] The same study reported that in 2008, this relationship had largely shifted as the percentage of level I and level IV

evidence studies was estimated to be 21% and 48%, respectively. While randomized controlled trials and higher level of evidence studies have and continue to grow, there remains many challenges to conducting these higher level of evidence studies.

As mentioned previously, the variation in surgical technique amongst surgeons is one of those challenges. No two surgeons, even those performing the exact same technique, perform an operation exactly the same way. These two surgeons also more than likely have different skill levels. Consequently, unlike drug trials where the treatment is standardized via dosing, the same cannot be done in surgical trials. Other challenges to carrying out high level of evidence studies in orthopaedic surgery include but is not limited to current orthopaedic culture, strong patient preferences, the availability of treatment outside of the study, and low patient enrollment. [67] These challenges may partly explain why Bhandari et al. determined only 60% of the randomized controlled trials published from 1988 to 2000 were lower in quality.[69] These troubling results led Poolman et al. to conclude that a randomized controlled trial did not necessarily indicate a higher quality study than a level II study.[70]

Patient preference has also played a role in challenging the feasibility of higher level of evidence studies in the field of orthopaedic surgery. Different from a clinical trial involving pharmaceuticals, it is harder to convince patients to be randomly allocated in a surgical trial. Often times, for ethical reasons, patients maintain control of their treatment choice. Even if the patients were somehow convinced to participating in the randomization process, there is a strong possibility that at some point during the trial they will lose faith in the process and become unhappy with their designated treatment plan. This would lead to crossover to the other treatment and, ultimately, a contamination of the randomization process. Thereby, a high crossover rate has the potential to undermine the original intent of the trial and render the intention- to- treat results

meaningless. Consequently, a high crossover rate in a randomized trial would lead to a lower level of evidence study that is observational in nature.

Placebo Effects of Surgery

With any field of medicine, clinical trials should thoroughly assess any potential ethical dilemmas the conduction of the study may bring up. One area of concern in surgical trials involves the use of sham procedures. Sham procedures are to surgical trials what placebo drugs are to drug trials. Placebo drugs are often used in the control arm of a randomized control drug trial in order to determine the effects of a drug. While this is a widely accepted practice for drug trials, the implementation of placebo procedures is highly controversial.

All surgical procedures involve a ritualistic process from the preoperative stage all the way to the postoperative recovery room. The scenery of nurses, surgical technicians, and physicians all adorned with masks and gowns have been documented to instill an aura of expectation within the patient undergoing the procedure.[71] This setting along with the general expectation one has after deciding to undergo a procedure, all contribute to the placebo effect in surgery. [72]

Leading up to the actual incision, the ethical issue that must be considered is informed consent. For a surgical trial to use a sham procedure as its control, there must be explicit understanding on the part of the subjects that they may be placed under anesthesia just to receive a skin incision. For a subject's acknowledgement to be considered valid they must demonstrate mental competence; given time to consider the presented risk and benefits; and given the right to later withdraw from consent among other essential rights.[73]

During the time when the subject is actually under anesthesia, the ethical issue is the potential risks the subject in the sham arm of the trial is being placed under. In order for the

subject to fully receive the placebo effect of the surgery, the full guise of the treatment must be presented to them. That is accomplished in part by the ritualistic process as described above, but the post- surgical expectations of finding incision sites is also an important part of the placebo effect. However, by incising the skin, no matter the size, the subject is exposed to an actual risk of bleeding and infection. On the other hand, there are actual benefits of participating in a research trial. One of these is the close monitoring and additional attention these subjects are given by virtue of being in the study.[74]

After the procedure, the ethical issue becomes the need to deceive the patient throughout the subsequent follow- up visits. This becomes an ethical dilemma for the surgeon who performed the procedure be it sham or treatment. Since it is impossible for the surgeon in this scenario to be blinded to what arm of the trial the subject belongs to, the surgeon may be put into a situation where he must deliberately deceive the subject. Dowrick and Bhandari's solution to this ethical challenge is to involve another surgeon, who is completely blinded to which treatment the subject received, to perform the follow- up assessments.[72]

The research benefits of incorporating a sham procedure in a surgical trial are undeniable. Being able to do so would potentially provide invaluable information regarding the effectiveness of a surgical procedure that goes beyond just the placebo effect of a surgical procedure. Moseley et al. were able to demonstrate there was no additional therapeutic value of performing a knee arthroscopic debridement for knee osteoarthritis using an effectively designed sham protocol.[75] As long as the ethical issues are thoroughly explored and addressed by the study, there is a strong argument for incorporating sham procedures as the control arm in surgical trials. Being able to do so would certainly help raise the level of evidence for the field of orthopaedic surgical science.

Spine Patient Outcomes Research Trial (SPORT)

The Spine Patient Outcomes Research Trial (SPORT) was a project funded by the National Institutes of Health (NIH). It was designed to compare the relative clinical and cost effectiveness of surgical and nonsurgical interventions for low back and leg pain.[76] Specifically, the project examined three common low back disorders: intervertebral disc herniation, degenerative spondylolisthesis, and lumbar spinal stenosis. SPORT was a 5 year-long study, involved 13 different sites, and enrolled approximately 2500 subjects. The primary results of this project have been published in 3, level I evidence publications and 1, level II evidence publication.[77-80]

These results have had a large impact in the spine surgery field from the knowledge gained from both treatment and cost effectiveness. SPORT managed to achieve such results in spite of the challenges that surgical trials face. The challenge of standardizing surgical procedure and technique was addressed by the collective agreement of participating physicians to use general approaches.[76] Even still, when it came time for surgery, the techniques used varied widely especially for the degenerative spondylolisthesis cohort.[79] Surgical technique for this cohort included decompression alone, decompression with fusion, and anterior-posterior fusion. However, all patients at the very least received a decompressive laminectomy.

Additionally, to avoid the loss of potentially valuable data, the project incorporated a prospective, observational arm in addition to the randomization control trial. This allowed the inclusion of patients who did not feel comfortable with the randomization process to make the treatment decision for themselves. Additionally, the patients who initially chose to be randomized were given the option of which treatment they would ultimately receive. Thereby, the project was able to account for a potentially high crossover rate. This foresight was proven to

be appropriate when the high crossover rate in the degenerative spondylolisthesis cohort led to one of their publications being downgraded to a level II designation.[81] To account for high crossover rates, the data analysis followed both the intent- to- treat and as- treated principles.

The SPORT project continues to provide valuable evidence from the wide swath of data it collected over five years.[76] It serves as an example of a surgical trial that was thoroughly designed and successfully maneuvers the challenges that it came across. Though it is not without limitations, the information gained has undoubtedly filled a gap in knowledge.

In summary, there is a trend toward the establishment of higher level of evidence studies to base clinical practice. The field of shoulder surgery, especially in those who may benefit the most from such procedures, still lacks any veritable study to base clinical practice on. In light of this, we propose a study that will accomplish this task in the following chapter.

Chapter 4

This chapter contains a proposal for a surgical trial organized in a manner similar to that found in a grant proposal. A brief background will go over the procedures of concern: massive rotator cuff repair with subacromial decompression and subacromial decompression alone. Then a detailed description of the proposed study design is given followed by the dissemination and the implementation potential of the results of this trial. Finally, ethical concerns as it pertains to the proposed study and the involved patient population will also be discussed. The purpose of this proposal is to demonstrate not only the need for high- level of evidence studies in this patient population but also the feasibility of conducting them.

Study Proposal

A. Synopsis & Study Aims

Massive rotator cuff tears are a severely debilitating problem for a wheelchair- bound, paraplegic patient. This patient population is almost exclusively reliant on their upper extremities for independence, so to lose stabilization afforded by the rotator cuffs can be detrimental to the overall quality of life of the patient. There are several options for treating reparable massive rotator cuff tears. However, there are not many high level of evidence studies that look at comparative effectiveness of these different options. As a result, there is no guideline based on high level of evidence to guide treatment in the wheelchair- bound, paraplegic population. Consequently, it is essential to be able to provide rotator cuff care based on better evidence for this patient population. This multisite randomized surgical trial will compare the relative effectiveness of two surgical techniques to treat massive rotator cuff tears. The primary goal of

this study is to provide better evidence for the care of the wheelchair, bound paraplegic population.

Study Aims

I. Determine the relative effectiveness of a rotator cuff repair for massive rotator cuff tears versus a subacromial decompression in the wheelchair- bound, paraplegic population in the short term, mid term and long term.

II. Determine variables that may act as covariates for the outcome of either surgical procedure.

The results of this study will lead to a better understanding of the proper surgical measures to employ when caring for a wheelchair – bound, paraplegic patient with a massive rotator cuff tear.

B. Background

In 1993, a reported 100,000 spinal cord injured persons used wheelchairs out of 700,000 wheelchair users in the United States.[61] The recent estimate placed the total number of manual wheelchair numbers in the US at 1.6 million.[1] While no data exists on what percentage of that number is represented by spinal cord injury patients, the National Spinal Cord Injury Statistical Center estimates that the prevalence of spinal cord injury in the US is approximately 276,000 with an annual incidence of about 12,500 cases.[2] With an estimated 62% of wheelchair-dependent individuals eventually developing pain and overuse injuries of the upper extremities, the preservation of upper extremity function is a key issue in the paraplegic population.[18] The dependence on the upper extremities in this patient population have coined the term "weight – bearing shoulder".

Wheelchair- bound, paraplegic patients are heavily reliant on their upper extremities in order to be independent. It is thought that this same reliance is the key reason behind the high

prevalence of shoulder pain in this population.[10, 11, 25] One biomechanical study estimated that the act of wheelchair propulsion increases the vertical shear force across the shoulder joint by 360%.[24] Wheelchair users subject their shoulder joints to these increased stresses not just from propulsion but from other activities of daily living as well.[10] Activities like weight- relief raises and transfers may trigger shoulder pain, and repetition of these activities throughout the day may exacerbate the pain.[11, 82] The issue is further compounded by the fact that these wheelchair bound patients are unable to give their painful shoulders the same level of rest their able- bodied counterparts are able to. As a result, any condition that limits upper extremity function will burden both the patient as well as the potential caretaker.[83]

In the able – bodied population, rotator cuff disease is the most common cause of shoulder pain, and encompasses a spectrum of disorders involving the rotator cuff muscles. This includes subacromial/subcoracoid impingement, calcific tendinitis, rotator cuff tear, and rotator cuff arthropathy. By some estimates, up to 17 million individuals are at risk for rotator cuff disease in the United States, and the disease's annual incidence is approximately 4 million. [27-29] The reported prevalence of shoulder pain of 7 % - 26% in the able- bodied population is comparatively much less than that reported in the wheelchair – bound, paraplegic population of 30% - 73%.[3-5] Additionally, the reported prevalence of rotator cuff tears in this patient population with shoulder pain is 65% - 73%.[11, 38] Along the same lines, the proportion of massive rotator cuff tears in the able- bodied population has been reported to be as high as 40% of all rotator cuff tears while the same statistic in the wheelchair – bound, paraplegic population has been much higher at 75%.[37, 84]

The management of rotator cuff tears, and massive rotator cuff tears specifically, is a hotly contested and controversial area in clinical medicine. There is wide variability in the use of

surgical intervention for this problem. The indications are not clearly delineated even for the able- bodied population that has been more widely studied for rotator cuff disease.[85] Therefore, reparable, massive rotator cuff tears is a challenging problem in the able- bodied population and possibly even more so in the wheelchair- bound paraplegic population.[37] Symptoms that have been associated with massive tears include shoulder pain and weakness with reaching overhead. Rotator cuff tear repair failure rate has been shown to have a positive correlation with the size of the tear.[48-50] This risk of repair failure is thought to be even higher for wheelchair- bound patients.[37] Despite these high failure rates, the functional and clinical outcomes as assessed in both populations have been shown to have a seemingly paradoxical relationship with these failure rates.[37, 48-50] In spite of high failure rates, the satisfaction and functional outcome scores were found to be high in these studies. Furthermore, many studies have demonstrated satisfactory results after performing an arthroscopic debridement and decompression without repair.[86-88]

Subacromial decompression is often performed in conjunction with a repair and involves resection of the subacromial bursa and burring of the subacromial bone to leave a smooth surface. There have been multiple repair techniques for massive rotator cuff tears that have been introduced over the past several decades including partial repairs, tendon slides and complete repairs. However, as mentioned the longevity of said repairs are suspect at best with a dearth of long- term prospective studies. While the legions of physicians that learned a specific repair technique remain steadfast in defending their technique, there still remains a question that remains unanswered that may prove to be fundamental in the creation of standardized practice guideline: Is a repair necessary? The findings from case studies and other low level of evidence

studies are inconclusive and beg the question whether a repair is necessary to achieve good clinical and functional outcomes.

Significance

The limitations in the available evidence regarding rotator cuff repair in general has already been well established by the clinical practice guideline published by the AAOS. However, this is even further limited in the wheelchair, bound paraplegic population, which the aforementioned guideline was not designed to address. Consequently, it is impossible to make an evidence- guided decision in the rotator cuff care of these individuals. It is arguable that finalizing a guideline for this patient population is more urgent considering the incredible dependence these patients have on their upper extremities. It is, therefore, paramount to increase the number of high level of evidence studies within this field. This study will address one of the knowledge gaps that currently exist. The study as described in the following pages, will utilize thoroughly designed methodology to provide evidence for or against repairs for massive rotator cuff tears in the wheelchair- bound, paraplegic population. The findings of this study will help to better tailor the care for massive rotator cuff tears in this patient population and avoid potentially unnecessary, costly interventions.

Research Questions

The primary research questions for this study are as follows:

1. What is the relative effectiveness of a repair for a massive rotator cuff tear with a subacromial decompression versus a simple subacromial decompression in the short term? Mid term? Long term?

2. What factors are covariates for these surgical procedure and, as a result, are partially responsible for the clinical and functional outcomes in the short term? Mid term? Long term?

Hypothesis

Given the high energy demand of manual wheelchair users, we expect that a repair will convincingly demonstrate advantages in outcomes along all time points of the study. The factors that will be associated with the outcomes will include tear size, smoking, and age.

C. Research Design & Methods

This study will be a randomized, single- blinded surgical trial involving multiple sites. Patients who meet inclusion criteria will be randomly assigned to either have their rotator cuff repaired with concomitant subacromial decompression or just the subacromial decompression. Specifically, the control group in this scenario will be the relatively more conservatively treated subacromial decompression group. The repair method will obviously vary by institution but given the small prevalence of these patients, it would be impossible to narrow down the repair technique to just one. The technique undertaken by each involved institution will, however, represent the technique that the involved surgeons feel the most comfortable with and therefore should be theoretically yield the best results. Subacromial decompression, on the other hand, has been fairly standardized across institutions and involves resecting the thickened and possibly inflamed subacromial bursa followed by a smoothing procedure of the subacromial bone. Patients will be randomly assigned to one of these two treatment conditions. The first condition will involve a repair of a massive rotator cuff tear along with a subacromial decompression. The second condition will involve only a subacromial decompression with no repair.

Patient Population

The target population for this study will be wheelchair- bound, paraplegics with a massive rotator cuff tear. To meet inclusion criteria, the patient's spinal cord injury level will not be high enough such that they are effectively more quadriplegic than paraplegic. Additionally, the patient will need to demonstrate weight- bearing use of their shoulders through manual wheelchair use or crutches. Electronic wheelchair users will be excluded from the study. The subject will also have to display minimal baseline independence level. This will be determined either by previous records or patient report of the ability to perform wheelchair propulsion, weight- relief lifts, and transfers effectively on their own. The massive rotator cuff tear will also have to be reparable and relatively acute. In other words, the tears must not display chronic degenerative changes including atrophy, fatty infiltration, retraction, and glenohumeral arthritis. Massive rotator cuff tears will be assessed by physical exam, MRI and plain film.

Sample Recruitment

The only feasible method of sampling for a study involving a population as specific as the one of concern is convenience sampling. This sampling method involves drawing samples from a population that is available and easily accessible. Over an 18- 24 month period, patients will be recruited on a rolling basis at all involved sites. As soon as they are enrolled, each patient will immediately receive the intervention they are assigned to. Initial contact with the patients will be undertaken by the coordinating nurses or physicians. These caretakers will also, at that time, introduce the study to the patients. A videotape detailing the overall project and the aims of the study will be shown during the visit. This will detail both treatment arms as well as the contact information for the study team member at the participating site. The patients will then be

asked if they would be willing to provide their contact information so that a study team member might contact them to provide further details. Should the patient agree to be contacted, their information will be passed on to a study team member who has been trained to recruit. This team member will contact the patient via the preferred medium of contact that the patient selected. The patient's eligibility as well as any further questions regarding the study will be addressed at that time. All qualifying patients who agree to be included in the study will be mailed an enrollment packet. This packet will contain another copy of the recruitment brochure, a detailed description of the study, informed consent documents, as well as a pre- addressed stamped return envelope to be used to mail in the signed consent forms. All the aforementioned documentation will undergo institutional review by all participating sites' IRB. Additionally, all patients must have failed a trial of nonsurgical treatment for at least 6 weeks.

Patients will be excluded if they have not attempted a trial of nonsurgical management. If a patient experienced significant improvement with nonsurgical care, this will also qualify a patient for exclusion. The remaining exclusion criteria will include: poor overall health making surgery too high a risk, pregnancy, active malignancy, prior or current fracture/ infection / deformity of the involved shoulder joint, < 18 years of age, prior shoulder surgery, and if the patient does not have the means to be available for regular follow- up.

Random Assignment Procedures

All random assignment will be carried out at one central location to be chosen out of the participating sites. The actual process will be a computer- based random assignment algorithm. This procedure will be carried out as soon as all the patent's required documentation has been received and reviewed by the study team.

Treatment Enrollment and the Blinding Process

After the randomization process has designated a subject to a certain treatment arm, they will be blinded from which procedure they will be receiving throughout the duration of the study. This should technically be a feasible feat considering a subacromial decompression is often performed in conjunction with a rotator cuff repair using the same instruments and involves making similar incisions on the patient's shoulder.

Surgical technique

The standardization of surgical approaches to a massive rotator cuff tear is one of the biggest issues this study will face and one that may not be feasible. There are a large number of arthroscopic repair techniques available and not a lot of agreement between practicing surgeons as to which technique is superior. To that end, the only feasible method is to allow each participating surgeon to perform the technique they feel the most comfortable with. Argument for this approach is that restricting the study to a specific technique may place technical strain on some participating surgeons who are not as well versed in that technique. This may have the detrimental effect of skewing outcomes and, most importantly, would be an ethical issue as the patient would technically not be receiving the best available care at that site.

Outcome Measures

Functional and clinical outcomes will be measured using several instruments already employed in clinical practice. These will be measured by the clinician who, as mentioned before, was not involved in the actual surgical procedure in order to preserve the blinding process. Assessments will occur preoperatively, two weeks postoperatively, 6 months postoperatively, 1

year postoperatively, 3 years postoperatively, 5 years postoperatively, and 10 years postoperatively.

Two pain and functional assessment instruments will be used at each assessment. A large number of assessment tools for the shoulder have been used in the past. Each one has been determined to have their respective limitations. Consequently, utilizing multiple different assessment tools is important to attain a complete picture of a patient's function and pain.

Demographic and Background

A survey consisting of questions will be formulated in order to gather data on the subjects' demographic and background. Demographic data collected will include age, gender, race/ ethnicity, socioeconomic status, and education level. Other background data will include smoking status, alcohol and other substance use, chronic illnesses (i.e. hypertension, diabetes, rheumatoid arthritis), and prior surgeries.

American Shoulder and Elbow Surgeons (ASES)

The American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form (ASES) was originally published in 1994. The ASES is a 17- item instrument that assesses pain and function. This functional assessment tool contains a self- report section for patients and a professional assessment section to be used by medical professionals. This is a widely used instrument and has been determined to be reliable, valid and responsive.[89] How are you going to code the responses to ensure a consist method of analyzing the responses?

Simple Shoulder Test (SST)

The Simple Shoulder Test (SST) was developed by the Shoulder Service at the University of Washington. It assesses the degree to which an affected shoulder limits a patient's

function in terms of activities of daily living. This instrument has also been determined to be reliable, valid and responsive.[90]

Wheelchair Users Shoulder Pain Index (WUSPI)

The Wheelchair Users Shoulder Pain Index (WUSPI) is a 15- item instrument used to assess the effect of shoulder pain on activities of daily living. Each item in the instrument are self- graded by the subject on a scale of zero to 10, where 0 is "no pain" and 10 is "worst pain ever experienced". The maximum possible score on the WUSPI is 150 with a minimum possible score of 0. Curtis et al. has demonstrated the reliability and validity of this instrument. [91] The WUSPI is useful for assessing the pain level during the 15 defined activities, but it is limited in that it does not reflect the actual grade of activity performance.[14] Consequently, this measure may be used to replace the traditional pain scale.

Data Analysis

The Checklist to Evaluate a Report of a Nonpharmacological Trial (CLEAR- NPT) instrument will be used to document the enrollment procedure as well as the data collection events. This instrument contains 10 items and 5 subitems and was designed to critically appraise literature, assess the quality of trials reported in systematic reviews, and help in the design of nonpharmacological treatment trials.[92] The ten items are the following: (1) adequate allocation sequence, (2) concealed allocation, (3) details of intervention for each group, (4) appropriate skill/ experience of providers in each group, (5) participant adherence (not applicable for one-time surgical treatments), (6) blinded participants, (7) blinded providers, (8) blinded assessors, (9) same follow-up for reach group, and (10) intention- to – treat analysis.

The primary groups involved in this project will be the cohort receiving a repair and subacromial decompression and the cohort receiving a subacromial decompression alone. Our analysis will determine the impact estimate for the former against the latter. The outcomes for each treatment arm will be collected via the follow-up appointments. These follow-up appointments will occur preoperatively, two weeks postoperatively, 6 months postoperatively, 1 year postoperatively, 3 years postoperatively, 5 years postoperatively, and 10 years postoperatively. A multivariate regression model will be used to assess procedure differences (rotator cuff repair + subacromial decompression versus subacromial decompression) in outcome scores after adjusting for age, smoking, tear size, race/ ethnicity, insurance status, education, comorbidities, symptom duration, site and tear progression. At the conclusion of the study, a linear mixed- effects models with repeated measures will be used to account for the time variant variable introduced by the various follow- up points. Mixed effects linear models with repeated measures are used to handle time variant variables.

One of the more difficult factors to adjust for will be with site selection. Spinal cord injury centers across the United States obviously have geographic variation and with this geographic variation comes an inherent variation in the patient population. For example, a spinal cord injury center that is closer to Los Angeles may have a younger patient population than say a center that is in Oklahoma. As a result, this may lead to relatively better outcomes in the site with a younger population. We will attempt to account for this by coding sites and adjusting for them in our model.

Along the same lines, we have to consider the effect that individual surgeons within a site will have on patient outcomes. Not all surgeons have the same skill level or experience. Consequently, even within institutions, there may be variable outcomes. However, we do not

believe that this may play a large factor. Most institutions generally hire clinicians who practice similar techniques and should have similar outcomes as a result. Consequently, we believe that adjusting for sites will be simultaneously have the effect of adjusting for surgeon. There is still the issue of being able to adjust for experience level, and this will unfortunately be one of the limitations of this study. If the individual sites provide an adequate number of subjects, this factor will be stratified per site. It should be noted, however, that while stratification would for many of the variables listed would be ideal, it may not necessarily be practical given the specificity of the patient population.

Another factor that must be given consideration is the impact the length of follow up will have on the outcomes being followed. Our last follow up will be 10 years postoperatively, consequently there is a very high chance that there will be loss to follow up. Our strategy for dealing with missing data is further detailed in a later section. However, something that is more concerning is the practicality of such a long follow- up within this patient population. For example, there is a problem of adjusting for how long a patient receives physical therapy. Furthermore, therapeutic measures will undoubtedly evolve over such a long time frame, so this is also another variable that will need to be accounted for during the duration of the study.

While crossover rates are certainly a reality in surgical trials, the primary analysis will be performed by following the intent- to- treat principle. This will allow us to preserve the treatment effects the randomization process should allow the study to calculate. A secondary analysis will be carried out by following the as- treated principle, where the outcomes of a patient will be based on the actual treatment received and not what was originally intended. We will compare the results with sensitivity analysis to determine impact on study findings as further detailed in the "Differential Attrition & Missing Data" section.

Sample Size Calculation

Our sample size calculation is based on the outcome measures and the reported minimal clinically important scores.[93] Minimal clinically important scores are the smallest difference in an outcome score that a patient will be able to perceive as an improvement. Tashjian et al.'s 2010 study measured this minimal score for the Simple Shoulder Test (SST) and the American Shoulder and Elbow Surgeons (ASES) score in 81 patients with rotator cuff tears managed nonoperatively.[93] The study determined that the minimal clinically important score for SST is a 2- point change while the same for the ASES score ranged from 12 to 17.

The formula we used for sample size calculation is the following:

$$n = \frac{2\sigma^2}{(\mu_2 - \mu_1)^2} \cdot f_{(\alpha,\beta)}$$

This equation provides an estimate of the necessary number of subjects for *each* treatment arm in order to attain a result with a desired power. In this equation, "σ" denotes the standard deviation for the outcome measure and "μ" denotes the mean for the population of interest.[94] Consequently, the term "(μ_2- μ_1)" denotes the minimal difference in mean outcome score between our two populations of interest that will have a meaningful clinical effect. Godfrey et al.'s study determined that the standard deviation for the simple shoulder test in 335 individuals with rotator cuff injury was "3.25".[90] We also know the minimal score difference in the simple shoulder test that will have clinically relevant effect is a 2- point difference.[93] The constant, *f,* represents a function of the values α and β, which are type I and II error, respectively. The value for this constant when the desired α is "0.05" and the desired β is "0.2" is "7.9".[94] Plugging these values into the equation above yields:

$$n = \frac{2(3.25)^2}{(2)^2} \cdot 7.9$$

$$n = 41.7$$

For the American Shoulder and Elbow Surgeons score, the standard deviation amongst a population of 63 patients with various shoulder pathologies was determined to be 17.3.[89] We also know the minimal score difference in the American Shoulder and Elbow Surgeons that will have a clinically relevant effect is a 17- point difference. Using the same formula, the sample size needed is:

$$n = 15.9$$

Rounding up these values and multiplying by two for each treatment arm indicates that for the simple shoulder test we would need at least 84 patients. Since the sample size needed for the American Shoulder and Elbow Surgeons score is only 32, we will use the estimated 84 patients as the minimum necessary amount necessary. However, this calculation is based on the assumption of 1 independent variable. Our analysis, as stated above, will rely on multivariate regression modeling based on 10 separate independent variables. As a result, the calculated 84 patients would not be a big enough sample size for the model we intend to use. Using a smaller sample size may have the inadvertent effect of "overfitting" the data or, in other words, the model may fit the sample well but not be generalizable. Consequently, we will follow the rule of thumb proposed by Harrell of 10 subjects per independent variable in order to attain a model that provides accurate predictions.[95] Consequently, we require at least 100 subjects with 50 subjects in each treatment arm.

Minimizing Attrition

As with any clinical trial, there is certainly a risk for attrition and loss to follow- up. Several mechanisms to minimize this will be put into place including a thorough follow- up procedure for non- respondents. A maximum of 10 attempts will be made by telephone to reach a

patient who has failed to follow- up at an interval of 2 to 3 days between attempts. If all attempts are unsuccessful, a team member will contact the site that enrolled the patient and will obtain medical records to determine if the patient is still receiving treatment or if there is some other reason for the lack of communication (i.e. passing away).

Differential Attrition & Missing Data

With ten variables of primary concern, it is highly probable that there will be missing data for some subjects and there is a possibility of differential attrition for any given subset of the patient population. To determine whether there is a systematic bias for the missing data, analysis will be carried out in both an intent to treat and as treated manner. The results from these two separate analyses will be compared to determine whether there is a systematic bias. If the results indicate that there is no systematic bias, in other words the data is missing at random, analysis of the available data will be conducted. However, if the results indicate there is a systematic bias, in other words the data is not missing at random, multiple imputation will be used. Sensitivity analysis will follow and will be done on the original and imputed data separately. If this analysis produces similar results between the two groups of data, the results from the imputed analysis will be reported.

Project Milestones

The project will have 3 overall phases. The first year will consist of finalizing the data collection plan and randomization protocol for patients. The first 2 years will involve patient recruitment across all involved sites. Following recruitment, the subjects will be randomized by a centralized database. Intervention will then follow thereafter. Prior to receiving interventions, the patients will be asked to take a baseline survey along with the ASES and SST assessments. Follow- up assessments will occur two weeks postoperatively, 6 months postoperatively, 1 year

postoperatively, 3 years postoperatively, 5 years postoperatively, and 10 years postoperatively. Data collected from these surveys will be analyzed at one central site. Interim reports will be sent to the funding agency at the end of each fiscal year with updates on progress. We will plan to publish results in a peer- reviewed journal after data is analyzed and finalized from the major postoperative follow- up time points: 3, 5, and 10 year marks.

	Year 1		Year 2		Years 3-5		Year 12
Advisory Panel Meeting	■						
Patient Recruitment		■	■				
Intervention			■	■			
Patient interviews					■	■	■
Interim reports		■		■		■	
Data analyses					■	■	■
Final Research Report					■	■	■
Dissemination Activities					■	■	■

Table 4. Project Milestones

D. Dissemination and Implementation Potential

The proposed project has the potential to revise indications for the surgical management of massive rotator cuff tears in the wheelchair- bound, paraplegic population. This is a matter of importance for clinicians and patients alike, so there will most likely be a wide range of interest both domestically and internationally. Additionally, the research team will consist of healthcare professionals from multiple disciplines. Consequently, the results of this project will be widely disseminated throughout all involved disciplines. This will involve not only the peer-reviewed journal publications but also professional organizational meetings and conferences.

E. Caveats and Potential Pitfalls for Each Study Aim

This project will have several limitations. Some of these have been addressed in the "Research Design" and "Data Analysis" sections. Another limitation is that the surgical techniques used by each involved clinician will be impossible to standardize. Massive rotator cuff repairs are arguably one of the most hotly contested and controversial repairs in the upper extremity surgical field. With so many different techniques currently being practiced, it will be impossible to avoid a heterogeneous treatment in our subjects. We take solace in the fact that published outcomes data has generally been fairly consistent with regards to the various involved techniques, so while this study will lack efficacy, it should maintain effectiveness.

There is also the issue of heterogeneity of treatment effects. Depending on the subgroup of patients looked at the outcomes may be significantly different. This will be in part accounted for by our linear, mixed effects model as outlined in the "Data Analysis" section. Furthermore, the generalizability of our findings will be suspect as well. While we will include a variety of spinal cord injury centers in our study, it may not be possible to definitively say that our sample population is representative of this specific patient population as a whole.

Another potential pitfall for this project will be a high crossover rate. With our plan to analyze the data following the intent- to – treat analysis, a crossover rate approaching 50% would technically render such an analysis meaningless. We will, however, be analyzing the data following the as- treated principle as well. While the treatment effect gathered from such an analysis will be prone to biases that an intent- to- treat analysis would not, it represents the next best mode of analysis to determine treatment effect.

F. Ethical Considerations

All trials involving human subjects should address the issue of vulnerable populations. In other words, will the project be taking advantage of a disadvantaged group of individuals. Historically, vulnerable populations have referred to children, prisoners, and those in low socioeconomic backgrounds. Consequently, it is reasonable to question whether conducting a research trial involving disabled individuals, as in this project, would be violating a critical ethical code. The first step is to assess the risk and benefit of the project and the involved procedures. Given the fact that the procedures in question are minimally invasive and are commonly used in practice for both able- bodied and paraplegics, we believe that the benefits of the procedure far outweigh the risks.

The second step is to ensure the affected individuals are fully informed of what the project will entail. This will involve a thorough reporting of the risks and benefits of each surgical technique as well as a detailed explanation of the follow- up and rehabilitation procedures. We believe that our recruitment protocol along with the informational videos and readily accessible study team will give our subjects all the information they will require to make a fully informed decision.

The final step may be to involve an independent governing research body, such as an IRB, which will continually monitor the safety and quality of care being given to the involved research subjects. The roles of such a governing body should be emphasized throughout the duration of the project. Specifically, the roles of such a governing body would include the safeguarding of a subject's rights, well-being, and safety.

Conclusion

The original purpose of this thesis was to investigate the effectiveness of rotator cuff repairs in the wheelchair- bound, paraplegic population. This group of patients are of particular interest to the shoulder community due to the overwhelming burden their shoulders take on to allow them to be independent. The first half of this thesis overviews the systematic review process through which it was determined that the available evidence was not amenable to meta-analysis. The systematic search results yielded 6 uncontrolled case series. While case series are valuable as an initial assessment and for hypothesis creation, they are not useful to demonstrate effectiveness. The heterogeneity of preoperative assessment, surgical procedures, patient population, and postoperative assessment were other factors that precluded the ability to perform a meaningful meta- analysis.

In light of the dearth of available evidence regarding rotator cuff repairs in this population, the second half of this thesis was dedicated to outlining exactly what the levels of evidence are in orthopaedic surgery scientific literature. This eventually culminates in a study proposal for a high- level of evidence study that would be able to overcome the confines of the challenges of performing such high level of evidence of studies in orthopaedic surgery.

Future Directions

To be clear, the feasibility of said study is yet to be determined. One of the biggest pitfalls of such a study may possibly be the simple lack in the number of patients to be able to generate meaningful data. The inclusion criteria of the proposed study are strict to allow for internal validity. However, the same restrictions may also limit the number of patients who will be available for inclusion to a degree that will weaken the study.

Regardless, the value of randomized trials and other higher level of evidence studies to the practice of orthopaedic surgery cannot be understated as it is in other medical fields. If a study is thoroughly planned and carried out it may have the potential to alter the standard of care for common maladies. Evidence gained from such a study may cause surgical treatments to be abandoned, revision of indications for said treatment, or clearly demonstrate its superiority.

If a study similar to the one designed here is carried out, the implications of the study may be far greater than the immediate aims of the study. Not only would the scientific community now have high level of evidence for directing the surgical management of a debilitating problem, but a foundation for future studies will have been built by the data collected. A robust database may lead to further studies that allow a highly tailored treatment algorithm within this patient population. The importance of identifying risk factors as well as factors that will benefit surgical outcomes is a goal that many of us in the scientific community share.

Additionally, if this proposed study is undertaken and the results are "promising", it should not end there. That would be just the beginning. The results from one promising study is not as strong as reproduced results in many studies demonstrating a homogeneity of findings. Consequently, the next step in such a situation would be to validate the findings with further studies that perhaps involve different institutions.

Personal Knowledge Gained

The process this thesis has taken me through has taught me numerous things. I had the opportunity to learn more about the history of evidence- based medicine and how it eventually became adapted by the Orthopaedic Surgery community. Secondly, it has taught me the complex nature of designing a high level of evidence study from randomized clinical trials all the way to

systematic reviews and clinical practice guidelines. Finally, it has given me an appreciation for the scientific method and provided a context through which I will hopefully draw from to conduct research in the future. Most importantly, I have learned how much more work there is to be done toward achieving a truly evidence- based practice of Orthopaedic Surgery.

References

1. LaPlante, M.P. and H.S. Kaye, *Demographics and trends in wheeled mobility equipment use and accessibility in the community.* Assist Technol, 2010. **22**(1): p. 3-17; quiz 19.
2. *Facts 2015 Aug.pdf*. 2015 [cited 2015 November 28]; Available from: https://www.nscisc.uab.edu/Public/Facts 2015 Aug.pdf.
3. Ballinger, D.A., D.H. Rintala, and K.A. Hart, *The relation of shoulder pain and range-of-motion problems to functional limitations, disability, and perceived health of men with spinal cord injury: a multifaceted longitudinal study.* Arch Phys Med Rehabil, 2000. **81**(12): p. 1575-81.
4. Pentland, W.E. and L.T. Twomey, *The weight-bearing upper extremity in women with long term paraplegia.* Paraplegia, 1991. **29**(8): p. 521-30.
5. Luime, J.J., et al., *Prevalence and incidence of shoulder pain in the general population; a systematic review.* Scand J Rheumatol, 2004. **33**(2): p. 73-81.
6. Brose, S.W., et al., *Shoulder ultrasound abnormalities, physical examination findings, and pain in manual wheelchair users with spinal cord injury.* Arch Phys Med Rehabil, 2008. **89**(11): p. 2086-93.
7. Jayaraman, C., et al., *Shoulder pain and cycle to cycle kinematic spatial variability during recovery phase in manual wheelchair users: a pilot investigation.* PLoS One, 2014. **9**(3): p. e89794.
8. Rice, I.M., et al., *Relationship between shoulder pain and kinetic and temporal-spatial variability in wheelchair users.* Arch Phys Med Rehabil, 2014. **95**(4): p. 699-704.
9. Sosnoff, J.J., et al., *Variability in Wheelchair Propulsion: A New Window into an Old Problem.* Front Bioeng Biotechnol, 2015. **3**: p. 105.
10. Collinger, J.L., et al., *Shoulder biomechanics during the push phase of wheelchair propulsion: a multisite study of persons with paraplegia.* Arch Phys Med Rehabil, 2008. **89**(4): p. 667-76.
11. Bayley, J.C., T.P. Cochran, and C.B. Sledge, *The weight-bearing shoulder. The impingement syndrome in paraplegics.* J Bone Joint Surg Am, 1987. **69**(5): p. 676-8.
12. Nawoczenski, D.A., et al., *Clinical trial of exercise for shoulder pain in chronic spinal injury.* Phys Ther, 2006. **86**(12): p. 1604-18.
13. Wang, J.C., et al., *The influence of shoulder pain on functional limitation, perceived health, and depressive mood in patients with traumatic paraplegia.* J Spinal Cord Med, 2015. **38**(5): p. 587-92.
14. Samuelsson, K.A., H. Tropp, and B. Gerdle, *Shoulder pain and its consequences in paraplegic spinal cord-injured, wheelchair users.* Spinal Cord, 2004. **42**(1): p. 41-6.
15. Silfverskiold, J. and R.L. Waters, *Shoulder pain and functional disability in spinal cord injury patients.* Clin Orthop Relat Res, 1991(272): p. 141-5.
16. Hastings, J. and B. Goldstein, *Paraplegia and the shoulder.* Phys Med Rehabil Clin N Am, 2004. **15**(3): p. vii, 699-718.
17. Dyson-Hudson, T.A. and S.C. Kirshblum, *Shoulder pain in chronic spinal cord injury, Part I: Epidemiology, etiology, and pathomechanics.* J Spinal Cord Med, 2004. **27**(1): p. 4-17.

18. Finley, M.A. and M.M. Rodgers, *Prevalence and identification of shoulder pathology in athletic and nonathletic wheelchair users with shoulder pain: A pilot study.* J Rehabil Res Dev, 2004. **41**(3b): p. 395-402.
19. Isaacs, D. and D. Fitzgerald, *Seven alternatives to evidence based medicine.* BMJ, 1999. **319**(7225): p. 1618.
20. *The American Academy of Orthopaedic Surgeons: AAOS Evidence-based Clinical Practice Guidelines.* [cited 2016 May 10, 2016]; Available from: http://www.aaos.org/research/guidelines/guide.asp.
21. Sawatzky, B., et al., *The need for updated clinical practice guidelines for preservation of upper extremities in manual wheelchair users: a position paper.* Am J Phys Med Rehabil, 2015. **94**(4): p. 313-24.
22. Paralyzed Veterans of America Consortium for Spinal Cord, M., *Preservation of upper limb function following spinal cord injury: a clinical practice guideline for health-care professionals.* J Spinal Cord Med, 2005. **28**(5): p. 434-70.
23. Khan, K.S., et al., *Five steps to conducting a systematic review.* J R Soc Med, 2003. **96**(3): p. 118-21.
24. Kulig, K., et al., *Shoulder joint kinetics during the push phase of wheelchair propulsion.* Clin Orthop Relat Res, 1998(354): p. 132-43.
25. Akbar, M., et al., *Prevalence of rotator cuff tear in paraplegic patients compared with controls.* J Bone Joint Surg Am, 2010. **92**(1): p. 23-30.
26. Akbar, M., et al., *Do overhead sports increase risk for rotator cuff tears in wheelchair users?* Arch Phys Med Rehabil, 2015. **96**(3): p. 484-8.
27. Oh, L.S., et al., *Indications for rotator cuff repair: a systematic review.* Clin Orthop Relat Res, 2007. **455**: p. 52-63.
28. Sher, J.S., et al., *Abnormal findings on magnetic resonance images of asymptomatic shoulders.* J Bone Joint Surg Am, 1995. **77**(1): p. 10-5.
29. Milgrom, C., et al., *Rotator-cuff changes in asymptomatic adults. The effect of age, hand dominance and gender.* J Bone Joint Surg Br, 1995. **77**(2): p. 296-8.
30. Tashjian, R.Z., *Epidemiology, natural history, and indications for treatment of rotator cuff tears.* Clin Sports Med, 2012. **31**(4): p. 589-604.
31. Yamaguchi, K., et al., *Natural history of asymptomatic rotator cuff tears: a longitudinal analysis of asymptomatic tears detected sonographically.* J Shoulder Elbow Surg, 2001. **10**(3): p. 199-203.
32. Yamaguchi, K., et al., *The demographic and morphological features of rotator cuff disease. A comparison of asymptomatic and symptomatic shoulders.* J Bone Joint Surg Am, 2006. **88**(8): p. 1699-704.
33. Lazarides, A.L., et al., *Rotator cuff tears in young patients: a different disease than rotator cuff tears in elderly patients.* J Shoulder Elbow Surg, 2015. **24**(11): p. 1834-43.
34. Downie, B.K. and B.S. Miller, *Treatment of rotator cuff tears in older individuals: a systematic review.* J Shoulder Elbow Surg, 2012. **21**(9): p. 1255-61.
35. Morse, K., et al., *Arthroscopic versus mini-open rotator cuff repair: a comprehensive review and meta-analysis.* Am J Sports Med, 2008. **36**(9): p. 1824-8.
36. Nho, S.J., et al., *Systematic review of arthroscopic rotator cuff repair and mini-open rotator cuff repair.* J Bone Joint Surg Am, 2007. **89 Suppl 3**: p. 127-36.

37. Kerr, J., et al., *Arthroscopic rotator cuff repair in the weight-bearing shoulder.* J Shoulder Elbow Surg, 2015. **24**(12): p. 1894-9.
38. Escobedo, E.M., et al., *MR imaging of rotator cuff tears in individuals with paraplegia.* AJR Am J Roentgenol, 1997. **168**(4): p. 919-23.
39. Moosmayer, S., et al., *The natural history of asymptomatic rotator cuff tears: a three-year follow-up of fifty cases.* J Bone Joint Surg Am, 2013. **95**(14): p. 1249-55.
40. Mall, N.A., et al., *Symptomatic progression of asymptomatic rotator cuff tears: a prospective study of clinical and sonographic variables.* J Bone Joint Surg Am, 2010. **92**(16): p. 2623-33.
41. Gerber, C., et al., *Effect of tendon release and delayed repair on the structure of the muscles of the rotator cuff: an experimental study in sheep.* J Bone Joint Surg Am, 2004. **86-A**(9): p. 1973-82.
42. Goutallier, D., et al., *Influence of cuff muscle fatty degeneration on anatomic and functional outcomes after simple suture of full-thickness tears.* J Shoulder Elbow Surg, 2003. **12**(6): p. 550-4.
43. Cofield, R.H., et al., *Surgical repair of chronic rotator cuff tears. A prospective long-term study.* J Bone Joint Surg Am, 2001. **83-A**(1): p. 71-7.
44. Kuhn, J.E., et al., *Interobserver agreement in the classification of rotator cuff tears.* Am J Sports Med, 2007. **35**(3): p. 437-41.
45. DeOrio, J.K. and R.H. Cofield, *Results of a second attempt at surgical repair of a failed initial rotator-cuff repair.* J Bone Joint Surg Am, 1984. **66**(4): p. 563-7.
46. Abrams, J.a.B., RH, *Arthroscopic Rotator Cuff Surgery: A Practical Approach to Management*. 2008, New York, New York: Springer Science + Business.
47. Morrow, M.M., et al., *Detailed shoulder MRI findings in manual wheelchair users with shoulder pain.* Biomed Res Int, 2014. **2014**: p. 769649.
48. Zumstein, M.A., et al., *The clinical and structural long-term results of open repair of massive tears of the rotator cuff.* J Bone Joint Surg Am, 2008. **90**(11): p. 2423-31.
49. Paxton, E.S., et al., *Clinical and radiographic outcomes of failed repairs of large or massive rotator cuff tears: minimum ten-year follow-up.* J Bone Joint Surg Am, 2013. **95**(7): p. 627-32.
50. Galatz, L.M., et al., *The outcome and repair integrity of completely arthroscopically repaired large and massive rotator cuff tears.* J Bone Joint Surg Am, 2004. **86-A**(2): p. 219-24.
51. Geary, M.B. and J.C. Elfar, *Rotator Cuff Tears in the Elderly Patients.* Geriatr Orthop Surg Rehabil, 2015. **6**(3): p. 220-4.
52. Sackett, D.L., et al., *Evidence based medicine: what it is and what it isn't.* BMJ, 1996. **312**(7023): p. 71-2.
53. Tsay, M.Y. and Y.H. Yang, *Bibliometric analysis of the literature of randomized controlled trials.* J Med Libr Assoc, 2005. **93**(4): p. 450-8.
54. Wright, J.G., M.F. Swiontkowski, and J.D. Heckman, *Introducing levels of evidence to the journal.* J Bone Joint Surg Am, 2003. **85-A**(1): p. 1-3.
55. Wright, J.G., *A practical guide to assigning levels of evidence.* J Bone Joint Surg Am, 2007. **89**(5): p. 1128-30.

56. Guidelines, C.o.S.f.D.T.C.P., *Clinical Practice Guidelines We Can Trust*, ed. R.M. Graham, M; Wolman, DM; Greenfield, S; Steinberg, E. 2011, Washington, D.C.: The National Academies Press.
57. Research, C.o.S.f.S.R.o.C.E., *Findings What Works in Health Care: Standards for Systematic Reviews*, ed. J.L. Eden, L; Berg, A; Morton, S. 2011, Washington, D.C.: The National Academies Press.
58. Russell, R., et al., in *Issues and Challenges in Conducting Systematic Reviews to Support Development of Nutrient Reference Values: Workshop Summary: Nutrition Research Series, Vol. 2*. 2009: Rockville (MD).
59. Moher, D., et al., *Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement.* J Clin Epidemiol, 2009. **62**(10): p. 1006-12.
60. Goldstein, B., J. Young, and E.M. Escobedo, *Rotator cuff repairs in individuals with paraplegia.* Am J Phys Med Rehabil, 1997. **76**(4): p. 316-22.
61. Robinson, M.D., R.W. Hussey, and C.Y. Ha, *Surgical decompression of impingement in the weightbearing shoulder.* Arch Phys Med Rehabil, 1993. **74**(3): p. 324-7.
62. Popowitz, R.L., et al., *Rotator cuff repair in spinal cord injury patients.* J Shoulder Elbow Surg, 2003. **12**(4): p. 327-32.
63. Fattal, C., et al., *Rotator cuff surgery in persons with spinal cord injury: relevance of a multidisciplinary approach.* J Shoulder Elbow Surg, 2014. **23**(9): p. 1263-71.
64. Jung, H.J., et al., *Reconstruction of rotator cuff tears in wheelchair-bound paraplegic patients.* J Shoulder Elbow Surg, 2015. **24**(4): p. 601-5.
65. Obremskey, W.T., et al., *Level of evidence in orthopaedic journals.* J Bone Joint Surg Am, 2005. **87**(12): p. 2632-8.
66. Cochrane. *Data collection forms for intervention reviews*. 2014 [cited 2017 January 3]; Available from: http://training.cochrane.org/resource/data-collection-forms-intervention-reviews.
67. Bederman, S.S. and J.G. Wright, *Randomized trials in surgery: how far have we come?* J Bone Joint Surg Am, 2012. **94 Suppl 1**: p. 2-6.
68. Hanzlik, S., et al., *Levels of evidence in research published in The Journal of Bone and Joint Surgery (American Volume) over the last thirty years.* J Bone Joint Surg Am, 2009. **91**(2): p. 425-8.
69. Bhandari, M., et al., *The quality of reporting of randomized trials in the Journal of Bone and Joint Surgery from 1988 through 2000.* J Bone Joint Surg Am, 2002. **84-A**(3): p. 388-96.
70. Poolman, R.W., et al., *Does a "Level I Evidence" rating imply high quality of reporting in orthopaedic randomised controlled trials?* BMC Med Res Methodol, 2006. **6**: p. 44.
71. Johnson, A.G., *Surgery as a placebo.* Lancet, 1994. **344**(8930): p. 1140-2.
72. Dowrick, A.S. and M. Bhandari, *Ethical issues in the design of randomized trials: to sham or not to sham.* J Bone Joint Surg Am, 2012. **94 Suppl 1**: p. 7-10.
73. Striefel, S., *Ethical research issues: going beyond the Declaration of Helsinki.* Appl Psychophysiol Biofeedback, 2001. **26**(1): p. 39-59; discussion 67-71.
74. Stock, G., *If the goal is relief, what's wrong with a placebo?* Am J Bioeth, 2003. **3**(4): p. 53-4.

75. Moseley, J.B., et al., *A controlled trial of arthroscopic surgery for osteoarthritis of the knee.* N Engl J Med, 2002. **347**(2): p. 81-8.
76. Birkmeyer, N.J., et al., *Design of the Spine Patient outcomes Research Trial (SPORT).* Spine (Phila Pa 1976), 2002. **27**(12): p. 1361-72.
77. Weinstein, J.N., et al., *Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial.* JAMA, 2006. **296**(20): p. 2441-50.
78. Weinstein, J.N., et al., *Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT) observational cohort.* JAMA, 2006. **296**(20): p. 2451-9.
79. Weinstein, J.N., et al., *Surgical versus nonsurgical treatment for lumbar degenerative spondylolisthesis.* N Engl J Med, 2007. **356**(22): p. 2257-70.
80. Weinstein, J.N., et al., *Surgical versus nonsurgical therapy for lumbar spinal stenosis.* N Engl J Med, 2008. **358**(8): p. 794-810.
81. Weinstein, J.N., et al., *Surgical compared with nonoperative treatment for lumbar degenerative spondylolisthesis. four-year results in the Spine Patient Outcomes Research Trial (SPORT) randomized and observational cohorts.* J Bone Joint Surg Am, 2009. **91**(6): p. 1295-304.
82. Nawoczenski, D.A., et al., *Clinical trial of exercise for shoulder pain in chronic spinal injury.* Physical Therapy, 2006. **86**(12): p. 1604-1618.
83. van den Dolder, P.A., P.H. Ferreira, and K.M. Refshauge, *Effectiveness of soft tissue massage and exercise for the treatment of non-specific shoulder pain: a systematic review with meta-analysis.* Br J Sports Med, 2014. **48**(16): p. 1216-26.
84. Bedi, A., et al., *Massive tears of the rotator cuff.* J Bone Joint Surg Am, 2010. **92**(9): p. 1894-908.
85. Pedowitz, R.A., et al., *Optimizing the management of rotator cuff problems.* J Am Acad Orthop Surg, 2011. **19**(6): p. 368-79.
86. Levy, H.J., R.D. Gardner, and L.J. Lemak, *Arthroscopic subacromial decompression in the treatment of full-thickness rotator cuff tears.* Arthroscopy, 1991. **7**(1): p. 8-13.
87. Ellman, H., *Arthroscopic subacromial decompression: analysis of one- to three-year results.* Arthroscopy, 1987. **3**(3): p. 173-81.
88. Esch, J.C., *Arthroscopy update #4. Arthroscopic subacromial decompression. Surgical technique.* Orthop Rev, 1989. **18**(6): p. 733-5, 738-42.
89. Michener, L.A., P.W. McClure, and B.J. Sennett, *American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form, patient self-report section: reliability, validity, and responsiveness.* J Shoulder Elbow Surg, 2002. **11**(6): p. 587-94.
90. Godfrey, J., et al., *Reliability, validity, and responsiveness of the simple shoulder test: psychometric properties by age and injury type.* J Shoulder Elbow Surg, 2007. **16**(3): p. 260-7.
91. Curtis, K.A., et al., *Functional reach in wheelchair users: the effects of trunk and lower extremity stabilization.* Arch Phys Med Rehabil, 1995. **76**(4): p. 360-7.
92. Boutron, I., et al., *A checklist to evaluate a report of a nonpharmacological trial (CLEAR NPT) was developed using consensus.* J Clin Epidemiol, 2005. **58**(12): p. 1233-40.

93. Tashjian, R.Z., et al., *Minimal clinically important differences in ASES and simple shoulder test scores after nonoperative treatment of rotator cuff disease.* J Bone Joint Surg Am, 2010. **92**(2): p. 296-303.
94. Pocock, S., *Clinical Trials: A Practical Approach*. 1984, Great Britain: John Wiley & Sons Ltd.
95. Harrell, F.J., *Regression modeling strategies*. 2001, New York, NY: Springer- Verlag.

Appendix

Pubmed Search Strategy

#1 Shoulder pain OR Should pains OR Shoulder OR shoulders
#2 Paraplegia OR paraplegic OR spinal cord injury OR spinal cord injuries OR wheelchair
#3 Rotator cuff OR rotator cuff repair OR rotator cuff surgery OR arthroplasty OR arthroplasties OR decompression
#4 #1 AND #2 AND #3 Filters: English

Web of Science Search Strategy

Topic: (((Paraplegia OR paraplegic OR spinal cord injury OR spinal cord injuries)) OR wheelchair) AND **Topic:** ((((shoulder pain OR shoulder pains)) OR shoulder) OR shoulders) AND **Topic:** (rotator cuff OR rotator cuff repair OR rotator cuff surgery OR arthroplasty OR arthroplasties OR decompression)

Cochrane Search Strategy

'shoulder* OR shoulder pain in Title, Abstract, Keywords and parapleg* OR spinal cord injur* OR wheelchair* and rotator cuff OR rotator cuff repair* OR rotator cuff surgery OR arthroplast* OR decompression

Robinson MD et al., 1993 Study Information	
Country	United States of America
Level of Evidence	4
Total # of Patients/ Shoulders	4/6
Obremsky	$^{3}/_{9}$
All patients have same diagnosis	Yes, Grade II/III shoulder impingement
Strict inclusion and exclusion criteria	No
Prospective patient enrollment	Unclear
Standard treatment protocol	Yes, all included patients had failed
Follow-up at specified time intervals	No
Outcome Measures	Yes, ROM and assessment of activities of daily living
Patient derived validated instruments for functional asssessment	No
Follow up >80%	N/A
Missing data accounted for?	N/A
Outcome	All involved patients reportedly improved in some aspect to pre-morbid functionality
Level of SCI	C5-T12
Time since injury	Unavailable
Means of cuff tear diagnosis	Physical Exam
Rotator cuff tear	Supraspinatus tears were noted in ¾ patients but the size or involvement of other tendons were not described.
Intervention	Decompression & rotator cuff repair (“when warranted”)
Follow up	No standardized follow- up period

Goldstein B et al., 1997 Study Information	
Country	United States of America
Level of Evidence	4
Total # of Patients/ Shoulders	5/6
Obremsky	$^{1}/_{9}$
All patients have same diagnosis	No
Strict inclusion and exclusion criteria	No
Prospective patient enrollment	No
Standard treatment protocol	No
Follow-up at specified time intervals	Unclear
Outcome Measures	Yes, over head reach and activities of daily living
Patient derived validated instruments for functional asssessment	Unclear
Follow up >80%	N/A
Missing data accounted for?	N/A
Outcome	1 patient with partial tear reported improvements after procedure but the remaining 4 with large tears did not improve and one reportedly had worsened symptoms.
Level of SCI	T3- L1
Time since injury	6- 31 years
Means of cuff tear diagnosis	Physical Exam and MRI
Rotator cuff tear	Large (4)
Intervention	Repair and decompression
Follow up	5 years for two but unclear for other subjects

Popowitz et al., 2003 Study Information	
Country	United States of America
Level of Evidence	4
Total # of Patients/ Shoulders	5/ 8
Obremsky	$^{3}/_{9}$
All patients have same diagnosis	No (7/8 had acute injuries, sizes of tears are not mentioned)
Strict inclusion and exclusion criteria	No
Prospective patient enrollment	No
Standard treatment protocol	Yes
Follow-up at specified time intervals	No
Outcome Measures	ASES and Shoulder score index
Patient derived validated instruments for functional asssessment	Yes
Follow up >80%	N/A
Missing data accounted for?	N/A
Outcome	7/8 returned to pre- injury level of function at most recent followup
Level of SCI	C5 – T10
Time since injury	1-3 years
Means of cuff tear diagnosis	Physical Exam and MRI
Rotator cuff tear	Unclear
Intervention	Arthroscopic rotator cuff repair
Follow up	12 – 72 months (avg. 40.1 months)

Fattal et al., 2014 Study Information	
Country	France
Level of Evidence	4
Total # of Patients/ Shoulders	28/ 38
Obremsky	$^{5}/_{9}$
All patients have same diagnosis	No
Strict inclusion and exclusion criteria	Yes
Prospective patient enrollment	Yes
Standard treatment protocol	No
Followup at specified time intervals	No
Patient derived validated instruments for fucntional asssessment	Yes
Follow up >80%	Yes
Missing data accounted for?	Unclear
Level of SCI	C5 – L4
Time since injury	unclear
Means of cuff tear diagnosis	Physical Exam and MRI
Rotator cuff tear	Wide range of tears
Intervention	Open and Arthroscopic rotator cuff repairs; Nonoperative
Follow up	0.2 – 2.9 years (avg. 1.5 years)
Outcome Measures	Functional Independence Measure (FIM), mean pain intensity, max pain intensity

Outcome	The most prominent advantage in operative shoulders was pain relief with small improvements in FIM score and Range of Motion.

Kerr et al., 2015 Study Information	
Country	Switzlerland
Level of Evidence	4
Total # of Patients/ Shoulders	46
Obremsky	$^{3}/_{9}$
All patients have same diagnosis	No
Strict inclusion and exclusion criteria	No
Prospective patient enrollment	No
Standard treatment protocol	Yes
Follow-up at specified time intervals	No
Outcome Measures	Constant Murley, Subjective shoulder value, and ASES
Patient derived validated instruments for fucntional asssessment	Yes
Follow up >80%	N/A
Missing data accounted for?	N/A
Outcome	Pre/postop: CS – 50/80; ASES – 56/92; SSV 84% (postop)
Level of SCI	C5-L3
Time since injury	Unavailable
Means of cuff tear diagnosis	Physical Exam and MRI
Rotator cuff tear	Wide range of tears
Intervention	Repair and subacromial decompression
Follow up	24- 82 months (avg. 46 months)

Jung et al., 2015 Study Information	
Country	South Korea
Level of Evidence	4
Total # of Patients/ Shoulders	13/16
Obremsky	$^{1}/_{9}$
All patients have same diagnosis	No
Strict inclusion and exclusion criteria	No
Prospective patient enrollment	No
Standard treatment protocol	No
Follow-up at specified time intervals	No
Outcome Measures	ASES and Constant and Murley
Patient derived validated instruments for fucntional asssessment	No
Follow up >80%	N/A
Missing data accounted for?	N/A
Outcome	Pre/postop: ASES – 53/85; Constant – 48/75; Even in the retear group, the function scores improved.
Level of SCI	C5- T10
Time since injury	Unavailable
Means of cuff tear diagnosis	Physical Exam and MRI
Rotator cuff tear	Medium (2), large (3), massive (11)
Intervention	Open or Arthroscopic rotator cuff repair
Follow up	Avg. 31.2 months