Clinical and functional outcomes for patients following rotator cuff repair surgery, with or without adjuvant platelet rich plasma injections


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Clinical and functional outcomes for patients following rotator cuff repair surgery, with or without adjuvant platelet rich plasma injections.

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This thesis is presented for the degree of Master of Science of

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ABSTRACT

**Background:** Tendon-bone healing following rotator cuff repair correlates with a successful outcome. With the relatively high re-tear rates reported in the literature despite multiple surgical and suture anchor techniques, there has been an increase in research into biological adjuvant therapies that elevate local growth factor concentrations, to assist structural tendon healing following rotator cuff surgery.

**Purpose:** To determine if postoperative and repeated application of platelet-rich plasma (PRP) to the tendon repair site improves early tendon healing and enhances functional recovery following double row arthroscopic supraspinatus repair. A secondary objective was to determine if partial re-tears early post-surgery reveal differences in subjective function, or objective isokinetic strength, compared to completely intact tendon repairs; and if early tendon healing can be predicted using these measures, independent of medical imaging.

**Study Design:** Randomised controlled trial; Level of evidence = 2.

**Methods:** 60 patients underwent arthroscopic, double row supraspinatus tendon repair. Following post-surgery randomisation, 30 patients received two ultrasound-guided injections of PRP to the repair site at 7 and 14 days post-surgery. Functional scores were recorded pre-surgery and post-surgery, at 6, 12 and 16 weeks; and included the Oxford Shoulder Score (OSS), the Quick Disability of the Arm, Shoulder and Hand (QuickDASH), Visual Analogue Scale (VAS) for pain and the Short Form-12 (SF-12) quality of life score. Isokinetic strength and active range of motion were also recorded at 16 weeks post-surgery. Early post surgery structural healing of the tendon was assessed.
with Magnetic Resonance Imaging (MRI) at 16 weeks, with cuff appearance graded according to the Sugaya classification.

**Results:** PRP treatment did not improve early functional recovery, strength or range of motion, nor influence pain scores at any time point following arthroscopic supraspinatus repair. No difference was seen in MRI structural integrity between treatment and control groups (p=0.35). At 16 weeks post-surgery, the PRP group had 0% full thickness tear; 23% partial tear and 77% intact, compared to the control group with 7% full-thickness tear; 23% partial tear and 70% intact.

In the secondary study, full-thickness tears were excluded and the treatment and control groups pooled to determine if functional and strength differences were observed between Sugaya classified MRI groups (36% of the cohort had grade one classification; 40% grade two; and 24% grade three). No significant differences were observed between MRI groups for functional scores (VAS, OSS and QuickDASH) or isokinetic strength at 4 months post-surgery. Only 64% of the partial tear group, and 13% of the intact repair group were correctly classified with five variables entered into a discriminant analysis prediction equation.

**Conclusion:** Ultrasound-guided PRP injections on two occasions post-surgery does not improve early tendon-bone healing, or functional recovery. Correct tendon healing classification early post rotator cuff surgery must include medical imaging, and reliance on functional scores and isokinetic strength alone to assess early tendon healing is not supported.
ACKNOWLEDGEMENTS

I would like to take the time to thank all of the people that have contributed to getting me to this point. This thesis has taken me a lot longer than it should have, and I appreciate the interest my family, friends and colleagues have taken in my progress.

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The paper detailed below is included as Chapter 3 in my thesis. Though I am listed as third author, I managed the collection, storage and analysis of data, as well as created the tables and drafted the text for the manuscript.

The paper detailed below is included as Chapter 4 in my thesis. As first author, I managed the collection, storage and analysis of data, as well as created the tables and drafted the text for the manuscript.

Student Signature

Coordinating Supervisor Signature
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INTRODUCTION

Rotator cuff tendon tear is one of the most common injuries of the shoulder joint (Mitchell, et al., 2005), with a reported incidence rate ranging from 5 to 40% (Baydar, et al., 2009) and over 250,000 rotator cuff repairs performed annually in the United States alone (Yamaguchi et al., 2006). The prevalence of rotator cuff pathology increases with age (Bokor, et al., 1993; Kinsella & Velkoff, 2001; Murrell & Walton, 2001), with Yamaguchi, et al. (2006) also reporting an increase in the likelihood of bilateral rotator cuff pathology among patients over the age of 60 years. As the population continues to age, degenerative rotator cuff tears are likely to become an increasing problem.

Failure to heal and tendon re-tearing following rotator cuff surgery is not uncommon. Re-tear rates have been reported as high as 90% in the radiology literature, and as high 57% in orthopaedic literature, depending on patient age, the size of the tendon tear and level of degeneration, fatty infiltration, type of suture anchors, surgical technique and compliance with post-surgery rehabilitation guidelines (Boileau, et al., 2005; Galatz, et al., 2004; Gulotta & Rodeo, 2009; Sugaya, et al., 2007). It has been widely reported that those over the age of 60 years have significantly poorer rates of healing following rotator cuff repair surgery (Boileau, et al., 2005; DeFranco, et al., 2007; Oh, et al., 2010; Thomazeau, et al., 1997). The absence of tendon healing and recurrent tears following rotator cuff surgery lead to poor functional strength (Boileau, et al., 2005; Cho & Rhee, 2009; Galatz, et al., 2001; Harryman, et al., 1991).
The goal of rotator cuff surgery is to decrease pain and improve patient function. While the majority of patients who undergo this type of surgery see this result, there are some who continue to experience pain and loss of function and who are left unsatisfied due to recurrent tendon tearing or failed healing. Younger, more active patients may need to return to employment in physical roles or even to sport. Due to the lengthy nature of post-surgical recovery, patients often require early confirmation of tendon healing so as to tailor their rehabilitation programs accordingly.

**STATEMENT OF THE PROBLEM**

Despite the advances in surgical and suture anchoring techniques to improve rotator cuff tendon-to-bone fixation, failure of the tendon repair occurs often (Boileau, et al., 2005; Galatz, et al., 2004; Sugaya, et al., 2005; 2007). While tendon re-tears may be due to a specific injury at the site, it may also be caused by incomplete or failed primary healing following rotator cuff repair surgery (Boileau, et al., 2005; Carpenter, et al., 1998).

In a bid to improve early primary tendon healing, there has been an increase in research effort related to the use of biological adjuvant therapies that elevate local growth factor concentrations. In particular, many studies have investigated platelet-rich plasma (PRP) products, where a supra physiological concentration of platelets is delivered to the tendon-bone repair site at the time of surgery. The term “PRP” remains controversial in the literature, as this generic terminology does not differentiate between the various commercial products available, or their respective protocols and differing platelet concentrations (Lopez-Vidriero, et al., 2010; Sanchez, et al., 2010), with is no current
consensus on the actual platelet concentration required to have a clinically significant effect (Barber, et al., 2011).

While numerous studies have been published on the topic, the success of PRP use in improving outcomes following rotator cuff repair remains unclear. Reviewing the related literature is complicated by variations in the tendon pathologies treated, which range from small single tendon tears to large multi-tendon tears, concomitant use of acromioplasty (Castricini et al., 2011; Jo et al., 2011), and the formulations of PRP used, ranging from intra-tendon injections (Kesikburun, et al., 2013; Randelli, et al., 2008), spray application (Randelli, et al., 2011; Ruiz-Moneo, et al., 2013) or the incorporation of a platelet-rich fibrin matrix (PRFM) (Barber, et al., 2011; Castricini, et al., 2010; Gumina, et al., 2012) to the tendon repair site. Another factor affecting PRP is the timing of delivery, with the majority of studies to date using time zero delivery at the time of surgery, with Gulotta and Rodeo (2009) stating that biological augmentation too early in the tendon healing cascade may be ineffective.

This thesis addresses two primary questions and these have been presented as journal manuscripts in Chapters 3 and 4. The first paper (Wang, et al., 2015) sought to determine if injections of PRP would enhance early tendon healing and functional recovery following double row arthroscopic supraspinatus tendon repair surgery. The primary outcome in this study was improved early tendon healing, assessed with MRI, and the secondary outcomes related to patient-reported shoulder function and isokinetic shoulder strength as a measure of functional recovery.

The second paper (Colliver, et al. 2015, under review) aimed to determine if patients with an intact repair or partial re-tear in the early stages following rotator cuff repair
surgery display differences in common shoulder patient reported outcome measures and isokinetic strength tests; and if early post-surgical tendon healing could be predicted using these common clinical shoulder evaluations.

RESEARCH HYPOTHESIS

The following hypotheses were developed and tested for study 1 (Wang, et al., 2015).

1. The use of delayed and repeated PRP ultrasound-guided injections following supraspinatus tendon repair will improve early structural tendon healing, as assessed by MRI, when compared to no PRP treatment.

2. The use of delayed and repeated PRP ultrasound-guided injections following supraspinatus tendon repair will improve early patient-reported shoulder function and isokinetic shoulder strength, compared to no PRP treatment.

In study 2 (Colliver, et al., under review), the following hypotheses were developed and tested.

1. Following supraspinatus repair, differences in patient shoulder function and isokinetic shoulder strength will be detected in those patients with partial tendon re-tears or high MRI signal intensity, compared to those with intact repairs at 4 months post-surgery, regardless of their initial PRP group allocation.

2. Following supraspinatus repair, patients with partial re-tears and incomplete healing can be predicted on the basis of patient function and strength tests alone, without the need for post-surgery imaging.
PATIENT INCLUSION AND EXCLUSION CRITERIA

The methodology for each of the papers is contained in the relevant sections of the journal manuscripts shown in Chapters 3 and 4. However, journal papers are limited by strict word counts, which do not allow for a full description of patient selection criteria, or data collection and analysis methods. Therefore, a complete list of patient selection criteria is presented here.

Inclusion Criteria

1. Patients were male or female, aged between 25-80 years.
2. Full-thickness, symptomatic tear of supraspinatus tendon as identified by preoperative imaging and confirmed by arthroscopic evaluation.
3. Patients agreed to wear a dedicated arm sling for 4-6 weeks, as directed by the surgeon.
4. Patients needed to be in a non-dependent relationship.

Exclusion Criteria

1. Previous history of rotator cuff repair surgery.
2. Rotator cuff tears secondary to fracture.
3. Concomitant labral tear or significant degenerative glenohumeral osteoarthritis.
4. Contralateral shoulder symptoms.
5. Prior PRP injections.
7. Presence of rheumatalogical, neuromuscular or autoimmune disease.

8. Pre-existing conditions associated with upper extremity pain, including arthritis, ongoing infection, carpal tunnel syndrome, cervical disc herniation, cervical neuropathy or other nerve pathology.

9. Metabolic bone or blood disorders that could impair bone or soft tissue function.


11. Contraindication to postoperative MRI evaluation.

12. Likely problems with follow-up (i.e. patients with no fixed address, reported plan to move out of town, uncooperative or patients without adequate family support).

13. Patients who were participating in an existing ongoing trial that would interfere with assessment of the primary or secondary outcomes.

14. Patients who did not read or speak English.

REFERENCES


CHAPTER 2
REVIEW OF LITERATURE

ROTATOR CUFF TENDON TEARS

Full thickness rotator cuff tendon tear is one of the most common injuries affecting the shoulder joint (Mitchell, et al., 2005; Seitz, et al., 2011), with the incidence rate ranging from 5 to 40% of the general population (Baydar, et al., 2009; Gialanella & Prometti, 2011). Those with rotator cuff tears can experience pain and decreased functional ability (Ainsworth & Lewis, 2007; MacDermid, et al., 2004), reduction of range of motion (ROM) in the glenohumeral joint and muscular atrophy (Maniscalco, et al., 2008; Mitchell, et al., 2005); having an impact on health-related quality of life (MacDermid, et al., 2004). Reduced function may include difficulty or inability to dress independently, attending to personal hygiene and using utensils to eat. The pain can be so severe that the patient’s sleep is also affected (Ainsworth & Lewis, 2007).

Incidence of rotator cuff tendon tears

True prevalence of rotator cuff tears is difficult to determine in the general population, as a tendon tear can cause significant pain, weakness and disability in some, whereas others experience little to no pain or disability (Ainsworth & Lewis, 2007; Fehringer, et al., 2008; Gialanella & Prometti, 2011). As a result, reported incidence of rotator cuff tendon tears varies widely throughout the literature.

Cadaveric studies have demonstrated the incidence of rotator cuff tendon tears in subjects aged over 60 years to be at least 30%, compared with 6% in those younger than 60 years
Tempelhof, et al. (1999) investigated the prevalence of rotator cuff tears in asymptomatic shoulders, and found that of a total 411 subjects, 96 (23.4%) had a full-thickness rotator cuff tear. Sher, Uribe, Posada, Murphy and Zlatkin (1995) conducted a prospective study investigating the prevalence of rotator cuff tendon tears in asymptomatic individuals of varying ages, with varying activities. More than half (54%) of the cohort over the age of 60 years had either a partial or full thickness rotator cuff tear, confirming age-related changes of the rotator cuff consistent with other studies, identified with MRI.

The incidence of degenerative rotator cuff tendon tears increases with age, even in the asymptomatic population (Boileau, et al., 2005; Bokor, et al., 1993; Cheung, et al., 2010; Oh, et al., 2010; Tempelhof, et al., 1999). A study conducted by Murrell and Walton (2001) found that rotator cuff tear frequency increased linearly with age from 30 years (increasing from 33% in the 40s to 55% the in 50s). As the ageing population continues to increase worldwide, degenerative rotator cuff tendon tears will become more prevalent in the future.

**Aetiology of rotator cuff tendon tears**

A tendon is a tough band of fibrous connective tissue, usually connecting muscle to bone, and capable of withstanding tension loads (Del Buono, et al., 2011; Notarnicola & Moretti, 2012). Tendons are often subjected to tendinopathies, as a result of trauma and overuse, which may lead to inflammation and degeneration of the tendon and, in turn, to a tendon tear or rupture (Notarnicola & Moretti, 2012). While most tendons have the ability to heal following injury, the repair tissue is functionally inferior to that of normal healthy tendon, and carries with it an increased risk of further injury.
Factors causing rotator cuff tendinopathies and tendon tears have traditionally been described as extrinsic, intrinsic or a combination of the two (Seitz, et al., 2011). Extrinsic factors are those causing compression of the rotator cuff tendons due to narrowing of the subacromial space (Carpenter, et al., 1998; Mishra, et al., 2009), and can be related to anatomical and/or biomechanical factors (Seitz, et al., 2011). Anatomical factors that can contribute to the narrowing of the subacromial space include variations in the acromion shape, orientation of the slope or angle of the acromion, or ossification of the inferior aspect of the acromioclavicular joint or coracoacromial ligament (Seitz, et al., 2011). Biomechanical factors may also contribute to extrinsic compression and can include abnormal scapular and humeral kinematics, abnormalities in posture, muscular deficits and soft tissue tightness (Seitz, et al., 2011). Intrinsic factors that affect the rotator cuff tendons result in degeneration of the tendons caused by the natural ageing process, decreased vascularity and blood flow (Mishra, et al., 2009), altered biology and fibrocartilagenous changes (Carpenter, et al., 1998) associated with previous tendon damage, and tensile tissue overload (Seitz, et al., 2011).

Although rotator cuff tears can occur as a result of an acute injury, most tears result from gradual degeneration of the tendon and tendon-to-bone interface (Bokor, et al., 1993; Cheung, et al., 2010). Chronic tendon tears are known to induce structural changes within the tendon (fibro-vascular scar tissue forms during the healing process) (Anitua, et al., 2005), rendering the tendon prone to re-tearing, as well as muscular atrophy (Liem, Lichtenberg, et al., 2007).

Rotator cuff tendon tears can be caused by degeneration and overuse with repetitive extrinsic compression, eccentric overload of the tendon, or by differential strains being
placed on the tendon (Millett, et al., 2006). Reilly and colleagues (2003) found that in cadaveric shoulders, maximal differential strain was reached at approximately 120 degrees of shoulder abduction. Partial tears can also create tension overload in the remaining tendon, which may increase the force concentration in the remainder of the tendon tissue and over time, can lead to complete full-thickness rotator cuff tendon tear (Millett, et al., 2006). While the rotator cuff tendons are able to tolerate huge tensile stresses, compressive and sheer forces are poorly tolerated (Millett, et al., 2006).

**Diagnosis of rotator cuff tendon tears**

Rotator cuff pathologies are a major cause of shoulder pain. Ostor, et al., 2005 reported that rotator cuff tendinopathy was present in 85% of patients presenting with shoulder pain to a general medical practice. Rotator cuff tendon tears may account for up to 50% of major shoulder injuries and, while clinical testing is the recommended first line investigation (Beaudreuil, et al., 2009), an accurate diagnosis can be difficult with clinical tests alone (Ainsworth & Lewis, 2007; Hughes, et al., 2008; Murrell & Walton, et al., 2001). Investigative techniques such as magnetic resonance imaging (MRI) or ultrasound (US) are commonly used to confirm or dismiss the presence of a rotator cuff tear (Bennell, et al., 2007; Codsi, et al., 2014; Kluger, et al., 2011; Liem, Lichtenberg, et al., 2007; Teefey, et al., 2004).

The diagnostic accuracy of common clinical tests for rotator cuff pathology has been questioned in a number of reviews (Hughes, et al., 2008; Mitchell, et al., 2005; Murrell & Walton, 2001). A clinical review conducted by Mitchell and colleagues (2005) of the diagnosis and management of shoulder pain suggested that clinical investigation and diagnosis should take into account the patient’s history (e.g. onset of pain, age, pain
during active and/or passive movements or at rest, patient’s occupation) as well as a physical examination (palpation of the shoulder joints, comparison of power, stability and ROM in both shoulders – active, passive and resisted, look for painful abduction arc and the “drop arm test” where the patient lowers an abducted arm to the waist slowly; a positive test result is indicated by the inability to hold the arm at 90 degrees of abduction, or a patient’s inability to smoothly control the lowering of their arm). Patients presenting with rotator cuff pathologies may have muscle wastage, active and resisted arm movements are usually painful and often partially restricted (Mitchell, et al., 2005). And while passive ROM may be full, it is usually painful, and history is a strong indicator; young people often present following a traumatic incident, with atraumatic presentation common among the elderly (Mitchell, et al., 2005). Mitchell and colleagues (2005) also suggested that partial tears can be difficult to differentiate from rotator tendinopathy upon physical examination, as weakness during resisted movement can occur with either condition. The authors stated that the “drop arm test”, can be used to detect a large or complete tear.

In a bid to improve the clinical diagnosis of rotator cuff tears, Murrell and Walton (2001) conducted a prospective study to determine if any of 23 clinical tests commonly used in assessment of the shoulder were predictive of a rotator cuff tear. They found that most clinical tests could not distinguish between the group that had rotator cuff tears (partial or full thickness tears and no other major shoulder pathology) and those with a shoulder pathology not involving a rotator cuff tear. However, the researchers did find that three clinical features were more positive in patients with tears and were predictors for this condition. These were supraspinatus weakness, weakness in external rotation and impingement. It was suggested that the “drop arm” test was also a predictor of a rotator cuff tear due to its high specificity, however, it had a low sensitivity within the tear group.
These results show that patients presenting with these three clinical features, or with a positive test for two of the three and who are over 60 years of age, there is a 98% chance of having a rotator cuff tear. If only one of those three tests is positive, the result is inconclusive and further imaging is required to confirm the diagnosis.

A systematic review conducted by Hughes, et al. (2008) of the diagnostic accuracy of clinical tests for rotator cuff pathology suggested that most tests cannot be recommended for clinical use. At best, suspicion may be heightened by positive palpitation, combined Hawkins/painful arc/infraspinatus, among others; and suspicion may be reduced upon negative palpation, empty can or Hawkins-Kennedy test. It has also been suggested that the poor accuracy of common clinical tests for diagnosis of rotator cuff pathology and tears may be attributed to the lack of anatomical validity of the tests, or that the complex relationships of the shoulder structures make it difficult to identify specific pathologies (Ainsworth & Lewis, 2007; Hughes, et al., 2008), highlighting the importance of medical imaging in conjunction with clinical investigations.

US and MRI are non-invasive techniques used widely to identify rotator cuff tears and tear size (Codsi, et al., 2014; Ianotti, et al., 2005; Kluger, et al., 2011; Naqvi, et al., 2009; Seibold, et al., 1999; Teefey, et al., 2004). Assessment of the rotator cuff using US was first published in 1979 (Seltzer, et al.) , and 1986 for MRI (Kneeland et al.). Initially, there was a great variety of results in the detection of rotator cuff tears with US (Brandt, et al., 1989), which was thought to be due to the limited experience of examination procedures and use of low frequency transducers (Naqvi, et al., 2009; Teefey, et al., 2004). As a result, MRI became the “gold standard” technique for diagnosis of partial and full thickness rotator cuff tears, due to its high sensitivity and accuracy, despite the relatively high cost (Iannotti, et al., 1991; Naqvi, et al., 2009). More recently though,
technical improvements and increased experience have led to a significant improvement in US reliability (Teefey, et al., 2004).

A number of studies have re-evaluated the accuracy of both US and MRI in the detection of partial and full rotator cuff tendon tears with modern equipment, standardised techniques and imaging diagnostic criteria. Teefey, et al. (2004) found the overall accuracy of diagnosing full thickness, partial thickness and intact rotator cuff tendons was 87%. Naqvi, et al. (2009) evaluated the accuracy of US and MRI in detection of full thickness rotator cuff tears, with the overall accuracy of US being repeated as 89%, compared with 80% for MRI. Codsi, et al. (2014) suggested US was comparable to MRI when evaluating rotator cuff integrity, and that post-surgical US results should be compared with MRI results for a period of time before relying solely on US for diagnosis. Ardic, et al. (2006) however, reported MRI to be superior to US, while reported that US was not a reliable tool for diagnosing full-thickness rotator cuff tears. Sonnabend, et al. (1997) reported on the accuracy of US in diagnosing full thickness rotator cuff tears and as a “useful adjunct” to the diagnosis of partial tears; however they also noted it was operator-dependent.
TREATMENT OF ROTATOR CUFF TENDON TEARS

The optimal treatment for rotator cuff tears, particularly large tears, varies for each patient. Decisions on how to treat patients should take into account the severity of symptoms, patient functional requirements, and the presence of any concomitant diseases that could complicate treatment (Gialanella & Prometti, 2011). The treatment for rotator cuff tendon degeneration and injury ranges from conservative to surgical treatment.

Non-surgical treatment of rotator cuff tendon tears

Conservative treatments include exercise, physiotherapy (electrotherapy, ultrasound, acupuncture and taping) and injection therapy (steroidal and non-steroidal) (Ainsworth & Lewis, 2007; Lewis, 2010; Ruotolo & Nottage, 2002). Exercise or other conservative treatment is often offered as the initial management approach, as satisfactory results cannot be guaranteed with surgical intervention (Ainsworth & Lewis, 2007; Gialanella & Prometti, 2011). The goals of non-surgical management of a rotator cuff tendon tear are to eliminate pain and restore function (Ainsworth & Lewis, 2007; Millett, et al., 2006), however, recommendations vary on the length of time conservative care should be undertaken before seeking a surgical opinion (Ainsworth & Lewis, 2007; Itoi & Tabata, 1992).

Reviews of interventions for rotator cuff pathologies suggest that exercise may be an effective treatment (Ainsworth & Lewis, 2007; Kuhn, 2009). Both Brox et al. (1999) and Haahr et al. (2005) reported active physiotherapy to be superior to a placebo or control. Physiotherapy aims to decrease shoulder pain and disability by improving joint biomechanics and movement patterns, rather than treating the pathology, using a range
of modalities (Bennell, et al., 2007). Both exercise and physiotherapy are often used in combination to treat rotator cuff tendon tears.

There is currently no consensus view on the ideal exercise or physiotherapy program for patients with rotator cuff tendon pathologies. Many rehabilitation protocols in the literature are based on empirical clinical evidence, which indicate a specific exercise or activity progression based on tendon healing timelines (Millett, et al., 2006). An evaluation-based protocol not only takes into account healing timelines, but also the attainment of specific clinical goals, before progressing exercises (Millett, et al., 2006). This makes good sense, considering patients with rotator cuff tendon tears do not all progress through their rehabilitation phases at the same rate. Guidance as to the most appropriate exercise treatment (including intensity, duration and frequency) remains speculative (Ainsworth & Lewis, 2007).

Lewis (2010) suggested exercises that reduce superior migration of the humeral head may be beneficial, as well as a graduated program of tendon reloading, including concentric, isometric and eccentric exercises, in a pain-free manner. Millett and colleagues (2006) discuss exercise rehabilitation of both partial and full-thickness tears of the rotator cuff. Rehabilitation goals of both are to re-establish full range of motion, synchronise the firing of the rotator cuff and periscapular muscles, and re-establish normal glenohumeral and scapulothoracic kinematics. A graduated strength program was suggested by Ruotolo and Nottage (2002); once shoulder pain has been controlled, focusing of scapular stabilisation and removing deltoid work until pain is completely diminished. Range of motion was observed to increase following a carefully designed exercise program, however strength using manual testing remained unchanged (Bokor, et al., 1993; Itoi & Tabata, 1992; Ruotolo & Nottage, 2002).
While physiotherapy is one of the most commonly prescribed conservative treatments of rotator cuff pathology, there appears to be little evidence to support its effectiveness, with many trials treating a single modality rather than multiple modalities; despite being the most common way to treat shoulder pathologies in clinical practice (Bennell, et al., 2007). The lack of consensus of this treatment is most likely due to the lack of good quality, randomised controlled trials available in the literature focusing on clinical outcomes.

Corticosteroids are often prescribed for rotator cuff tears (Gialanella & Prometti, 2011), however, evidence of the effectiveness of steroid injections for rotator cuff pathologies is unconvincing, despite extensive research in this area (Ekeberg, et al., 2009; Gialanella & Prometti, 2011). Therapeutic mechanisms of corticosteroid injections may include anti-inflammatory effects, relaxation of reflex muscle spasm, influence on local tissue metabolism, pain relief, mechanical improvements and placebo effect (Neustadt, 1991).

Research conducted by Bokor, et al. (1993) and Koubaa, et al. (2006) in patients with rotator cuff tears showed positive results when treated with a combination of rehabilitation, anti-inflammatories and local corticosteroid injections. Similarly, Yamada, et al. (2000) saw improvements in pain, muscular strength and ROM in those treated with conservative measures, including corticosteroids. Shibata, et al. (2001) also showed pain relief in patients with rotator cuff tears. A recent study conducted by Gialanella and Prometti (2011) demonstrated that patients receiving local corticosteroid injections and rehabilitation had pain relief when compared to those with rehabilitation alone. However, Darlington and Coomes (1977) found that while patients with supraspinatus tendon tears had some relief from pain with local corticosteroids, there was
no improvement in ROM or the painful arc; concluding there was no objective evidence that corticosteroids improve the condition.

Some studies reported that there is no reliable proof to suggest that corticosteroids injected at the peritendinous level had adverse effects (Nichols, 2005; Paavola et al., 2002); with Bhatia, et al. (2009) concluding that the use of corticosteroids should not be considered a cause of rotator cuff tendon tears. Despite the suggestion of positive results of steroid injections in conjunction with other therapies, subacromial and intra-articular injections of corticosteroids remains controversial, with respect to it deleterious effects. Tillander, et al. (1999) showed that after five corticosteroid injections into the subacromial space of rats there was focal inflammation, necrosis and fragmentation of collagen bundles, but no change was seen after three injections. Studies have reported that intraarticular steroid injections had adverse effects on cartilage and tendons, and osteoarthritic changes and tendon tears have been observed (Stannard & Bucknell, 1993; Tillander, et al., 1999).

Mitchell (2005) suggests subacromial corticosteroids should be considered for short term pain relief and to facilitate rehabilitation. Smidt et al. (2002) showed that in patients with lateral epicondylitis, corticosteroid injections are merely the best treatment option in the short term, compared to a physiotherapy and “wait-and-see” policy, however poor results were reported after the 12 week follow-up. Similar results were found by Verhaar, et al. (1996) and Hay, et al. (1999). It is thought that this could be due to the intratendinous injection causing permanent adverse changes within the structure of the tendon, and that patients may tend to overuse the arm following injection because they have experienced pain relief (Peerbooms, et al., 2010; Smidt, et al, 2002).
Patient satisfaction with non-operative treatment of rotator cuff tears has been reported widely in the literature with varied results; Itoi and Tabata (1992) reported 82%, Bokor, et al. (1993) 56% and Bartolozzi, et al. (1994) 25% satisfaction. While partial-thickness tears of the rotator cuff can usually be treated successfully with non-surgical interventions, full-thickness tears treated non-surgically provide inconsistent and often unacceptable results, with Millet and colleagues (2006) suggesting there are no reliable methods of predicting successful treatment of these full-thickness tears. Bartolozzi, et al. (1994) suggest that of patients with full thickness rotator cuff tears with symptoms for more than 1 year, only 13% reported a satisfactory end result with non-surgical treatment.

A review conducted by Downie and Miller (2012) comparing non-operative and operative treatment of rotator cuff tears in older patients (mean age of 60 years) was unable to find sufficient evidence to recommend treatment. And while the reviewed studies reported favourable operative outcomes, there was a lack of good quality non-operative treatment studies in this age group for comparison; highlighting a gap in the research for this age group.

**Surgical treatment of rotator cuff tendon tears**

Rotator cuff repair surgery is one of the most common orthopaedic procedures, with over 250,000 performed annually in the United States (Castricini, et al., 2010; Gulotta & Rodeo, 2009). The procedure is generally offered for the painful rotator cuff that has failed non-surgical treatment (Castricini, et al., 2010; Millett, et al., 2006). Surgery can include a rotator cuff tendon repair with or without subacromial decompression (Ainsworth & Lewis, 2007); and in more severe cases where osteoarthritis is involved, shoulder joint replacement may be the only solution (Ainsworth & Lewis, 2007). The goal of this type of surgery is to eliminate pain and improve shoulder function with
increased strength and ROM of the shoulder (Boissonault, et al., 2007; Ghodadra, et al., 2009).

Optimal repair of the rotator cuff requires high fixation strength, minimal gap formation, maintenance of mechanical stability under cyclic loads, and proper healing of the tendon to the bone (Ghodadra, et al., 2009). The majority of studies reported excellent outcomes following rotator cuff tendon repair surgery, with the integrity of repair generally being shown to have a negative correlation with age (Boileau, et al., 2005; DeFranco, et al., 2007; Ghodadra, et al., 2009; Oh, et al., 2010; Thomazeau, et al., 1997). However, healing of the repair is also dependent on the number of tendons involved and the pre-surgery tear size (Barber, et al., 2011). Cofield (1985) reviewed published results of open rotator cuff repair, noting an average pain relief of 87%; ranging between 71% to 100%, and a patient satisfaction rate of 77%.

In the past 15 years, the surgical treatment for rotator cuff tears has evolved from the traditional open procedure, to a mini-open (arthroscopic-assisted) technique, to an all-arthroscopic technique (Nho, et al., 2007). The traditional open approach was associated with severe early post-operative pain, deltoid detachment and/or weakness, and arthrofibrosis (Bennett, 2003a; 2003b; Bigliani, et al., 1992; Nho, et al., 2007). The mini-open repair technique was developed with the potential advantage of less deltoid morbidity, while demonstrating outcomes that were similar to those with the open procedure (Levy, et al., 1990; Liu & Baker, 1994; Nho, et al., 2007; Paulos & Kody, 1994). More recently, surgeons are performing complete arthroscopic rotator cuff repairs, with potential advantages including less pain, more rapid rehabilitation, the ability to treat intra-articular lesions, smaller skin incisions, less soft tissue dissection and a very low risk of deltoid detachment (Nho, et al., 2007). This technique has shown
promising results in both the short and long term (Bennett, 2003a; Galatz, et al., 2004; Galatz, et al., 2001; Gartsman, 2001). Despite these advantages, the procedure is technically demanding and requires a large amount of practice for the surgeon to be proficient in this procedure (Nho, et al., 2007; Norberg, et al., 2000). Due to the technical demands of the arthroscopic approach, a large number of orthopaedic surgeons favour the mini-open procedure (Yamaguchi, et al., 2003).

The first documented rotator cuff repair was performed by Dr Codman, in 1911, using an open technique, and further modifications to this technique were proposed by Neer in 1972 (Yamaguchi, et al., 2003). With an open rotator cuff repair approach, the patient is placed in the “beach-chair” position, and a 3-6 cm incision is made parallel to the lateral border of the acromion, in line with Langer’s lines (Figure 1). The deltoid is taken off the anterior aspect of the acromion, usually beginning at the acromioclavicular joint, extending along the anterior border of the acromion, then splitting the deltoid laterally 3-5 cm. Following rotator cuff repair, the deltoid is reattached to the acromion, and the longitudinal split of the deltoid repaired. Deltoid dysfunction has been a reported complication with this surgical approach.

![Figure 1](image.jpg)

**Figure 1.** Open rotator cuff repair, landmarks and incision marked (Ghodadra, et al., 2009).
Levy and colleagues (1990) described an arthroscopically assisted repair, where arthroscopy was used to form a subacromial decompression and avoid deltoid takedown. To perform the mini-open repair the arthroscopic portal is extended by 1-2 cm and the deltoid fibres are split in line to obtain access to the repair site (Figure 2).

![Figure 2](image.png)

**Figure 2.** Mini-open rotator cuff repair (Ghodadra, et al., 2009).

An all-arthroscopic procedure requires only a small incision for insertion of several cannulas 7-8 mm in diameter, and the only disruption to the deltoid is from insertion of the cannula, as no tissue retraction is required. Following identification of the appropriate anatomical landmarks, all arthroscopic portals are marked (Figure 3). Various surgical instruments can be introduced through these portals into the shoulder to immobilise the cuff, implant suture anchors and tie arthroscopic knots to hold the tendon to the bone.
In addition to the surgical approach, much research has centred around suture anchoring technique to establish a normal rotator cuff footprint (anatomic contact area between the tendon and the bone of the humeral greater tuberosity) in order to optimise healing potential and increase the mechanical strength of the primary fixation of the tendon repair (Lo & Burkhart, 2003; Milano, et al., 2008). While excellent clinical results of arthroscopic rotator cuff repair have been documented (Bennett, 2003a, 2003b; DeFranco, et al., 2007; Kasten, et al., 2011; Liem, Bartl, et al., 2007), there has been criticism of suture anchor repair techniques and repair integrity (Kim et al., 2006; Lo & Burkhart, 2003). In the past, most arthroscopic rotator cuff repairs were done with a single row of suture anchors, to anchor the free edge of the tendon to the bone (Milano, et al., 2008). Imaging studies of rotator cuff integrity have shown that single row arthroscopic repairs had a greater rate of structural failure than open rotator cuff repairs (Galatz, et al., 2004; Liu & Baker, 1994; Thomazeau, et al., 1997). Gerber, et al. (1994, p. 378) stated “the ideal repair should have high initial fixation strength, allow minimal gap formation, and maintain mechanical stability until solid healing; it is clear that weak initial fixation leads to gap formation under load, poor healing and possible complete failure”.

Figure 3. Arthroscopic rotator cuff repair (Ghodadra, et al., 2009).
A study conducted by Apreleva and colleagues (2002) evaluated the three-dimensional rotator cuff footprint in the normal rotator cuff and after several methods of arthroscopic supraspinatus tendon repair. They determined that 67% of the original rotator cuff footprint was restored using a single row of suture anchors, while the double-row suture repairs restored up to 85% of the surface area. The results showed that the rotator cuff footprint is a complex three-dimensional structure, covering a large surface of the humerus, that cannot be restored with a simple single row of sutures (Apreleva, et al., 2002). Similarly, Kim, et al. (2006) found that the use of a double-row suture technique created a more superior suture construct, with greater strength and stiffness, resulting in less gap formation and less strain over the rotator cuff footprint, compared with a single-row repair. By providing a double row of fixation, the number of fixation points doubles compared with a single-row repair, potentially improving mechanical strength and function by providing more complete healing across the rotator cuff footprint (Lo & Burkhart, 2003).

Despite the many surgical repair techniques, there remains concern regarding the ability of the rotator cuff insertion to fully heal following the repair (Castricini, et al., 2010; Gulotta & Rodeo, 2009; Kovacevic & Rodeo, 2008), with recurrent tearing occurring frequently (Cheung, et al., 2010). Re-tears have been reported to occur in 11-94% of rotator cuff repair surgeries – dependent upon the size of the tear, the level of tendon degeneration, and fatty infiltration present at the time of surgery, type of suture anchors and suture method used during surgery, compliance with post-operative rehabilitation guidelines and patient age (Boileau, et al., 2005; Cheung, et al., 2010; Cho & Rhee, 2009; Galatz, et al., 2004; Gulotta & Rodeo, 2009; Sugaya, et al., 2007). The authors that published these re-tear rates reported the predictors of re-tear included: larger tear size,
greater levels of tendon degeneration and fatty infiltration, and increased age at the time of surgery, as well as non-compliance with the post-operative rehabilitation guidelines. The large range in re-tear rates is likely due to differences in research methodology and study follow up timeframes.

There are a variety of re-tear rates reported in the literature, with comparisons between the open, mini-open and arthroscopic surgical approaches. Re-tear rates have been reported as high as 80-90% in the radiology literature, and as high as 57% in orthopaedic literature (Barber, et al., 2011; Charousset, et al., 2010; Liem, Bartl, et al., 2007; Liem, Lichtenberg, et al., 2007).

A study conducted by Kluger, et al. (2011) reported the overall failure rate of patients having mini-open rotator cuff repair surgery was 33% (n=107, average age=59.5 ± 9.2 years). Furthermore, they reported that 74% of the failures occurred atraumatically in the first 3 months, 11% occurred between 3-6 months following surgery, and the remaining failures occurred 2 to 5 years post surgery, and were related to sporting activities or direct trauma. Miller, et al. (2011) reported 41% of their arthroscopically repaired rotator cuffs had re-torn (n=22); with seven of the nine (78%) re-tears occurring within the first 3 months after surgery. Another study found that 100% of re-tears occurred in the first 3 months post surgery (Nho, et al., 2009).

DeFranco, et al. (2007) reported a 40% re-tear rate (n=30, average age=56.3 ±12.3 years) in patients who underwent isolated supraspinatus repair arthroscopically, using a single-row suture technique. They noted that patients in the no-tear group were significantly younger than those in the re-tear group (51 ± 12 vs 64 ± 9 years, p<0.01).
Oh, et al. (2010) reported similar results; patients with an intact repair were significantly younger than the failed repair group (58.4 ± 8.7 years vs 63.7 ± 7.5 years). Similarly, Boileau, et al. (2005) reported that only 43% of the patients over the age of 65 years had completely healed tendons (p=0.001). In this study, the rotator cuff was completely healed in 71% of the patients, 62 of the 65 patients reported they were satisfied with the result, and those with intact repairs had significantly greater shoulder strength. Charousset, et al. (2010) showed that patients older than 65 (mean age 70 years, range = 65-85 years) who underwent an arthroscopic rotator cuff surgery at 6 months post-surgery had a re-tear rate of 42%. Furthermore, the isolated supraspinatus tears showed superior healing (28.9% failure rate), however those that had a massive tear (supraspinatus retracted to the glenoid) had 100% failure rate. This indicated that arthroscopic tendon repair can be considered a successful procedure for the older patient with a small or medium tear, particularly where the tear is isolated to the supraspinatus tendon (Charousset, et al., 2010).

There has been much debate about whether the integrity of repair of the rotator cuff tendon affects functional outcome, with the trend being towards a better outcome with an intact repair (DeFranco, et al., 2007; Galatz, et al., 2004; Lafosse, et al., 2007; Liem, Bartl, et al., 2007; Oh, et al., 2010). While the radiographs may show failures at the repair site, often the patient may still have pain relief; however, studies have shown they have inferior function results when compared to patients with healed repairs (Boileau, et al., 2005; Galatz, et al., 2004; Gulotta & Rodeo, 2009; Lafosse, et al., 2007). Lam and Mok (2004), and Verma, et al. (2010) reported in older patients treated for rotator cuff repair (open and arthroscopic respectively), that over 90% had reduced pain post-surgery. They did not, however, consider the structural integrity of the repair sites.
ATTEMPTS TO REDUCE HIGH ROTATOR CUFF TENDON RE-TEAR RATES

Though surgery is successful for many patients, the quality and speed of post-operative healing remains problematic, with a number of studies demonstrating that native tendon-to-bone insertions were not restored after tendon repair surgery (Carpenter, et al., 1998; Kovacevic & Rodeo, 2008; Rodeo, et al., 2007). Tendons comprise specialised cells including tenocytes and water (Cheung, et al., 2010; Molloy, et al., 2003; Sampson, et al., 2008), as well as type I collagen fibres which orient towards a continuous insertion point on the humerus (Clark & Harryman, 1992; Sampson, et al., 2008). The vasculature is organised and dispersed through the tendon, however, the vessels decrease in number and size closer to the bone (Cheung, et al., 2010; Clark & Harryman, 1992). There are four distinct zones of tissue running longitudinally; tendon, non-mineralised fibrocartilage, mineralised fibrocartilage and bone (Carpenter, et al., 1998; Clark & Harryman, 1992).

Tendons are required to transfer great forces and, as a result, can be susceptible to injury when overloaded (Sampson, et al., 2008). With continuous overuse, micro tears can form in the collagen fibres, which may lead to tendinosis or tendinopathy (Millett, et al., 2006; Mishra, et al., 2009; Sampson, et al., 2008). When this occurs, the injured tendon heals by scarring, and with its inferior biomechanical properties, affects function and increases the risk of re-injury (Carpenter, et al., 1998; Sampson, et al., 2008). Tendons tend to heal at a slower rate compared with other connective tissues, due to poor vascularisation (Castricini, et al., 2010; Jo, et al., 2011; Sampson, et al., 2008).

General healing follows a pathway, beginning with inflammation, continuing with cellular and matrix proliferation, followed by tissue formation and maturation, and finally
tissue remodelling (Lopez-Vidriero, et al., 2010); this can also be applied to tendon healing. Tendon-to-bone healing is divided into three stages: the inflammatory stage, the repair stage and the remodelling stage (Carpenter, et al., 1998; Cheung, et al., 2010; Gulotta & Rodeo, 2009; Mishra, et al., 2009; Molloy, et al., 2003). Following a tendon injury or surgical repair, the final bone-to-tendon insertion point bears little resemblance to the original insertion (Kovacevic & Rodeo, 2008). The overall structure, composition and organisation of the normal insertion site does not regenerate (Kovacevic & Rodeo, 2008). Instead of the four distinct zones following the remodelling stage of healing, the tendon and bone become joined by a layer of fibrovascular scar tissue dominated by poorly organised type III collagen fibres (Carpenter, et al., 1998; Cheung, et al., 2010). Mechanically, this fibrous scar tissue is weaker than the native insertion site, and may contribute to the high number of repair failures (Carpenter, et al., 1998; Cheung, et al., 2010).

In an attempt to reduce the number of rotator cuff repair failures, researchers have focused their attention on ways to minimise the scar tissue formation and at the same time, promote the regeneration of the fibrocartilagenous insertion zones (Gulotta & Rodeo, 2009; Maniscalco, et al., 2008). Initially, studies looked at improving the biomechanical strength of the repair site by using stronger sutures and double row repairs (Apreleva, et al., 2002; Gulotta & Rodeo, 2009; Kim, et al., 2006; Lo & Burkhart, 2003), however, even with these techniques, failed healing and/or re-tears still occurred in up to 12% of cases (Lafosse, et al., 2007). Although improved biomechanics may slightly improve tendon healing, it has been suggested that biologic augmentation of the healing process may be required to further reduce the scar tissue formation at the repair site, and help regenerate a normal fibrocartilagenous transition zone (Gulotta & Rodeo, 2009; Maniscalco, et al., 2008), which may improve the strength of the repair.
Because of the problems faced with tendon healing following injury or surgical repair, much of the research has been directed towards understanding the mechanisms of tendon healing at the molecular level (Anitua, et al., 2005; Anitua, et al., 2007; Lyras, et al., 2010; Molloy, et al., 2003; Randelli, et al., 2009). This research has been undertaken in an effort to develop complimentary therapies to facilitate tendon healing via individual and groups of molecules that are known to have beneficial roles in the healing process. The more recent knowledge gained about tissue biology and the complexity of the regulation of growth factors in normal tissue structure, as well as in reaction to tissue damage, shows the important and effective role of an application of growth factors in the healing of damaged tissue (Filardo, et al., 2010).

Growth factors have an essential role in the body’s healing process and tissue formation (Anitua, et al., 2006). All stages of the repair process are controlled by a variety of cytokines and growth factors that act as regulators of the majority of basic cell functions (Anitua, et al., 2006). Growth factors influence many of the processes common to tissue repair and disease, including angiogenesis, chemotaxis and cell proliferation, as well as controlling the synthesis and degradation of extracellular matrix proteins (Anitua, et al., 2006).

As mentioned earlier, tendon healing follows a pattern (inflammatory phase, repair phase and remodelling phase). When tissue is damaged, blood vessels rupture which signals the release of molecules to trigger coagulation to coordinate the formulation of a clot around the affected area (Molloy, et al., 2003). The clot contains cells and platelets that immediately release a variety of molecules (including growth factors), causing acute and local inflammation (Molloy, et al., 2003). It is during the inflammatory phase that
extrinsic cells (neutrophils and macrophages) which are responsible for phagocytosis, and intrinsic cells (endotenon and epitenon cells) produce another battery of cytokines which initiates the repair phase (Molloy, et al., 2003). At this stage that we see the collagen deposition and granular tissue formation, as well as neovascularisation, extrinsic fibroblast migration and intrinsic fibroblast proliferation (Anitua, et al., 2005; Molloy, et al., 2003).

Platelets are responsible for haemostasis and coagulation (Anitual, et al., 2004; Lopez-Vidriero, et al., 2010), and also contain alpha granules with various molecules (growth factors, endostatins, antipoietsins and thrombospondin) that are secreted upon activation during the healing process (Anitua, et al., 2004; Lopez-Vidriero, et al., 2010), assisting in the construction of new connective tissue and revascularisation, making up approximately 6% of a blood specimen (Sampson, et al., 2008).
Growth factors important in tendon healing/regeneration

Growth factors have a number of crucial roles in tendon healing. Numerous studies have revealed the complexity of the regulation of growth factors in response to tissue damage and the important role they play in tendon healing (Anitua, et al., 2005; Anitua, et al., 2007; Lyras, et al., 2010; Molloy, et al., 2003; Randelli, et al., 2009; Rodeo, et al., 2007). Factors secreted from platelets such as transforming growth factor-ß (TGF-ß), platelet-derived growth factor (PDGF), vascular endothelial growth factors (VEGF), basic fibroblast growth factor (bFGF) and insulin-like growth factor (IGF-1) are markedly up-regulated throughout the tendon repair process (Anitua, et al., 2005; Molloy, et al., 2003; Randelli, et al., 2009). They can be potentially produced by both intrinsic and extrinsic cells, often have dose-dependent effects, require specific receptors to be active, and usually work in synergy with other signalling molecules (Molloy, et al., 2003). Growth factors are one of the largest groups of molecules involved in the healing process of tendons and ligaments (Molloy, et al., 2003), with an outline provided below of some of their functions and behaviours.

TGF-ß is active in almost all stages of tendon healing, having varied effects such as stimulating extrinsic cell migration, regulating proteinases, fibronectin binding interactions, termination of cell proliferation via cyclin-dependent kinase inhibitors and stimulation of collagen production (Anitua, et al., 2005; Molloy, et al., 2003; Randelli, et al., 2009). TGF-ß levels have been shown to dramatically increase following tendon injury, and it is believed to play an important role in the initial inflammatory response to tissue damage (Molloy, et al., 2003).
PDGF is secreted by platelets during the early phases of inflammation and has been identified at fracture sites (Randelli, et al., 2009). It is thought that PDGF may play a significant role in the early stages of healing by inducing the synthesis of other growth factors, such as IGF-1 (Molloy, et al., 2003; Randelli, et al., 2009). The role of PDGF in tendon repairs appears to be most relevant in the remodelling phase where it has been observed to stimulate collagen and non-collagen protein production, and DNA synthesis, in a dose-dependent manner.

VEGF has a small role in early cellular migration and proliferation, however, has been found to be most active after the inflammation phase during the proliferation and remodelling phases, where it is a powerful stimulator of angiogenesis (Anitua, et al., 2005; Molloy, et al., 2003). Increased levels of VEGF at the site of injury correlate with a well-defined pattern of vascular ingrowth from the epi- and intra-tendinous blood supply towards the site of repair. This increased vascularisation proceeds along the epitenon, through a normally avascular area, providing extrinsic cells, nutrients and growth factors to the injured site.

The bFGF promotes growth and differentiation in a range of cells, including epithelial cells, myocytes, osteoblasts and chondocytes (Molloy, et al., 2003; Randelli, et al., 2009). In tendons it has been shown to be a potent stimulator of angiogenesis, cellular migration and proliferation. Kobayashi and colleagues (1997) found that bDGF provided a boost to the initial stages of healing, and that all the subsequent steps proceeded with significantly greater speed and efficiency.

IGF-1 is an important mediator in all phases of wound healing, particularly in the inflammatory and proliferative phases (Molloy, et al., 2003). It is a versatile signal
molecule, having numerous and varied activities during tendon healing, especially when working in synchrony with other growth factors (Molloy, et al., 2003). Its primary role is to stimulate the proliferation and migration of fibroblasts and other cells at the repair site, and subsequently increase the production of collagens and other extracellular matrix structures during the remodelling phase (Anitua, et al., 2005; Molloy, et al., 2003).

It has been suggested that the concentrated addition of the above mentioned growth factors might improve tissue healing. Recently a technique has been developed to extract useable growth factors from autologous blood, which can be injected around an injury or repair site, called platelet rich plasma (PRP).

**Platelet rich plasma**

Platelets contribute to haemostasis by preventing blood loss at sites of vascular injury, and contain large numbers of cytokines and growth factors that play a key role in bone regeneration and soft tissue maturation (Anitua, et al., 2006). PRP has emerged as a new technology believed to stimulate the revascularisation of soft tissue and increase the concentration of growth factors to improve and accelerate wound, bone, muscle and tendon healing (Barber, et al., 2011; Peerbooms, et al., 2010). It is an autologous concentration of platelets in a small volume of plasma, which, once activated, undergoes degranulation to release growth factors with healing properties (Kajikawa, et al., 2008; Lopez-Vidriero, et al., 2010). Because the PRP preparation is obtained from the patient’s own blood, concerns regarding immunogenic reactions and disease transmission are eliminated (Anitua, et al., 2006). Important growth factors identified in PRP include TGF- β, PDGF, VEGF, bFGF and IGF-1 (Lyraa et al., 2010). As well as containing platelets and concentrated growth factors, PRP also consists of plasma with fibrin, which
acts as a scaffold for primary cell migration and differentiation, functioning as a biological glue (Anitua, et al., 2006; Lopez-Vidriero, et al., 2010).

The concept of using growth factors to assist healing dates back to the early 1980’s, where it was first used to assist in wound healing (Knighton, et al., 1982). Initially it was thought that platelets acted exclusively during clotting; however it has since been discovered that platelets also release many bioactive proteins responsible for attracting microphages, mesenchymal stem cells and osteoblasts, which promote the removal of necrotic tissue, as well as enhancing tissue regeneration and healing (Sampson, et al., 2008). The early use of PRP in the 1990’s was as a biological glue (Gibble & Ness, 1990). Because of the high proportions of fibrin, these “glues” were used primarily in maxillofacial surgery (Lopez-Vidriero, et al., 2010). It was during this time that PRP preparations were discovered to have bone-forming properties, as well as anti-inflammatory and antibacterial qualities, attributed mainly to the high concentration of platelets (Lopez-Vidriero, et al., 2010).

Since then, research has been conducted using PRP in a variety of tissues to accelerate and assist the healing process. Such areas include cosmetic surgery and wound healing (Eppely, et al., 2004), as well as most orthopaedic disciplines, such as chronic patella tendon injuries (Filardo, et al., 2010) and defects (Lytras, et al., 2010), lateral epicondylitis (Mishra & Pavelko, 2006; Peerbooms et al., 2010), Achilles tendon injuries (Aspenberg & Virchenko, 2004; Sanchez, et al., 2007), bone allograft integration, rotator cuff tendon tears (Maniscalco, et al., 2008) and rotator cuff tendon repair surgery (Barber, et al., 2011; Castricini, et al., 2010; Kovacevic, et al., 2008; Randelli, et al., 2008; Randelli, et al., 2011).
Lopez-Vidrierio and colleagues (2010) described the characteristics of the main PRP commercial products currently available on the market. The term “PRP” has been controversial in the literature, because this generic terminology doesn’t differentiate between the various commercial products available, and their respective protocols (Lopez-Vidriero, et al., 2010; Sanchez, et al., 2010). Concerns have been raised because different products show varying biologic effects (Anitua, et al., 2009). The main differences between commercial PRP systems are: speed and number of centrifugations that lead to different platelet concentrations, the use of anticoagulant, the presence of leukocytes in the preparation and the use of an activator (Anitua, et al., 2009; Lopez-Vidriero, et al., 2010). The actual platelet concentration required to have a clinically significant effect has not yet been determined, and a higher concentration may not necessarily be superior (Barber, et al., 2011). It is important that these factors be taken into account when analysing published results, and when surgeons are deciding on which system to use (Anitua, et al., 2006; Castillo, et al., 2011; Lopez-Vidriero, et al., 2010).

**Platelet-rich plasma and tendon injury**

Aspenberg and Virchenko (2004) investigated the use of PRP to augment rat Achilles tendon tears, finding greater maturation in tendon callus, but also reported increased force to failure and ultimate stress in PRP treated animals (Virchenko & Aspenberg, 2006). PRP was found by Kajikawa, et al. (2008) to enhance mobilisation of circulation-derived cells to the injection area, and that PRP induced type I collagen production and increased the proliferation of microphages at three and seven days.

Mishra and Pavelko (2006) reported on the use of PRP in patients with chronic severe elbow tendinitis, who had failed a standardised, non-operative treatment protocol. They
found a 60% improvement in pain scores for those patients treated with PRP, compared with a 16% improvement in the control group at 8 weeks following treatment. At final follow-up, the PRP recipients reported over 90% reduction in pain compared to their pre-treatment scores, and 93% of PRP patients were fully satisfied with this treatment. It should be noted however, that this was a small sample, non-randomised study.

Anitua and colleagues (2007) reported faster recovery in athletes who underwent PRP-enhanced Achilles tendon repair, compared to a retrospective control group of athletes who had surgery alone. Those treated with PRP recovered their range of motion earlier, had no wound complications and returned to training activities earlier than the control patients.

**Platelet-rich plasma preparations and rotator cuff tendon repair**

Review of the literature reveals substantial rates of failure in the surgical treatment of smaller tears. A number of studies have looked into the use of PRP constructs to potentially enhance rotator cuff healing (Barber, et al., 2011; Castricini, et al., 2010; Gumina, et al., 2012; Randelli, et al., 2008; Randelli, et al., 2011), but currently there are no clear guidelines or agreement on the safest or most effective augmentation. A pilot study conducted by Randelli and colleagues (2008) demonstrated the application of PRP during arthroscopic rotator cuff repair is safe and effective, and results remained stable with time.

Castricini, et al. (2010) suggest that the use of autologous platelet-rich fibrin matrix (PRFM) for augmentation of a repair of a small or medium rotator cuff tear does not improve shoulder function or cuff integrity, when compared to a control group at 16
months post-surgery. They suggested that, given the variety of PRP products on the market, there might be another preparation that could be more effective. Barber and colleagues (2011) also used a PRP fibrin matrix (Cascade, by Musculoskeletal Transplant Foundation, NJ), which did not have thrombin activation, nor contain leukocytes, opting to suture two lots of the construct into the repair. While there was no statistical difference between the PRP and control groups in terms of functional outcomes, the MRI results indicated that the PRP group had significantly lower re-tear rates (P=0.03), with MRI follow-up at 4 months post surgery.

A study by Gumina, et al. (2012) compared clinical and MRI results of arthroscopic rotator cuff repair with and without the use of platelet-leukocyte membrane (n=80), stating that the use of the membrane was associated with significantly better repair integrity (p=0.04). However, this improvement in integrity was not associated with greater improvement in functional outcomes.

Randelli, et al. (2011) published long-term results from the use of an intra-operative application of PRP in combination with a rotator cuff repair of small to massive tears (n=53; treatment group n=26, control group n=27) completed by a single surgeon. Pain scores in the treatment group were significantly lower than the control group at 3, 7, 14 and 30 days post surgery (p<0.05). Functional scores (Simple Shoulder Test (SST), University of California (UCLA and Constant) and strength in external rotation were significantly higher in the treatment group at 3 months post surgery; however, there was no significant difference between the groups after 6, 12 and 24 months. The 12-month MRI analysis showed no difference in the rotator cuff healing rate between the two groups. They concluded that the PRP application reduced pain in the first post-operative months, and that smaller tears with less retraction would benefit from PRP.
More recently, Werthel and colleagues (2014) reported long term results (mean 19 month follow-up ± 4.2) on the use of an intra-operative injection of PRP during surgical rotator cuff repair of full thickness symptomatic supraspinatus tendon tear (retraction less than 3 in the Patte classification). No significant differences were noted functionally or structurally between the treatment and control groups, except for a lower VAS for pain score at final follow-up (p < 0.001). There were some limitations of this study; subjects were not randomised, and a different surgeon operated on the subjects in each group. There was also a significant age difference between the treatment and control groups, and the authors suggest this may have contributed to the difference in pain reported at final follow-up.

**SUMMARY**

Significant re-tear rates reported in the literature despite advancements in surgical and suture anchor technique, along with the lengthy tendon healing timeline, has established the need to investigate biological therapies that may improve and/or accelerate tendon healing. Biological augmentation in conjunction with rotator cuff repair has the potential to improve tendon healing. While research in this area has shown it to be safe, results remain inconclusive, and have not been demonstrated sufficiently to warrant regular clinical use.

While it has been well established that the longer-term structural and functional results (>12 months follow-up) have not differed significantly, little research has centred on the early tendon healing. In a primate model, Sonnabend, et al. (2010) showed that a significant proportion of Sharpey fibres begin to reconstitute at 3 months, with maturation
at 4 months following surgery. It has also been well documented that the majority of re-tears occur within the first 3 months of surgery (Kluger, et al., 2011; Miller, et al. 2011; Nho, et al., 2009), suggesting that the early tendon healing stage is critical for long term success.

There are a number of variables that may affect the efficacy of PRP in combination with rotator cuff repair, including tendon tear size, formulation of PRP used and timing of delivery; with all previous studies to our knowledge using time zero delivery at the time of surgery. We propose that the delayed and repeated injection of PRP (Arthrex) at 7 and 14 days post-surgery will give the best opportunity to enhance early tendon healing and functional recovery following rotator cuff repair.

REFERENCES


CHAPTER 3
PAPER 1

Do postoperative platelet-rich plasma injections accelerate early tendon healing and functional recovery after arthroscopic supraspinatus repair?

A randomized controlled trial

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ABSTRACT

\textbf{Background:} Tendon bone healing after rotator cuff repair directly correlates with a successful outcome. Biological therapies that elevate local growth factor concentrations may potentiate healing following surgery.

\textbf{Purpose:} To ascertain whether postoperative and repeated application of platelet-rich plasma (PRP) to the tendon repair site improves early tendon healing and enhances early functional recovery following double row arthroscopic supraspinatus repair.

\textbf{Study Design:} Randomized controlled trial; Level of evidence, 1.
Methods: Sixty patients underwent arthroscopic double row supraspinatus tendon repair. Following randomization, half the patients received two ultrasound-guided injections of PRP to the repair site at day 7 and day 14 post-surgery. Early structural healing was assessed with Magnetic Resonance Imaging (MRI) at 16 weeks and cuff appearances graded according to the Sugaya classification. Functional scores were recorded with the Oxford Shoulder Score (OSS), the Quick Disability of the Arm, Shoulder and Hand (Quick-DASH), Visual Analogue Scale (VAS) for pain and Short From-12 (SF-12) quality of life score both pre-surgery and post-operatively at 6, 12 and 16 weeks, isokinetic strength and active range of motion was measured at 16 weeks.

Results: PRP treatment did not improve early functional recovery, range of motion, strength or influence pain scores at any time point after arthroscopic supraspinatus repair. There was no difference in MRI structural integrity of the supraspinatus repair between groups (p=0.35) (PRP group 0% full thickness re-tear; 23% partial tear; 77% intact), compared with the control group (7% full thickness re-tear; 23% partial tear; 70% intact) at 16 weeks post-operatively.

Conclusion: Following arthroscopic supraspinatus tendon repair, image guided PRP treatment on two occasions does not improve early tendon bone healing or functional recovery.
INTRODUCTION

Despite the advent of new surgical techniques to improve rotator cuff fixation to bone, failure of the tendon repair often occurs (Galatz, et al., 2004; Sugaya, et al., 2007). Tendon re-tears may be due to a specific re-injury at the repair site, but also may reflect incomplete or failed primary healing after surgery (Boileau, et al., 2005; Carpenter, et al., 1998).

Sonnabend, et al. (2010) in a primate model of rotator cuff repair, showed that a significant proportion of Sharpey fibres begin to reconstitute at 3 months with maturation at 4 months after surgery. Thus the early tendon healing stage is critical for long-term success of rotator cuff repair. Accelerated rotator cuff rehabilitation programs which allow active exercises sooner than 3 to 4 months before early tendon bone healing occurs, risk early failure (Parsons, et al., 2010; Zhang, et al., 2013).

Hence, there has been increasing interest in adjuvant biological therapies to improve early primary tendon healing. In particular, many studies have investigated platelet-rich plasma (PRP) products, where a supra physiological concentration of platelets is delivered to the tendon-bone repair site at the time of surgery. Activated platelets degranulate to release multiple growth factors that modulate the cascade of chemotaxis, cell proliferation and differentiation, which assist in the tendon healing process (Bedi, et al., 2012; Eppely, et al., 2004; Galatz, et al., 2007; Gulotta & Rodeo, 2009; Isaac, et al., 2012; Kobayashi, et al., 2006; Manning, et al., 2011; Molloy, et al., 2003; Plate, et al., 2013).
Published studies reporting the use of PRP administration have met with mixed success in improving outcomes after rotator cuff repair. Appraisal of the literature is complicated by the range of treated pathologies, varying from small, single tendon tears to massive multitendon tears; concomitant use of acromioplasty or not; (Castricini, et al., 2011; Jo, et al., 2011) and the formulation of PRP used, which ranged from intra-tendon injection (Kesikburun, et al., 2013; Randelli, et al., 2008), spray application (Randelli, et al., 2008; Ruiz-Moneo, et al., 2013), or incorporation of a platelet-rich fibrin matrix (PRFM) into the tendon repair site (Barber, et al., 2011; Castricini, et al., 2011; Gumina, et al., 2012; Weber, et al., 2013).

A further variable affecting the efficacy of PRP is the timing of delivery. All previous PRP augmented rotator cuff studies to date have used time zero delivery at the time of surgical repair. Following activation, platelets release growth factors almost immediately with total elution within 1 hour (Arnoczky, et al., 2011), and the half-life of growth factors is a matter of minutes to hours (Mooren, et al., 2010), however it has been acknowledged that biological augmentation of tendon repairs too early in the tendon healing cascade may be ineffective (Gulotta & Rodeo, 2009). Differing classes of growth factors are active at specific time points (Kobayashi, et al., 2006); for example, animal studies have shown that application of platelet-derived growth factors at day-7 have a more pronounced effect on tendon cellular maturation and biomechanical strength than earlier application (Chan, et al., 2006). Growth factors including BMP-13, platelet-derived growth factor-B and transforming growth factor B1 are expressed maximally at days 7 and 14 (Wurgler-Hauri, et al., 2007) and the cytokine mediated temporal expression of collagen type I and III increases from day-7 onward (Dahlgren, et al., 2005).
Hence, timing for PRP delivery remains an important consideration for optimizing tendon healing. In this study we hypothesized that delayed and repeated injection of PRP at days 7 and 14 after surgery would firstly avoid the potential dilution and washout effect of arthroscopic administration and secondly, produce a sustained up regulation of the tendon healing process. The purpose of this study is to determine if this PRP delivery protocol would enhance early tendon healing and functional recovery after arthroscopic supraspinatus tendon repair. The primary study outcome is improved early tendon healing as assessed by MRI scanning. The secondary outcome is patient rated function as a measure of functional recovery.

METHODS

Patient Selection

Institutional Ethics Committee approval was granted for this study. Patients with MRI or ultrasound proven rotator cuff tears were identified over the period from November 2011 to February 2013. A power calculation was performed to determine the required number of patients to detect a significant difference of one Sugaya grade classification between the treatment and control groups based on previously published MRI classification scores for post-rotator cuff repair patients (Sugaya, et al., 2007). The power analysis used an effect size of 0.769 (moderate effect), with significance of p<0.05 and a power of 80%, giving a minimum sample size of 56 participants (28 participants in each group). More participants (n=60) were recruited to allow for attrition.

The inclusion criteria comprised the presence of a symptomatic full thickness tear of supraspinatus in an active adult identified by preoperative imaging and confirmed by
arthroscopic evaluation. All patients also received a series of plain radiographs (anteroposterior, outlet and axillary views) for evaluation of arthritic change. Exclusion criteria included: patients with a history of previous rotator cuff surgery, subscapularis or infraspinatus tear identified on preoperative imaging or arthroscopic evaluation; labral tear; significant degenerative glenohumeral osteoarthritis; contralateral shoulder symptoms; rheumatalogical, neuromuscular or autoimmune disease; cervical disc herniation; ongoing workers compensation claims; or contraindication to postoperative MRI evaluation (Figure 1).
Figure 1. CONSORT (Consolidated Standards of Reporting Trials) flowchart.
PASTA = partial articular supraspinatus tendon avulsion; US = ultrasound; PRP = platelet-rich plasma
Surgical Technique

All surgery was performed by the senior author. All procedures were performed in the lateral decubitus position under general anaesthesia with an interscalene nerve block. The arm was placed in 4 kg of traction and positioned in 30 degrees of arm flexion and abduction. Initial diagnostic glenohumeral arthroscopy was performed and the presence of a full thickness supraspinatus tear confirmed. After debridement of the bursal tissue and tendon margins, the tear morphology was assessed and tear size measured with a calibrated probe with 5 mm increments. Tears over 20 mm in the anterioposterior dimension were excluded, as were partial tears. Supraspinatus tears associated with subscapularis or infraspinatus tears were excluded from the study. Following acromioplasty, rotator cuff reconstruction was performed. The footprint was prepared with a full-radius resector to decorticate the greater tuberosity. A double row suture bridge repair (Park, et al., 2006) with bioabsorbable anchors was performed (Arthrex Bio-Corkscrew 5.5mm FT, Biocomposite Pushloc 3.5mm, Arthrex, Naples, FL, USA). The same reconstructive technique was utilized in each case. Concomitant shoulder pathology was treated as clinically or radiographically indicated. Acromioclavicular joint arthropathy was treated with arthroscopic excision of the lateral end of the clavicle and long head of biceps tendinopathy was treated with tenotomy (Table 1).
Table 1. Group demographics with concomitant procedures and complications $^a$

<table>
<thead>
<tr>
<th></th>
<th>PRP Group (n=30)</th>
<th>Control Group (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male/female)</td>
<td>11/19</td>
<td>17/13</td>
</tr>
<tr>
<td>Mean age (years) [range]</td>
<td>59.8 [28-77]</td>
<td>58.4 [38-76]</td>
</tr>
<tr>
<td>Acromioplasty (n)</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Biceps tenotomy (n)</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Acromioclavicular joint excision (n)</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Complications (n)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Supraspinatus tear size (mm)</td>
<td>14.60 (3.78)</td>
<td>13.70 (3.27)</td>
</tr>
</tbody>
</table>

$^a$PRP = Platelet Rich Plasma.

Post-operative Protocol

All patients were immobilized in a sling (Ultrasling III, Don Joy, Carlsbad, CA, USA) for 6 weeks postoperatively and followed a standard rehabilitation program under the supervision of physical therapists. This consisted of passive range of motion exercises in the first 6 weeks, followed by active assisted range of motion exercises from 6 to 10 weeks and finally, a guided strengthening program from 10 to 16 weeks. All patients followed this program consistently.

Randomisation Procedure

Patients were reviewed on the fifth post-operative day, and following arthroscopic evaluation and confirmation study inclusion criteria were met, randomized to PRP or control groups. A computer block permutation method was prepared to generate a simple randomised computer-generated table of blocks of 10 (5 PRP; 5 Control), stratified by the treating surgeon at the five day post-surgical follow up. Sixty consecutive patients meeting the study inclusion criteria, and consenting to the study were randomized via the
above procedure, with thirty in each arm of the study. The average age was 59.1 years (range: 28-77 years). Patient demographics along with details of concomitant surgical procedures are illustrated in Table 1.

**Preparation of Platelet-rich Plasma**

The group randomized to the treatment arm of the study underwent ultrasound guided PRP injection to the rotator cuff repair site on two separate occasions, at days 7 and 14 post-surgery. The platelet concentrate was obtained using the Arthrex Autologous Conditioned Plasma (ACP) system (Arthrex, Naples, FL, USA). A PRP injection was prepared from 10 ml of autologous peripheral blood. Following the addition of 1 ml of Anticoagulant Citrate Dextrose Solution (ACD-A), the blood was spun in a centrifuge (ROTOFIX 32 A, Andreas Hettich GmbH & Co. KG, Tuttingen, Germany) at 1500 revolutions per minute (RPM) for 5 minutes. Following centrifugation, the PRP supernatant (approximately 2-4 ml) was removed and stored in a separate sterile syringe in preparation for point of care delivery.

The ACP system produces a platelet concentration of approximately 470,000 platelets/μL, (2.1 times greater than the level in whole blood) with an estimated concentration of growth factor reported as five to 25 times that of normal physiologic levels. It is free of both residual erythrocytes and leucocytes, which may impair local growth factor activity by free radical activation (Jiang, et al., 2007; Scott, et al., 2004). Immediately prior to injection, the preparation was activated with 2 ml of CaCl₂ (Nikolidakis & Jansen, 2008). The injection was delivered at the tendon repair site under direct visualisation with ultrasound by an experienced fellowship-trained musculoskeletal
radiologist. Needle placement was aided by the identification of the echogenic sutures at the tendon repair site (Figure 2). The control group did not receive a placebo injection.

Figure 2. Ultrasound image of needle placement directly at the tendon repair site (arrow).

Outcome Assessments

Radiographic analysis was performed with MR imaging at 16 weeks. All scans utilized a 1.5 Telsa unit (Sonata Maestro Class; Siemens, Erlangen, Germany) with 40 mT/m gradient power. Multiple images were obtained in oblique coronal, oblique sagittal and axial planes with both short-tau inversion recovery (STIR) and turbo spin echo (TSE) T1-weighted sequence. MRI assessment was performed by an experienced fellowship trained musculoskeletal radiologist, who had not performed the PRP injections and was blinded to patient allocation to treatment or control group. Multiple images were evaluated and graded as per the Sugaya classification (Figure 3) (Sugaya, et al., 2007).
Outcomes were assessed clinically and radiologically. Patients were assessed using the Oxford Shoulder Score (OSS), Quick Disability of the Arm, Shoulder and Hand (Quick DASH), Visual Analogue Scale (VAS) for pain and Short Form-12 (SF-12); pre-surgery and at 6, 12 and 16 weeks post-surgery. All assessors were blinded as to the identity of the treatment and control groups, nor were they involved in any stage of the recruitment or surgery.

Active range of motion was assessed at 16 weeks using a goniometer. Absolute values were recorded for arm flexion, abduction and external humeral rotation in both the operated and un-operated shoulders, using anatomical landmarks for accuracy and consistency. Range of motion was performed within the participants’ pain tolerance to minimise any injury risk and discomfort.
Isokinetic strength was also assessed at 16 weeks with the patient seated in a Biodex Isokinetic Dynamometer (Biodex, System 4, Shirley, NY) and a series of standardized measurements performed with the patient instructed to produce a maximum muscular force at speeds of 60 and 90 degrees/s. External humeral rotation was performed in the modified-neutral position, with the elbow at 90 degrees of flexion and the forearm in a neutral position throughout. Arm flexion was performed with the elbow fully extended. Values for both peak torque and total work performed over the range of motion were noted. Data were recorded as both absolute values and as a percentage of the scores obtained on the contralateral, un-operated shoulder. A difference of 10-15% in the strength between shoulders is regarded as physiologically normal in the general population and in those patients undergoing surgery (Bigoni, et al., 2009).

**Statistical Analysis**

Values are presented as means with associated standard deviations. A series of two-factor, repeated measures ANOVA was performed to assess for difference between the treatment and control groups over time for continuous variables. For continuous data recorded at a single time point only, a series of independent t-tests were performed, whereas a Mann-Whitney U test was employed for the MRI rating primary outcome variable. Statistical analyses used SPSS software (SPSS, Chicago, IL). For all tests, a p<0.05 was considered significant.

**RESULTS**

All patients complied with the study protocol, and no patient was lost to follow up. There were no significant complications such as infection, neurological or vascular deficit for
any patient in either arm of the study. In the control group mean tendon tear size treated was 1.37 cm, and in the PRP group, mean tendon tear size treated was 1.46 cm. The adjunctive procedures of acromioclavicular joint excision and biceps tenotomy are shown in Table 1. No patient underwent a cortisone injection for pain, capsulitis or bursitis within the study period.

**Structural Evaluation**

Using the Sugaya classification, the grade of supraspinatus tendon healing for the PRP and control group is reported in Table 2. In both groups, 23% of subjects had a partial thickness tendon repair (Sugaya grade 3). No full thickness re-tears were noted in the PRP treatment group, two (7%) full thickness re-tears (Sugaya grades 4 and 5) occurred in the control group. One patient in the PRP treatment group did not tolerate the postoperative MRI scan and so underwent an ultrasound performed by an experienced musculoskeletal radiologist. This tendon repair was intact and without any evidence of thinning or discontinuity and so, for the purposes of the study, was included in the grade 1 group of that cohort. In the PRP treatment group, 23 subjects (77%) exhibited a healed repair or an intact repair with high signal intensity (Sugaya grades 1 and 2), compared to 21 subjects (70%) in the control group. A Mann-Whitney U test demonstrated no difference (p=0.351) between groups on MRI rating at 16 weeks (PRP group mean ± SD = 1.8 ± 0.8; Control = 2.1 ± 1.0).
### Table 2. Sugaya classification of MRI scans of patient treatment groups

<table>
<thead>
<tr>
<th>Sugaya Classification a</th>
<th>Group</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 (no tear)</td>
<td>PRP</td>
<td>12</td>
<td>40.0</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>9</td>
<td>30.0</td>
</tr>
<tr>
<td>Grade 2 (sufficient tendon thickness but with high signal change)</td>
<td>PRP</td>
<td>11</td>
<td>36.6</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>12</td>
<td>40.0</td>
</tr>
<tr>
<td>Grade 3 (insufficient thickness but no tendon discontinuity)</td>
<td>PRP</td>
<td>7</td>
<td>23.0</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>7</td>
<td>23.0</td>
</tr>
<tr>
<td>Grade 4 (small full thickness re-tear)</td>
<td>PRP</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>1</td>
<td>3.3</td>
</tr>
<tr>
<td>Grade 5 (large full thickness re-tear)</td>
<td>PRP</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>1</td>
<td>3.3</td>
</tr>
</tbody>
</table>

a Values are reported as n (%), PRP = platelet-rich plasma.

b From Sugaya, et al., (2007). Grade 1 = no tear; grade 2 = sufficient tendon thickness but with high signal change; grade 3 = insufficient thickness but no tendon discontinuity; grade 4 = small full-thickness re-tear; grade 5 = large full-thickness re-tear.

### Functional Scores

Outcome scores for all patients improved following surgery. At 12 and 16 weeks postoperatively, the OSS (F=75.803; df 3; p<0.001), the QuickDASH (F=53.939; df 3; p<0.001) and the VAS pain scores (F=75.499; df 3; p<0.001) all improved significantly from pre-surgery. Similarly, the SF-12 quality of life indicators improved with time: Physical Component score (F=13.967; df 3; p<0.001) and Mental Component score (F=5.401; df 3; p=0.001). There was, however, no statistical difference (p>0.05) between the PRP treatment and control groups for any of these functional scores at any time point postoperatively (Table 3).
Table 3. Functional scores

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Pre-surgery Mean</th>
<th>Pre-surgery SD</th>
<th>6 weeks post-surgery Mean</th>
<th>6 weeks post-surgery SD</th>
<th>12 weeks post-surgery Mean</th>
<th>12 weeks post-surgery SD</th>
<th>16 weeks post-surgery Mean</th>
<th>16 weeks post-surgery SD</th>
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<tbody>
<tr>
<td>QuickDASH Symptoms</td>
<td>PRP</td>
<td>42.27</td>
<td>17.06</td>
<td>51.17</td>
<td>19.54</td>
<td>33.14</td>
<td>19.27</td>
<td>22.58</td>
<td>14.36</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>37.16</td>
<td>20.38</td>
<td>53.48</td>
<td>13.27</td>
<td>36.33</td>
<td>17.40</td>
<td>17.23</td>
<td>13.56</td>
</tr>
<tr>
<td>VAS</td>
<td>PRP</td>
<td>6.37</td>
<td>1.59</td>
<td>3.26</td>
<td>2.43</td>
<td>2.35</td>
<td>2.01</td>
<td>1.75</td>
<td>1.68</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>5.38</td>
<td>2.43</td>
<td>1.19</td>
<td>2.34</td>
<td>2.23</td>
<td>1.91</td>
<td>1.36</td>
<td>1.51</td>
</tr>
<tr>
<td>OSS</td>
<td>PRP</td>
<td>27.63</td>
<td>6.90</td>
<td>23.57</td>
<td>9.61</td>
<td>33.38</td>
<td>8.93</td>
<td>38.17</td>
<td>7.19</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>30.68</td>
<td>7.76</td>
<td>21.48</td>
<td>6.61</td>
<td>32.53</td>
<td>6.92</td>
<td>40.37</td>
<td>5.12</td>
</tr>
<tr>
<td>SF-12 PCS</td>
<td>PRP</td>
<td>35.17</td>
<td>8.43</td>
<td>36.31</td>
<td>7.40</td>
<td>38.73</td>
<td>7.06</td>
<td>41.78</td>
<td>8.34</td>
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<tr>
<td></td>
<td>Control</td>
<td>37.92</td>
<td>7.97</td>
<td>34.98</td>
<td>5.75</td>
<td>39.08</td>
<td>6.94</td>
<td>43.08</td>
<td>6.26</td>
</tr>
<tr>
<td>SF-12 MCS</td>
<td>PRP</td>
<td>52.16</td>
<td>12.24</td>
<td>49.87</td>
<td>12.94</td>
<td>52.75</td>
<td>11.90</td>
<td>53.81</td>
<td>11.21</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>50.47</td>
<td>12.56</td>
<td>49.69</td>
<td>13.63</td>
<td>53.47</td>
<td>10.55</td>
<td>55.17</td>
<td>7.41</td>
</tr>
</tbody>
</table>

*Values are reported as mean ± SD. MCS = mental component score; OSS = Oxford Shoulder Score; PCS = physical component score; PRP = platelet-rich plasma; QuickDASH = Quick Disability of the Arm, Shoulder and Hand; SF-12 = Short Form-12; VAS = visual analogue scale for pain.

Strength

Isokinetic strength values were obtained for active arm flexion and external rotation movements at two speeds. Values were expressed as a percentage of the strength recorded in the contralateral shoulder. Within the control group the relative scores for arm flexion peak torque at 90 and 60 degrees/s were 68.7% and 75.4% respectively, and 75.6% and 74.0% respectively for external rotation peak torque. Relative scores were similar in the PRP treatment group for arm flexion peak torque at 90 and 60 degrees/s (74.1% and 76.3%) and external rotation peak torque (72.1% and 77.3%) respectively. No group differences (p>0.05) for strength scores at 16 weeks post-surgery were evident (Table 4).
Table 4. Group mean scores (as percentage of the contralateral, un-operated arm) and t-test results for strength measures at 16 weeks post-surgery.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Mean (%)</th>
<th>SD</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm flexion peak torque 90°/s</td>
<td>PRP</td>
<td>74.1</td>
<td>10.8</td>
<td>-0.122</td>
<td>0.266</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>68.7</td>
<td>24.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arm flexion total work 90°/s</td>
<td>PRP</td>
<td>55.5</td>
<td>23.2</td>
<td>0.107</td>
<td>0.915</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>56.3</td>
<td>34.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arm flexion peak torque 60°/s</td>
<td>PRP</td>
<td>76.3</td>
<td>22.0</td>
<td>-0.190</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>75.4</td>
<td>22.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arm flexion total work 60°/s</td>
<td>PRP</td>
<td>61.7</td>
<td>21.8</td>
<td>-0.150</td>
<td>0.881</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>60.8</td>
<td>27.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>External rotation peak torque 90°/s</td>
<td>PRP</td>
<td>72.2</td>
<td>15.7</td>
<td>0.470</td>
<td>0.640</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>75.6</td>
<td>37.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>External rotation total work 90°/s</td>
<td>PRP</td>
<td>51.9</td>
<td>30.1</td>
<td>0.712</td>
<td>0.371</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>55.1</td>
<td>35.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>External rotation peak torque 60°/s</td>
<td>PRP</td>
<td>77.3</td>
<td>17.8</td>
<td>-0.64</td>
<td>0.525</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>74.0</td>
<td>21.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>External rotation total work 60°/s</td>
<td>PRP</td>
<td>59.8</td>
<td>24.3</td>
<td>0.277</td>
<td>0.783</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>62.3</td>
<td>44.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Strength was calculated as a percentage of the contralateral, un-operated arm. Results are reported as mean ± SD, PRP = platelet-rich plasma.*

**Range of Motion**

The analysis revealed no significant differences (p>0.05) in any active range of motion measure between the two groups at 16 weeks post-surgery. Complete values are displayed in Table 5.
Table 5. Group mean scores and t-test results for range of motion for the operated limb at 16 weeks post-surgerya

<table>
<thead>
<tr>
<th>Range of Motion (degrees)</th>
<th>Mean (deg)</th>
<th>SD</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm flexion</td>
<td></td>
<td></td>
<td>1.274</td>
<td>0.208</td>
</tr>
<tr>
<td>PRP</td>
<td>144.8</td>
<td>22.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>151.8</td>
<td>19.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arm abduction</td>
<td></td>
<td></td>
<td>0.342</td>
<td>0.734</td>
</tr>
<tr>
<td>PRP</td>
<td>134.8</td>
<td>28.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>137.4</td>
<td>29.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>External rotation</td>
<td></td>
<td></td>
<td>0.69</td>
<td>0.493</td>
</tr>
<tr>
<td>PRP</td>
<td>41.1</td>
<td>10.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>42.8</td>
<td>9.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a PRP = platelet-rich plasma

DISCUSSION

The purpose of the study was to evaluate the efficacy of a protocol of sequential PRP administration following arthroscopic supraspinatus repair. All previous studies have utilized a single delivery of a PRP product at the time of surgery. The current protocol delivered a PRP product under ultrasound guidance to the tendon repair site at 7 and 14 days after surgery to avoid a possible dilution or washout effect of PRP, which may occur with arthroscopic fluid lavage. This protocol also allows a potentially prolonged up-regulation of growth factors involved in the tendon-healing cascade. Our hypothesis was that this post-surgical and sequential PRP delivery protocol would firstly improve rotator cuff healing and secondly accelerate early functional recovery following arthroscopic rotator cuff repair.

This study finds that at 16 weeks post-surgery, no full thickness tendon re-tears occurred in the PRP group however, there were two (7%) full thickness re-tears in the control
group. Although this difference was not statistically significant, our findings are consistent with previous reports. Castricini, et al. (2012) examined the effects of PRFM augmentation in rotator cuff repair and reported the re-rupture rate was higher in the control group (10.5% versus 2.5%). In contrast, Gumina, et al. (2012), using a novel platelet rich fibrin matrix allowing slow release of growth factors on the tendon repair site, found a 14% re-tear rate in isolated supraspinatus tears (between 2 to 4 cm) in the PRP group compared to 50% in the control group at 13 months. However Rodeo, et al. (2007), also using PRFM in 79 patients undergoing arthroscopic cuff repair found no difference in tendon bone healing on ultrasound at 6 weeks and 12 weeks after surgery.

The secondary outcomes of this study were to evaluate early functional recovery in patients receiving PRP treatment following supraspinatus repair. In a prospective RCT of 53 patients, Randelli, et al. (2011) reported that PRP administered by spray, produced statistically better early function scores and strength at 3 months post-surgery. No imaging was performed at this stage, though it was concluded that PRP administration accelerates early recovery following surgery. Zumstein, et al. (2012) also showed an early benefit of PRP administration with improved revascularization of the tendon-bone repair site. Doppler ultrasonography was used to assess the vascularization index of 20 shoulders at 6 and 12 weeks following surgery (Zumstein, et al., 2012). At 6 weeks, those shoulders treated with a leucocyte rich PRP product showed significantly better vascularization, however this was not sustained at 12 weeks.

Our study can report that early functional recovery was not improved with a sequential post-surgical PRP delivery protocol. At 6, 12 and 16 weeks, clinical function scores were equivalent between PRP and control group participants. Furthermore, objective testing of shoulder function at 16 weeks showed no difference between groups in recovery of
active arm flexion, abduction, or external rotation range of motion. Similarly, isokinetic peak torque and the work done through the active range of motion during each movement was not different between groups.

PRP delivery by injection under ultrasound guidance into the supraspinatus tendon repair site may be less accurate than injection under arthroscopic visualization. However, the surgical technique employed in this study comprised a double row suture bridge technique and the echogenic suture knots were readily identified on ultrasound. Moreover, the oblique and interlocking sutures of the suture bridge potentially retains the injected PRP at the repair site better than the single row repair site technique used in previous studies (Randelli, et al., 2011).

As an imaging modality, ultrasound has been shown to be reliable in obtaining a precise placement of PRP at the site of tendon injury (Wiegerinck, et al., 2011). PRP delivery by direct injection under ultrasound guidance has been used to treat injuries of the Achilles tendon (de Vos et al., 2010), the common extensor tendon origin (Mishra, et al., 2006; Mishra, et al., 2014; Peerbooms, et al., 2010) and the rotator cuff. Kesikburun, et al. (2013) demonstrated that PRP injection to non-surgically treat rotator cuff tendinopathy and partial thickness tendon tears has no significant clinical benefit over saline injections at 3, 6, 12 and 52 weeks. The findings of our study are consistent with this work, and even with a second PRP injection, there was no significant clinical or functional benefit up to 16 weeks post-surgery. Our study focus is early outcomes, however definitive clinical outcomes require 12 to 24 month postoperative evaluation.

This study has some limitations to be acknowledged. Firstly, the follow-up was limited to 16 weeks. It is possible that more structural tendon failures would have been seen if
MRI evaluation was repeated at a later time interval such as 12 months. However, it was the primary aim of this study to assess the effects of PRP treatment on the early phases of tendon healing. Animal models have demonstrated that a significant proportion of Sharpey’s fibres at the tendon repair site have reconstituted and matured at the bone-tendon repair by 3 to 4 months (Sonnabend, et al., 2010), thus supporting the validity of assessment at the 16-week time point.

A second limitation is the non-blinding of subjects in both PRP and control groups. As the study protocol required two separate post-surgical injections, we considered that it would be impractical to have patients agreeing to complete two placebo injections. Patients in the PRP treatment group may have had the benefit of a placebo as well as a possible PRP treatment effect in their clinical and functional evaluation. Similarly, those patients who did not receive injections may have responded differently in clinical testing. The non-blinding of subjects could be expected to cause a positive bias in the PRP group however, groups were equivalent in their study outcomes. MRI evaluation was performed by an independent musculoskeletal radiologist, who had not been involved in previous diagnostic imaging or PRP injections, and was blinded to group allocation.

A further possible study limitation was the PRP product used in this study, does not achieve the very high concentration of platelets reported with some other PRP products (Arnoczky, et al., 2011; Eppely, et al., 2004; Geaney, et al., 2011). Sundman, et al. (2011), in a laboratory study suggested that markedly elevated supra physiological levels of platelets and growth factors may be of no additional benefit due to cell-surface receptor saturation, or may actually be detrimental to tendon healing. Optimal tendon healing requires not only the appropriate concentration of growth factors, but those growth factors
be delivered at the appropriate time in the tendon healing cascade, to be maximally effective.

CONCLUSION

This study is the first to evaluate the efficacy of a post-surgical PRP delivery protocol to improve healing and functional outcomes after arthroscopic rotator cuff repair. Sequential delivery of the specific injectable PRP preparation used in this study under ultrasound guidance, at days 7 and 14 post-surgery, does not improve early rotator cuff healing or functional recovery. Future research should include randomized controlled trials of other PRP products with alternate delivery vehicles and dosing regimes.

REFERENCES


CHAPTER 4
PAPER 2

Early postoperative repair status after rotator cuff repair cannot be accurately classified using questionnaires of patient function and isokinetic strength evaluation.

PREAMBLE

Research conducted by Sonnabend and colleagues (2010), shows the reconstitution and maturation of Sharpey fibres at 3-4 months post rotator cuff repair. Kluger, et al. (2011) have shown that the majority of recurrent tears occurred in the first 3 months following rotator cuff surgery, highlighting that this early tendon healing phase is critical for longer term success. The early confirmation that tendon healing is progressing (or not), is of benefit, and could affect post-surgery management (rehabilitation and/or revision surgery), as well as individual structured return to work and/or sport. It is common to introduce return-to-work strategies at 4 months post rotator cuff repair and therefore, we believe that the prediction of tendon healing at this stage using low cost functional and strength outcomes could prove beneficial.

The post-operative use of MRI and/or US to evaluate rotator cuff repair tendon healing can be costly and time consuming. Studies have investigated the diagnostic accuracy of common clinical shoulder tests for conservatively treated rotator cuff tendon tears, and concluded that most tests are inaccurate and cannot be recommended for clinical diagnosis (Ainsworth & Lewis, 2007; Hughes, et al., 2008; Murrell & Walton, 2001; Hegedus, et al., 2008; 2012). This may well be the case post-operatively, and more robust testing in this area is required (Hegedus, et al., 2008; 2012).
As the results of Wang, et al. (2015) showed no significant difference between the PRP and control groups in structural tendon healing, function or strength outcomes, we saw an opportunity to combine the original groups into one cohort, to further investigate this gap in the research.

REFERENCES


Early post-operative repair status after rotator cuff repair cannot be accurately classified using questionnaires of patient function and isokinetic strength evaluation.

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\(^4\) Perth Radiological Clinic, Subiaco, Perth, Western Australia.

**Level of Evidence:** Level IV prospective study.

**ABSTRACT**

**Purpose:** To investigate if patients with an intact repair or partial re-tear in the early stages (16 weeks) after rotator cuff repair surgery display differences in common shoulder patient-reported outcome (PRO) measures and isokinetic strength tests, and whether early post-surgical tendon healing could be predicted using these clinical shoulder evaluations.

**Methods:** This study was undertaken in 60 patients undergoing arthroscopic double-row supraspinatus tendon repair. All patients were assessed clinically at 16 weeks post-
surgery using the Oxford Shoulder Score, the Quick Disability of the Arm, Shoulder and Hand (QuickDASH), a Visual Analogue Pain Scale and the 12-item Short Form Health survey, as well as isokinetic strength evaluation (external humeral rotation and arm flexion). Magnetic Resonance Imaging (MRI) was undertaken at 16 weeks post-surgery. Independent t-tests were employed to investigate clinical differences in patients group-stratified based on the Sugaya MRI classification for rotator cuff tears (Grades 1, 2 or 3). Discriminant analysis was employed to determine whether intact repairs (Sugaya Grade 1) and partial re-tears (Sugaya Grades 2 and 3) could be predicted based on clinical scores.

**Results:** No significant differences (p<0.05) in any of the PRO or strength measures were observed between groups at 16 weeks post-surgery. Discriminant analysis revealed the QuickDASH alone produced a 97% true positive rate for predicting partial re-tears, but also a 90% false positive rate. The ability to discriminate between groups was enhanced with up to five variables entered; however, only 87% of the partial re-tear group, and 36% of the intact repair group, were correctly classified.

**Conclusion:** We observed no difference in clinical scores between patient groups stratified by the Sugaya MRI classification system at 16 weeks post-surgery, while the presence of an intact repair or partial re-tear after surgery could not be accurately predicted by these shoulder evaluations. Our results suggest that correct classification of tendon healing in the early stage following surgery must involve medical imaging.

**Keywords:** rotator cuff repair surgery, shoulder, patient-reported outcome measures, isokinetic strength, magnetic resonance imaging.
INTRODUCTION

Rotator cuff surgical repair is common with in excess of 250,000 performed each year (Gulotta & Rodeo, 2009). However, despite several proposed surgical techniques and the increasing use of adjunct biological therapies to stimulate and/or enhance repair, the post-operative failure rate remains relatively high (Barber, et al., 2011; Charousset, et al., 2010; Cheung, et al., 2010). It is well documented in the literature that increased patient age, tear size and severity of pre-operative fatty muscular degeneration contribute to an increased incidence of post-operative rotator cuff re-tears (Boileau, et al., 2005; Cho & Rhee, 2009; Cho, et al., 2010; Galatz, et al., 2004; Murrell & Walton, 2001; Oh, et al., 2010). While patients with re-tears or failed healing may experience a reduction in pain, functional outcomes including strength levels are significantly lower when compared to patients with evidence of healed tendons (Boileau, et al., 2005; Cho & Rhee, 2009; Galatz, et al., 2004; Harryman, et al., 1991; Sugaya, et al., 2007). These inferior functional results may be satisfactory for an older and/or less active population, but for patients requiring a return to sport or work, especially in roles where physical strength is important, many are likely to be dissatisfied with the outcome.

In a primate model of rotator cuff repair, it has been shown that a significant proportion of Sharpey fibres start to reconstitute at 3 months, with maturation seen at four months (Sonnabend, et al., 2010). Kluger, et al. (2011) reported that the majority of recurrent tears occurred in the first three months after rotator cuff surgery, highlighting that this early tendon healing phase up to 3-4 months post-operatively is critical for longer term success. Early confirmation that healing is progressing well (or not) is therefore of benefit, and could affect post-surgery management (rehabilitation and/or re-operation), as well as the patient’s individualised structured return to work and/or sport. For the
aforementioned reasons, it is commonplace to introduce return-to-work strategies at four months post-surgery and, therefore, prediction of tendon-healing at this stage using low cost functional and strength outcomes could prove beneficial.

The use of post-operative magnetic resonance imaging (MRI) and/or ultrasound (US) to evaluate the outcome of rotator cuff surgery can be costly and time consuming. Several researchers have attempted to determine whether the healing progress of a conservatively treated rotator cuff tendon tear can be predicted using common, clinical shoulder assessments, albeit with limited success (Ainsworth & Lewis, 2007; Hughes, et al., 2008; Murrell & Walton, 2001). At the time of writing, the authors are unaware of any other studies that have investigated the ability of common shoulder clinical assessments to predict the early post-operative success of rotator cuff repair surgery, independent of radiological assessment (MRI and/or US).

Therefore, this study aimed to: a) investigate if differences in common shoulder patient-reported outcome (PRO) measures and isokinetic strength tests could be observed between patients with intact repairs or partial re-tears, classified by MRI, at 16 weeks after rotator cuff repair surgery, and; (b) determine if early post-surgical tendon healing could be predicted using these PRO measures and strength tests alone, without the need for radiological assessment.

**METHODS**

**Patients**

Between November 2011 and February 2013, patients with rotator cuff tears isolated to the supraspinatus, confirmed via US or MRI, were invited to participate in this project.
This study was part of a larger, published randomized controlled trial (RCT) that sought to ascertain whether platelet-rich plasma (PRP) applied to the tendon repair site after double-row arthroscopic supraspinatus repair (PRP group), improved early tendon healing and functional recovery, compared to no adjunct post-operative treatment (control group) (Wang, et al., 2015). Therefore, inclusion and exclusion criteria for this RCT have been published (Wang, et al., 2015). In brief, inclusion criteria required patients to have a symptomatic full thickness tear of supraspinatus, confirmed pre-operatively via MRI or US and intra-operatively by arthroscopic evaluation. Patients with supraspinatus partial tears or tears over 20 mm in the anteroposterior dimension were excluded, as were patients with concomitant subscapularis and/or infraspinatus tears identified on pre-operative US/MRI or intra-operative examination. Patients were excluded if they had a history of previous rotator cuff surgery, labral tearing, significant osteoarthritis of the glenohumeral joint, rheumatological, neuromuscular or autoimmune disease and/or cervical disc herniation. Patients were further excluded if they presented with any contralateral shoulder symptoms or had ongoing workers’ compensation claims.

Over the study recruitment period, a total of 305 patients were assessed for study eligibility. A CONSORT (Consolidated Standards of Reporting Trials) flowchart has been previously published (Wang, et al., 2015). As part of the primary RCT, (Wang, et al., 2015) all patients that consented to the study and subsequently underwent supraspinatus repair, were reviewed on the fifth post-operative day and then randomized by a computer block permutation method into either the PRP injection group or the control group. Therefore, a total of 60 consecutive patients (30 PRP; 30 control) meeting the study inclusion criteria and consenting to the study were randomized via the aforementioned procedure. Patient demographics with concomitant surgical procedures are presented in Table 1. A priori power calculation was performed for the primary RCT.
(Wang, et al., 2015) which indicated that for an anticipated moderate effect size of 0.769 in the primary outcome variable (the Sugaya classification system of rotator cuff tear severity (Sugaya, et al., 2007)), a total of 56 patients (28 PRP; 28 control) were required to reveal differences at the 5% significance level, with 80% power. Therefore, a total of 60 participants were initially recruited to allow for attrition. This research was approved by the relevant Institutional Review Board (IRB).

Table 1. Group demographics with details of concomitant procedures and complications.

<table>
<thead>
<tr>
<th></th>
<th>PRP Group (n=30)</th>
<th>Control Group (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male/female)</td>
<td>11/19</td>
<td>17/13</td>
</tr>
<tr>
<td>Mean age (years) [range]</td>
<td>59.8 [28-77]</td>
<td>58.4 [38-76]</td>
</tr>
<tr>
<td>Acromioplasty (n)</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Biceps tenotomy (n)</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Acromioclavicular joint excision (n)</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Complications (n)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Supraspinatus tear size (mm)</td>
<td>14.6 (3.8)</td>
<td>13.7 (3.4)</td>
</tr>
</tbody>
</table>

PRP = Platelet Rich Plasma.

Surgical Technique

All surgery was performed by the senior author and has been previously published (Wang, et al., 2015). Briefly, all procedures were performed in the lateral decubitus position under general anesthesia with an interscalene nerve block. The arm was placed in 4 kg of traction and positioned in 30° of arm flexion and abduction. The presence of a full thickness supraspinatus tear was initially confirmed via diagnostic glenohumeral arthroscopy. Tear type and size were assessed using a calibrated probe with 5 mm increments, following debridement of bursal tissue and tendon margins. After
acromioplasty, rotator cuff reconstruction was performed. The footprint was prepared with a full-radius resector to decorticate the greater tuberosity. A double-row suture-bridge repair (Park, et al., 2006) technique with bioabsorbable anchors was performed (Arthrex Bio-Corkscrew 5.5 mm–FT, Biocomposite Pushloc 3.5 mm; Arthrex) in all cases. Concomitant shoulder injuries were treated as clinically or radiographically indicated. Acromioclavicular joint arthropathy was treated with arthroscopic excision of the lateral end of the clavicle, and long head of biceps tendinopathy was treated with tenotomy (Table 1).

**Post-operative Management**

All patients were immobilized in an abduction sling (Ultrasling III, Don Joy, Carlsbad, CA, USA) for 6 weeks post-operatively and underwent a standard rehabilitation program under the supervision of a physical therapist. Briefly, patients underwent an initial 6 weeks of passive range of motion exercises, followed by active-assisted range of motion exercises from 6-10 weeks and a conservative strengthening program from 10-16 weeks. All patients followed the aforementioned protocol consistently.

**Patient-reported Outcome (PRO) Measures**

Four PRO measures were employed pre- and post-operatively at 16 weeks, including: 1) the Oxford Shoulder Score (OSS); 2) the Quick Disability of the Arm, Shoulder and Hand (QuickDASH) questionnaire; 3) a Visual Analogue Pain Scale (VAS), and; 4) the 12-item Short Form Health survey (SF-12). Firstly, the OSS is a 12-item questionnaire evaluating pain and function, which has been validated against both general health and clinical measures and has demonstrated good reliability in evaluating outcome after
shoulder surgery (Dawson, et al., 1996; Dawson, et al., 2001; Olley & Carr, 2008). The QuickDASH is an 11-item questionnaire evaluating pain, symptoms and physical function in patients with upper limb musculoskeletal disorders, (Beaton, et al., 2005) and has also demonstrated good reliability, validity and responsiveness (Beaton, et al., 2005; Gummesson, et al., 2006). The VAS required patients to rate their pain intensity on a 0-10cm sliding scale (0 = no pain, 10 = worst pain imaginable) in the preceding 24 hours. A 1.4cm improvement on the VAS has previously been reported as the minimal clinically important change in patients undergoing non-operative treatment for rotator cuff disease (Tashjian, et al., 2009). Finally, the SF-12 is a generic health-related quality of life score, (Ware, et al., 1996) that produces a physical (PCS) and mental (MCS) component subscale.

Isokinetic Strength Evaluation

Isokinetic strength was assessed at 16 weeks post-surgery in all patients using a Biodex Isokinetic Dynamometer (Biodex, System 4, Shirley, NY). Patients were seated with the trunk stabilized using rigid straps, and adjustments made for humeral and forearm length, in accordance with each patient’s stature. Patients were instructed to undertake maximal concentric external/internal humeral rotation (Figure 1), followed by arm flexion, at an angular velocity of 60°/s. External/internal humeral rotation was performed in the modified-neutral position, with the elbow in 90° of flexion and the forearm in a neutral position. Arm flexion was performed with the elbow fully extended. Each trial consisted of three maximal repetitions. Two trials on each upper limb were undertaken, alternating between the non-operated and operated limbs, with the first trial always undertaken on the non-operated side. During each maximal effort, patients were asked to perform to their maximal muscle strength, while verbal encouragement was provided, standardized
across all patients and trials. Patients were given adequate rest in between trials to minimize fatigue, though this was not standardized and based upon the patient’s individual readiness to proceed. For all trials, the peak torque (Nm), time to peak torque (secs) and total work (J) performed over the range of motion were obtained, and data were recorded as absolute values.

Figure 1. A patient performing humeral (A) internal and (B) external rotation on the Biodex Isokinetic Dynamometer.
Radiological Evaluation

Radiographic analysis was performed with MRI at 16 weeks post-surgery. All scans utilized a 1.5T unit (Sonata Maestro Class; Siemens, Erlangen, Germany) with 40mT/m gradient power. Multiple images were obtained in oblique coronal, oblique sagittal and axial planes with both short-tau inversion recovery (STIR) and turbo spin echo (TSE) T1-weighted sequence. MRI assessment was performed by an experienced radiologist, who did not perform the PRP injections as part of the primary RCT and was therefore blinded to patient group allocation. MR images were graded as per the Sugaya classification (Sugaya, et al., 2007): Grade 1 = no tear; Grade 2 = sufficient tendon thickness but with high signal change; Grade 3 = insufficient thickness but no tendon discontinuity; Grade 4 = small full-thickness re-tear; Grade 5 = large full-thickness re-tear.

Statistical Analysis

Firstly, statistical procedures were performed with both groups as part of the primary RCT (PRP and control) pooled together (n=60). Independent sample t-tests were initially employed to determine if partial thickness tendon re-tears led to poorer strength and functional scores, compared to an intact repair. Participants were grouped according to their 16-week post-operative MRI Sugaya grading (Grade 1, 2 or 3), while those with Grade 4 or 5 were omitted from the analysis (n=2). Group means (SD) for the Sugaya grading classifications were presented.

A series of discriminant analyses were employed to determine if the Sugaya grading (presence and severity of a tear) could be predicted using PRO measures and/or strength data. Linear combinations of predictor variables were formed to serve as the basis for
classifying cases into two groups: a partial re-tear group (Sugaya Grades 2 and 3) and an intact repair group (Sugaya Grade 1). When using discriminant analysis, it is recommended that the number of variables should be used so that there are data for at least three subjects per variable, and the number of variables should not exceed the number of subjects in the smallest group (Carter & Ackland, 1998; Tatsuoka, 1971). These requirements were satisfied in our analysis. The discriminant analysis used the method of Wilks’ lambda and a stepwise forward inclusion model. Analyses were evaluated in terms of a high eigenvalue, high canonical correlation squared, low and significant Wilks’ lambda (p<0.001), and a high percentage of correctly classified subjects, as suggested by Carter and Ackland (1998), and successful classification would be above 80%. We began the analysis with the variable that had the highest prediction (QuickDASH), and then added variables to a maximum of five. Statistical analysis was performed using SPSS software (SPSS, Version 22.0, SPSS Inc., USA), while statistical significance was determined at $P < 0.05$.

RESULTS

Group means (SD) are presented for patients classified by Sugaya Grades 1 (n=21, 35%), 2 (n=23, 38%) or 3 (n=14, 23%), and these groups were compared at 16 weeks post-surgery (Table 2). One patient did not tolerate the post-operative MRI scan due to claustrophobia, instead undergoing an US performed by an experienced musculoskeletal radiologist. This tendon repair was intact, with no evidence of thinning or discontinuity, so for the purpose of this study it was included in the Grade 1 Sugaya classification. No significant differences (p>0.05) in PRO or isokinetic strength measures were observed between these three groups based on the Sugaya tear classification system, at 16 weeks post-surgery.
Table 2. Mean (SD) scores for the patient-reported outcome (PRO) and isokinetic maximal strength measures (at an angular velocity of 60°/s) employed, for patients with intact (Grade 1) and partial (Grade 2 and 3) supraspinatus tendon re-tears. Independent sample t-test comparisons are provided between groups (p values).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sugaya Classification</th>
<th>Group Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade 1 (n=21)</td>
<td>Grade 2 (n=23)</td>
</tr>
<tr>
<td>OSS</td>
<td>38.9 (6.4)</td>
<td>39.2 (5.1)</td>
</tr>
<tr>
<td>VAS</td>
<td>1.5 (1.4)</td>
<td>1.3 (1.3)</td>
</tr>
<tr>
<td>QuickDASH</td>
<td>21.9 (12.4)</td>
<td>17.5 (11.9)</td>
</tr>
<tr>
<td>SF-12 (PCS)</td>
<td>42.1 (8.1)</td>
<td>42.7 (5.8)</td>
</tr>
<tr>
<td>SF-12 (MCS)</td>
<td>53.7 (11.6)</td>
<td>55.3 (7.7)</td>
</tr>
<tr>
<td>Arm Flexion Peak Torque (Nm)</td>
<td>77.1 (22.6)</td>
<td>76.5 (15.4)</td>
</tr>
<tr>
<td>Arm Flexion Total Work (J)</td>
<td>61.7 (26.5)</td>
<td>63.2 (21.3)</td>
</tr>
<tr>
<td>External Humeral Rotation Peak Torque (Nm)</td>
<td>75.8 (21.2)</td>
<td>71.1 (16.8)</td>
</tr>
<tr>
<td>External Humeral Rotation Total Work (J)</td>
<td>68.2 (49.5)</td>
<td>53.7 (22.7)</td>
</tr>
</tbody>
</table>

OSS = Oxford Shoulder Score; VAS = Visual Analogue Pain Scale for pain; QuickDASH = Quick Disability of the Arm, Shoulder and Hand; SF-12 = 12-item Short Form Health survey; PCS = Physical Component Subscale; MCS = Mental Component Subscale.

Descriptive statistics for the intact (Grade 1) and partial re-tear (Grade 2 and 3 pooled) groups are shown in Table 3. At 16 weeks post surgery, mean scores for strength and function for the intact repair group compared to the partial re-tear group were not
significant. Discriminant analysis results in Table 4 revealed the QuickDASH alone produced a 97% true positive rate for predicting partial re-tears, but also a 90% false positive rate. The ability to discriminate between groups was enhanced with up to five variables entered; however, only 87% of the partial re-tear group, and 36% of the intact repair group were correctly classified.

Table 3. Descriptive statistics (mean ± SD) for patients with intact repairs (Grade 1) and partial (Grade 2 and 3 pooled) supraspinatus tendon re-tears.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intact repair Group (n=21)</th>
<th>Partial re-tear Group (n=37)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>OSS</td>
<td>38.9 ± 6.4</td>
<td>40.1 ± 6.3</td>
<td>39.6 ± 6.3</td>
</tr>
<tr>
<td>VAS</td>
<td>1.5 ± 1.4</td>
<td>1.4 ± 1.6</td>
<td>1.4 ± 1.5</td>
</tr>
<tr>
<td>QuickDASH</td>
<td>20.9 ± 12.4</td>
<td>18.1 ± 14.6</td>
<td>19.2 ± 13.7</td>
</tr>
<tr>
<td>External Humeral Rotation Peak Torque (Nm)</td>
<td>76.9 ± 20.6</td>
<td>75.0 ± 19.9</td>
<td>75.7 ± 20.0</td>
</tr>
<tr>
<td>Arm Flexion Peak Torque (Nm)</td>
<td>77.3 ± 22.0</td>
<td>76.0 ± 17.0</td>
<td>76.5 ± 18.9</td>
</tr>
<tr>
<td>Time to Peak Torque for External Humeral Rotation (s)</td>
<td>0.54 ± 0.45</td>
<td>0.60 ± 0.42</td>
<td>0.58 ± 0.43</td>
</tr>
</tbody>
</table>

OSS = Oxford Shoulder Score; VAS = Visual Analogue Pain Scale for pain; QuickDASH = Quick Disability of the Arm, Shoulder and Hand.
Table 4. Discriminant analysis for variables predicting an intact repair (n=21, Grade 1 Sugaya Classification) or partial re-tears (n=37, Grade 2 and 3 Sugaya Classification).

<table>
<thead>
<tr>
<th>Prediction variables entered ²</th>
<th>Statistic ¹</th>
<th>Number Classified (%)</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>Actual Group Membership</th>
<th>Predicted Group Membership</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EV</td>
<td>CC</td>
<td>WL</td>
<td>Sig</td>
<td></td>
<td></td>
<td>Intact repair</td>
<td>Partial re-tear</td>
</tr>
<tr>
<td>A. QuickDASH</td>
<td>0.011</td>
<td>0.104</td>
<td>0.989</td>
<td>0.465</td>
<td></td>
<td></td>
<td>2 (10%)</td>
<td>19 (90%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 (3%)</td>
<td>30 (97%)</td>
</tr>
<tr>
<td>B. QuickDASH, ER Pk Tq</td>
<td>0.034</td>
<td>1.82</td>
<td>0.967</td>
<td>0.429</td>
<td></td>
<td></td>
<td>4 (18%)</td>
<td>18 (82%)</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3 (10%)</td>
<td>28 (90%)</td>
</tr>
<tr>
<td>C. QuickDASH, ER Pk Tq, OSS</td>
<td>0.039</td>
<td>0.194</td>
<td>0.962</td>
<td>0.594</td>
<td></td>
<td></td>
<td>5 (23%)</td>
<td>17 (77%)</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>4 (13%)</td>
<td>27 (87%)</td>
</tr>
<tr>
<td>D. QuickDASH, ER Pk Tq, OSS, TPT ER</td>
<td>0.045</td>
<td>0.207</td>
<td>0.957</td>
<td>0.717</td>
<td></td>
<td></td>
<td>7 (32%)</td>
<td>15 (68%)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4 (13%)</td>
<td>26 (87%)</td>
</tr>
<tr>
<td>E. QuickDASH, ER Pk Tq, OSS, TPT ER, AF Pk Tq</td>
<td>0.045</td>
<td>0.207</td>
<td>0.957</td>
<td>0.837</td>
<td></td>
<td></td>
<td>8 (36%)</td>
<td>14 (64%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4 (13%)</td>
<td>26 (87%)</td>
</tr>
</tbody>
</table>

¹ EV = eigenvalue, CC = canonical correlation, WL = Wilks’ lambda, Sig = prediction significance of the discriminant function.
² ER Pk Tq = Peak torque for humeral external rotation at $60^\circ /s$; AF Pk Tq = Peak torque for arm flexion at $60^\circ /s$; TPT ER = time to peak torque in humeral external rotation.
DISCUSSION

The use of post-operative MRI and/or US to evaluate the outcome of rotator cuff surgery can be costly and time consuming. Several researchers have attempted to determine whether the healing progress of a conservatively treated rotator cuff tendon tear can be predicted using common, clinical shoulder assessments, with little success (Ainsworth & Lewis, 2007; Hughes, et al., 2008; Murrell & Walton, 2001). This study aimed to: a) investigate if differences in common shoulder PRO measures and isokinetic strength tests could be observed between patients with intact or partial re-tears, classified by MRI, at 16 weeks after rotator cuff repair surgery, and; (b) determine if early post-surgical tendon healing could be predicted using these PRO measures and strength tests alone, without the need for radiological assessment.

This study found no significant difference in the employed shoulder PRO measures, nor isokinetic strength evaluation, between patient groups stratified by the Sugaya MRI classification system (Grades 1, 2 or 3) for rotator cuff tears at 16 weeks post-surgery. Studies have investigated the diagnostic accuracy of clinical tests for rotator cuff pathology (Hegedus, et al., 2008; Hegedus, et al., 2012; Hughes, et al., 2008), and concluded that most tests are inaccurate and cannot be recommended for clinical diagnosis alone. This may well be the case post-operatively, and more robust testing in this area is required. When employing radiology to investigate rotator cuff pathology, it has been reported in a number of studies that both US and MRI are accurate in the detection of rotator cuff lesions (Kluger, et al., 2003; Teefey, et al., 2004). Codsi, et al. (2014) suggested US was comparable to MRI when evaluating rotator cuff integrity, and that post-surgical US results should be compared with MRI results for a period of time before relying solely on US for diagnosis. However, Ardic, et al. (2006) reported MRI
to be superior to US, while Goldberg, et al. (2003) reported that US was not a reliable tool for diagnosing full thickness rotator cuff tears. Sonnabend, et al. (1997) reported on the accuracy of US in diagnosing full thickness rotator cuff tears and as a “useful adjunct” in the diagnosis of partial tears; however, they also noted it was operator-dependent. For these reasons, we chose to use MRI for confirmation of tendon healing.

The discriminant analysis showed the QuickDASH alone produced a 97% true positive rate for predicting partial re-tears, but also a 90% false positive rate, revealing the test to be sensitive but not specific. The addition of other shoulder PRO measures or isokinetic strength evaluations did not greatly improve the predictive capability of the patient’s early tendon repair outcome, and so we must conclude that combining such measures does not give confidence in the diagnosis of partial re-tears. At this stage, we must conclude that some form of radiological assessment (MRI or US) be used for this purpose. However, it should also be noted that the concurrent use of shoulder-specific PRO measures and/or strength evaluation remain important in guiding the rehabilitation process after rotator cuff repair, as well as the patient’s specific return to work or sport. Furthermore, while Nho, et al. (2009) reported that 100% of re-tears occurred in the first three months post-surgery, Kluger, et al. (2009) reported that most early post-operative re-tears appear to be a failure to heal, and that repair site integrity at six months was a predictor of 7-year clinical outcome. Therefore, based on our results and pre-existing literature, if a patient has a QuickDASH score that is greater (i.e. worse) than the mean value we report at 16 weeks post-surgery, then it may be likely they have incomplete healing or partial re-tearing of the tendon. This would then warrant adjunct radiological assessment. While these results suggest that PRO measures and shoulder strength in a patient with a completely intact repair is equivalent to that of a partial re-tear, at least at 16 weeks post-surgery, the natural history in ongoing high demand work or sport is for partial tears to
deteriorate. Therefore, subsequent imaging in these patients may allow for a decelerated rehabilitation program or vocational counselling on restricted work duties and prognosis.

This study has some acknowledged inherent limitations. Firstly, the patient follow-up was limited to 16 weeks. Research by Sonnabend, et al. (1997) has previously demonstrated that a significant portion of Sharpey fibres have reconstituted and matured at the tendon repair site by 3-4 months. Furthermore, accurate classification of rotator cuff tendon healing has been suggested to be importance at this time as it affects the rehabilitation strategy, especially for patients who intend to return to employment in physical work or to physically demanding sports. However, if MRI evaluations were to be repeated at a later time (such as 12 months) it is possible that more structural tearing may be observed, contributing to more pain and diminished function. While the primary aim of this study was to assess early post-operative tendon healing, future research may include a longer-term follow-up.

A second limitation may result from the primary RCT, whereby half of this patient cohort received two PRP injections post-surgery. However, as reported previously there were no differences observed between the PRP and control groups at 16 weeks post surgery in any of the assessments employed, including the shoulder-specific PRO measures, shoulder range of motion, isokinetic strength evaluation and MRI-based assessment (Wang, et al., 2015). This result created the opportunity to combine the original groups (PRP or control) into one cohort for this analysis.

Thirdly, we employed PRO instruments used routinely through our clinical practice and research, and we appreciate other shoulder-specific scores are available. It is possible that differences (or an improved predictive capacity) may be observed in other clinical
and functional shoulder evaluations. Fourthly, strength tests also have some inherent limitations as they are unable to differentiate between true muscular weakness and pain-related weakness (Bigoni, et al., 2009). The results of the isokinetic strength tests also rely upon a maximal effort being made by the patient. While clear, standardized instructions and verbal encouragement were provided to all participants, it must be acknowledged that this was the first time many of the patients would have maximally stressed their operated limb since surgery, and some may have been hesitant to exert maximal effort. Protocols for future research may require a familiarisation session prior to the testing session. Furthermore, Bigoni, et al. (2009) has previously reported that isokinetic strength testing is a powerful tool for evaluating strength following rotator cuff surgery, so it may be that alternate testing protocols, incorporating shoulder abduction, may more accurately discriminate between groups.

**CONCLUSION**

This study found no significant difference in the employed shoulder PRO measures, nor isokinetic strength evaluation, between patient groups stratified by the Sugaya MRI classification system for rotator cuff tears at 16 weeks post-surgery. Furthermore, the presence of an intact repair or partial re-tear after rotator cuff surgery could not be accurately predicted by these clinical and functional shoulder evaluations. Our results suggest that correct classification of tendon healing in the early stage following rotator cuff surgery must involve medical imaging. This will give confidence in patient management of appropriate return-to-work and/or sport rehabilitation programs. Reliance on PRO measures and/or functional scores alone to make an accurate assessment is not supported by our data.
REFERENCES


CHAPTER 5

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

The main purpose of this thesis was to investigate the effect of PRP injections following rotator cuff repair surgery on early tendon healing and functional recovery. Current research in the area of PRP augmentation following rotator cuff repair surgery remains controversial. This is complicated by a lack of standardisation of PRP products, differences in timing of delivery protocols, and optimal platelet concentrations. The research investigated if delayed and repeated PRP injections would accelerate the early structural healing following surgical repair of supraspinatus tendon as well as improving patient function and strength (see Paper 1 in Chapter 3). In addition, the research also aimed to determine if early post-surgery tendon healing could be predicted independently of an MRI scan, using a combination of patient-reported functional and quality of life questionnaires and isokinetic strength data (see Paper 2 in Chapter 4).

In Paper 1 a prospective, randomised controlled study design was used to investigate radiological and functional assessment up to and including 16 weeks post rotator cuff repair surgery in 60 patients (30 treatment, 30 control group). Patients randomly assigned to the treatment group received two PRP injections under guided-US (at 7 and 14 days post-surgery), while the control group received no placebo injection. MRI was used to assess the structural tendon healing at 4 months, with rotator cuff appearances graded according to the Sugaya classification. Functional assessment was undertaken pre-surgery, and at 6, 12 and 16 weeks post-surgery. These included the OSS, QuickDASH, VAS and SF-12 inventories. Isokinetic strength and ROM were also measured at 16 weeks post-surgery.
No significant difference was observed in structural healing of the tendon at 16 weeks between the treatment and control groups, a finding that did not support our first hypothesis. Functional outcome scores improved in all patients following surgery - at 12 and 16 weeks the OSS, VAS and SF-12 improved significantly from pre-surgery. However, no significant difference was observed in the functional scores between the treatment and control groups at any of the post-surgery time points. In addition, no significant difference was observed for strength or ROM between the groups at 16 weeks. This finding did not support the second hypothesis of Paper 1, that PRP would improve early function and strength compared to the control group.

Participants from Paper 1 were able to be pooled for analysis in Paper 2 since no significant differences were observed between the treatment and control groups in MRI classification, patient reported functional scores and isokinetic strength (Wang et al., 2015). Paper 2 aimed to determine if it were possible to predict the success of the tendon repair at 16 weeks post-surgery without the costly and time-consuming requirement of MRI. Previous research had shown that Sharpey fibres begin to reconstitute at 3 months, with maturation seen at 4 months. Furthermore, it was reported that the majority of recurrent tears occurred in the first 3-4 months (Kluger, et al., 2011; Miller, et al., 2011; Nho, et al., 2009); highlighting this early tendon healing phase as being critical for long-term success. Prediction of tendon healing at this early stage using low cost strength and functional outcomes could prove useful, as this could influence early post-surgical management as well as the patient’s individual return to work and/or sport strategy. Paper 2 sought to determine if differences in patient shoulder function and strength could be detected for those patients with partial tendon re-tears compared to those with intact repairs 16 weeks post surgery, regardless of their initial PRP group allocation. The second aim of Paper 2 was to determine if patients with partial re-tears and incomplete healing
could be predicted based on function and strength alone, without the need for early post-surgery imaging.

No significant differences were observed in patient shoulder function or isokinetic strength at 16 weeks post rotator cuff repair between those with an intact repair and those with a partial tendon re-tear; this finding did not support the first hypothesis of Paper 2. Discriminant analysis showed that while the QuickDASH produced a 97% true positive rate for predicting partial re-tears, it also produced a 90% false positive rate. With the addition of up to five variables entered, the ability to discriminate between intact repairs and partial re-tears was enhanced; only 87% of the partial re-tear group and 36% of the intact repair group were correctly classified, thus not supporting the second hypothesis. The results of this study suggest that correct classification of early tendon healing following rotator cuff repair surgery must involve medical imaging.

A number of limitations should be acknowledged within these studies. Firstly, the patient follow-up period was limited to 16 weeks. Research has previously demonstrated that a significant proportion of Sharpey fibres have reconstituted and matured at the tendon-repair site by 3-4 months (Sonnabend, et al., 2010). Also, accurate classification of rotator cuff tendon healing has been suggested to be important at 16 weeks, as it affects the rehabilitation strategy, especially for those returning to physically demanding employment or sports. However, we acknowledge that should MRI evaluations be repeated at a later time, more structural tearing may be observed, which would contribute to more pain and decreased function. While this study focused on the early assessment of tendon healing, future research should include a longer follow-up period.
Patients were not blinded as to their grouping in Paper 1, as it was considered impractical to having patients complete two placebo injections. Patient knowledge of their intervention group may cause a positive bias among members of the PRP group, however, both groups were equivalent in terms of the study outcomes. An independent, experienced radiologist who was blinded to the participants’ group allocation, and who was not involved in the PRP injections, performed all MRI evaluations.

The PRP product used in Paper 1 does not achieve the high concentration of platelets that some other commercially available PRP products report. However, it has been suggested that markedly elevated supra physiological levels of platelets and growth factors may not be of benefit, and could in fact be detrimental to tendon healing (Barber, et al., 2011; Sundman, et al., 2011). Optimal tendon healing requires the appropriate concentration of growth factors, as well as appropriate timing of delivery in the tendon-healing cascade in order to be maximally effective. This highlights the need for a standardised protocol to be developed for future research.

The functional scores used in both papers are used routinely in clinical practice and research, however, we appreciate there are other shoulder-specific scores available, and it is possible that differences, or an improved prediction capacity, may be observed with other clinical shoulder evaluations. Strength tests also have some inherent limitations, as they are unable to differentiate between true muscular weakness and pain-related weakness (Bigoni, et al., 2009). The results of the isokinetic strength tests also rely on a maximal effort being made by the patient. Whilst clear, standardised instructions and verbal encouragement was provided, it is acknowledged that some patients may have been hesitant to exert maximal strength. The tests undertaken at 16 weeks post-surgery were the first time most patients would have maximally exerted their shoulder since their
operation. Future research protocols might require a familiarisation session prior to the testing session. Furthermore, isokinetic strength testing has been reported to be a powerful tool for evaluating strength following rotator cuff surgery (Bigoni, et al., 2009), so it may be that alternate testing protocols, incorporating shoulder abduction could be considered in future research. We did not include shoulder abduction in our protocol as it was considered too early post-surgery to directly stress the repaired tendon.

A perceived limitation of Paper 2 may result from the primary RCT (Paper 1), where half of the cohort received two PRP injections post-surgery. However, as previously reported, there were no observed differences in any of the outcome measures between the PRP and control groups at 16 weeks post-surgery (Wang, et al., 2015). This result created the opportunity for us to combine the original groups into one cohort for this analysis.

This is the first study to our knowledge that evaluated the efficacy of a post-surgical PRP delivery protocol to improve tendon healing and functional outcomes following rotator cuff repair. While this research reiterated that PRP injections post rotator cuff surgery are safe, we concluded that PRP does not accelerate early tendon healing nor improve functional or strength outcomes. Future research might include randomised controlled trials of other commercially available PRP products with alternative delivery vehicles and dosing regimes, and with longer post-surgery follow-up.
REFERENCES


APPENDIX 1

UNIVERSITY OF WESTERN AUSTRALIA NOTIFICATION OF RESEARCH

PROPOSAL APPROVAL
Dear Miss Colliver

RESEARCH PROPOSAL - MASTER OF SCIENCE - RESEARCH

I am pleased to inform you that the Board of the Graduate Research School has considered your Research Proposal and, it is accepted without the requirement for changes or clarification.

In addition your research proposal is accepted subject to:

- Your proposal indicates that approval from UWA Human Research Ethics Committee, is currently being sought in relation to your research. Until you provide us with notification that you have approval, or otherwise, from the UWA Human Research Ethics Committee, the status of your research proposal will be marked as provisional.

The supervisors for your research are recorded as being:

- **Coordinating supervisor:** Winthrop Professor T Ackland (40%)
- **Co supervisor:** Prof A Wang (40%)
- **Co supervisor:** Adj/A/Prof B Joss (20%)

On behalf of the Board please accept my best wishes for the remainder of your candidature.

Yours sincerely

Barbara Telfer
Administrative Officer, Candidature

cc Professor A Gordon (Graduate Research Coordinator)  
Winthrop Professor T Ackland

SCHOOL OF SPORT SCIENCE, EXERCISE AND HEALTH

**Students please note:**
* Please activate your UWA student email account and check it regularly. [http://www.its.uwa.edu.au/student/email](http://www.its.uwa.edu.au/student/email)

Click on the "Course and Unit" link in the list on the left side of the page, and you should see your current and previous courses displayed. For the course in which you are enrolled currently, click on the "Milestones" link under the course details. You will see your list of milestones and the current status of each. There is a description of what each milestone status means. If you believe that there is an error in the list, please contact barbara.telfer@uwa.edu.au. Please note that your re-enrolment each year is dependent on all your milestones being up to date.
APPENDIX 2

UNIVERSITY OF WESTERN AUSTRALIA NOTIFICATION OF ETHICS APPROVAL
Dear Professor Ackland

HUMAN RESEARCH ETHICS OFFICE – RECOGNITION OF ETHICS APPROVAL FROM ANOTHER HUMAN RESEARCH ETHICS COMMITTEE

Project: Does autologous conditioned plasma enhance rotator cuff healing after surgery?

Thank you for your correspondence enclosing the necessary documents to facilitate recognition of the ethics approval for the above project granted by an external Human Research Ethics Committee (HREC) registered with the National Health and Medical Research Council (NHMRC).

It is noted that you have ethics approval from South Metropolitan, approval number 11/75.

The UWA students and researchers identified as working on this project are:

UWA Researchers:

<table>
<thead>
<tr>
<th>Name</th>
<th>Faculty / School</th>
<th>Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>Winthrop Professor Timothy Robert Ackland</td>
<td>Sport Science, Exercise &amp; Health (School of)</td>
<td>Chief Investigator</td>
</tr>
<tr>
<td>Clinical Associate Professor Allan Wenli Wang</td>
<td>Sport Science, Exercise &amp; Health (School of)</td>
<td>Co-Inv</td>
</tr>
<tr>
<td>Dr Brendan Keith Joss</td>
<td>Sport Science, Exercise &amp; Health (School of)</td>
<td>Co-Inv</td>
</tr>
</tbody>
</table>

Student(s): Jessica Anne Colliver

Although The University of Western Australia reserves the right to subject any research involving its staff and students to its own ethics review process, in this case, the Human Research Ethics Office has recognised the existing approval of the external HREC. The project is exempt from ethics review at UWA and the involvement of the above-listed researchers has been authorised. Any conditions for the recognition of the external HREC’s existing approval are listed below:

Special Conditions

None specified

You are reminded that it will be the responsibility of the approving HREC to ensure compliance with all ethics requirements and to monitor and report on the project. However, should any relevant ethics issues arise during the course of the project; you should inform the Human Research Ethics Office of The University of Western Australia.

If you have any queries, please do not hesitate to contact Kate Kirk on (08) 6488 3703.

Please ensure that you quote the file reference – RA/4/1/4872 – and the associated project title in all future correspondence.

Yours sincerely
Peter Johnstone
Manager
Human Research Ethics Committee
APPENDIX 3

SOUTH METROPOLITAN AREA HEALTH SERVICE NOTIFICATION OF
ETHICS APPROVAL
Professor Allan Wang  
School of Sport Science, Exercise and Health  
M408, University of Western Australia  
35 Stirling Highway  
Crawley WA 6009  

Dear Professor Wang,  

Re: Does Autologous Conditioned Plasma Enhance Rotator Cuff Tendon Healing After Surgery.  

Thank you for your correspondences dated 20 October 2011 enclosing, a Protocol Amendment and revised Patient Information Sheet and Consent Form, for the above study. Your correspondence and attachments were reviewed by the SMAHS Human Research Ethics Committee at its meeting on 8 November 2011.  

At the meeting the Committee resolved to approve the Protocol Amendment and revised PICF:  

Please quote the following reference number on any future correspondence with the Committee regarding this protocol: 11/75  

Yours sincerely  

MR RICHARD WOJNAR-HORTON  
A/CHAIRMAN  
HUMAN RESEARCH ETHICS COMMITTEE  

cc: Dr Eamon Koh, Consultant Radiologist, Radiology Department B4, Fremantle Hospital
APPENDIX 4

STUDY INFORMATION SHEET
Information Sheet

Does autologous conditioned plasma enhance rotator cuff healing after surgery?

TO BE USED IN CONJUNCTION WITH THE CONSENT FORM

Chief Investigator
Dr Allan Wang, Consultant Orthopaedic Surgeon and Clinical Professor, UWA
awang@westnet.com.au

Co Investigators
Dr Eamon Koh, Consultant Radiologist, Fremantle Hospital
Ms Jessica Colliver, Exercise Physiologist and Study Coordinator
Prof Timothy Ackland, Winthrop Professor, UWA
Dr Brendan Joss, Clinic Director, HFRC
Prof Ming Hao Zheng, Winthrop Professor, UWA

We invite you to participate in this research study, supported by Arthrex Medical Company, concerning patients who have undergone surgery for a rotator cuff tendon tear, and comparing the efficacy of post-surgery injections of autologous conditioned plasma (ACP) versus usual care. This study has been approved by the Human Research Ethics Committees of the South Metropolitan Area Health Service and the University of Western Australia.

If you decide to take part in this study, it is important that you understand the purpose of the study and the procedures you will be asked to undergo. Please read the following pages, which will provide you with information about the treatments involved and the potential benefits, discomforts and precautions of the study. If you are currently involved in a research study you will be ineligible to participate in this one.

What is the purpose of this research?
Your family doctor has referred you for treatment of a rotator cuff tendon tear in your shoulder, which requires surgical repair. Unfortunately, surgical repair is sometimes unsuccessful, due to retraction of the torn tendon or poor tissue quality and occasionally following surgery the tendon may fail to heal well, or re-tear and further surgery is sometimes required.

To combat these problems your surgeon has been investigating other options. There is increasing evidence that tendon healing is improved by ACP injection. Plasma is the component of blood with the red blood cells removed, and containing platelets and proteins which have been shown to improve tendon healing and function with Achilles tendon injuries, tennis elbow tendon damage and shoulder rotator cuff tendon tears\(^1,2,3\). The plasma is obtained by taking 10 ml of your own blood (“autologous plasma”) and spinning it in a centrifuge for 5 minutes just prior to injection.
The purpose of this research study is to investigate the benefit of autologous plasma injections for patients following rotator cuff tendon repair surgery.

**Duration of study**
If you choose to participate in this study you will be evaluated at regular intervals by Prof. Wang and the research team for 4 months after surgery.

**Clinical procedure**
Your shoulder will be evaluated with radiological studies including ultrasound or a MRI scan to assess the extent of rotator cuff damage. The standard surgical procedure to arthroscopically decompress then repair the rotator cuff tendon will be performed. After discharge from hospital you will be reviewed one week after surgery by Prof. Wang, who will then discuss this research study and if you agree to participate, we will enter you into the program. At this time, you will choose an envelope at random containing notification regarding which arm of the study you will enter (ie. the “treatment group” or the “control group”). The study coordinator, Miss Jess Colliver will then schedule you for post-operative care and assessment sessions.

Patients assigned to the treatment group will be seen by Dr Eamon Koh, consultant radiologist at Fremantle Hospital. Patients in this group will have 10 ml (approximately two teaspoons) of their own blood taken, spun down, calcium chloride is added, and then 1-2 ml of this autologous conditioned plasma (ACP) is injected under ultrasound guidance into the rotator cuff repair site. Dr Koh will repeat this injection two weeks later.

Regardless of whether you are an ACP treatment patient or control patient, your post-operative care and assessments will be identical.

**Pre- and post-surgery tests**
All patients who are referred to Prof. Wang for surgical treatment of a rotator cuff repair have a standard history, examination and radiology tests performed routinely. In addition, assessments of pain and function of the shoulder musculature will have been performed. If you agree to participate in this trial, we will use these data as your “pre-surgery” baseline scores.

The post-surgical management is identical between Treatment and Control groups. Post-operative questionnaires are administered at 6, 12 and 16 weeks post-surgery (in Prof. Wang’s rooms). A routine post-operative MRI scan will be performed at 16 weeks to check the tendon repair site.

Questionnaires administered to both groups include the Quick Disabilities of the Arm, Shoulder and Hand (QDASH), Oxford Shoulder Score (OSS), and Short Form-12 (SF-12). These questionnaires ask you to report on your shoulder pain, symptoms and how it affects your activities of daily living. At the time of the two injections we will also ask you for information regarding the levels of pain in your shoulder.

Strength and range of motion testing post-surgery (at 16 weeks) is performed under the supervision of Miss Jessica Colliver who is an accredited Exercise Physiologist, at the UWA School of Sport Science, Exercise & Health in Crawley. The strength tests are performed within your level of tolerance to minimise any risk of injury or discomfort. Post-operative strength and ROM testing will only be performed once you have been cleared by Prof. Wang at the post-surgery clinical examination.
Testing time points:

<table>
<thead>
<tr>
<th>Measures</th>
<th>Pre-op</th>
<th>6 weeks post-op</th>
<th>12 weeks post-op</th>
<th>16 weeks post-op</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Strength</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROM</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>VAS (pain)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>QuickDASH</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>OSS</td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>SF-12</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

What happens if I choose not to participate in this study?
This will not affect your medical treatment from Prof. Wang. Your routine post-surgical rehabilitation and follow up will still go ahead as planned.

What are the possible benefits for me to participate in this study?
In both Treatment and Control groups, patients will receive a more in depth evaluation of the shoulder, before and after surgery by the research team, compared to patients not participating in this study. If you are allocated to the ACP treatment group, your outcome following surgery may or may not be better than the control group. This study will determine if there are significant positive benefits of ACP treatment. Previous studies of this type of injection have suggested less post-surgical pain\(^4\), earlier return to function\(^3\), and possibly lower rates of infection\(^5\).

What are the possible side effects and risks of participating in this study?
Autologous plasma injection to potentially enhance the outcome of tendon repair surgery is relatively new technology. Recent, similar studies have shown no adverse effects from platelet rich plasma injections\(^3,4,5\). However, there are general risks of surgery and anaesthesia for both participants and non-participants in this research study. There is a possible, minor increased risk from the ACP injection, including infection and pain after surgery. In the event of any complications in either the Treatment or Control group, all necessary medical care will be provided. Your participation in this study does not prejudice the right to compensation, which you may have under Statute or Common Law.

The post-surgery MRI scans, which are performed to evaluate the healing of the rotator cuff tendon, may be claustrophobic for some patients.

Will my personal information be kept confidential?
Yes, your personal medical details will be kept private and confidential, and accessible only by the study Investigators. However, authorisation may be given to the hospital or Human Research Ethics Committee to verify the study procedures and conduct.

The results of this research may be made available to other professionals at medical meetings or publications in medical journals. However, no personal identifying data will be used. By taking part in this study, you agree to not restrict the use of this de-identified data.

Voluntary participation and withdrawal from the study
Participation in this study is voluntary. If you choose not to participate, Prof. Wang will continue to provide the standard treatment for your shoulder condition. You may also withdraw from this study at any time, for whatever reason. Such withdrawal will not in any
way influence decisions regarding future standard or conventional medical treatment you may require.

Further information
If you have any questions about the study please contact the study coordinator, Ms Jessica Colliver on 0488 367 626, or by email to jessicacolliver@gmail.com.

References:
2. Mishra & Pavelko Treatment of chronic elbow tendonosis with buffered platelet rich plasma. AJSM 2006 34: 1774-1778

Approval to conduct this research has been provided by the South Metropolitan Area Health Service and The University of Western Australia, in accordance with their ethics review and approval procedures. Any person considering participation in this research project, or agreeing to participate, may raise any questions or issues with the researchers at any time. If you have any complaints or concerns about the way in which the study is being conducted, you may contact the Chairman of the South Metropolitan Area Health Service Human Research Ethics Committee on 9431 2929. Alternatively, you may contact the Human Research Ethics Office at The University of Western Australia on (08) 6488 3703 or by emailing to hreo-eresearch@uwa.edu.au.

Prof. Allan Wang
Principal Investigator

Ms Jessica Colliver
AEP & Study Coordinator

Dr Eamon Koh
Consultant Radiologist
APPENDIX 5

PATIENT CONSENT FORM
Consent Form

Does autologous conditioned plasma enhance rotator cuff healing after surgery?

TO BE USED IN CONJUNCTION WITH THE INFORMATION SHEET

Participant’s Name: ___________________________  Date of Birth: ________________________

1. I agree entirely voluntarily to take part in this study, supported by Arthrex Medical Company. I am 18 years of age or over.

2. I have been given a full explanation of the purpose of this study, of the procedures involved and of what will be expected of me. The doctor has explained the possible problems that might arise as a result of my participation in this study.

3. I agree to inform the supervising doctor of any unexpected or unusual symptoms I may experience.

4. I understand that I am entirely free to withdraw from the study at any time and that this withdrawal will not in any way affect my future treatment or medical management.

5. I understand that the information in my medical records is essential to evaluate the results of this study. I agree to the release of this information to the research staff and the clinical trial staff on the understanding that it will be treated confidentially.

6. I understand that I will not be referred to by name in any report concerning this study. In turn, I cannot restrict in any way the use of the results that arise from this study.

7. I have been given and read a copy of this Consent Form and Information Sheet.

Participant Signature: ___________________________  Date ______________________

Signature of Principal Investigator: ______________________  Date ______________________

Approval to conduct this research has been provided by the South Metropolitan Area Health Service and The University of Western Australia, in accordance with their ethics review and approval procedures. Any person considering participation in this research project, or agreeing to participate, may raise any questions or issues with the researchers at any time. In addition, any person not satisfied with the response of researchers may raise ethics issues or concerns, and may make any complaints about this research project by contacting the Human Research Ethics Office at The University of Western Australia on (08) 6488 3703 or by emailing to hreo-eresearch@uwa.edu.au
APPENDIX 6

VISUAL ANALOGUE SCALE (VAS) FOR PAIN
Visual Analogue Scale (VAS)

Please rate how **severe** the **pain** in your affected shoulder has been (in the **past 7 days**) along the line below.

How severe is your pain?

<table>
<thead>
<tr>
<th>No pain</th>
<th>Worst pain imaginable</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX 7

OXFORD SHOULDER SCORE (OSS)
**Oxford Shoulder Score**

Please circle the most appropriate answer of each of the following questions for your *affected shoulder*:

1. How would you describe the worst pain from your shoulder?

<table>
<thead>
<tr>
<th>Unbearable</th>
<th>Severe</th>
<th>Moderate</th>
<th>Mild</th>
<th>None</th>
</tr>
</thead>
</table>

2. How would you describe the pain you usually get from your shoulder?

<table>
<thead>
<tr>
<th>Unbearable</th>
<th>Severe</th>
<th>Moderate</th>
<th>Mild</th>
<th>None</th>
</tr>
</thead>
</table>

3. How much has the pain from your shoulder interfered with your work (including housework)?

<table>
<thead>
<tr>
<th>Totally</th>
<th>Greatly</th>
<th>Moderately</th>
<th>A little bit</th>
<th>Not at all</th>
</tr>
</thead>
</table>

4. Have you been troubled by pain in your shoulder in bed at night?

<table>
<thead>
<tr>
<th>Every night</th>
<th>Most nights</th>
<th>Some nights</th>
<th>Only 1 to 2 nights</th>
<th>No nights</th>
</tr>
</thead>
</table>

5. Have you had any trouble dressing yourself because of your shoulder?

<table>
<thead>
<tr>
<th>Impossible to do</th>
<th>Extreme difficulty</th>
<th>Moderate difficulty</th>
<th>Very little difficulty</th>
<th>No difficulty at all</th>
</tr>
</thead>
</table>

6. Have you had any trouble getting in and out of the car or using public transport because of your shoulder? (Whichever one you tend to use)

<table>
<thead>
<tr>
<th>Impossible to do</th>
<th>Extreme difficulty</th>
<th>Moderate difficulty</th>
<th>Very little difficulty</th>
<th>No difficulty at all</th>
</tr>
</thead>
</table>

7. Have you been able to use a knife and fork at the same time?

<table>
<thead>
<tr>
<th>No.</th>
<th>Impossible</th>
<th>With extreme difficulty</th>
<th>With moderate difficulty</th>
<th>With little difficulty</th>
<th>Yes, easily</th>
</tr>
</thead>
</table>

8. Could you do the household shopping on your own?

<table>
<thead>
<tr>
<th>No.</th>
<th>Impossible</th>
<th>With extreme difficulty</th>
<th>With moderate difficulty</th>
<th>With little difficulty</th>
<th>Yes, easily</th>
</tr>
</thead>
</table>

9. Could you carry a tray containing a plate of food across the room?

<table>
<thead>
<tr>
<th>No.</th>
<th>Impossible</th>
<th>With extreme difficulty</th>
<th>With moderate difficulty</th>
<th>With little difficulty</th>
<th>Yes, easily</th>
</tr>
</thead>
</table>

10. Could you brush/comb your hair with the affected arm?

<table>
<thead>
<tr>
<th>No.</th>
<th>Impossible</th>
<th>With extreme difficulty</th>
<th>With moderate difficulty</th>
<th>With little difficulty</th>
<th>Yes, easily</th>
</tr>
</thead>
</table>

11. Could you hang your clothes up in a wardrobe with your affected arm?

<table>
<thead>
<tr>
<th>No.</th>
<th>Impossible</th>
<th>With extreme difficulty</th>
<th>With moderate difficulty</th>
<th>With little difficulty</th>
<th>Yes, easily</th>
</tr>
</thead>
</table>

12. Have you been able to wash and dry yourself under both arms?

<table>
<thead>
<tr>
<th>No.</th>
<th>Impossible</th>
<th>With extreme difficulty</th>
<th>With moderate difficulty</th>
<th>With little difficulty</th>
<th>Yes, easily</th>
</tr>
</thead>
</table>
APPENDIX 8

QUICK DEFORMITIES OF THE ARM, SHOULDER AND HAND (QUICKDASH)

OUTCOME MEASURE
# Quick DASH

This questionnaire asks you about your symptoms as well as your ability to perform certain activities. Please answer *every question*, based on you condition *in the past week*, by circling the number of the appropriate answer. If you did not have the opportunity to perform a certain activity in the past week, please make your best estimate of which response would be most accurate. It doesn’t matter which arm you use to perform the activity; please answer based on your ability regardless of how you perform the task.

<table>
<thead>
<tr>
<th></th>
<th>NO DIFFICULTY</th>
<th>MILD DIFFICULTY</th>
<th>MODERATE DIFFICULTY</th>
<th>SEVERE DIFFICULTY</th>
<th>UNABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Open a tight or new jar</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2.</td>
<td>Do heavy household chores (e.g. wash floors)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3.</td>
<td>Carry a shopping bag or briefcase</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4.</td>
<td>Wash your back</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5.</td>
<td>Use a knife to cut food</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6.</td>
<td>Recreational activities in which you take some force or impact through your arm, shoulder or hand (e.g. golf, hammering, tennis etc.)</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>NOT AT ALL</th>
<th>SLIGHTLY</th>
<th>MODERATELY</th>
<th>QUITE A BIT</th>
<th>EXTREMELY</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.</td>
<td>During the past week, to what extent has you arm, shoulder or hand problem interfered with your normal social activities with friends, family or groups?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>NOT AT ALL LIMITED</th>
<th>SLIGHTLY LIMITED</th>
<th>MODERATELY LIMITED</th>
<th>VERY LIMITED</th>
<th>UNABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.</td>
<td>During the past week, were you limited in your work or other regular daily activities as a result of you arm, shoulder or hand problem?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

**Rate the severity of these symptoms in the past week:**

<table>
<thead>
<tr>
<th></th>
<th>NONE</th>
<th>MILD</th>
<th>MODERATE</th>
<th>SEVERE</th>
<th>EXTREME</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.</td>
<td>Arm, shoulder or hand pain</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>10.</td>
<td>Tingling (pins and needles) in your arm, shoulder or hand</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>NO DIFFICULTY</th>
<th>MILD DIFFICULTY</th>
<th>MODERATE DIFFICULTY</th>
<th>SEVERE DIFFICULTY</th>
<th>UNABLE TO SLEEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.</td>
<td>During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
WORK MODULE (optional):
The following questions ask about the impact of your arm, shoulder or hand problem on your ability to work (including homemaking if that is your main work role).

Please indicate what your job is: ____________________________

☐ I do not work. (You may skip this section)

Please circle the number that best describes your physical ability in the past week at work:

<table>
<thead>
<tr>
<th>Did you have any difficulty?</th>
<th>NO DIFFICULTY</th>
<th>MILD DIFFICULTY</th>
<th>MODERATE DIFFICULTY</th>
<th>SEVERE DIFFICULTY</th>
<th>UNABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Using your usual technique for your work?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. Doing your usual work because of your arm, shoulder or hand problem?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. Doing your work as well as you would like?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. Spending your usual amount of time doing your work?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

SPORTS/PERFORMING ARTS MODULE (optional)
The following questions ask about the impact of your arm, shoulder or hand problem on playing your musical instrument or sport or both. If you play more than one sport or musical instrument (or play both), please answer with respect to that activity which is most important to you.

Please indicate the sport or instrument that is most important to you: ____________________________

☐ I do not play a sport or musical instrument. (You may skip this section)

Please circle the number that best describes your physical ability in the past week playing sport or your musical instrument:

<table>
<thead>
<tr>
<th>Did you have any difficulty?</th>
<th>NO DIFFICULTY</th>
<th>MILD DIFFICULTY</th>
<th>MODERATE DIFFICULTY</th>
<th>SEVERE DIFFICULTY</th>
<th>UNABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Using you usual technique for playing sport or your instrument?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. Playing sport or your instrument because of your affected arm, shoulder or hand problem?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. Playing sport or your instrument as well as you would like?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. Spending your usual amount of time practicing or playing sport or your musical instrument?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
APPENDIX 9

SHORT FORM-12 (SF-12) HEALTH SURVEY
Short Form – 12 (SF-12)

This questionnaire asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Please answer every question by marking one box. If you are unsure about how to answer, please give the best answer you can.

1. In general, would you say your health is:

- [ ] Excellent
- [ ] Very good
- [ ] Good
- [ ] Fair
- [ ] Poor

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If limited, how much?

2. Moderate activities such as moving a table, pushing a vacuum cleaner, bowling or playing golf

- [ ] Yes, limited a lot
- [ ] Yes, limited a little
- [ ] No, not limited at all

3. Climbing several flights of stairs

- [ ] Yes, limited a lot
- [ ] Yes, limited a little
- [ ] No, not limited at all

During the past month, have you had any of the following problems with work or other regular activities as a result of your physical health?

4. Accomplished less than you would like

- [ ] Yes, limited a lot
- [ ] Yes, limited a little
- [ ] No, not limited at all

5. Were limited in the kind of work or other activities

- [ ] Yes, limited a lot
- [ ] Yes, limited a little
- [ ] No, not limited at all

During the past month, have you had any of the following problems with work or other regular activities as a result of any emotional problems (such as feeling depressed or anxious)?

6. Accomplished less than you would like

- [ ] Yes, limited a lot
- [ ] Yes, limited a little
- [ ] No, not limited at all
7. Didn’t do work or other activities as carefully as usual

8. During the past month, how much did pain interfere with your normal work (both outside of the house and housework)?

These questions are about how you feel and how things have been with you during the past month. For each question, please give one answer that comes closest to the way you have been feeling. How much of the time during the past month:

9. Have you felt calm and peaceful?

10. Did you have a lot of energy?

11. Have you felt downhearted and blue?

12. During the past month, how much of the time has your physical health or emotional problems interfered with you social activities (such as visiting with friends, relatives etc.)?
APPENDIX 10

MANUSCRIPT ACCEPTED FOR PUBLICATION IN THE AMERICAN JOURNAL OF SPORTS MEDICINE: DO POSTOPERATIVE PLATELET-RICH PLASMA INJECTIONS ACCELERATE HEALING AND EARLY FUNCTIONAL RECOVERY AFTER ARTHROSCOPIC SUPRASPINATUS REPAIR?: A RANDOMIZED CONTROLLED TRIAL
Do Postoperative Platelet-Rich Plasma Injections Accelerate Early Tendon Healing and Functional Recovery After Arthroscopic Supraspinatus Repair?

A Randomized Controlled Trial

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Investigation performed at St John of God Hospital and University of Western Australia, Perth, Australia

Background: Tendon-bone healing after rotator cuff repair directly correlates with a successful outcome. Biological therapies that elevate local growth-factor concentrations may potentiate healing after surgery.

Purpose: To ascertain whether postoperative and repeated application of platelet-rich plasma (PRP) to the tendon repair site improves early tendon healing and enhances early functional recovery after double-row arthroscopic supraspinatus repair.

Study Design: Randomized controlled trial; Level of evidence, 1.

Methods: A total of 60 patients underwent arthroscopic double-row supraspinatus tendon repair. After randomization, half the patients received 2 ultrasound-guided injections of PRP to the repair site at postoperative days 7 and 14. Early structural healing was assessed with MRI at 16 weeks, and cuff appearances were graded according to the Sugaya classification. Functional scores were recorded with the Oxford Shoulder Score; Quick Disability of the Arm, Shoulder and Hand; visual analog scale for pain; and Short Form–12 quality-of-life score both preoperatively and at postoperative weeks 6, 12, and 16; isokinetic strength and active range of motion were measured at 16 weeks.

Results: PRP treatment did not improve early functional recovery, range of motion, or strength or influence pain scores at any time point after arthroscopic supraspinatus repair. There was no difference in structural integrity of the supraspinatus repair on MRI between the PRP group (0% full-thickness retear; 23% partial tear; 77% intact) and the control group (7% full-thickness retear; 23% partial tear; 70% intact) at 16 weeks postoperatively (P = .35).

Conclusion: After arthroscopic supraspinatus tendon repair, image-guided PRP treatment on 2 occasions does not improve early tendon-bone healing or functional recovery.

Keywords: platelet-rich plasma; rotator cuff repair; growth factors; tendon healing; early functional recovery.

Despite the advent of new surgical techniques to improve rotator cuff fixation to bone, failure of the tendon repair often occurs.12,38 Tendon retears may be due to a specific reinjury at the repair site but also may reflect incomplete or failed primary healing after surgery.5,6

Sonnabend et al,37 in a primate model of rotator cuff repair, showed that a significant proportion of Sharpey fibers begin to reconstitute at 3 months with maturation at 4 months after surgery. Thus, the early tendon healing stage is critical for long-term success of rotator cuff repair.

Accelerated rotator cuff rehabilitation programs that allow active exercises sooner than 3 to 4 months before early tendon-bone healing occurs risk early failure.29,43

Hence, there has been increasing interest in adjuvant biological therapies to improve early primary tendon healing. In particular, many studies have investigated platelet-rich plasma (PRP) products, where a supra physiological concentration of platelets is delivered to the tendon-bone repair site at the time of surgery. Activated platelets degranulate to release multiple growth factors that modulate the cascade of chemotaxis, cell proliferation, and differentiation, which assist in the tendon healing process.9

References 3, 11, 13, 15, 17, 21, 22, 25, 31.
Published studies reporting the use of PRP administration have met with mixed success in improving outcomes after rotator cuff repair. Appraisal of the literature is complicated by the range of treated injuries, varying from small, single-tendon tears to massive multitenor tears; concomitant use of acromioplasty or not\textsuperscript{1,19,20}; and the formulation of PRP used, which ranged from intratendon injection,\textsuperscript{2,7,16,40} spray application\textsuperscript{33,35} or incorporation of a platelet-rich fibrin matrix into the tendon repair site.\textsuperscript{2,7,16,40}

A further variable affecting the efficacy of PRP is the timing of delivery. All previous PRP augmented rotator cuff studies to date have used time zero delivery at the time of surgical repair. After activation, platelets release growth factors almost immediately with total elution within 1 hour,\textsuperscript{3} and the half-life of growth factors is a matter of minutes to hours.\textsuperscript{26} However, it has been acknowledged that biological augmentation of tendon repairs too early in the tendon healing cascade may be ineffective.\textsuperscript{15} Differing classes of growth factors are active at specific time points\textsuperscript{21}, for example, animal studies have shown that application of platelet-derived growth factors at day 7 have a more pronounced effect on tendon cellular maturation and biomechanical strength than earlier application.\textsuperscript{8} Growth factors, including bone morphogenetic protein–13 (BMP-13), platelet-derived growth factor–B, and transforming growth factor–B1, are expressed maximally at days 7 and 14,\textsuperscript{42} and the cytokine-mediated temporal expression of collagen types I and III increases from day 7 onward.\textsuperscript{9}

Hence, timing for PRP delivery remains an important consideration for optimizing tendon healing. In this study, we hypothesized that delayed and repeated injection of PRP at days 7 and 14 after surgery would first avoid the potential dilution and washout effect of arthroscopic administration and second, produce a sustained up-regulation of the tendon healing process. The purpose of this study was to determine if this PRP delivery protocol would enhance early tendon healing and functional recovery after arthroscopic supraspinatus tendon repair. The primary study outcome was improved early tendon healing as assessed by magnetic resonance imaging (MRI). The secondary outcome was patient-rated function as a measure of functional recovery.

METHODS

Patient Selection

Institutional ethics committee approval was granted for this study. Patients with rotator cuff tears verified by MRI or ultrasound were identified over the period from February 2011 to February 2013. A power calculation was performed to determine the required number of patients to detect a significant difference of 1 Sugaya grade classification between the treatment and control groups based on previously published MRI classification scores for post–rotator cuff repair patients.\textsuperscript{38} The power analysis used an effect size of 0.769 (moderate effect), with significance of $P < .05$, and a power of 80%, giving a minimum sample size of 56 participants (n = 28 participants in each group). More participants (n = 60) were recruited to allow for attrition.

The inclusion criteria comprised the presence of a symptomatic full-thickness tear of supraspinatus in an active adult identified by preoperative imaging and confirmed by arthroscopic evaluation. All patients also received a series of plain radiographs (anteroposterior, outlet, and axillary views) for evaluation of arthritic changes. Exclusion criteria included patients with a history of previous rotator cuff surgery, subscapularis or infraspinatus tear identified on MRI or ultrasound.
Sex, Male/ Female, n  
Age, y, Mean (Range)  
Acromioplasty, n  
Biceps Tenotomy, n  
Acromioclavicular Joint Excision, n  
Complications, n  
Tear Size, mm  

PRP group (n = 30)  
11/19  
59.8 (28-77)  
30  
3  
4  
0  
15 (10-20)  
14.60 ± 3.78  

Control group (n = 30)  
17/13  
58.4 (38-76)  
30  
5  
5  
0  
15 (10-20)  
13.70 ± 3.27  

PRP, platelet-rich plasma.

preoperative imaging or arthroscopic evaluation; labral tear; significant degenerative glenohumeral osteoarthritis; contralateral shoulder symptoms; rheumatological, neuromuscular, or autoimmune disease; cervical disc herniation; ongoing workers’ compensation claims; or contraindication to postoperative MRI evaluation (Figure 1).

Surgical Technique

All surgery was performed by the senior author. All procedures were performed in the lateral decubitus position under general anesthesia with an interscalene nerve block. The arm was placed in 4 kg of traction and positioned in 30° of arm flexion and abduction. Initial diagnostic glenohumeral arthroscopy was performed and the presence of a full-thickness supraspinatus tear confirmed. After debridement of the bursal tissue and tendon margins, the tear type was assessed and tear size measured with a calibrated probe with 5 mm increments. Tears over 20 mm in the anteroposterior dimension were excluded, as were partial tears. Supraspinatus tears associated with subscapularis or infraspinatus tears were excluded from the study. After acromioplasty, rotator cuff reconstruction was performed. The footprint was prepared with a full-radius resector to decorticate the greater tuberosity. A double-row suture-bridge repair with bioabsorbable anchors was performed (Arthrex Bio-Corkscrew 5.5 mm–PT, Biocomposite Pushloc 3.5 mm; Arthrex). The same reconstructive technique was utilized in each case. Concomitant shoulder injuries were treated as clinically or radiographically indicated. Acromioclavicular joint arthroplasty was treated with arthroscopic excision of the lateral end of the clavicle, and long head of biceps tendinopathy was treated with tenotomy (Table 1).

Postoperative Protocol

All patients were immobilized in a sling (Ultrasling III; Don Joy) for 6 weeks postoperatively and followed a standard rehabilitation program under the supervision of physical therapists. This consisted of passive range of motion exercises in the first 6 weeks, followed by active assisted range of motion exercises from 6 to 10 weeks, and finally, a guided strengthening program from 10 to 16 weeks. All patients followed this program consistently.

Randomization Procedure

Patients were reviewed on postoperative day 5 and, after arthroscopic evaluation and confirmation study inclusion criteria were met, randomized to PRP or control groups. A computer block permutation method was prepared to generate a simple randomized computer-generated table of blocks of 10 (5 PRP; 5 control) stratified by the treating surgeon at the 5-day postsurgical follow-up. Sixty consecutive patients meeting the study inclusion criteria and consenting to the study were randomized via the aforementioned procedure, with 30 in each arm of the study. The average age was 59.1 years (range, 28-77 years). Patient demographics along with details of concomitant surgical procedures are illustrated in Table 1.

Preparation of PRP

The group randomized to the treatment arm of the study underwent ultrasound-guided PRP injection to the rotator cuff repair site on 2 separate occasions, at days 7 and 14 after surgery. The platelet concentrate was obtained using the Arthrex Autologous Conditioned Plasma (ACP) system. A PRP injection was prepared from 10 mL of autologous peripheral blood. After the addition of 1 mL of Anticoagulant Citrate Dextrose Solution (ACD-A), the blood was spun in a centrifuge (ROTOFIX 32 A; Andreas Hettich GmbH & Co KG) at 1500 RPM for 5 minutes. After centrifugation, the PRP supernatant (approximately 2-4 mL) was removed and stored in a separate sterile syringe in preparation for point-of-care delivery.

The ACP system produces a platelet concentration of approximately 470,000 platelets/μL (2.1 × greater than the level in whole blood), with an estimated concentration of growth factor reported as 5 to 25 times that of normal physiologic levels. It is free of both residual erythrocytes and leucocytes, which may impair local growth factor activity by free radical activation. Immediately before injection, the preparation was activated with 2 mL of CaCl₂. The injection was delivered at the tendon repair site under direct visualization with ultrasound by an experienced fellowship-trained musculoskeletal radiologist. Needle placement was aided by the identification of the echogenic sutures at the tendon repair site (Figure 2). The control group did not receive a placebo injection.
Outcome Assessments

Radiographic analysis was performed with MRI at 16 weeks. All scans utilized a 1.5-T unit (Sonata Maestro Class; Siemens) with 40 mT/m gradient power. Multiple images were obtained in oblique coronal, oblique sagittal, and axial planes with both short-tau inversion recovery (STIR) and turbo spin echo (TSE) T1-weighted sequence. MRI assessment was performed by an experienced fellowship-trained musculoskeletal radiologist who had not performed the PRP injections and was blinded to patient allocation to treatment or control group. Multiple images were evaluated and graded as per the Sugaya classification (Figure 3).38

Outcomes were assessed clinically and radiologically. Patients were assessed using the Oxford Shoulder Score (OSS); Quick Disability of the Arm, Shoulder and Hand (QuickDASH); visual analog scale (VAS) for pain (noting maximum pain in the prior 7-day period); and Short Form–12 (SF-12) preoperatively and at 6, 12, and 16 weeks postoperatively. All assessors were blinded as to the identity of the treatment and control groups, nor were they involved in any stage of the recruitment or surgery.

Active range of motion was assessed at 16 weeks using a goniometer. Absolute values were recorded for arm flexion, abduction, and external humeral rotation in both the operated and unoperated shoulders, using anatomic landmarks for accuracy and consistency. Range of motion was performed within the participants’ pain tolerance to minimize any injury risk and discomfort.

Isokinetic strength was also assessed at 16 weeks with the patient seated in a Biodex isokinetic dynamometer, and a series of standardized measurements were performed with the patient instructed to produce a maximum muscular force at speeds of 60 and 90 deg/s. External humeral rotation was performed in the modified-neutral position, with the elbow at 90° of flexion and the forearm in a neutral position throughout. Arm flexion was performed with the elbow fully extended. Values for both peak torque and total work performed over the range of motion were noted. Data were recorded as both absolute values and as a percentage of the scores obtained on the contralateral, unoperated shoulder. A difference of 10% to 15% in the strength between shoulders is regarded as physiologically normal in the general population and in those patients undergoing surgery.4

Statistical Analysis

Values are presented as means with associated standard deviations. A series of 2-factor, repeated-measures ANOVAs were performed to assess for difference between the treatment and control groups over time for continuous variables. For continuous data recorded at a single time point only, a series of independent t tests were performed, whereas a Mann-Whitney U test was employed for the MRI rating primary outcome variable. Statistical analyses used SPSS software (IBM Corp). For all tests, \( P < .05 \) was considered significant.

RESULTS

All patients complied with the study protocol, and no patient was lost to follow-up. There were no significant complications such as infection or neurological or vascular deficit for any patient in either arm of the study. In the control group, mean tendon tear size treated was 1.37 cm, and in the PRP group, mean tendon tear size treated was 1.46 cm. The adjunctive procedures of acromioclavicular joint excision and biceps tenotomy are shown in Table 1. No patient underwent a cortisone injection for pain, capsulitis, or bursitis within the study period.

Structural Evaluation

With use of the Sugaya classification, the grade of supraspinatus tendon healing for the PRP and control group is reported in Table 2. In both groups, 23% of subjects had a partial-thickness tendon repair (Sugaya grade 3). No
full-thickness retears were noted in the PRP treatment group; 2 (7%) full-thickness retears (Sugaya grades 4 and 5) occurred in the control group.

One patient in the PRP treatment group did not tolerate the postoperative MRI scan and so underwent an ultrasound performed by an experienced musculoskeletal radiologist. This tendon repair was intact and without any evidence of thinning or discontinuity and so, for the purposes of the study, was included in the grade 1 group of that cohort. In the PRP treatment group, 23 subjects (77%) exhibited a healed repair or an intact repair with high signal intensity (Sugaya grades 1 and 2), compared with 21 subjects (70%) in the control group. A Mann-Whitney U test demonstrated no difference (P = .351) between groups on MRI rating at 16 weeks (PRP group mean, 1.8 ± 0.8; control group mean, 2.1 ± 1.0).

Functional Scores

Outcome scores for all patients improved after surgery. At 12 and 16 weeks postoperatively, the Oxford Shoulder Score (F = 75.803; df = 3; P < .001), the QuickDASH (F = 53.939; df = 3; P < .001), and the VAS pain scores (F = 75.499; df = 3; P < .001) all improved significantly from before surgery. Similarly, the SF-12 quality-of-life indicators (physical component score: F = 13.967; df = 3; P < .001; mental component score: F = 5.401; df = 3; P = .001) improved with time. There was, however, no statistical difference (P > .05) between the PRP treatment and control groups for any of these functional scores at any time point postoperatively (Table 3).

### Strength

Isokinetic strength values were obtained for active arm flexion and external rotation movements at 2 speeds. Values were expressed as a percentage of the strength recorded in the contralateral shoulder. Within the control group, the relative scores for arm flexion peak torque at 90 and 60 deg/s were 68.7% and 75.4%, respectively, and 75.6% and 74.0%, respectively, for external rotation peak torque. Relative scores were similar in the PRP treatment group for arm flexion peak torque at 90 and 60 deg/s (74.1% and 76.3%, respectively) and external rotation peak torque (72.1% and 77.3%, respectively). No group differences (P > .05) for strength scores at 16 weeks after surgery were evident (Table 4).

### Range of Motion

The analysis revealed no significant differences (P > .05) in any active range of motion measure between the 2

---

**Table 2**

<table>
<thead>
<tr>
<th>Sugaya Classification&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRP group (n = 30)</td>
<td>12 (40.0)</td>
<td>11 (36.6)</td>
<td>7 (23.0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Control group (n = 30)</td>
<td>9 (30.0)</td>
<td>12 (40.0)</td>
<td>7 (23.0)</td>
<td>1 (3.3)</td>
<td>1 (3.3)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Values are reported as n (%). PRP, platelet-rich plasma.

<sup>b</sup>From Sugaya et al.<sup>38</sup> Grade 1 = no tear; grade 2 = sufficient tendon thickness but with high signal change; grade 3 = insufficient thickness but no tendon discontinuity; grade 4 = small full-thickness retear; grade 5 = large full-thickness retear.

**Table 3**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Preoperative</th>
<th>6 wk</th>
<th>12 wk</th>
<th>16 wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>QuickDASH symptoms (transformed)</td>
<td>PRP</td>
<td>42.27 ± 17.06</td>
<td>51.17 ± 19.54</td>
<td>33.14 ± 19.27</td>
<td>22.58 ± 14.36</td>
</tr>
<tr>
<td>VAS</td>
<td>Control</td>
<td>37.16 ± 20.38</td>
<td>53.48 ± 13.27</td>
<td>36.33 ± 17.40</td>
<td>17.23 ± 13.56</td>
</tr>
<tr>
<td>OSS</td>
<td>PRP</td>
<td>6.37 ± 1.59</td>
<td>3.26 ± 2.43</td>
<td>3.25 ± 2.01</td>
<td>1.75 ± 1.68</td>
</tr>
<tr>
<td>SF-12</td>
<td>Control</td>
<td>5.38 ± 2.43</td>
<td>1.19 ± 2.34</td>
<td>2.23 ± 1.91</td>
<td>1.36 ± 1.51</td>
</tr>
<tr>
<td>PCS</td>
<td>PRP</td>
<td>27.63 ± 6.90</td>
<td>23.57 ± 9.61</td>
<td>33.38 ± 8.93</td>
<td>38.17 ± 7.19</td>
</tr>
<tr>
<td>MCS</td>
<td>Control</td>
<td>30.68 ± 7.76</td>
<td>21.48 ± 6.61</td>
<td>32.53 ± 6.92</td>
<td>40.37 ± 5.12</td>
</tr>
</tbody>
</table>

<sup>a</sup>Values are reported as mean ± SD. MCS, mental component score; OSS, Oxford Shoulder Score; PCS, physical component score; PRP, platelet-rich plasma; QuickDASH, Quick Disability of the Arm, Shoulder and Hand; SF-12, Short Form–12; VAS, visual analog scale for pain.
Table 4

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Isokinetic Strength, %</th>
<th>t</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm flexion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak torque 90 deg/s PRP</td>
<td>74.1 ± 10.8</td>
<td>-122</td>
<td>.266</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>68.7 ± 24.2</td>
<td>.107</td>
<td>.915</td>
<td></td>
</tr>
<tr>
<td>Total work 90 deg/s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRP</td>
<td>55.5 ± 23.2</td>
<td>.190</td>
<td>.85</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>56.3 ± 34.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak torque 60 deg/s PRP</td>
<td>76.3 ± 22.0</td>
<td>-.150</td>
<td>.881</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>75.4 ± 22.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total work 60 deg/s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRP</td>
<td>61.7 ± 21.8</td>
<td>-.150</td>
<td>.881</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>60.8 ± 27.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>External rotation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak torque 90 deg/s PRP</td>
<td>72.2 ± 15.7</td>
<td>.470</td>
<td>.640</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>75.6 ± 37.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total work 90 deg/s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRP</td>
<td>51.9 ± 30.1</td>
<td>.712</td>
<td>.371</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>55.1 ± 35.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak torque 60 deg/s PRP</td>
<td>77.3 ± 17.8</td>
<td>-.64</td>
<td>.525</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>74.0 ± 21.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total work 60 deg/s</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRP</td>
<td>59.8 ± 24.3</td>
<td>.277</td>
<td>.783</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>62.3 ± 44.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Strength was calculated as a percentage of the contralateral, unoperated arm. Results are reported as mean ± SD. PRP, platelet-rich plasma.**

Table 5

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Range of Motion, deg</th>
<th>t</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arm flexion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRP</td>
<td>144.8 ± 22.8</td>
<td>1.274</td>
<td>.208</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>151.8 ± 19.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arm abduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRP</td>
<td>134.8 ± 28.2</td>
<td>0.342</td>
<td>.734</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>137.4 ± 29.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>External rotation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRP</td>
<td>41.1 ± 10.2</td>
<td>0.69</td>
<td>.493</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>42.8 ± 9.3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**PRP, platelet-rich plasma.

The secondary outcomes of this study were to evaluate early functional recovery in patients receiving PRP treatment after supraspinatus repair. In a prospective randomized controlled trial of 53 patients, Randelli et al reported that PRP administered by spray produced statistically better early function scores and strength at 3 months after surgery. No imaging was performed at this stage, although it was concluded that PRP administration accelerates early recovery after surgery. Zumstein et al also showed an early benefit of PRP administration with improved revascularization of the tendon-bone repair site. Doppler ultrasonography was used to assess the vascularization index of 20 shoulders at 6 and 12 weeks after surgery. At 6 weeks, those shoulders treated with a leukocyte-rich PRP product showed significantly better vascularization; however, this was not sustained at 12 weeks.

Our study can report that early functional recovery was not improved with a sequential postsurgical PRP delivery protocol. At 6, 12, and 16 weeks, clinical function scores were equivalent between PRP and control group participants. Furthermore, objective testing of shoulder function at 16 weeks showed no difference between groups in recovery of active arm flexion, abduction, or external rotation range of motion. Similarly, isokinetic peak torque and the work done through the active range of motion during each movement was not different between groups. PRP delivery by injection under ultrasound guidance into the supraspinatus tendon repair site may be less significant, our findings are consistent with previous reports. Castricini et al examined the effects of platelet-rich fibrin matrix augmentation in rotator cuff repair and reported the re-rupture rate was higher in the control group (10.5% vs 2.5%). In contrast, Gumina et al using a novel platelet-rich fibrin matrix allowing slow release of growth factors on the tendon repair site, found a 14% retear rate in isolated posterosuperior cuff tears in the PRP group compared with 50% in the control group at 13 months.

The purpose of the study was to evaluate the efficacy of a protocol of sequential PRP administration after arthroscopic supraspinatus repair. All previous studies have utilized a single delivery of a PRP product at the time of surgery. The current protocol delivered a PRP product under ultrasound guidance to the tendon repair site at 7 and 14 days after surgery to avoid a possible dilution or washout effect of PRP, which may occur with arthroscopic fluid lavage. This protocol also allows a potentially prolonged up-regulation of growth factors involved in the tendon healing cascade. Our hypothesis was that this postsurgical and sequential PRP delivery protocol would (1) improve rotator cuff healing and (2) accelerate early functional recovery after arthroscopic rotator cuff repair.

This study finds that at 16 weeks after surgery, no full-thickness tendon retears occurred in the PRP group; however, there were 2 (7%) full-thickness retears in the control group. Although this difference was not statistically significant, our findings are consistent with previous reports. Castricini et al examined the effects of platelet-rich fibrin matrix augmentation in rotator cuff repair and reported the re-rupture rate was higher in the control group (10.5% vs 2.5%). In contrast, Gumina et al using a novel platelet-rich fibrin matrix allowing slow release of growth factors on the tendon repair site, found a 14% retear rate in isolated posterosuperior cuff tears in the PRP group compared with 50% in the control group at 13 months. However Rodeo et al also using platelet-rich fibrin matrix in 79 patients undergoing arthroscopic cuff repair, found no difference in tendon bone healing on ultrasound at 6 weeks and 12 weeks after surgery.

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accurate than injection under arthroscopic visualization. However, the surgical technique employed in this study comprised a double-row suture bridge technique, and the echogenic suture knots were readily identified on ultrasound. Moreover, the oblique and interlocking sutures of the suture bridge potentially retain the injected PRP at the repair site better than the single-row repair site technique used in previous studies.33

As an imaging modality, ultrasound has been shown to be reliable in obtaining a precise placement of PRP at the site of tendon injury.31 PRP delivery by direct injection under ultrasound guidance has been used to treat injuries of the Achilles tendon,10 the common extensor tendon origin,23,24,30 and the rotator cuff. Kesikburun et al20 demonstrated that PRP injection to nonsurgically treat rotator cuff tendinopathy and partial-thickness tendon tears has no significant clinical benefit over saline injections at 3, 6, 12, and 52 weeks. The findings of our study are consistent with this work, and even with a second PRP injection, there was no significant clinical or functional benefit up to 16 weeks after surgery. Our study focus is early outcomes, however; definitive clinical outcomes require 12- to 24-month postoperative evaluation.

This study has some limitations to be acknowledged. First, the follow-up was limited to 16 weeks. It is possible that more structural tendon failures would have been seen if MRI evaluation was repeated at a later time interval such as 12 months. However, it was the primary aim of this study to assess the effects of PRP treatment on the early phases of tendon healing. Animal models have demonstrated that a significant proportion of Sharpey fibers at the tendon repair site have reconstituted and matured onstrated that a significant proportion of Sharpey fibers early phases of tendon healing. Animal models have demonstrated that PRP injection to nonsurgically treat rotator cuff tendinopathy and partial-thickness tendon tears has no significant clinical benefit over saline injections at 3, 6, 12, and 52 weeks. The findings of our study are consistent with this work, and even with a second PRP injection, there was no significant clinical or functional benefit up to 16 weeks after surgery. Our study focus is early outcomes, however; definitive clinical outcomes require 12- to 24-month postoperative evaluation.

A second limitation is the nonblinding of subjects in both PRP and control groups. As the study protocol required 2 separate postsurgical injections, we considered that it would be impractical to have patients agreeing to complete 2 placebo injections. Patients in the PRP treatment group may have had the benefit of a placebo as well as a possible PRP treatment effect in their clinical and functional evaluation. Similarly, those patients who did not receive injections may have responded differently in clinical testing. The nonblinding of subjects could be expected to cause a positive bias in the PRP group; however, groups were equivalent in their study outcomes. MRI evaluation was performed by an independent musculoskeletal radiologist who had not been involved in previous diagnostic imaging or PRP injections and was blinded to group allocation.

A further possible study limitation was the PRP product used in this study does not achieve the very high concentration of platelets reported with some other PRP products.3,11,14 Sundman et al.,39 in a laboratory study, suggested that markedly elevated supra physiological levels of platelets and growth factors may be of no additional benefit due to cell-surface receptor saturation or may actually be detrimental to tendon healing.39 Optimal tendon healing requires not only the appropriate concentration of growth factors but that those growth factors be delivered at the appropriate time in the tendon healing cascade to be maximally effective.

CONCLUSION

This study is the first to evaluate the efficacy of a postsurgical PRP delivery protocol to improve healing and functional outcomes after arthroscopic rotator cuff repair. Sequential delivery of the specific injectable PRP preparation used in this study under ultrasound guidance, at days 7 and 14 after surgery, does not improve early rotator cuff healing or functional recovery. Future research should include randomized controlled trials of other PRP products with alternative delivery vehicles and dosing regimes.

REFERENCES


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APPENDIX 11

MANUSCRIPT ACCEPTED FOR PUBLICATION IN THE JOURNAL OF SHOULDER AND ELBOW SURGERY: EARLY POSTOPERATIVE REPAIR STATUS AFTER ROTATOR CUFF REPAIR EVALUATION. CANNOT BE ACCURATELY CLASSIFIED USING QUESTIONNAIRES OF PATIENT FUNCTION AND ISOKINETIC STRENGTH EVALUATION
Background: This study investigated if patients with an intact tendon repair or partial-thickness retear early after rotator cuff repair display differences in clinical evaluations and whether early tendon healing can be predicted using these assessments.

Methods: We prospectively evaluated 60 patients at 16 weeks after arthroscopic supraspinatus repair. Evaluation included the Oxford Shoulder Score, 11-item version of the Disabilities of the Arm, Shoulder and Hand, visual analog scale for pain, 12-item Short Form Health Survey, isokinetic strength, and magnetic resonance imaging (MRI). Independent \( t \) tests investigated clinical differences in patients based on the Sugaya MRI rotator cuff classification system (grades 1, 2, or 3). Discriminant analysis determined whether intact repairs (Sugaya grade 1) and partial-thickness retears (Sugaya grades 2 and 3) could be predicted.

Results: No differences (\( P < .05 \)) existed in the clinical or strength measures. Although discriminant analysis revealed the 11-item version of the Disabilities of the Arm, Shoulder and Hand produced a 97% true-positive rate for predicting partial thickness retears, it also produced a 90% false-positive rate whereby it incorrectly predicted a retear in 90% of patients whose repair was intact. The ability to discriminate between groups was enhanced with up to 5 variables entered; however, only 87% of the partial-retear group and 36% of the intact-repair group were correctly classified.

Conclusions: No differences in clinical scores existed between patients stratified by the Sugaya MRI classification system at 16 weeks. An intact repair or partial-thickness retear could not be accurately predicted. Our results suggest that correct classification of healing in the early postoperative stages should involve imaging.
Rotator cuff surgical repair is common, with in excess of 250,000 performed each year. Despite advances in surgical techniques and the increasing use of adjunct biologic therapies to stimulate or enhance repair, or both, the postoperative failure rate remains a concern. Although patients with retears or failed healing may experience a reduction in pain, functional outcomes, including strength levels, are significantly lower compared with patients with evidence of completely healed tendons. These inferior functional results may be satisfactory for an older or less active population, or both, but patients who require a return to sport or work where physical strength is important may be dissatisfied with the outcome.

A primate model of rotator cuff repair showed that a significant proportion of Sharpy fibers start to reconstitute at 3 months, with maturation seen at 4 months. Kluger et al reported that most recurrent tears occur in the first 3 months after rotator cuff surgery, highlighting that this early phase of tendon healing up to 3 to 4 months postoperatively is critical for longer-term success. Early confirmation of tendon healing is reassuring for the patient in the early postoperative stages. Likewise, identification of impaired healing or partial disruption of the tendon repair could affect management after surgery. This may include modifying the patient’s ongoing rehabilitation program, more focused patient education on potentially provocative or damaging movements and activities, recommending restrictions in future work and sport practices, ongoing surveillance of future patient symptoms and imaging, and even consideration for further surgery. Therefore, identifying the presence of incomplete tendon healing at an early stage after surgery using clinical and strength evaluation could prove beneficial.

The routine use of postoperative imaging studies to evaluate the outcome of rotator cuff surgery can be costly. Ultrasound (US), although readily available and cost-effective, is operator dependent for accuracy. Magnetic resonance imaging (MRI) is generally considered to be superior to US but remains an expensive imaging modality. Several researchers have attempted to determine whether the clinical progress of a nonoperatively treated rotator cuff tendon tear can be predicted using common clinical shoulder assessments, albeit with limited success. At the time of writing, we are unaware of any other studies that have investigated whether common shoulder clinical assessments can predict the early postoperative success of rotator cuff repair surgery.

Therefore, this study aimed to (1) investigate if differences in common shoulder patient-reported outcome (PRO) measures and isokinetic strength tests could be observed between patients with completely intact repairs or partial-thickness tendon retears, classified by MRI, at 16 weeks after rotator cuff repair surgery; and (2) determine if these PRO measures and strength tests could predict the early (16 weeks) postoperative success of rotator cuff repair.

Materials and methods

Patients

This prospective comparative study recruited 60 consecutive patients with rotator cuff tears isolated to the supraspinatus (Table I). Patients were recruited between November 2011 and February 2013 and were included if they presented with a symptomatic full-thickness tear of the supraspinatus, confirmed preoperatively by MRI or US and intraoperatively by arthroscopic evaluation. Patients with supraspinatus partial tears or tears exceeding 20 mm in the anteroposterior dimension were excluded, as were patients with concomitant subscapularis or infraspinatus tears, or both, identified on preoperative US or MRI or intraoperative examination. Patients were excluded if they had any or all of a history of previous rotator cuff surgery, labral tearing, significant osteoarthritis of the glenohumeral joint, rheumatologic, neuromuscular, or autoimmune disease, or cervical disc herniation. Patients were further excluded if they presented with any contralateral shoulder symptoms or had ongoing workers’ compensation claims.

A priori power calculation based on our first study goal was determined from the recommendations of Cohen. The minimal clinically important difference reported for the 11-item version of the Disability of the Arm, Shoulder and Hand (QuickDASH) questionnaire varies, ranging from 14.0 to 17.1 for patients with shoulder pathology, equating to an effect size of 0.75 to 0.98. Therefore, to detect this degree of difference (effect size of 0.85) with 80% power at = 0.05, we estimated that 18 patients in each of the intact-repair (Sugaya grade 1) and partial-retear (Sugaya grade 2 and 3 pooled) groups would be required for this study.

Surgical technique

All surgery was performed by the senior author (A.W.). Briefly, all procedures were performed with the patient in the lateral decubitus position under general anaesthesia with an interscalene nerve block. The arm was placed in 4 kg of traction and positioned in 30° of arm flexion and abduction. The presence of a full-thickness supraspinatus tear was initially confirmed by diagnostic...
glenohumeral arthroscopy. Tear type and size were assessed using a calibrated probe with 5-mm increments after débridement of bursal tissue and tendon margins.

After acromioplasty, rotator cuff reconstruction was performed. The footprint was prepared with a full-radius resector to decorticate the greater tuberosity. A double-row suture-bridge formed. The footprint was prepared with a full-radius resector to bursal tissue and tendon margins.

Postoperative management

All patients were immobilized in an abduction sling (UltraSling III; DonJoy, Carlsbad, CA, USA) for 6 weeks postoperatively and underwent a standard rehabilitation program under the supervision of a physical therapist. Briefly, patients undertook an initial 6 weeks of passive range of motion exercises, followed by active-assisted range of motion exercises from 6 to 10 weeks, and a conservative strengthening program from 10 to 16 weeks. All patients followed the protocol consistently.

PRO measures

Four PRO measures were used at 16 weeks after surgery: (1) the Oxford Shoulder Score (OSS); (2) the QuickDASH questionnaire; (3) a visual analog scale (VAS) for rating pain, and (4) the 12-item Short Form Health Survey (SF-12). The OSS is a 12-item questionnaire evaluating pain and function that has been validated against general health and clinical measures and has demonstrated good reliability in evaluating outcome after shoulder surgery. The QuickDASH is an 11-item questionnaire evaluating pain, symptoms, and physical function in patients with upper limb musculoskeletal disorders and has also demonstrated good reliability, validity, and responsiveness. The VAS required patients to rate their pain intensity on a 0- to 10-cm sliding scale (0 = no pain, 10 = worst pain imaginable) in the preceding 24 hours. A 1.4-cm improvement on the VAS has been reported as the minimal clinically important change in patients undergoing nonoperative treatment for rotator cuff disease.

Finally, the SF-12 is a generic health-related quality of life score that produces a physical (PCS) and mental (MCS) component subscale.

Isokinetic strength evaluation

Isokinetic strength was assessed at 16 weeks after surgery in all patients using a Biodex Isokinetic Dynamometer (Biodex, System 4, Shirley, NY, USA). Patients were seated with the trunk stabilized using rigid straps, and adjustments were made for humeral and forearm length in accordance with each patient’s stature. Patients were instructed to undertake maximal concentric external/internal humeral rotation, followed by arm flexion, at an angular velocity of 60°/s. External/internal humeral rotation was performed in the modified-neutral position with the elbow in 90° of flexion and the forearm in a neutral position. Arm flexion was performed with the elbow fully extended. Each trial consisted of 3 maximal repetitions. Two trials on each upper limb were undertaken, alternating between the nonoperated and operated limbs, with the first trial always undertaken on the nonoperated side. During each effort, patients were asked to perform to their maximal muscle strength, although without exerting themselves to excessive pain. Verbal encouragement was provided, standardized across all patients and trials. Patients were given adequate rest between trials to minimize fatigue, although this was not standardized and was determined by the patient’s individual readiness to proceed. The peak torque (Nm) and time to peak torque (seconds) were obtained for all trials.

Radiologic evaluation

Radiographic analysis was performed using MRI at 16 weeks after surgery. A Sonata Maestro Class 1.5-T unit (Siemens, Erlangen, Germany) with 40 mT/m gradient power was used for all scans. Multiple images were obtained in oblique coronal, oblique sagittal, and axial planes with short-tau inversion recovery and turbo spin echo T1-weighted sequence. MRI assessment was performed by a fellowship-trained musculoskeletal radiologist with more than 20 years of experience. MRIs were graded according to the Sugaya classification: grade 1 = no tear (sufficient tendon thickness with homogeneously low intensity); grade 2 = sufficient tendon thickness but with partial high intensity; grade 3 = insufficient thickness but no tendon discontinuity; grade 4 = small full-thickness retear (the presence of a minor discontinuity); grade 5 = large full-thickness retear (the presence of a major discontinuity).

Statistical analysis

To address the first goal of this study, independent-sample t tests were used to determine if residual tendinopathy or partial-thickness tendon retears (Sugaya grade 2 or 3) led to poorer strength and functional scores compared with an intact repair (Sugaya grade 1). Participants were grouped according to their 16-week postoperative MRI Sugaya grading (grade 1, 2, or 3), and those with grade 4 or 5 were omitted from the analysis (n = 2). Group means (standard deviation) for the Sugaya grading classifications are presented.

To address the second study goal, discriminant analysis was used to determine if the Sugaya grading (presence and severity of

### Table I Group demographics with details of concomitant procedures and complications

<table>
<thead>
<tr>
<th>Variable</th>
<th>Result (n = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range) years</td>
<td>58.8 (28-77)</td>
</tr>
<tr>
<td>Acromioplasty, No.</td>
<td>60</td>
</tr>
<tr>
<td>Biceps tenotomy, No.</td>
<td>8</td>
</tr>
<tr>
<td>Acromioclavicular joint excision, No.</td>
<td>9</td>
</tr>
<tr>
<td>Complications, No.</td>
<td>0</td>
</tr>
<tr>
<td>Supraspinatus tear size, mean (SD) mm</td>
<td>14 (4)</td>
</tr>
<tr>
<td>SD</td>
<td></td>
</tr>
</tbody>
</table>

*SD = standard deviation.*
Results

Group means (standard deviations) are presented for patients classified by Sugaya grades 1 (21 [36%]), 2 (23 [40%]), or 3 (14 [24%]), and these groups were compared at 16 weeks after surgery (Table II). One patient did not tolerate the postoperative MRI scan due to claustrophobia and instead underwent an US performed by an experienced musculoskeletal radiologist. This tendon repair was intact, with no evidence of thinning or discontinuity, so for the purpose of this study, it was included in the grade 1 Sugaya classification. No significant differences (P > .05) in PRO or isokinetic strength measures were observed among these 3 groups by the Sugaya tear classification system at 16 weeks after surgery (Table II).

Descriptive variables for the groups with intact (Sugaya grade 1) and residual tendinopathy and partial retear (Sugaya grade 2 and 3 pooled) are reported in Table III, with differences (P > .05) observed at 16 weeks after surgery. Discriminant analysis results in Table IV revealed the QuickDASH produced a 97% true-positive rate for predicting partial retears but also a 90% false-positive rate. The ability to discriminate between groups was enhanced with up to 5 variables entered; however, only 87% of the partial-retear group and 36% of the intact-repair group were correctly classified.

Discussion

This study evaluated the early clinical, functional, and MRI status of the supraspinatus tendon after arthroscopic surgical repair. Firstly, we investigated whether differences in common shoulder PRO measures and isokinetic strength tests could be observed between patients with intact repairs or partial-thickness tendon retears, classified by MRI, at 16 weeks after rotator cuff repair surgery. Secondly, we determined whether early postsurgical tendon healing could be predicted using these PRO measures and strength tests.

This study found no significant difference in shoulder PRO and strength measures between patients stratified by the Sugaya MRI classification system (grades 1, 2, or 3) for rotator cuff tears at 16 weeks after surgery. Studies have investigated the diagnostic accuracy of clinical examination
for rotator cuff pathology and concluded that most clinical tests are inaccurate. This study showed that clinical evaluation is also inaccurate after surgery in differentiating a completely intact supraspinatus tendon repair from a repair with residual tendinopathy or partial-thickness retear at 16 weeks after surgery. In this study, all concomitant pathology (lesions of the long head of biceps, acromial spurs and acromioclavicular arthropathy) that might have affected the outcome evaluations had been treated at the time of surgery.

Although discriminant analysis revealed that the QuickDASH produced a 97% true-positive rate for predicting partial retears, it also produced a 90% false-positive rate whereby it incorrectly predicted a retear in 90% of patients whose repaired tendons were in fact intact. The addition of other shoulder PRO measures or isokinetic strength evaluations did not greatly improve the capability of predicting the patient’s early tendon repair outcome. This study concludes that combining such measures does not give confidence in the diagnosis of partial-thickness tendon retears. Some form of imaging assessment (MRI or US) should be used if necessary for the purpose of diagnosing residual tendinopathy or partial-thickness tendon retearing after arthroscopic supraspinatus repair.

However, the early use of shoulder-specific PRO measures or strength evaluations remain important in guiding the rehabilitation process after rotator cuff repair as well as the patient’s specific return to work or sport. Although not specific, these measures appear sensitive for identifying incomplete tendon tearing at 16 weeks after surgical repair. Nho et al reported that 100% of retears occurred in the first 3 months after surgery. Kluger et al reported that most early postoperative retears appear to be a failure to heal and that repair site integrity at 6 months was a predictor of 7-year clinical outcome. On the basis of our results, if a patient has a QuickDASH score that is greater than the mean value we report at 16 weeks after surgery, then incomplete healing or partial-thickness retearing of the tendon requires exclusion by an imaging assessment. Although these results suggest that PRO measures and shoulder strength in a patient with a completely intact repair is equivalent to that of a partial-thickness tendon retear at 16 weeks after surgery, the natural history in ongoing high-demand work or sport is for partial tears to deteriorate. Therefore, early diagnosis of a failing cuff repair by subsequent imaging in these patients may allow for a decelerated rehabilitation program or vocational counselling on restricted work duties and prognosis.

This study has some acknowledged inherent limitations. Firstly, the patient follow-up was limited to 16 weeks. In a primate model of rotator cuff repair, Sonnabend et al reported that a significant proportion of Sharpey fibers start to reconstitute at 3 months, with maturation seen at 4 months. However, if clinical, functional and MRI evaluations were to be repeated at a later time (such as 12 months), it is possible that more structural tearing might be observed, contributing to more pain, diminished function, and improved diagnostic accuracy of the combined testing protocol. Although the primary aim of this study was to assess early postoperative tendon healing, future research may include a longer-term follow-up.

A second limitation is that the PRO instruments we used are used routinely through our clinical practice and research, and we appreciate other shoulder-specific scores are available. It is possible that differences (or an improved predictive capacity) may be observed in other clinical and functional shoulder evaluations.

Thirdly, strength tests also have some inherent limitations because they are unable to differentiate between true muscular weakness, muscular inhibition, and pain-related weakness. The results of the isokinetic strength tests also rely on the patient making a maximal effort. Clear, standardized instructions and verbal encouragement were provided to all participants, but we acknowledged that this was the first time many of the patients would have maximally stressed their operated-on limb since surgery and that some may have been hesitant to exert maximal effort. However, Bigoni et al reported that isokinetic strength testing is a powerful tool for evaluating strength after rotator cuff surgery, so it may be that alternate testing protocols, incorporating shoulder abduction, may more accurately discriminate between groups. Although maximal loading of the supraspinatus during shoulder abduction may be more

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intact repair (n = 21)</th>
<th>Partial retear (n = 37)</th>
<th>Total (n = 58)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxford Shoulder Score</td>
<td>39.2 (6.4)</td>
<td>40.1 (6.3)</td>
<td>39.6 (6.3)</td>
</tr>
<tr>
<td>Visual analog scale for pain</td>
<td>1.5 (1.4)</td>
<td>1.4 (1.6)</td>
<td>1.4 (1.5)</td>
</tr>
<tr>
<td>QuickDASH</td>
<td>21.7 (12.4)</td>
<td>18.1 (14.6)</td>
<td>19.2 (13.7)</td>
</tr>
<tr>
<td>SF-12 (PCS)</td>
<td>42.1 (8.1)</td>
<td>43.2 (7.5)</td>
<td>42.6 (7.6)</td>
</tr>
<tr>
<td>SF-12 (MCS)</td>
<td>53.7 (11.6)</td>
<td>55.1 (8.1)</td>
<td>54.5 (9.6)</td>
</tr>
<tr>
<td>Arm flexion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak torque, Nm</td>
<td>77.1 (22.6)</td>
<td>76.0 (17.0)</td>
<td>76.5 (18.9)</td>
</tr>
<tr>
<td>Time to peak torque, sec</td>
<td>0.53 (0.36)</td>
<td>0.52 (0.44)</td>
<td>0.52 (0.41)</td>
</tr>
<tr>
<td>External humeral rotation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak torque, Nm</td>
<td>75.8 (21.2)</td>
<td>75.0 (19.9)</td>
<td>75.7 (20.0)</td>
</tr>
<tr>
<td>Time to peak torque, sec</td>
<td>0.54 (0.45)</td>
<td>0.60 (0.42)</td>
<td>0.58 (0.43)</td>
</tr>
</tbody>
</table>

MCS, Mental Component Subscale; PCS, Physical Component Subscale; QuickDASH, 11-item version of the Disabilities of the Arm, Shoulder and Hand; SD, standard deviation; SF-12, 12-item Short Form Health Survey.
specific for eliciting pain and weakness, the aim of this study was to evaluate whether these tests could predict early (16-week) outcome, which we consider too early to maximally stress the supraspinatus. Again, this also highlights the need for longer-term evaluation.

Finally, our sample size had 80% power to detect only a large effect size of 0.85 as estimated from prior studies, and therefore, we can be confident that our data provide evidence that such large differences in outcome between groups do not exist. We may have failed to detect smaller group differences with the available sample size.

**Conclusion**

This study found no significant difference in the shoulder PRO measures used or in the isokinetic strength evaluation between patient groups stratified by the Sugaya MRI rotator cuff classification system at 16 weeks after surgery. Furthermore, the presence of an intact repair or partial-thickness tendon retear after rotator cuff surgery could not be accurately predicted by these clinical and functional shoulder evaluations at 16 weeks. Our results suggest that if accurate classification of tendon healing is required in the early stage after rotator cuff surgery, then medical imaging should be used. This will give confidence in patient management of appropriate return to work or sport rehabilitation programs. Reliance on PRO measures and functional scores alone to make an accurate assessment is not supported by our data.

**Acknowledgments**

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**References**


