



# Evidence-based Management of Rotator Cuff Tears (Acute and Chronic)

Rosa M. Pasculli<sup>1</sup> · Robert L. Bowers<sup>1</sup>

Accepted: 1 July 2022

© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2022

## Abstract

**Purpose of Review** This paper should serve as a guide for nonoperative physicians in the management of rotator cuff tears and provide an algorithm of when to refer patients for potential operative repair.

**Recent Findings** While physical therapy remains the mainstay of conservative treatment, recent studies have examined various injections to improve pain and function in partial- and/or full-thickness rotator cuff tears, such as suprascapular nerve blocks, subacromial hyaluronic acid, and intratendinous platelet-rich plasma.

**Summary** Patients who experience an acute, full-thickness rotator cuff tear should be referred as soon as possible for potential surgical repair; however, clinicians should consider the patient's age and activity level. The algorithms for both acute partial-thickness tears and chronic degenerative rotator cuff tears are similar and should initially include a conservative approach of pain control, physical therapy, and potentially various injections before possible referral for surgical evaluation. We anticipate future research examining the role for biologic agents in the conservative treatment of rotator cuff tears.

**Keywords** Rotator cuff tear · Rotator cuff disease · Nonoperative treatment · Conservative management

## Introduction

The rotator cuff (RTC) is a group of four muscles (supraspinatus, infraspinatus, teres minor, and subscapularis) originating from the scapula and inserting on the humerus to provide motion and dynamic stability to the glenohumeral joint. Rotator cuff disease is a wide spectrum that includes acute injury, chronic injury, tendinitis, tendinosis, partial tears, and complete tears. It is a common cause of shoulder pain leading to more than 4.5 million physician visits per year; rotator cuff tears have a prevalence of 13–54% in the general population, with higher rates in patients over 60 years old [1, 2, 3]. The

incidence of rotator cuff repair (RCR) has increased over the past two decades to become the most commonly performed shoulder surgery in the USA with an estimated annual cost of \$1.2–1.6 billion [4, 5, 6].

Most rotator cuff tears involve the supraspinatus tendon; however, they can extend posteriorly or anteriorly to involve the infraspinatus or the subscapularis and long head of the biceps tendon, respectively. Partial-thickness tears can be interstitial (intrasubstance) or involve either the articular (undersurface) or bursal-sided surface of the tendon, whereas a full-thickness tear extends through both surfaces [7]. Articular-sided partial tears are more common due to the decreased strength and hypovascularity of the undersurface compared to the bursal surface [8]. Partial-thickness tears are graded using the Ellman classification according to depth: grade I (< 3 mm), grade II (3–6 mm), or grade III (> 6 mm) [9]. A full-thickness tear can be further subcategorized into focal versus incomplete for small tears, or complete if it encompasses the full width of a tendon. These can also be graded using the classification described by DeOrto and Cofield as either small (< 1 cm), medium (1–3 cm), large (3–5 cm), or massive (> 5 cm or involving two or more tendons) [10].

This article is part of the Topical Collection on *Sports Medicine Rehabilitation*

✉ Robert L. Bowers  
rlbower@emory.edu

Rosa M. Pasculli  
rmpascu@emory.edu

<sup>1</sup> Department of Orthopedics, Division of Sports Medicine, Emory University, Atlanta, GA, USA

Rotator cuff tears can present acutely related to shoulder trauma or as a chronic finding related to overload, subacromial impingement, and gradual degeneration of the tendons. Practitioners should rely on the patient's history of symptoms, as well information from diagnostic imaging to determine an acute versus chronic tear. MRI findings of a chronic tear include cephalad migration of the humeral head and fatty atrophy of the supraspinatus and infraspinatus, whereas edema of the associated muscle and kinking of the central tendon are associated with traumatic tears [11, 12]. Musculoskeletal ultrasound in the hands of an appropriately experienced practitioner can provide additional detail as to the nature of the rotator cuff tear. Acute tears tend to occur more proximally and are filled with anechoic fluid, while cortical irregularity of the greater tuberosity next to a hypoechoic tendon abnormality suggests a chronic tear [13, 14]. The purpose of this review is to discuss the nonoperative and surgical treatment options that are available for both acute and chronic rotator cuff tears, as well as suggested practice guidelines for how to approach treatment.

## Management of Chronic Rotator Cuff Tears

### Physical Therapy

Physical therapy has become the mainstay of conservative treatment for symptomatic chronic rotator cuff tears, including both partial and full-thickness tears; however, the success is variable. Physical therapy for rotator cuff tears focuses on strengthening of the scapular stabilizers and rotator cuff muscles, as well as improving range of motion and stretching of the shoulder capsule [15]. An important consideration when initiating treatment is the natural progression of rotator cuff tears managed nonoperatively. Patients with rotator cuff tears have a risk of developing a larger tear, fatty infiltration, and/or muscle atrophy if treated conservatively; these risks appear to be higher in patients over 60 years old and in those with a full-thickness tear [16, 17]. Patients with a full-thickness tear appear to have approximately 50% chance of progressing the size of their tear; however, Moosmayer and colleagues demonstrated deterioration of functional outcomes at 8.8 years was only associated with an increased tear size of  $\geq 20$  mm in the anterior–posterior plane [16]. The risk of tear progression was similar in other studies with shorter follow-up periods as well [17, 18]. While the risk of tear progression is overall lower in partial rotator cuff tears, high-grade partial-thickness tears involving  $> 50\%$  of tendon thickness are more likely to progress in size compared to low-grade partial-thickness tears [19].

There are few studies directly comparing physical therapy to other treatment options, including operative management of rotator cuff tears, and there is significant heterogeneity,

incomplete outcome reporting, and high risk of bias in the available literature; however, there is evidence to support the use of exercise in treating both partial- and full-thickness rotator cuff tears [20, 21, 22]. In patients with small and medium full-thickness rotator cuff tears ( $< 3$  cm), there was no significant difference in patient-reported outcomes at 5 years in cohorts treated with physical therapy or operative RCR, and both groups demonstrated meaningful improvement in their strength and function compared to baseline [23]. Another study demonstrated similar findings in patients treated with either operative repair or physical therapy, with no significant difference in pain, patient satisfaction, or shoulder function at 2-year follow-up [24]. We recommend that all patients with chronic partial- or full-thickness rotator cuff tears undergo at least 6 weeks of physical therapy either preceding or concomitant to an injection, or prior to consideration of operative intervention.

### Extracorporeal Shockwave Therapy

Extracorporeal shockwave therapy (ESWT) is a non-invasive therapy that involves soundwave delivery to a focused area of the body. It was initially developed for the treatment of nephrolithiasis and is now being extensively studied for musculoskeletal conditions [25, 26]. There have been several studies examining ESWT for both calcific and non-calcific rotator cuff tendinopathy, and more recent studies examining its use in rotator cuff tears [27, 28]. One small study examining the effect of ESWT in both athletes and older patients with rotator cuff tendinopathy and partial rotator cuff tears demonstrated high patient satisfaction with significantly improved pain and function at 1-year post-treatment [29]. A recent case series looked at the effect of ESWT in multiple shoulder conditions including partial rotator cuff tears and found significantly improved pain and function in all groups at 3 months post-treatment, as well as improved tendon appearance on MRI 6 months after shockwave treatment [30]. Prior animal studies have shown that ESWT stimulates neovascularization of tendons and is associated with early release of markers related to angiogenesis, which authors hypothesized may play a role in improving the blood supply and regenerating the tendon at the tendon-bone junction [31, 32]. Large, prospective randomized-controlled trials are needed to further examine this modality; however, ESWT may represent a potential treatment option for patients looking to avoid operative intervention.

### Injections: Corticosteroid, Suprascapular Nerve Block, Hyaluronic Acid, Platelet-rich Plasma, Mesenchymal Stromal Cells

Corticosteroid injections (CSI) are used often in treating musculoskeletal complaints; however, there is concern

for the use of steroids in or around tendons as they can contribute to collagen collapse, loss of tensile strength, and tendon rupture [33, 34]. Steroids can also predispose patients to infection with future surgical procedures, and there is some evidence that they can increase the risk of rotator cuff failure if performed in the 6 months prior to surgery [35, 36]. A Cochrane review of multiple randomized-controlled trials of varying sample sizes and quality found that while subacromial corticosteroid injections provide short-term pain relief from rotator cuff tears, the effects tend to be temporary [37]. Corticosteroid injections may be useful in symptom relief in patients with significant pain associated with their RTC tear not managed with oral pain medications, but the risks should be carefully reviewed with the patients. Another option for those looking to avoid the potential risks of corticosteroid is a subacromial injection with the non-steroidal anti-inflammatory drug (NSAID) ketorolac, which has been shown to significantly improve pain and function in patients with subacromial impingement syndrome [38]. The basic science literature has demonstrated varying results of NSAIDs on tendon histology; however, they may have positive effects in the maturation and remodeling phases seen in degenerative processes [39, 40]. Although future studies are needed to further explore this, a subacromial ketorolac injection is a potential therapeutic option for patients with pain due to chronic partial- or full-thickness rotator cuff tears.

Another option for potential pain relief is a suprascapular nerve block (SSNB). The suprascapular nerve is a peripheral nerve that originates from the ventral rami of C5 and C6 roots and comes off the upper trunk of the brachial plexus. It contains both motor and sensory nerve fibers. After passing through the suprascapular notch, the sensory fibers depart as the superior articular branch to innervate the coracoclavicular and coracohumeral ligaments, the acromioclavicular and glenohumeral joints, and the subacromial bursa [41]. While the injectate type and volume varies in the literature, 5 cc of bupivacaine 0.25% or 0.5% is commonly used and a steroid can potentially be added for a therapeutic effect [42, 43]. Ultrasound (US) guidance can be used to identify the nerve at the floor of the suprascapular fossa, as well as to identify the nearby suprascapular artery to avoid during the procedure [44]. Several small studies have examined the utility of SSNB in chronic rotator cuff tendinitis/tendinosis and have demonstrated temporary improvement in pain and range of motion after SSNB alone or in addition to physical therapy [45, 46]. A small double-blinded, randomized-controlled trial compared SSNB to subacromial CSI in patients with symptomatic partial- and full-thickness RTC tears and found significantly improved pain and function at 12 weeks in the SSNB compared to the subacromial group [47•]. US-guided suprascapular nerve block is a safe injection that can provide temporary relief in patients with rotator cuff disease,

especially in those with concomitant arthritis or potentially awaiting surgical repair. We recommend 2 cc of lidocaine 1% plus 2 cc of ropivacaine 0.2% for a diagnostic injection, with the option to add 0.5 cc of dexamethasone 4 mg/mL for therapeutic effect.

Hyaluronic acid (HA) is a naturally produced polysaccharide with viscoelastic properties that contributes to the lubrication, shock absorption, and nutrition of joint tissues and is a commonly used and well-tolerated treatment for knee osteoarthritis; however, it is also thought to have anti-inflammatory and pain-relieving properties which may lend itself to treatment of soft tissue pathologies [48]. HA injections (weekly  $\times$  3–5 weeks) into the subacromial bursa have been shown to improve pain and function associated with partial rotator cuff tears but were not found to improve either outcome in complete tears [49, 50, 51]. The HA injections were well tolerated in all studies and no significant adverse effects were reported. A recent systematic review and meta-analysis found support for the efficacy of HA injections in improving pain and function related to partial rotator cuff tears [52]. Additional prospective randomized-controlled trials are needed to further examine the efficacy of HA in RTC tears, as well as data to determine the most effective molecular weight of HA and the frequency at which it should be injected.

Platelet-rich plasma (PRP) is an autologous concentration of platelets with at least 1,000,000 platelets/ $\mu$ L in 5 mL of plasma isolated from the patient's whole blood using centrifugation. PRP is thought to accelerate the healing process through modulating the inflammatory response and pain-relieving pathways via the release or attraction of growth factors, cytokines, and mesenchymal stromal cells [53, 54]. The literature related to PRP as a potential treatment for rotator cuff pathology is growing; however, studies are mixed in relation to its efficacy. One open study examined the safety and efficacy of a dual PRP injection into the supraspinatus insertion and glenohumeral joint space and found significantly improved pain and functional scores that persisted at 2 years. There were no adverse effects and no patient with a partial tear progressed to a full-thickness tear [55•]. A recent randomized-controlled trial compared a subacromial injection of either leukocyte-poor PRP or corticosteroid and found significantly improved pain and function in the PRP cohort at 3 months, but no significant change between the two groups at 12 months with similar failure rates [56]. There have been several recent systematic reviews with meta-analyses examining the use of PRP for rotator cuff disease in a nonoperative setting (inclusive of both partial tears and tendinopathy) also reporting conflicting results [57, 58, 59, 60, 61]. The PLRA classification system described by Mautner and colleagues discusses the important characteristics to report when conducting research using PRP; however, the authors of these recent review articles note

the wide heterogeneity in the methodology as well as the reporting of how the PRP was prepared, including the total administered platelet count, leukocyte content (leukocyte-rich versus leukocyte-poor), and type of leukocytes present, and the use of an activating agent [62].

While we acknowledge the mixed evidence, it appears that PRP can provide relief to patients with partial RTC tears. Giovannetti and colleagues conducted a systematic review examining the effect of various subacromial injections in partial rotator cuff tears (corticosteroids, PRP, prolotherapy) and found that while corticosteroid injections significantly reduced pain in the short and medium term (< 12 weeks) compared to other injections, PRP provided significant pain reduction and better functional outcomes at all points, including long term (> 24 weeks) [63]. A combined injection of hyaluronic acid and PRP (weekly  $\times$  4 weeks) into the subacromial space was found to significantly improve pain and function of partial small to medium bursal-sided tears compared to either PRP, hyaluronic acid, or normal saline alone, with associated significant reduction of anterior to posterior tear size as measured by MRI at 12 months in both the PRP and PRP + HA groups [64]. We recognize the need for standardization of PRP preparation methods as well as the consistent reporting of cellular content. Once this is homogenized, then the optimal PRP injection and possible combination with current therapies can be better determined. However, it is our opinion that intratendinous PRP is a safe treatment option for patients who wish to pursue additional nonoperative treatments for rotator cuff tendinopathy and tears.

Mesenchymal stromal cells (MSCs) are multipotent cells that can be isolated from different tissues, including adipose, bone marrow, synovium, and umbilical cord blood. They can affect the healing response via activation of cell proliferation and differentiation, as well as decreased inflammation and cell apoptosis [65, 66]. There are few case reports and low-level clinical studies in the literature examining the effects of stromal cell injections on rotator cuff tears. Recent case studies and small pilot studies have examined micro-fragmented adipose tissue (MFAT) injections  $\pm$  additional PRP injections as a possible treatment option for chronic partial supraspinatus tears with resulting improvements in pain and function [67, 68, 69]. A small open study found that an intratendinous injection of adipose tissue-derived mesenchymal stromal cells (AD-MSCs) significantly reduced shoulder pain and increased RTC strength at 1 and 2 years post-injection with associated decreased size of the tear seen on corresponding MRI [70]. In a small case-controlled study, Kim and colleagues compared a combination of bone marrow-derived mesenchymal stem cells (BM-MSCs) + PRP injected into the rotator cuff tear to a control group who received daily physical therapy and demonstrated significantly decreased pain and significantly improved shoulder

function at 3 months in the injection group [71]. In a similar small case-controlled study, Centeno and colleagues compared a BM-MSCs + PRP + platelet lysate intratendinous injection to home exercise program in patients with partial to full-thickness RTC tears and found significantly improved pain and function in the biologics cohort at 3 and 6 months [72]. Larger, prospective randomized-controlled studies are needed to examine the value of mesenchymal stromal cells in the treatment of rotator cuff tears.

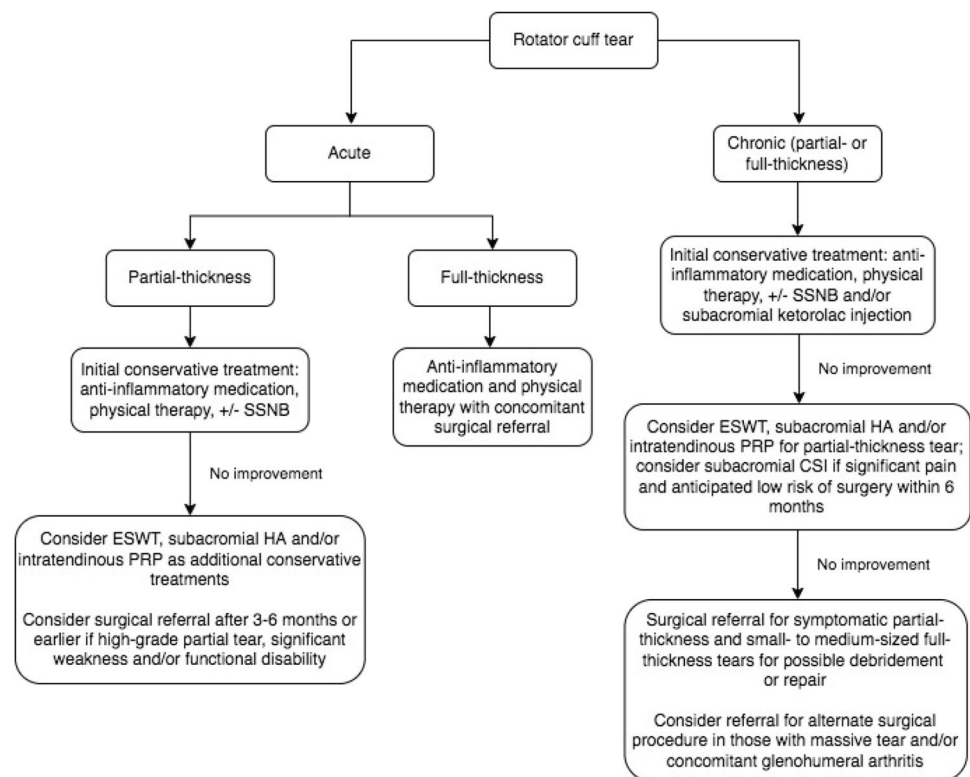
### Additional Nonoperative Treatments

There are other modalities that are used by practitioners in the treatment of rotator cuff tears (therapeutic ultrasound, acupuncture, transcutaneous electromagnetic stimulation, low-level laser therapy); however, there is insufficient evidence as to their benefits in this specific injury population. We recognize these are low-risk procedures and may be considered as adjunctive treatment with experienced practitioners.

### Operative Repair

Surgical intervention for chronic rotator cuff tears should be considered only after the patient has failed a trial of conservative management, as rotator cuff repair has not consistently been shown to result in superior pain control or functional outcomes compared to nonoperative management [73]. Surgical approaches include rotator cuff debridement or rotator cuff repair (arthroscopic or open). For patients with massive rotator cuff tears, concomitant glenohumeral arthritis, or significantly limited function, surgeons may consider an alternate procedure such as a tendon transfer or reverse total shoulder arthroplasty [74, 75]. Surgical outcomes depend on several variables. There is strong evidence that older age is associated with increased re-tear rates and worse patient-reported outcomes [76, 77, 78]. Increased tear size is a risk factor for poor healing after rotator cuff repair, as well as baseline fatty degeneration and muscle atrophy, which do not improve after rotator cuff repair [76, 78]. While the number of comorbidities does not necessarily predict worse outcomes after rotator cuff repair, patients with diabetes and current smokers were found to have worse patient-reported outcomes and higher re-tear rates after rotator cuff repair [79, 80, 81]. As discussed previously, physical therapy was shown to be non-inferior to rotator cuff repair at 5 years for small- to medium-sized full-thickness tears; however, a follow-up study was published showing that the operative group had significantly improved pain and function compared to the PT group at 10 years [82•]. We recommend a surgical consult for patients with symptomatic small- to medium-sized full-thickness tears who have failed a course of physical therapy and conservative management.

**Fig. 1** Recommendations for the nonoperative physician's approach to the management of rotator cuff tears



PRP has also been examined as an adjunct to the operative management of RTC tears; however, the outcomes are mixed. The American Academy of Orthopaedic Surgeons does not recommend the use of PRP with rotator cuff repair in their clinical practice guidelines as it has not been shown to improve postoperative patient-reported outcomes [75]. There have been studies that suggest biologic augmentation with PRP could decrease re-tear rates after surgery; however, as we have noted above, there is a lack of standardization of PRP formulation [83, 84]. While there are fewer studies examining MSCs as an adjuvant to rotator cuff repair, a case-controlled study comparing intra-operative BM-MSCs during arthroscopic rotator cuff repair to a control group found significantly increased intact single-row repairs at 6 months and 10 years in the stem BM-MSC group [85]. We anticipate future studies examining biologic augmentation of rotator cuff repair with PRP and MSCs for various sized tears.

## Management of Acute Rotator Cuff Tears

Acute rotator cuff tears typically occur in younger patients (under 60 years old), more commonly in males, who experience a traumatic event (i.e., falling on an outstretched arm or a trauma involving an abducted arm in external rotation) [86]. Patients with acute, partial-thickness tears have been

shown to have significant functional improvement with conservative treatment [87]. While the literature suggests that high-grade partial-thickness tears involving > 50% of the tendon are more likely to progress in tear size following nonoperative treatment, there is evidence that patients who perform at least 6 months of conservative treatment prior to surgical repair of a partial-thickness tear have improved postoperative outcomes compared to patients who undergo immediate surgical repair following their injury [88]. We recommend patients with a partial-thickness rotator cuff tear follow a similar algorithm as described above beginning with pain control and physical therapy with consideration of adjunct modalities and injections if warranted [89]. We recommend a trial of conservative treatment for 3–6 months before initiating surgical referral for a partial-thickness tear, but of course, this may occur sooner based on the shared decision making between the patient and physician, especially in the setting of high-grade tears, significant weakness, and/or functional disability [1]. Initial nonoperative treatment is typically recommended for athletes as well, including overhead and master athletes, with operative management reserved for those who fail to improve with consistent conservative treatment [15, 90]. We do not recommend the use of subacromial corticosteroid injections in the setting of an acute partial- or full-thickness tear due to the risk of further tendon degeneration. A suprascapular nerve block may



provide further pain relief in addition to or instead of oral anti-inflammatory medications. Shockwave treatment and intratendinous PRP may be considered as well for partial-thickness tears that do not improve with anti-inflammatory medications and physical therapy in patients who are interested in deferring surgical referral.

In otherwise healthy patients who have sustained an acute, full-thickness rotator cuff tear, there is strong evidence that surgical repair should be performed to improve function and prevent tear enlargement and significant muscle atrophy [91, 92]. While the timing is debated in the literature, there is evidence that repair should be performed within 4 months of injury, but ideally within several weeks [93, 94, 95]. We recommend that all patients with acute full-thickness tears be evaluated by a surgeon for potential repair, even though they may ultimately defer operative repair after considering the size of the tear, the patient's age, and their activity level.

We have summarized our recommendations and general approach for the treatment acute and chronic partial-thickness and full-thickness rotator cuff tears in Fig. 1.

## Conclusion

Rotator cuff tears are one of the most common presenting etiologies of shoulder pain; however, treatment can be challenging, especially the decision for when nonoperative physicians should refer patients to an orthopedic surgeon to discuss operative repair. Patients who experience an acute, partial-thickness rotator cuff tear should be managed conservatively with pain control, physical therapy, and potential injections. Patients who experience an acute, full-thickness rotator cuff tear should be referred as soon as possible for potential surgical repair; however, clinicians should consider the patient's age and activity level. Patients with chronic degenerative rotator cuff tears (both partial- and full-thickness) should be managed initially with a conservative approach that includes pain control, physical therapy, and potentially injections, and can potentially be referred for a surgical evaluation after treatment failure. We anticipate future research examining the role for biologic agents in conservative treatment of rotator cuff tears.

## Declarations

**Conflicts of Interest** The authors declare no competing interests.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

## References

Papers of particular interest, published recently, have been highlighted as:

### • Of importance

1. Oh LS, Wolf BR, Hall MP, Levy BA, Marx RG. Indications for rotator cuff repair: a systematic review. *Clin Orthop Relat Res.* 2007;455:52–63. <https://doi.org/10.1097/BLO.0b013e31802fc175>.
2. Sher JS, Uribe JW, Posada A, Murphy BJ, Zlatkin MB. Abnormal findings on magnetic resonance images of asymptomatic shoulders. *J Bone Joint Surg Am.* 1995;77(1):10–5. <https://doi.org/10.2106/00004623-199501000-00002>.
3. Löhr JF, Uthoff HK. Epidemiology and pathophysiology of rotator cuff tears. *Orthopade.* 2007;36(9):788–95. <https://doi.org/10.1007/s00132-007-1146-8>.
4. Chalmers PN, Granger E, Nelson R, Yoo M, Tashjian RZ. Factors affecting cost, outcomes, and tendon healing after arthroscopic rotator cuff repair. *Arthroscopy.* 2018;34(5):1393–400. <https://doi.org/10.1016/j.arthro.2017.11.015>.
5. Ensor KL, Kwon YW, Dibeneditto MR, Zuckerman JD, Rokito AS. The rising incidence of rotator cuff repairs. *J Shoulder Elbow Surg.* 2013;22(12):1628–32. <https://doi.org/10.1016/j.jse.2013.01.006>.
6. Jain NB, Higgins LD, Losina E, Collins J, Blazar PE, Katz JN. Epidemiology of musculoskeletal upper extremity ambulatory surgery in the United States. *BMC Musculoskelet Disord.* 2014;15:4. <https://doi.org/10.1186/1471-2474-15-4>.
7. Jacobson JA. *Fundamentals of musculoskeletal ultrasound.* 3rd ed. Philadelphia, PA: Elsevier; 2018.
8. Matava MJ, Purcell DB, Rudzki JR. Partial-thickness rotator cuff tears. *Am J Sports Med.* 2005;33(9):1405–17. <https://doi.org/10.1177/0363546505280213>.
9. Ellman H, Kay SP. Arthroscopic subacromial decompression for chronic impingement. Two- to five-year results. *J Bone Joint Surg Br.* 1991;73(3):395–8. <https://doi.org/10.1302/0301-620X.73B3.1670435>.
10. DeOrto JK, Cofield RH. Results of a second attempt at surgical repair of a failed initial rotator-cuff repair. *J Bone Joint Surg Am.* 1984;66(4):563–7.
11. Loew M, Magosch P, Lichtenberg S, Habermeyer P, Porschke F. How to discriminate between acute traumatic and chronic degenerative rotator cuff lesions: an analysis of specific criteria on radiography and magnetic resonance imaging. *J Shoulder Elbow Surg.* 2015;24(11):1685–93. <https://doi.org/10.1016/j.jse.2015.06.005>.
12. Iannotti JP, Zlatkin MB, Esterhai JL, Kressel HY, Dalinka MK, Spindler KP. Magnetic resonance imaging of the shoulder. Sensitivity, specificity, and predictive value. *J Bone Joint Surg Am.* 1991;73(1):17–29.
13. Wohlwend JR, van Holsbeeck M, Craig J, Shirazi K, Habra G, Jacobsen G, et al. The association between irregular greater tuberosities and rotator cuff tears: a sonographic study. *AJR Am J Roentgenol.* 1998;171(1):229–33. <https://doi.org/10.2214/ajr.171.1.9648794>.
14. Teefey SA, Middleton WD, Bauer GS, Hildebolt CF, Yamaguchi K. Sonographic differences in the appearance of acute and chronic full-thickness rotator cuff tears. *J Ultrasound Med.* 2000;19(6):377–8; quiz 83. <https://doi.org/10.7863/jum.2000.19.6.377>.
15. Rodriguez-Santiago B, Castillo B, Baerga-Varela L, Mícheo WF. Rehabilitation management of rotator cuff injuries in the master

- athlete. *Curr Sports Med Rep.* 2019;18(9):330–7. <https://doi.org/10.1249/JSR.0000000000000628>.
16. Moosmayer S, Gärtner AV, Tariq R. The natural course of non-operatively treated rotator cuff tears: an 8.8-year follow-up of tear anatomy and clinical outcome in 49 patients. *J Shoulder Elbow Surg.* 2017;26(4):627–34. <https://doi.org/10.1016/j.jse.2016.10.002>
  17. Maman E, Harris C, White L, Tomlinson G, Shashank M, Boynton E. Outcome of nonoperative treatment of symptomatic rotator cuff tears monitored by magnetic resonance imaging. *J Bone Joint Surg Am.* 2009;91(8):1898–906. <https://doi.org/10.2106/JBJS.G.01335>.
  18. Safran O, Schroeder J, Bloom R, Weil Y, Milgrom C. Natural history of nonoperatively treated symptomatic rotator cuff tears in patients 60 years old or younger. *Am J Sports Med.* 2011;39(4):710–4. <https://doi.org/10.1177/0363546510393944>.
  19. Lo IK, Denkers MR, More KD, Nelson AA, Thornton GM, Boorman RS. Partial-thickness rotator cuff tears: clinical and imaging outcomes and prognostic factors of successful nonoperative treatment. *Open Access J Sports Med.* 2018;9:191–7. <https://doi.org/10.2147/OAJSM.S153236>.
  20. Page MJ, Green S, McBain B, Surace SJ, Deitch J, Lyttle N, et al. Manual therapy and exercise for rotator cuff disease. *Cochrane Database Syst Rev.* 2016(6):CD012224. <https://doi.org/10.1002/14651858.CD012224>
  21. Ainsworth R, Lewis JS. Exercise therapy for the conservative management of full thickness tears of the rotator cuff: a systematic review. *Br J Sports Med.* 2007;41(4):200–10. <https://doi.org/10.1136/bjism.2006.032524>.
  22. Jeanfavre M, Husted S, Leff G. Exercise therapy in the non-operative treatment of full-thickness rotator cuff tears: a systematic review. *Int J Sports Phys Ther.* 2018;13(3):335–78.
  23. Moosmayer S, Lund G, Seljom US, Haldorsen B, Svege IC, Hennig T, et al. Tendon repair compared with physiotherapy in the treatment of rotator cuff tears: a randomized controlled study in 103 cases with a five-year follow-up. *J Bone Joint Surg Am.* 2014;96(18):1504–14. <https://doi.org/10.2106/JBJS.M.01393>.
  24. Kukkonen J, Joukainen A, Lehtinen J, Mattila KT, Tuominen EK, Kauko T, et al. Treatment of nontraumatic rotator cuff tears: a randomized controlled trial with two years of clinical and imaging follow-up. *J Bone Joint Surg Am.* 2015;97(21):1729–37. <https://doi.org/10.2106/JBJS.N.01051>.
  25. Chaussy C, Schmiedt E, Jocham D, Brendel W, Forssmann B, Walther V. First clinical experience with extracorporeally induced destruction of kidney stones by shock waves. *J Urol.* 1982;127(3):417–20. [https://doi.org/10.1016/s0022-5347\(17\)53841-0](https://doi.org/10.1016/s0022-5347(17)53841-0).
  26. Reilly JM, Bluman E, Tenforde AS. Effect of shockwave treatment for management of upper and lower extremity musculoskeletal conditions: a narrative review. *PM R.* 2018;10(12):1385–403. <https://doi.org/10.1016/j.pmrj.2018.05.007>.
  27. Galasso O, Amelio E, Riccelli DA, Gasparini G. Short-term outcomes of extracorporeal shock wave therapy for the treatment of chronic non-calcific tendinopathy of the supraspinatus: a double-blind, randomized, placebo-controlled trial. *BMC Musculoskelet Disord.* 2012;13:86. <https://doi.org/10.1186/1471-2474-13-86>.
  28. Ioppolo F, Tattoli M, Di Sante L, Attanasi C, Venditto T, Servidio M, et al. Extracorporeal shock-wave therapy for supraspinatus calcifying tendinitis: a randomized clinical trial comparing two different energy levels. *Phys Ther.* 2012;92(11):1376–85. <https://doi.org/10.2522/ptj.20110252>.
  29. Chou WY, Wang CJ, Wu KT, Yang YJ, Cheng JH, Wang SW. Comparative outcomes of extracorporeal shockwave therapy for shoulder tendinitis or partial tears of the rotator cuff in athletes and non-athletes: Retrospective study. *Int J Surg.* 2018;51:184–90. <https://doi.org/10.1016/j.ijsu.2018.01.036>.
  30. Oliveira VOM, Vergara JM, Oliveira VF, Lara PHS, Nogueira LC, Arliani GG. Extracorporeal shockwave therapy in shoulder injuries: prospective study. *Acta Ortop Bras.* 2021;29(5):268–73. <https://doi.org/10.1590/1413-785220212905237628>.
  31. Wang CJ, Wang FS, Yang KD, Weng LH, Hsu CC, Huang CS, et al. Shock wave therapy induces neovascularization at the tendon-bone junction. A study in rabbits. *J Orthop Res.* 2003;21(6):984–9. [https://doi.org/10.1016/S0736-0266\(03\)00104-9](https://doi.org/10.1016/S0736-0266(03)00104-9)
  32. Chen YJ, Wang CJ, Yang KD, Kuo YR, Huang HC, Huang YT, et al. Extracorporeal shock waves promote healing of collagenase-induced Achilles tendinitis and increase TGF-beta1 and IGF-I expression. *J Orthop Res.* 2004;22(4):854–61. <https://doi.org/10.1016/j.orthres.2003.10.013>.
  33. Haraldsson BT, Langberg H, Aagaard P, Zuurmond AM, van El B, Degroot J, et al. Corticosteroids reduce the tensile strength of isolated collagen fascicles. *Am J Sports Med.* 2006;34(12):1992–7. <https://doi.org/10.1177/0363546506290402>.
  34. Mikolyzk DK, Wei AS, Tonino P, Marra G, Williams DA, Himes RD, et al. Effect of corticosteroids on the biomechanical strength of rat rotator cuff tendon. *J Bone Joint Surg Am.* 2009;91(5):1172–80. <https://doi.org/10.2106/JBJS.H.00191>.
  35. Weber AE, Trasolini NA, Mayer EN, Essilfie A, Vangsness CT, Gamradt SC, et al. Injections prior to rotator cuff repair are associated with increased rotator cuff revision rates. *Arthroscopy.* 2019;35(3):717–24. <https://doi.org/10.1016/j.arthro.2018.10.116>.
  36. Traven SA, Brinton D, Simpson KN, Adkins Z, Althoff A, Palsis J, et al. Preoperative shoulder injections are associated with increased risk of revision rotator cuff repair. *Arthroscopy.* 2019;35(3):706–13. <https://doi.org/10.1016/j.arthro.2018.10.107>.
  37. Buchbinder R, Green S, Youd JM. Corticosteroid injections for shoulder pain. *Cochrane Database Syst Rev.* 2003(1):CD004016. <https://doi.org/10.1002/14651858.CD004016>
  38. Min KS, St Pierre P, Ryan PM, Marchant BG, Wilson CJ, Arrington ED. A double-blind randomized controlled trial comparing the effects of subacromial injection with corticosteroid versus NSAID in patients with shoulder impingement syndrome. *J Shoulder Elbow Surg.* 2013;22(5):595–601. <https://doi.org/10.1016/j.jse.2012.08.026>.
  39. Almekinders LC, Banes AJ, Ballenger CA. Effects of repetitive motion on human fibroblasts. *Med Sci Sports Exerc.* 1993;25(5):603–7.
  40. Radi ZA, Khan NK. Effects of cyclooxygenase inhibition on bone, tendon, and ligament healing. *Inflamm Res.* 2005;54(9):358–66. <https://doi.org/10.1007/s00011-005-1367-4>.
  41. Ajmani ML. The cutaneous branch of the human suprascapular nerve. *J Anat.* 1994;185(Pt 2):439–42.
  42. Price DJ. What local anesthetic volume should be used for suprascapular nerve block? *Reg Anesth Pain Med.* 2008;33(6):571; author reply -3. <https://doi.org/10.1097/00115550-200811000-00010>
  43. Chan CW, Peng PW. Suprascapular nerve block: a narrative review. *Reg Anesth Pain Med.* 2011;36(4):358–73. <https://doi.org/10.1097/AAP.0b013e3182204ec0>.
  44. Harmon D, Hearty C. Ultrasound-guided suprascapular nerve block technique. *Pain Physician.* 2007;10(6):743–6.
  45. Vecchio PC, Adebajo AO, Hazleman BL. Suprascapular nerve block for persistent rotator cuff lesions. *J Rheumatol.* 1993;20(3):453–5.
  46. Di Lorenzo L, Pappagallo M, Gimigliano R, Palmieri E, Saviano E, Bello A, et al. Pain relief in early rehabilitation of rotator cuff

- tendinitis: any role for indirect suprascapular nerve block? *Eura Medicophys.* 2006;42(3):195–204.
47. ● Coory JA, Parr AF, Wilkinson MP, Gupta A. Efficacy of suprascapular nerve block compared with subacromial injection: a randomized controlled trial in patients with rotator cuff tears. *J Shoulder Elbow Surg.* 2019;28(3):430–6. <https://doi.org/10.1016/j.jse.2018.11.051>. (This study suggests that suprascapular nerve block can lead to significantly improved short-term pain and function for both partial- and full-thickness symptomatic rotator cuff tears.)
  48. Moreland LW. Intra-articular hyaluronan (hyaluronic acid) and hylans for the treatment of osteoarthritis: mechanisms of action. *Arthritis Res Ther.* 2003;5(2):54–67. <https://doi.org/10.1186/ar623>.
  49. Moghtaderi A, Sajadiyeh S, Khosrawi S, Dehghan F, Bateni V. Effect of subacromial sodium hyaluronate injection on rotator cuff disease: a double-blind placebo-controlled clinical trial. *Adv Biomed Res.* 2013;2:89. <https://doi.org/10.4103/2277-9175.122517>.
  50. Chou WY, Ko JY, Wang FS, Huang CC, Wong T, Wang CJ, et al. Effect of sodium hyaluronate treatment on rotator cuff lesions without complete tears: a randomized, double-blind, placebo-controlled study. *J Shoulder Elbow Surg.* 2010;19(4):557–63. <https://doi.org/10.1016/j.jse.2009.08.006>.
  51. Gigante A, Cecconi S, Enea D, Cesari E, Valeri G, Busilacchi A. Effect of subacromial injections of hyaluron on different grades of rotator cuff lesion: a prospective study. *Eur J Inflamm.* 2013;11(3):777–87. <https://doi.org/10.1177/1721727X1301100320>.
  52. Khan M, Shanmugaraj A, Prada C, Patel A, Babins E, Bhandari M. The role of hyaluronic acid for soft tissue indications: a systematic review and meta-analysis. *Sports Health.* 2022;19417381211073316. <https://doi.org/10.1177/19417381211073316>
  53. Foster TE, Puskas BL, Mandelbaum BR, Gerhardt MB, Rodeo SA. Platelet-rich plasma: from basic science to clinical applications. *Am J Sports Med.* 2009;37(11):2259–72. <https://doi.org/10.1177/0363546509349921>.
  54. Andia I, Rubio-Azpeitia E, Maffulli N. Platelet-rich plasma modulates the secretion of inflammatory/angiogenic proteins by inflamed tenocytes. *Clin Orthop Relat Res.* 2015;473(5):1624–34. <https://doi.org/10.1007/s11999-015-4179-z>.
  55. ● Prodromos CC, Finkle S, Prodromos A, Chen JL, Schwartz A, Wathen L. Treatment of rotator cuff tears with platelet rich plasma: a prospective study with 2 year follow-up. *BMC Musculoskelet Disord.* 2021;22(1):499. <https://doi.org/10.1186/s12891-021-04288-4>. (Findings from this study suggest that PRP can provide long-term improvements in pain and function in patients with partial rotator cuff tears.)
  56. Kwong CA, Woodmass JM, Gusnowski EM, Bois AJ, Leblanc J, More KD, et al. Platelet-rich plasma in patients with partial-thickness rotator cuff tears or tendinopathy leads to significantly improved short-term pain relief and function compared with corticosteroid injection: a double-blind randomized controlled trial. *Arthroscopy.* 2021;37(2):510–7. <https://doi.org/10.1016/j.arthro.2020.10.037>.
  57. Chen X, Jones IA, Togashi R, Park C, Vangsness CT. Use of platelet-rich plasma for the improvement of pain and function in rotator cuff tears: a systematic review and meta-analysis with bias assessment. *Am J Sports Med.* 2020;48(8):2028–41. <https://doi.org/10.1177/0363546519881423>.
  58. Xiang XN, Deng J, Liu Y, Yu X, Cheng B, He HC. Conservative treatment of partial-thickness rotator cuff tears and tendinopathy with platelet-rich plasma: a systematic review and meta-analysis. *Clin Rehabil.* 2021;35(12):1661–73. <https://doi.org/10.1177/02692155211011944>.
  59. Wang C, Zhang Z, Ma Y, Liu X, Zhu Q. Platelet-rich plasma injection vs corticosteroid injection for conservative treatment of rotator cuff lesions: a protocol for systematic review and meta-analysis. *Medicine (Baltimore).* 2021;100(7):e24680. <https://doi.org/10.1097/MD.00000000000024680>.
  60. Lui M, Shih W, Yim N, Brandstater M, Ashfaq M, Tran D. Systematic review and meta-analysis of nonoperative platelet-rich plasma shoulder injections for rotator cuff pathology. *PM R.* 2021;13(10):1157–68. <https://doi.org/10.1002/pmrj.12516>.
  61. Robinson DM, Eng C, Makovitch S, Rothenberg JB, DeLuca S, Douglas S, et al. Non-operative orthobiologic use for rotator cuff disorders and glenohumeral osteoarthritis: a systematic review. *J Back Musculoskelet Rehabil.* 2021;34(1):17–32. <https://doi.org/10.3233/BMR-201844>.
  62. Mautner K, Malanga GA, Smith J, Shiple B, Ibrahim V, Sampson S, et al. A call for a standard classification system for future biologic research: the rationale for new PRP nomenclature. *PM R.* 2015;7(4 Suppl):S53–9. <https://doi.org/10.1016/j.pmrj.2015.02.005>.
  63. Giovannetti De Sanctis E, Franceschetti E, De Dona F, Palumbo A, Paciotti M, Franceschi F. The efficacy of injections for partial rotator cuff tears: a systematic review. *J Clin Med.* 2020;10(1):51. <https://doi.org/10.3390/jcm10010051>
  64. Cai YU, Sun Z, Liao B, Song Z, Xiao T, Zhu P. Sodium hyaluronate and platelet-rich plasma for partial-thickness rotator cuff tears. *Med Sci Sports Exerc.* 2019;51(2):227–33. <https://doi.org/10.1249/MSS.0000000000001781>.
  65. Caplan AI. Adult Mesenchymal stem cells: when, where, and how. *Stem Cells Int.* 2015;2015:1–6. <https://doi.org/10.1155/2015/628767>.
  66. Caplan AI, Dennis JE. Mesenchymal stem cells as trophic mediators. *J Cell Biochem.* 2006;98(5):1076–84. <https://doi.org/10.1002/jcb.20886>.
  67. Marathe A, Song B, Jayaram P. Microfragmented adipose tissue with adjuvant platelet-rich plasma combination therapy for partial-thickness supraspinatus tear. *Cureus.* 2021;13(6):e15583. <https://doi.org/10.7759/cureus.15583>.
  68. Cherian C, Malanga GA, Hogaboom N, Pollack MA, Dyson-Hudson TA. Autologous, micro-fragmented adipose tissue as a treatment for chronic shoulder pain in a wheelchair using individual with spinal cord injury: a case report. *Spinal Cord Ser Cases.* 2019;5:46. <https://doi.org/10.1038/s41394-019-0186-8>.
  69. Hogaboom N, Malanga G, Cherian C, Dyson-Hudson T. A pilot study to evaluate micro-fragmented adipose tissue injection under ultrasound guidance for the treatment of refractory rotator cuff disease in wheelchair users with spinal cord injury. *J Spinal Cord Med.* 2021;44(6):886–95. <https://doi.org/10.1080/10790268.2021.1903140>.
  70. Jo CH, Chai JW, Jeong EC, Oh S, Yoon KS. Intratendinous injection of mesenchymal stem cells for the treatment of rotator cuff disease: a 2-year follow-up study. *Arthroscopy.* 2020;36(4):971–80. <https://doi.org/10.1016/j.arthro.2019.11.120>.
  71. Kim SJ, Kim EK, Song DH. Effects of bone marrow aspirate concentrate and platelet-rich plasma on patients with partial tear of the rotator cuff tendon. *J Orthop Surg Res.* 2018;13(1):1. <https://doi.org/10.1186/s13018-017-0693-x>.
  72. Centeno C, Fausel Z, Stemper I, Azuiki U, Dodson E. A Randomized controlled trial of the treatment of rotator cuff tears with bone marrow concentrate and platelet products compared to exercise therapy: a midterm analysis. *Stem Cells Int.* 2020;2020:5962354. <https://doi.org/10.1155/2020/5962354>.
  73. Brindisino F, Salomon M, Giaggio S, Pastore C, Innocenti T. Rotator cuff repair vs. nonoperative treatment: a systematic review



- with meta-analysis. *J Shoulder Elbow Surg.* 2021;30(11):2648–59. <https://doi.org/10.1016/j.jse.2021.04.040>
74. Lädermann A, Denard PJ, Collin P. Massive rotator cuff tears: definition and treatment. *Int Orthop.* 2015;39(12):2403–14. <https://doi.org/10.1007/s00264-015-2796-5>.
  75. Weber S, Chadal J. Management of rotator cuff injuries. *J Am Acad Orthop Surg.* 2020;28(5):e193–e201. <https://doi.org/10.5435/JAAOS-D-19-00463>.
  76. Rashid MS, Cooper C, Cook J, Cooper D, Dakin SG, Snelling S, et al. Increasing age and tear size reduce rotator cuff repair healing rate at 1 year. *Acta Orthop.* 2017;88(6):606–11. <https://doi.org/10.1080/17453674.2017.1370844>.
  77. Kim IB, Kim MW. Risk Factors for retear after arthroscopic repair of full-thickness rotator cuff tears using the suture bridge technique: classification system. *Arthroscopy.* 2016;32(11):2191–200. <https://doi.org/10.1016/j.arthro.2016.03.012>.
  78. Deniz G, Kose O, Tugay A, Guler F, Turan A. Fatty degeneration and atrophy of the rotator cuff muscles after arthroscopic repair: does it improve, halt or deteriorate? *Arch Orthop Trauma Surg.* 2014;134(7):985–90. <https://doi.org/10.1007/s00402-014-2009-5>.
  79. Kim YK, Jung KH, Kim JW, Kim US, Hwang DH. Factors affecting rotator cuff integrity after arthroscopic repair for medium-sized or larger cuff tears: a retrospective cohort study. *J Shoulder Elbow Surg.* 2018;27(6):1012–20. <https://doi.org/10.1016/j.jse.2017.11.016>.
  80. Tashjian RZ, Henn RF, Kang L, Green A. Effect of medical comorbidity on self-assessed pain, function, and general health status after rotator cuff repair. *J Bone Joint Surg Am.* 2006;88(3):536–40. <https://doi.org/10.2106/JBJS.E.00418>.
  81. Naimark M, Robbins CB, Gagnier JJ, Landfair G, Carpenter J, Bedi A, et al. Impact of smoking on patient outcomes after arthroscopic rotator cuff repair. *BMJ Open Sport Exerc Med.* 2018;4(1):e000416. <https://doi.org/10.1136/bmjsem-2018-000416>.
  82. Moosmayer S, Lund G, Seljom US, Haldorsen B, Svege IC, Hennig T, et al. At a 10-year follow-up, tendon repair is superior to physiotherapy in the treatment of small and medium-sized rotator cuff tears. *J Bone Joint Surg Am.* 2019;101(12):1050–60. <https://doi.org/10.2106/JBJS.18.01373>. **(Findings from this study suggest that patients with small- or medium-sized full thickness rotator cuff tears (<3cm) may have significantly improved pain and function long term after operative repair compared to physical therapy alone.)**
  83. Pandey V, Bandi A, Madi S, Agarwal L, Acharya KK, Maddukuri S, et al. Does application of moderately concentrated platelet-rich plasma improve clinical and structural outcome after arthroscopic repair of medium-sized to large rotator cuff tear? A randomized controlled trial. *J Shoulder Elbow Surg.* 2016;25(8):1312–22. <https://doi.org/10.1016/j.jse.2016.01.036>.
  84. Jo CH, Shin JS, Shin WH, Lee SY, Yoon KS, Shin S. Platelet-rich plasma for arthroscopic repair of medium to large rotator cuff tears: a randomized controlled trial. *Am J Sports Med.* 2015;43(9):2102–10. <https://doi.org/10.1177/0363546515587081>.
  85. Hernigou P, Flouzat Lachaniette CH, Delambre J, Zilber S, Duffiet P, Chevallier N, et al. Biologic augmentation of rotator cuff repair with mesenchymal stem cells during arthroscopy improves healing and prevents further tears: a case-controlled study. *Int Orthop.* 2014;38(9):1811–8. <https://doi.org/10.1007/s00264-014-2391-1>.
  86. Mall NA, Lee AS, Chahal J, Sherman SL, Romeo AA, Verma NN, et al. An evidenced-based examination of the epidemiology and outcomes of traumatic rotator cuff tears. *Arthroscopy.* 2013;29(2):366–76. <https://doi.org/10.1016/j.arthro.2012.06.024>.
  87. Matthewson G, Beach CJ, Nelson AA, Woodmass JM, Ono Y, Boorman RS, et al. Partial thickness rotator cuff tears: current concepts. *Adv Orthop.* 2015;2015:458786. <https://doi.org/10.1155/2015/458786>.
  88. Kim YS, Lee HJ, Kim JH, Noh DY. When should we repair partial-thickness rotator cuff tears? Outcome comparison between immediate surgical repair versus delayed repair after 6-month period of nonsurgical treatment. *Am J Sports Med.* 2018;46(5):1091–6. <https://doi.org/10.1177/0363546518757425>.
  89. Tashjian RZ. Epidemiology, natural history, and indications for treatment of rotator cuff tears. *Clin Sports Med.* 2012;31(4):589–604. <https://doi.org/10.1016/j.csm.2012.07.001>.
  90. Liu JN, Garcia GH, Gowd AK, Cabarcas BC, Charles MD, Romeo AA, et al. Treatment of partial thickness rotator cuff tears in overhead athletes. *Curr Rev Musculoskelet Med.* 2018;11(1):55–62. <https://doi.org/10.1007/s12178-018-9459-2>.
  91. Läähteenmäki HE, Virolainen P, Hiltunen A, Heikkilä J, Nelimarkka OI. Results of early operative treatment of rotator cuff tears with acute symptoms. *J Shoulder Elbow Surg.* 2006;15(2):148–53. <https://doi.org/10.1016/j.jse.2005.07.006>.
  92. Ranebo MC, Björnsson Hallgren HC, Holmgren T, Adolfsson LE. Surgery and physiotherapy were both successful in the treatment of small, acute, traumatic rotator cuff tears: a prospective randomized trial. *J Shoulder Elbow Surg.* 2020;29(3):459–70. <https://doi.org/10.1016/j.jse.2019.10.013>.
  93. Patel M, Amini MH. Management of acute rotator cuff tears. *Orthop Clin North Am.* 2022;53(1):69–76. <https://doi.org/10.1016/j.ocl.2021.08.003>.
  94. Hantes ME, Karidakis GK, Vlychou M, Varitimidis S, Dailiana Z, Malizos KN. A comparison of early versus delayed repair of traumatic rotator cuff tears. *Knee Surg Sports Traumatol Arthrosc.* 2011;19(10):1766–70. <https://doi.org/10.1007/s00167-011-1396-1>.
  95. Petersen SA, Murphy TP. The timing of rotator cuff repair for the restoration of function. *J Shoulder Elbow Surg.* 2011;20(1):62–8. <https://doi.org/10.1016/j.jse.2010.04.045>.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.