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# **Complete Rotator Cuff Tear: An Evidence-Based Conservative Management Approach**

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Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/intechopen.70270>

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## **Abstract**

Rotator cuff disease accounts for 10% of all shoulder pain and major shoulder disability, with limited information concerning the natural history and treatment approaches for the disorder. Our objective is to assess the available evidence for the efficacy and morbidity of commonly used systemic medications, physiotherapy, and injections alongside evaluating any negative long-term effects. Although there is conflicting literature, there appears to be some consensus on the best indicators for choosing to treat a full-thickness tears (FTT) non-operatively to reduce pain and improve function. The risks associated with these tears include the potential of the progression of the tear, a diminished healing potential due to age or longer symptom duration, muscle atrophy, and fatty infiltration. The indications for surgery following conservative treatment are becoming more defined, and an outline regarding what scenarios warrant a transition from an initial conservative treatment plan has been developed. The developing benefits of using mesenchymal stem cells (MSCs) and other biologics have the potential to be disruptive to current treatment protocols in the approaches to healing rotator cuff tears (RCTs). With improved imaging modalities, diagnostic accuracy, and sensitivity, practitioners of the future will hopefully be able to intervene earlier in the disease pathogenesis cycle.

**Keywords:** natural history, physiotherapy, risk, rotator cuff, biologics

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## **1. Introduction**

Rotator cuff disease is prevalent in the general population, accounting for 10% of all shoulder pain and resulting in major shoulder disability. Despite the large prevalence of rotator cuff

tears (RCTs), there is still limited information concerning the natural history and treatment approaches for the disorder. An RCT may initially present as a partial-thickness tear (PTT) that progresses to a full-thickness tear (FTT) in the seventh decade of life [1]. Currently, there are no comprehensive British National Institute of Clinical Excellence (NICE) guidelines and European guidelines on the management of RCTs in general, and conclusions made by the American Academy of Orthopaedic Surgeons (AAOS) show weak evidence. Through understanding the natural history of RCTs, the progression from PTT to FTTs, and the different factors that influence progression such as age and comorbidities that influence progression, we can better advise our patients regarding optimum therapy. Such therapies include rehabilitation, physiotherapy, systemic medications and progression to surgical intervention. Although studies regarding physical therapy and surgical interventions show success in the recovery process, it has become increasingly clear that some biologics may augment the healing of tendon to bone when used as a primary treatment or as an adjunct to surgical procedures [2]. However, there are risks of conservative management, and it is important to identify the indications for transition from conservative to surgical management and appreciate patient satisfaction indices. To do so, the authors performed a critical review of the most recent evidence, providing an overview of the best evidence-based management for complete RCTs.

## 2. Natural history

For appropriate management of RCTs, it is imperative to appreciate the stages of progression of PTTs to FTTs and the contributing factors that lead to symptoms. A thorough patient history includes age, occupation, activities, hand dominance, history of trauma, time since onset of symptoms, history of smoking, diabetes mellitus and patient's expectations. A clinical examination is then supplemented with imaging studies, in particular ultrasound and magnetic resonance imaging (MRI), to further identify the location, size, thickness, retraction of RCTs and any other shoulder pathology such as long head of biceps tendonitis, labral tears, glenohumeral chondrosis, and muscle atrophy.

It is thought that older patients, patients with diabetes mellitus and osteoporosis and smokers will have a less successful repair of a complete tear [3]; however, there is no strong evidence for this. Chronic tears may have poor healing due to associated surrounding fatty infiltration and muscle atrophy [4]. An elderly patient with limited activities may be able to manage activities of daily living with a full-thickness RCT. In contrast, an active young patient may require surgery, even with a small complete RCT.

### 2.1. Traumatic vs. atraumatic tears

From the patient history, we can establish whether the RCT is a traumatic or degenerative one. Studies by Hantes et al. [5] and Petersen et al. [6] advocate early surgical treatment of complete traumatic RCTs, regardless of size and patient age, to avoid further RCT progression, with subsequent degenerative changes, fatty infiltration of surrounding muscle and cuff

retraction. Early surgery should be performed to obtain the best functional results. Atraumatic (degenerative) tears usually occur in elderly patients with larger tears, retracted rotator cuff tendons, poor surrounding tissue and fatty infiltration. In addition, they are likely to have fewer demands from their shoulder. Therefore, surgery may provide a less favourable outcome, and treatment may be best managed conservatively.

## **2.2. Partial to full-thickness tears**

PTTs can be bursal-sided or articular-sided tears. Over the course of time, PTTs enlarge and propagate into FTTs, developing distinct chronic pathological changes due to muscle retraction, fatty infiltration and muscle atrophy. These changes lead to a reduction in tendon elasticity and viability. Although PTT to FTTs are described as a continuum in the literature, these tears can occur without following this natural history path. In its end-state, the glenohumeral joint experiences a series of degenerative alterations known as cuff tear arthropathy.

Maman et al. [7] reported that, based on MRI imaging over an 18-month period for 59 patients, 52% of FTTs will increase in size and were substantially less stable than PTTs. Each shoulder underwent a baseline MRI, and a repeat imaging performed at a minimum interval of 6 months. Progression of tear size was found in 48% of the tears that were followed for at least 18 months compared with just 19% of those followed for less than 18 months. This contrasts with a study by Fucentese et al. [8], who reported seemingly contradictory findings in their report of 24 patients refusing operative treatment for full-thickness supraspinatus tears. They used magnetic resonance arthrography (MRA) as their initial imaging modality and MR without arthrography for their follow-up imaging and reported no increase in the mean size of the RCTs 3.5 years after the initial MRA.

## **2.3. Small vs. large full-thickness tears**

The risk of tear enlargement is greater for shoulders with more advanced tears and is associated with a greater risk of cuff muscle degenerative changes. This group reported that tear enlargement is also associated with greater risk of pain development across all tear types (50% for FTTs) [9].

The same study by Fucentese et al. [8] concludes that small isolated FTTs of the supraspinatus in patients under the age of 65 do not necessarily progress over time. Yamaguchi et al. [10] reported no increase in tear size over 5 years in 23 patients evaluated by ultrasound. This contrasts with a larger case series of 51 patients by Safran et al. [11] which reports that FTTs tend to increase in size in approximately half of patients aged 60 years or younger.

## **2.4. Demographics**

### **2.4.1. Age**

Advancing age has been considered the most important prognostic factor for surgical outcome. Gumina et al. [12] reported that patients older than 60 years of age were twice as

likely to develop a tear that was likely to progress to full-thickness and larger tears (54% of tears in patients older than 60 years showed such progression compared to only 17% of tears in those younger than 60 years). A cohort of patients younger than 60 years who were treated non-operatively for FTTs was found to have a higher rate of tear progression than older patients. Of the 61 tears, 49% increased in size according to the findings of ultrasound imaging [11].

#### 2.4.2. *Sex*

It has generally been reported that there are comparable incidence and characteristics of RCTs in both males and females [12], although only one study by Abate et al. [13] that specifically assessed menopausal women suggested that these women had an increased prevalence of asymptomatic FTT in the postmenopausal period.

#### 2.4.3. *Comorbidities*

Patient factors such as diabetes mellitus, cigarette smoking and osteoporosis have been suggested to negatively affect the clinical outcomes and healing of RCTs [3, 14].

#### 2.4.4. *Hand dominance*

There is no clear evidence to associate hand dominance with the development of RCTs [15]; however, one study demonstrated that in the dominant shoulders of 150 veteran competitive tennis players, there were more frequent RCTs, suggesting an association of high-energy activity [16].

#### 2.4.5. *Contralateral shoulder*

Multiple authors have reported that those who have an established RCT, regardless whether partial or full-thickness and size, are at an increased risk of developing a contralateral RCT [17, 18]. Yamaguchi et al. [10] estimated the prevalence of full-thickness bilateral RCTs at 35%, increasing to as high as 50% in those over the age of 60 years.

#### 2.4.6. *Smoking*

It is well recognised that smoking reduces microvascular perfusion, possibly reducing rotator cuff tendon vascular perfusion and healing [19]. Baumgarten et al. [20] conducted a study of 375 patients with RCTs confirmed by ultrasound (of all patients presenting with shoulder pain in general, of all demographics and characteristics). Of these 375 patients, 232 (62%) were smokers with a mean 23.4 years of smoking 1.25 packs per day and 30.1 mean pack-years. This is confirmed by the systematic review by Bishop et al. [21] in which increased rates and sizes of rotator cuff degeneration and symptomatic RCTs were seen in smokers, which could consequently increased the number of surgical procedures in these patients. However, there is no case control in these studies, and therefore no strong dose- and time-dependent association between smoking and the development of RCTs could be established.

#### *2.4.7. Family history*

There is limited evidence regarding the genetic predisposition and hereditary component for RCTs; however, a study examining the genealogical database in Utah, USA by Tashjian et al. [22] a population-based controlled study of 3091 patients, with a subgroup analysis of 652 patients diagnosed before 40 years of age, showed a significant association between individuals with rotator cuff disease in close and distant relations (reportedly up to third cousin relations). This study was included in the systematic review conducted by Dabija et al. [23], which includes the study by Harvie et al. [24], concluding that siblings of patients diagnosed with RCTs were twice as likely to develop complete RCTs. In addition, they identified single-nucleotide polymorphisms (SNPs) associated with RCTs, indicating the future risk for development of RCTs to enable prophylactic rehabilitation techniques and to avoid the development of symptomatic RCTs [23].

#### *2.4.8. Posture*

The relationship between posture and shoulder pathology is still under investigation. For example, Gumina et al. [25] found a reduced subacromial space in 47 patients over the age of 60 years with hyperkyphosis, as compared to a control group. Yamamoto et al. [26] observed RCTs in 65.8% of patients with kyphotic-lordotic postures, 54.3% of patients with flat-back postures, and 48.9% with sway-back postures, whereas only 2.9% of patients with ideal alignment had symptomatic or asymptomatic RCTs. It is hypothesised that the reduced subacromial space is due to less posterior tilting and dyskinesis of the scapula, resulting in extrinsic impingement.

#### *2.4.9. Mental health*

Cho et al. [27] demonstrated that as many as 82% of patients with chronic shoulder pain had sleep disturbance and that rates of depression were significantly increased in patients with more than 3 months of shoulder pain. Educational level, employment status, pain levels and patient perception of percentage of shoulder normalcy were most predictive of emotional health in patients with complete RCTs [28].

#### *2.4.10. Symptoms and pain*

There is disagreement in the literature regarding the correlation between tear size and pain. These studies tend to be cross-sectional as opposed to prospective observational studies [11]. For example, in a prospective study of 50 patients, Moosmayer et al. [29] reported that 40% of asymptomatic RCTs became symptomatic and anatomically deteriorated, and that an increase in tear size and a decrease in muscle quality correlated with the development of symptoms. Mall et al. [30] who compared asymptomatic and symptomatic RCTs, determined that many with asymptomatic FTTs will develop symptoms with time and that pain development is associated with an increase in tear size and deterioration of shoulder function and active range of motion (ROM). In the study, this was primarily seen with larger tears and required significant time for progression to occur and for glenohumeral and scapular mechanical dysfunction to become apparent. There



is therefore the concern that through conservative management of tears, these tears may progress to become more painful. This is supported by the study by Yamaguchi et al. [10] a report of 45 patients, in which 23 (51%) patients became symptomatic at a mean of 2.8 years; however, just 9 of the 23 (39%) demonstrated tear progression; hence, this could mean that over time symptoms can be progressive and not necessarily due to tear size or progression.

Through multiple observational and cross-sectional studies on more than 400 patients with atraumatic, FTTs, the multicenter orthopaedic outcomes network (MOON) Shoulder Group have found that pain and duration of symptoms are not strongly associated with the severity of RCTs [31, 32]. This is supported by a recent cross-sectional study by Curry et al. [33], which found that in patients with RCTs undergoing operative and non-operative treatment, pain and functional status were not associated with tear size and thickness, fatty infiltration, and muscle atrophy.

#### *2.4.11. Radiographic changes*

There are studies following the progression of both asymptomatic and symptomatic tears, and most these studies conclude that there is a risk of tear progression according to ultrasound or MRI findings, regardless of whether they are partial or complete RCTs. However, the progression of these tears may not necessarily contribute to increase in symptoms [10]. One ultrasound investigation of 411 patients found the overall prevalence of asymptomatic FTTs to be 13% in patients over age 50 years, and 51% in subjects over 80 years of age [15]. Safran et al. [11] reported that 5 of 61 (8%) FTTs evaluated with ultrasound decreased in size over a 2-year follow-up period.

A recent study by Yang-Soo et al. [34] found that 28 of 34 patients (82.4%) with symptomatic FTTs and 23 of 88 patients (26.1%) with symptomatic PTTs had tears that increased in size over a follow-up period of 6 months to 8 years. The clinical relevance of these observations is that FTTs treated conservatively should be monitored more carefully than PTTs for progression. However, some study limitations should be noted: patients included were those who had refused surgery (allocation bias). In addition, assessor bias due to the reporting of outcomes was a factor; however, the musculoskeletal radiologist reporting the MR images was blind to the clinical data.

This study was supported by another previously described comparison study of 59 shoulders in 54 patients with 33 FTTs, 26 PTTs and 4 combined tears on MRI [7]. Seventeen of 33 (52%) FTTs and 2 of 26 PTTs progressed in size. Factors that were associated with the progression of RCTs were age greater than 60 years, FTTs and fatty infiltration of muscle.

Therefore, RCTs do not always progress, with FTTs demonstrating a higher rate of enlargement in time than PTTs.

### **3. Effectiveness of physiotherapy rehabilitation**

The role of physiotherapy as a form conservative treatment for complete RCTs to improve pain, function, and reduce disability has long been debated. Recently, there have been some studies that have compared the effectiveness of physiotherapy vs. surgical intervention for RCTs.

One systematic review assessed the effectiveness of surgery vs. conservative management of RCTs [35]. It concluded that the three randomised controlled trials that were included in this review showed no statistical or clinically significant difference in the patients' clinical outcomes. One of the limiting factors identified were that two of the studies had a 1-year follow-up in comparison to Moosmayer et al.'s [36] 5-year follow-up. It is therefore difficult to conclude whether the conservative management of the RCTs in the studies was more progressive, or if the surgical repairs failed and the shoulders become symptomatic again. In addition, the systematic review concluded that there were only three trials with adequately varied methods and appropriate inclusion criteria for the review, making it difficult to make a comparison on the overall outcome. This is also supported by a systematic review by Seida [37], who concluded that there was insufficient evidence to support conservative over surgical treatment and vice versa for the management of RCTs and suggested that further studies were required and standardised methods and inclusion criteria were warranted.

The first randomised controlled trial by Moosmayer et al. [36] after 5 years showed no significance between surgery and physiotherapy, as the mean difference in the Constant-Murley Score (CMS) was only 5, which is deemed less than that considered a clinically relevant score of 10.4 [38]. This study also had traumatic tears in the conservative group, which may have influenced the results as previous research has suggested that early surgical intervention is recommended for younger patients with traumatic tears and severe functional deficit to avoid delays in tendon healing or prevent healing beyond repair [39]. The sample size was small in this study; therefore, it is difficult to make a conclusion on the effect of having the two subgroups over the results in this study. In this study, nine patients failed physiotherapy and switched to tendon repair in small and medium tears. Rotator cuff repairs may be recommended to prevent delay in progression of muscle atrophy and tendon retraction beyond the point of tendon healing if physiotherapy failed, which is more likely in the younger patient population with acute tears than in the older population who are more likely to present with degenerative FTTs [40, 41]. This is further supported by an algorithm on the management of RCTs by Tashjian [42] according to size, nature of the tear, and age of the patient; however, there is not enough high-quality evidence to support this. Further studies comparing interventions for traumatic and atraumatic complete tears as well as age groups would be required to decide initial treatment. In addition, further research on how long conservative management should be continued before resorting to surgical intervention would be required. This finding has also been discussed by Abdulwahab et al. [43], who concluded that timing to the end of conservative treatment is unknown, but likely is indicated when a patient demonstrates increased weakness and loss of function not recoverable by physiotherapy.

Another randomised controlled trial by Heerspink et al. [44] was a small study of only 56 patients that showed no statistical or clinically significant difference. The CMS was 10.1 between surgery and physiotherapy. The patients in this study were atraumatic, which may have made the study more generalised compared to Moosmayer's randomised controlled trial [36]. There were more patients with a larger tear in the conservative treatment group, which could have created bias in the results of this study despite the random allocation. Further research on surgical intervention compared to physiotherapy for complete tears as a separate



entity from partial tears are needed. In addition, high-quality studies in which comparisons between different conservative interventions and surgical treatment are made to determine the optimal conservative management for RCTs are necessary.

The present study also had a high incidence (73%) of re-tears in the surgical repair group at 1-year follow-up. However, tear progression or failed rotator cuff repair may not be indicative of why the patients have more pain and less function, as studies have shown that large tears can be asymptomatic [45, 46]. This uncertainty in the extent of RCTs in relation to the patient's clinical presentation may not be an accurate representation of the outcome of the patient's pain and function post intervention in this study. The best pain and functional outcomes in this study were observed in surgical patients with an intact rotator cuff repair at the final follow-up, but the numbers to treat for successful rotator cuff repair would be high in this case considering the 73% of failed repairs that reported slightly less favourable outcome than the conservative approach. The insignificant difference in the outcome of this study demonstrates that physiotherapy may possibly be considered as an intervention due to it being less expensive than surgery as reported in this article. However, longer duration of follow-ups in this study would be beneficial to determine the outcome of both interventions in relation to MRI findings, pain, function and economic impact.

Kukkonen et al. [47] concluded in their 1-year follow-up study that there was no statistical significance between rotator cuff repair with acromioplasty and physiotherapy, or physiotherapy alone. There was only a difference in patient satisfaction scores in the first 3 and 6 months, where the two groups without repair reported higher patient satisfaction than the repair group. This may be due to the postoperative restrictions for the surgery group, leading to more dissatisfaction in this group. However, the overall outcome was the same by the 1-year follow-up.

Overall, the three studies showed low risk of bias that cannot completely be avoided because of the nature of interventions. Despite the conservative and surgical interventions in all three trials being standardised with the same treatment aims, the patients' irritability and severity of their symptoms and the effect on their daily function varied the intensity, dosage, and duration of treatment. This variation made it difficult to compare conservative and surgical approaches for the management of RCTs. The treatment strategies and aims among all three trials for physiotherapy were similar in that all three randomised controlled trials focused on initiating static and dynamic glenohumeral movement, scapulohumeral movement, and stabilisation, and increasing the level of progression from 6 to 12 weeks.

### **3.1. Physiotherapy treatment techniques**

There is some debate on the optimal conservative treatment and rehabilitation approach for RCTs and its role in improving the symptoms associated with an RCT.

Ainsworth et al. [48] conducted a systematic review of exercise therapy for the conservative management of RCTs. This review could not find any high-quality trials and found only 10 observational studies and 2 case studies. The primary conclusion of this review was that physiotherapy may have some benefit; however, the method of distinguishing the extent of

the patient's pain in relation to the tear as well as the level of exercise in terms of intensity and dosage are still unclear due to the poor quality of the trials.

The review also concluded that the size of the tear is not as important as the presence of pain in the patient. This is supported by the findings discussed previously with the current research and MRI scans in relation to the patient's clinical symptoms. It also highlighted that RCT repairs appear to be less successful in the elderly, and the review leans more towards conservative management as a first line of treatment. This idea is also supported by the Tashjian algorithm [42] and Levy [49], who further explain that due to older patients being more likely to have multiple comorbidities, RCTs should be managed conservatively.

The present study acknowledged that until there is more understanding of how some patients with FTTs can have a spectrum of symptoms from minimum to severe, it will be difficult to establish an optimal treatment and rehabilitation program for RCTs.

There are differences in opinion on the focus of rehabilitation between anterior deltoid retraining or working on the humeral head depressors to rehabilitate shoulder elevation in abduction only [50]. The anterior deltoid training is supported by Levy et al. [49] and by Ainsworth [51] on the basis of the biomechanics of how the anterior deltoid works. The anterior deltoid was believed to act as a humeral head elevator, but a study by Gagey and Hue [52] concluded that the deltoid functions to prevent upward migration of the humeral head. This theory is supported in present clinical practice of using the Torbay exercise program, which is proposed in the aforementioned studies. In the Levy et al. study [49] instructions were to exercise 3–5 times per day for the first 6 weeks, with the patient supine for the exercises, and progressing to an incline, and then standing. This study found that this technique would be beneficial for older patients with atraumatic, massive tears. However, this study was not compared with another intervention; therefore, there was no randomised allocation, and the lack of quality and a small study group of 17 patients made it difficult to form a significant conclusion.

Ainsworth et al.'s [48] prospective randomised controlled study had 60 patients over the course of 1 year. The intervention group consisted of anterior deltoid training as well as other treatment modalities such as functional exercises, proprioception and stretching. It is therefore difficult to establish which specific treatment modality had an impact on improving patient pain and function compared to the control group, whose treatment consisted of ultrasound, advice, and steroid injections, if required. The SF-36 score showed statistical significance in the intervention group over the control group at 3 and 6 months, but there were no differences by 12 months. Despite these improvements in functional and pain scores, further studies with standardised treatment interventions and larger numbers of patients over a longer period are needed to support the use of anterior deltoid training.

This study also highlighted the role of education in altering the patient's perception of pain and therefore reduce pain and disability, which is also supported in previous studies [53, 54]. It is believed that advice and education alone allow the patient to use the shoulder, by reducing their fears of causing more harm. This may have contributed to why the control group had no statistical difference from the intervention group. Despite these findings, physiotherapy with this specific anterior deltoid exercise program is deemed to

be beneficial because it allows patients to return to their activities of daily living (ADLs) earlier, which could impact aspects such as reducing time away from work and the risk of depression, and improving quality of life (which are associated with poor outcome). Future studies should further investigate this exercise program. Kuhn et al. [55] conducted a multi-centre prospective cohort study of 381 patients who underwent physiotherapy over a 12-week period with a 2-year follow-up. The patients' compliance diaries showed a variation in programs from no therapy to supervision and home, home only, and supervision only. If after 6 weeks the patients were no longer in pain and/or the pain was not affecting their ADLs, then conservative management was successful. Only 9% of patients had surgery after 6 weeks, and a total of 15% of patients had surgery in the first 12 months. After this time, it is deemed that the patient is unlikely to have surgery for RCT. This study was performed only on atraumatic patients only; thus, it is not a reflection of acute traumatic tears. The treatment strategies for these patients were primarily focused on exercise therapy, manual therapy, and heat and cold therapy. However, there were no comparison intervention groups to establish which treatment modality was superior to another, and the therapist could tailor the therapy to the patient's individual presentation, making it difficult to form a conclusion on the most effective aspect of the therapy program. Edwards et al. [56] conducted a review of the current treatment strategies during rehabilitation and concluded the use of anterior deltoid training allows adequate shoulder elevation without upward migration of the humeral head. In this review, the authors also noted the role of the teres minor during external rotation with infraspinatus tears as part of allowing the greater tuberosity of the humerus to clear the acromion during shoulder elevation. Studies that have been researched currently show a general trend of 10–15 repetitions twice a day; however, further research to justify using the prescription recommended for this specific type of training is warranted.

It appears that the nature of the studies that have been reviewed do not always focus on complete RCTs, which is due to the lack of available evidence on the management of complete RCTs. Therefore, the conclusions in this review are limited. More studies focusing on the surgical and conservative management of complete RCTs need to be completed to delve further into the optimal management of this pathology.

#### **4. Systemic medications**

It is unclear if there is a true inflammatory element to rotator cuff tendinopathy and whether non-steroidal anti-inflammatory drugs (NSAIDs) will address this pathophysiology [57]. Currently, no trial or study has been conducted for evaluating NSAIDs as an oral preparation or topically, or other analgesics specifically, for efficacy in the treatment of complete RCTs. Only investigations for shoulder pain in general have been conducted [43]. One meta-analysis of 12 studies concludes that oral NSAIDs can lead to a reduction in pain in individuals with rotator cuff tendinopathy, but there are gastrointestinal or cardiovascular-associated risks [58].

## 5. Injections

The concept of using injections for the treatment of RCTs is not new to the field of orthopaedic surgery, as the practice of using injections such as corticosteroids (CS) and sodium hyaluronate (HA) is common in many practices. CS and HA are both injectable pharmaceutical agents that can be used to decrease pain and stiffness, and they have demonstrated significant impact on improving quality of life for patients with RCTs.

A 2015 *in vitro* study found that CS injections decreased cell proliferation in rotator cuff tendons, and the resulting strength of these tendons decreased as compared to the strength after HA injections [59]. The same study also conducted an experiment on the effects of CS and HA injections in rats. Like the *in vitro* study, the animal study found apoptosis in rotator cuff tendons, inhibition of cell proliferation, a delay in tendon healing, and decreased biomechanical strength in CS subjects [59].

Clinical application of these agents is highlighted by a study conducted in 2001, in which 40% of a group with RCTs that received HA injections were satisfied with the durable effects produced at 24-weeks follow-up [60]. In addition, 35% of the group that received CS injections expressed satisfaction over a 5-week period with the injections [60]. Moreover, another study found statistically significant pain relief in groups with HA injections as compared to the control group [61]. In another study, a combination of HA injections and rehabilitation programs led to an improvement of mobility in elderly patients [62]. When using CS injections, no difference was found in groups with different frequencies of injections [63].

## 6. Biologics

### 6.1. Basic science

Biologics are similar to the aforementioned injections, as they are injected into the RCT zone to assist in regeneration of the tendons. Biologics are specific proteins and cells that are obtained from the patient; therefore, they are personalised for the individual [64].

Biological injections can include platelet-rich plasma (PRP), which is prepared from a patient's blood by concentrating thrombocytes, usually a multiple of the normal circulating concentration. This injection is produced through standardised preparations: blood is drawn from the patient and spun in a centrifuge to separate the parts of the blood, and the highly concentrated plasma is re-administered to the patient in the affected area [65]. The idea of PRP follows simple scientific logic as the platelets are the body's primary way of reaching structural defects and injuries through proteins, cytokines, and growth factors that stimulate healing. Once platelets reach the specific site, they release different growth hormones that trigger natural and regenerative healing processes [66]. PRP has been known to stimulate both the response of mesenchymal stem cells (MSCs) to the local area through growth factors such as platelet-derived growth factor (PDGF), fibroblast growth factor and vascular endothelial growth factor



(VEGF) and stimulate tendon stem cells to differentiate into tenocytes when certain growth factors are released, which promotes healing of the rotator cuff [67, 68]. Furthermore, PRP can also assist in the proliferation of muscle cells [69], promoting inflammation [70], and the use of adhesion molecules to repair the torn tendon [71]. The proliferation of muscle cells allows for an increased number of fibroblasts and myotubes, thereby decreasing the overall time of recovery and increasing the strength of the rotator cuff [69]. Non-growth factors released from platelets such as serotonin, histamine, dopamine, calcium and adenosine aid in inflammation proliferation [70]. Finally, adhesion molecules such as fibronectin, fibrin and vitronectin can be delivered in a clot [71].

MSCs can be found in a variety of locations throughout the human body, but are most commonly found around vascular tissue, bone marrow, and fat [72]. MSCs are derived from pericytes that detach from the blood vessels and become activated MSCs [72]. These stem cells, like many other stem cells, can proliferate and eventually differentiate into fully functional osteocytes, adipocytes, and fibroblasts or remain as activated MSCs [73]. MSCs can be both immunomodulatory and trophic, which aid in regeneration. The cells can act as an autoimmune response to combat pathogens that infect the ruptured tissue [74]. Further, MSCs inhibit both apoptosis (cell death) and scar formation while stimulating angiogenesis and mitosis (through the secretion of mitogens) [64]. Because of the many functions of MSCs, the activation of MSCs is critical in the healing process. These activated MSC cells provide the damaged part with necessary chemicals to heal itself more quickly.

## 6.2. Laboratory investigation

An in vitro study found that PRP stimulated cell proliferation and the synthesis of tenocytes in RCTs [75]. In an experiment in which rats were treated for RCT, the group given the PRP treatment demonstrated better collagen linear alignment. Furthermore, the research team found positive effects when administering the PRP injections 3 weeks after the initial surgery [76].

## 6.3. Clinical investigation

A clinical trial in 2012 found reduced pain and positive effects in the healing process of RCTs [77]. These clinical trials demonstrate the effect PRP has in stimulating the already present natural healing process.

A commonly used source for regenerative injection therapy (RIT) is bone marrow aspirate that is centrifuged to form a concentrate. Bone marrow aspirate concentrate (BMAC) can possess a number of different stem or progenitor cells that can aid in the body's natural self-regenerative processes [78]. BMAC can be used as a regenerative injection therapy for various injuries and primary conditions, as well as be used during surgery. One study compared BMAC augmented surgery vs. arthroscopic repair alone. Of the 45 patients augmented with BMAC, 100% of patients were healed 6 months after surgery compared to 67% of the 45 control patients. At 10-year follow-up found that 87% of patients in the BMAC group compared with 44% of control patients were healed [79].



## 7. Risks of conservative treatment in managing a rotator cuff tear

Non-operative treatment has been recommended as an initial treatment for patients with rotator cuff pathology ranging from tendinopathy to partial and even complete RCTs [80]. Although several reviews and studies have demonstrated the effectiveness of non-operative treatment in RCTs, as previously described, there are concerns regarding the risks of conservative treatment as well. The overall goal of conservative management is to diminish pain, increase ROM and strength, and to ultimately decrease the functional limitations of the patient [81]. There appears to be some consensus that a conservative treatment program is a reasonable approach within the first 6–12 weeks in patients with non-traumatic tears under the age of 60 years. If the patient does not respond within the initial 4–6 weeks, then it can be an indicator for transition to surgical treatment. Edwards et al. [56] has demonstrated that if the patient does respond well, the conservative treatment will be effective for up to 2 years. Tanaka et al. [81] reviewed the literature and noted that conservative treatment is an effective method for the treatment of RCTs, with success rates ranging from 33 to 88%. The large variability appears to be dependent on the method of treatment chosen, as well as the observations and monitoring that occurs in between the pre-established patient follow-up dates. Although effective, the benefits of non-operative treatment have also been accompanied by progression of the tear, muscle atrophy, fatty infiltration, worse surgical outcomes and increased pain and symptoms.

Tempelhof et al. [15] studied asymptomatic RCTs longitudinally to improve the understanding of the risks of tear progression and pain development over time. The study followed patients for a median of 5.1 years, following the identification of the asymptomatic degenerative tear. They observed that tear enlargement occurred in a time-dependent manner with greater risks of enlargement relative to larger and more severe tears. This was observed in 110 of 224 patients (~49%) over an average span of 2.8 years. FTTs were 1.5–4 times more likely to enlarge than PTTs. In addition to the risk of tear progression, the transition from an asymptomatic tear to a symptomatic tear was observed due to the development of new pain, and the median time until pain developed was roughly 2.6 years. The development of new pain occurred in 46% of the patients, and the occurrence of symptoms correlated with an average enlargement rate of 63%, whereas those who remained asymptomatic had a 38% increase in the size of their tears.

These results demonstrate the long-term potential for an FTT to increase in size over several years, which is in agreement with Hsu and Keener [82], who thought that the risks of tear progression and muscle atrophy are present early on, but the rate of progression is slow enough to allow adequate time to attempt conservative treatment [82]. They developed a stratification of the several treatment options in which the patients were categorised and recommended a treatment option based on their natural history and pathology. The system established by Hsu and Keener [82] contained three groups in which the risks of non-operative treatment varied and the potential benefits of surgery were optimised. The groups were assigned according to the symptoms presented at the time of the patient interview. In group I, early operative repair was recommended for acute tears, while those in group

II were initially treated conservatively and, if they did not respond, they were transitioned to surgical treatment. Furthermore, group III was concerned with maximising conservative treatment, where the healing of the patient's RCT was unlikely. This group typically included patients over the age of 65, with chronic tears and FTT. Patients in the group were shown to have retracted tendons and advanced muscle degeneration. The goal of conservative treatment was to improve the overall functioning level of the patient. This study demonstrated that although these variables improved, there was also a 50% chance of tear progression within 5 years, especially in the FTT [82].

Several other studies of asymptomatic tears followed by either an ultrasound or a MRI have been reported in the literature [2, 15, 83, 84]. Maman et al. [7] described age as a large determinant of progression, with 54% of the tears in the patients over 60 years of age demonstrating progression, in comparison to 17% of tears in subjects under the age of 60 years. Safran et al. [11] found that FTTs had a higher rate of progression in younger patients, with 49% of the tears increasing in size under ultrasound.

Tear progression as well as muscle atrophy and fatty infiltration have been directly associated with pain. In a study conducted by Moosmayer et al. [85], these three variables were found to correlate with the presence of symptoms in comparison to an asymptomatic group. The authors compared non-operative to operative treatment for smaller tears of 3 cm in size, and found a progression in tear size and structural deterioration over time, which resulted in the recurrence of symptoms and functional depreciation over time. In the cases in which the patients were asymptomatic, they found that progression of the tear was directly related with the development of pain [30].

In contrast to these studies, Fucentese et al. [8] found that after a follow-up period of 3.5 years following non-operative treatment, there was no increase in the average tear size and only 25% of the initial tears demonstrated progression. An issue with this study is that the average initial tear size was small, averaging 1.6 cm. This further supports the notion that the likelihood of progression is dependent on the initial size of the tear, with larger tears more likely to develop progression.

## 8. Surgical indications for a transition from non-operative treatment

Throughout the literature, it has been observed that the presence of certain independent "risk factors" may also serve as indicators for the physician to transfer the patient from non-operative management to operative treatment. Beyond the risks and concerns involved with the non-operative treatment option, there are also independent factors that serve as direct indicators to opt for operative treatment. These factors include the patient's demographics, the mechanism of injury, the degree of severity and depth of the tear, the duration of symptoms and the patient's expectations about whether operative or non-operative treatments are effective. Several studies [2, 82, 86] have shown that patient expectations are potentially one of the

strongest indicators when deciding how to treat a patient. Dunn et al. [87] and Fucentese et al. [8] demonstrated a direct correlation between the expectations of the patient and the results of conservative treatment.

The demographics of a patient have also been shown to directly correspond with a transition in treatment. The strongest of these include the patient's age, body mass index (BMI) score, and socioeconomic status. Interestingly, patients with a higher BMI score were shown to be more likely to adopt a nonsurgical option, where those with a lower BMI opted for surgical treatment [88].

Regarding age, patients under the age of 60 years are thought to have better outcomes with operative treatment, because of significant risks of irreversible changes with non-operative treatment and a high likelihood of healing if a repair was performed. It has been generally recommended that surgical repair be performed instead of an initial conservative treatment in active patients with acute tears following trauma [4]. Early operative treatment appears to be warranted in this case and in the case of poor function for the achievement of maximal return of shoulder function. The importance of the timing following the initial patient interview is critical and dependent on the factors associated with the tear as well as how long the tear has been present. In a systematic review, Lazarides et al. [40] reported that the RCTs present in patients younger than age 40 years are more commonly FTTs and of traumatic origin. These patients typically respond well to surgery in terms of pain relief due to the good tendon and muscle quality at the time of the repair. The definition of "early" repair is often unclear.

Bjornsson et al. [89] determined that there was no difference in tendon healing, pain, shoulder elevation, or functional outcomes when an acute tear was fixed within the first 3 months of injury compared to within the first 3 weeks. However, if symptoms have persisted for longer than a year, and functional impairment was observed, the expectation for a successful surgical approach is worse in patients with FTTs [56]. Patients over the age of 60 years were twice as likely to develop a tear that was larger than those under 60 years. With each decade after 60, the odds of tear enlargement increased 2.69-fold [90].

Importantly, the mechanism of injury plays a significant role in decision-making for operative treatment. Schmidt and Morrey [91] described a measurement of the "appropriateness" of the various treatment options available to assist in RCT treatment, which are dependent on the associated benefits and risks of each method. The scale is referred to as the appropriate use criteria (AUC), and it was developed by a voting panel composed of mostly orthopaedic surgeons. This panel determined the 'appropriateness' level of a treatment based on the current literature. The AUC determined that a treatment was deemed 'appropriate' if the benefits outweighed the risks, 'may be appropriate' if the difference was null, and 'rarely Appropriate' when the risks outweighed the benefits. A large indicator favouring non-operative treatment included the initial response a patient exhibited during their initial trial of conservative treatment. If there was a positive response noted by the patient, then they would continue with non-operative treatment. Conversely, if the initial trial of conservative

treatment was ineffective, then operative treatment would be recommended. The indications for surgery were 'may be appropriate' in the instances in which the patient responded positively to the conservative management, were healthy before the injury, were experiencing moderate-to-severe pain, as well as in those who were not responsive to non-operative care methods. The duration of time given to determine whether a conservative treatment option is successful is typically 12 weeks. Beyond this time, there was a concern regarding the risk of tear progression. In addition, the authors showed that in patients with a higher level of pain, they were more likely to recommend surgery.

If surgery is needed in case of failed conservative treatment, chances for tendon healing are much lower after the age of 60 years [92]. In selected cases, surgery may be limited to a simple arthroscopic biceps tenotomy while leaving the cuff unrepaired with good pain relief and shoulder function in the elderly [93]. In other cases, despite older age, repairing the cuff may still be an option with high subjective patient satisfaction rates [94].

## 9. Patient satisfaction indices

In a study of 20 patients conducted by Baydar et al. [86], 6 months following conservative treatment 55% of the patients reported that they were 'much better' and 45% said they were 'better'. At their 1-year follow-up, 50% rated themselves as 'much better' and 40% rated themselves as 'better'. This trend was also observed at the 3-year follow-up.

Kuhn et al. [55] conducted a study over a 3-month period and found that physiotherapy significantly improved pain, function and ROM. Wirth et al. [95] conducted a similar study of 60 patients, with a 2-year follow-up. On the basis of the American Shoulder and Elbow Surgeons evaluation (ASES) and the UCLA score, they found that the patients showed significant improvements. They noted improved pain ratings, strength, and ROM.

Boorman et al. [96] found 75% of the patients were successfully treated conservatively. They noted that the baseline rotator cuff quality-of-life index (RC-QOL) score was a significant predictor of the outcome. Eighty-nine percent of the patients maintained their 3-month outcome at the 2-year follow-up. Even subjects with increased pain and tear progression were shown to have a significant increase in their functional scores.

## 10. Discussion

RCTs in general are prevalent within the population of all age groups. FTTs can present acutely following trauma or as a degenerative process. We have examined the associations with genetic influences, comorbidities, and the complex relationship between tear size, symptoms, and pain. Although there is conflicting literature, there appears to be some consensus on the best indicators for choosing to treat a FTT non-operatively. The established



physiotherapy techniques include anterior deltoid training to allow adequate shoulder elevation without upward migration of the humeral head, as well as teres minor training to allow the greater tuberosity of the humerus to clear the acromion during shoulder elevation. Patients who will benefit the most from conservative treatment include those over the age of 60 years with a chronic degenerative tear that is unlikely to heal and with low functional demand. In this scenario, the goal is to improve the function and ROM. The risks associated with these tears include the potential of the progression of the tear, a diminished healing potential due to age or longer symptom duration, muscle atrophy, and fatty infiltration. In addition, poor outcomes have been noted in this group with surgical treatment. Moreover, the indications for surgery following conservative treatment are becoming more defined, and an outline regarding what scenarios warrant a transition from an initial conservative treatment plan has been developed. If the patient does not respond well within the first 6–12 weeks of the conservative treatment and is younger than 60 years, has a higher activity level, and has a healthy tendon and muscle environment, then early operative treatment is likely. Overall, the patient satisfaction indices, and in particular functional scores such as the RC-QOL score, have shown a consistent level of satisfaction regarding conservative management in patients followed from 2 years.

Although experiments using injections and biologics to specifically treat RCTs are limited, the literature available is promising in primary treatment, adjunctive care, and to augment surgical procedures. Both CS and HA injections offer modest benefits to the patient in terms of reduced pain and improved function. From an administrative perspective, the injections are practical as they are easily available pharmaceuticals, and are relatively low in prices compared to surgical intervention. These injections have demonstrated effectiveness in ameliorating symptoms following RCT.

The developing benefits of using MSCs, PRP, and other biologics have the potential to be disruptive to current treatment protocols, both conservative as well as surgical, in the approaches to healing RCTs. With improved imaging modalities, diagnostic accuracy, and sensitivity, practitioners of the future will hopefully be able to intervene earlier in the disease pathogenesis cycle. PRP can possibly be an effective method and strategy in the healing process of tendinopathy or PTTs. With standardised preparations and treatment protocols, only a short window of time is required to assess, prepare, and treat patients with this method (less than 30 minutes). The real benefit, although not fully realised at this time, is that PRP follows fundamental biological principles as it releases several growth hormones to stimulate the healing process. PRP also prompts MSC activation, creating a unique regenerative environment that modulates the immune system response and promotes trophic, anti-scarring, and cellular proliferation that in theory further aid the healing process. Regenerative injection therapy provides patients with specific cells and proteins that their body has produced, thus creating a healing environment at the site of injury and/or degeneration. Further studies in the basic science, translation, as well as with high-quality clinical trials are needed to shed further light on this very exciting and potentially game-changing technology.



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