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*REVIEW*

# Factors affecting healing after arthroscopic rotator cuff repair

Amir M Abtahi, Erin K Granger, Robert Z Tashjian

Amir M Abtahi, Erin K Granger, Robert Z Tashjian, Department of Orthopaedic Surgery, University of Utah, Salt Lake City, UT 84108, United States
Author contributions: Abtahi AM, Granger EK and Tashjian RZ solely contributed to the concept, writing and editing of this paper.

Correspondence to: Robert Z Tashjian, MD, Department of Orthopaedic Surgery, University of Utah, 590 Wakara Way, Salt Lake City, UT 84108,
United States. robert.tashijan@hsc.utah.edu
Telephone: +1-801-5875457
Fax: +1-801-5875411
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## Abstract

Rotator cuff repair has been shown to have good long-term results. Unfortunately, a significant proportion of repairs still fail to heal. Many factors, both patient and surgeon related, can influence healing after repair. Older age, larger tear size, worse muscle quality, greater muscle-tendon unit retraction, smoking, osteoporosis, diabetes and hypercholesterolemia have all shown to negatively influence tendon healing. Surgeon related factors that can influence healing include repair construct-single *vs* double row, rehabilitation, and biologics including platelet rich plasma and mesenchymal stem cells. Double-row repairs are biomechanically stronger and have better healing rates compared with single-row repairs although clinical outcomes are equivalent between both constructs. Slower, less aggressive rehabilitation programs have demonstrated improved healing with no negative effect on final range of motion and are therefore recommended after repair of most full thickness tears. Additionally no definitive evidence supports the use of platelet rich plasma or mesenchymal stem cells regarding improvement of healing rates and clinical outcomes. Further research is needed to identify effective biologically directed augmentations that will improve healing rates and clinical outcomes after rotator cuff repair.

**Key words:** Shoulder; Repair; Healing; Tendon; Rotator cuff tear



**Core tip:** Many factors, both patient and surgeon related, can influence healing after repair. Older age, larger tear size, worse muscle quality, greater muscle-tendon unit retraction, smoking, osteoporosis, diabetes and hypercholesterolemia have all shown to negatively influence tendon healing after rotator cuff repair. Smoking cessation and blood glucose and cholesterol control are methods to potentially improve healing rates. Slower, less aggressive rehabilitation programs may improve healing rates with no negative effect on final range of motion and are therefore recommended after arthroscopic repair of most full thickness tears. Finally, no definitive evidence supports the use of platelet rich plasma or mesenchymal stem cells regarding improvement of healing rates after rotator cuff repair. Routine use of these adjuvants is therefore not currently recommended.

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## INTRODUCTION

Rotator cuff tears are a common cause of pain and disability[1,2]. In patients meeting indications for surgery, rotator cuff repair has been shown to have good long-term clinical results[3,4]. Despite this, the literature suggests that a significant proportion of repairs fail to heal following rotator cuff repair. Reported healing rates vary from 91% for small tears to 6% for large and/or massive tears in some series[5-8]. Failure of tendon healing does not necessarily preclude satisfactory results, although improved results have been associated with intact repairs[9,10]. There is a large body of literature demonstrating that a number of different factors may influence the results following rotator cuff repair. In general, factors can be separated into patient-related (non-modifiable) and surgeon-related (modifiable). The purpose of this review is intended to provide a summary of the literature related to the major factors, both patient- and surgeon-related, influencing healing after rotator cuff repair.

## PATIENT-RELATED FACTORS

### *Age*

Increasing patient age has been associated with lower rates of tendon healing after rotator cuff repair in multiple studies[5,11-13]. The detrimental effect of age on rotator cuff tendon healing appears to be independent of the surgical technique utilized for repair. Boileau *et al*[5], in a series of 65 chronic full-thickness supraspinatus tears repaired *via* an arthroscopic single row technique, reported 43% healing in patients over 65% *vs* 86% healing in patients under age 65. Tashjian *et al*[11], in a series of 49 arthroscopic double-row rotator cuff repairs, reported that increased age was associated with lower rates of tendon healing. The average age of patients with unhealed repairs was 63.3 *vs* 55.1 for those with healed repairs[11]. Similarly, Cho *et al*[12], in a study of 123 arthroscopic double-row suture bridge repairs, demonstrated that increasing age was associated with lower rates of tendon healing. The average age of patients with unhealed repairs in their series was 60.1 compared to 53.8 in the healed group. Finally, Oh *et al*[13], in a study of 177 patients after arthroscopic and mini-open rotator cuff repairs of various techniques, also noted that increasing age was associated with lower rates of tendon healing. The average age of patients with unhealed repairs in their series was 63.7 compared to 58.4 in the healed group[13].

The detrimental effect of increasing age on tendon healing after rotator cuff repair may be due to other factors affecting tendon healing rather than to age itself. Chung *et al*[14], in a study of 272 patients after arthroscopic rotator cuff repair, found that bone mineral density, fatty infiltration, and retraction of the rotator cuff tendon were the only independent predictors of rotator cuff healing. Chung *et al*[15], in another study of 108 patients who underwent arthroscopic repair of massive rotator cuff tears, found that while several factors were associated with failure of cuff healing in the univariate analysis including age, only fatty infiltration was significantly related to healing failure in the multivariate analysis. Similarly, Oh *et al*[13] noted that age was not an independent predictor of tendon healing or functional outcome. Tear retraction and fatty atrophy were found to be the only independent predictors of tendon healing in their study[13]. Therefore, age may be a surrogate for other anatomical factors correlated with impaired healing after rotator cuff repair.

### *Tear size*

Several studies have shown that tear size affects rotator cuff tendon healing. Larger tears have lower healing rates after rotator cuff repair compared to smaller tears. Failure rates after arthroscopic repair of large and/or massive rotator cuff repairs have been reported to range from 34%-94% in various series[6,16-19]. Despite poor healing rates in patients with large and/or massive rotator cuff tears, functional outcomes have generally been reported to be good following repair. Galatz *et al*[6] reported that despite failure of healing in 94% of patients at 1 year follow-up, excellent pain relief and improvement in the ability to perform activities of daily living was noted although these results did deteriorate somewhat at 24 mo follow-up. Chung *et al*[15] reported significantly improved functional improvement in a series of arthroscopically repaired massive cuff tears despite an anatomic failure rate of 39.8%. Despite this, not all patients with an unhealed repair do well clinically[18-21]. Namdari *et al*[21] reviewed a series of patients with structural failure after rotator cuff repair and reported a successful outcome in only 54% of patients. Those individuals with labor-intensive jobs were also found to be at high risk for poor outcome after a failed rotator cuff repair[21]. Kim *et al*[20] reviewed a similar group and determined younger age, lower education level and a workers' compensation claim were all risk factors for poorer outcomes after a failed repair.

### *Fatty infiltration and rotator cuff atrophy*

Fatty infiltration and rotator cuff atrophy have been shown to affect healing and functional outcomes following rotator cuff repair[10,22,23]. Thomazeau *et al*[22] demonstrated that more severe preoperative atrophy was associated with worse postoperative repair integrity in 30 open repairs of chronic supraspinatus tears. Liem *et al*[10], in a series of 53 arthroscopic repairs of isolated supraspinatus tears, reported that both supraspinatus atrophy and fatty infiltration were predictive of healing. Goutallier *et al*[23], in a series of 220 shoulders, demonstrated that the likelihood of recurrent tear was greater in patients whose muscle demonstrated more advanced degrees of fatty atrophy. Despite lower rates of cuff healing, patients with fatty infiltration and rotator cuff atrophy may still benefit from rotator cuff repair. Burkhart *et al*[24] reported on 22 patients with massive rotator cuff tears and Goutallier stage 3 or 4 fatty degeneration undergoing arthroscopic rotator cuff repair and demonstrated significant overall functional improvement. Patients with a greater degree of fatty degeneration, however, were less likely to benefit from surgical intervention than those with less fatty degeneration[24]. Other studies have also shown that patients with fatty infiltration and rotator cuff atrophy have lower rates of tendon healing associated with inferior clinical outcomes[10,25]. Goutallier grade 2 or higher degrees of fatty infiltration are significantly associated with poorer healing after repair[10].

Although rotator cuff atrophy and fatty infiltration are both considered part of the same process, they have been found to independently predict outcome following rotator cuff repair[25]. Most studies indicate that fatty infiltration is irreversible, even in the presence of a successful repair. In the presence of an untreated or failed repair, fatty infiltration continues to progress. In some studies, atrophy has been shown to improve to a small degree after successful repair. Fuchs *et al*[26] in a series of single tendon rotator cuff repairs reported that muscular atrophy did not decrease significantly after repair. However, fatty infiltration of the supraspinatus and infraspinatus, increased significantly despite repair. Rotator cuff atrophy was significantly worse in patients with re-tears than in those with intact repairs. Gerber *et al*[27], in a study of 12 patients, noted that within one year after successful tendon repair, fatty infiltration did not improve but rotator cuff atrophy improved partially. In the presence of a failed repair, atrophy and infiltration progressed significantly. In a separate study, Gerber *et al*[19] studied 29 patients who underwent arthroscopic repair of massive rotator cuff tears and noted a 34% retear rate. Supraspinatus atrophy was mildly reversed after repair. Infraspinatus atrophy, however, worsened even after successful repair. Fatty infiltration was not reversible but progressed less in patients with intact repairs. Chung *et al*[28] reported, in a series of 191 patients who underwent arthroscopic rotator cuff repair, that 42.4% of patients showed improvement of atrophy and 17.3% of patients showed worsening. The change in atrophy was related to repair integrity. For patients with worsened atrophy, the cuff healing rate was 48.5% compared with 22.2% in patients with improved atrophy. Gladstone *et al*[25], in a study of 38 patients after arthroscopic rotator cuff repair found that both atrophy and infiltration progressed regardless of rotator cuff healing. In cases in which the tendon had re-torn however, the progression was noted to be more significant compared to those patients that had healed. Liem *et al*[10] in a series of 53 consecutive patients who underwent arthroscopic repair of an isolated supraspinatus tear, reported that in patients with intact repairs fatty infiltration and atrophy did not progress whereas in those with recurrent tears fatty infiltration and atrophy worsened significantly. So overall, fatty infiltration may halt after a repair if it remains intact but will progress with re-tears. Atrophy has the potential to reverse after repair if the repair remains intact but will likely progress if it fails.

#### *Muscle-tendon unit retraction*

Tendon retraction, or the gap between the greater tuberosity and the tendon edge, is either due to tendon shortening or muscle retraction. Muscle retraction can be defined by utilizing the position of the muscle-tendon junction (MTJ) in relation to landmarks on the scapula. Meyer *et al*[29] evaluated 118 shoulder MRIs for the MTJ position in the setting of a rotator cuff tear. They concluded that increasing stages of fatty infiltration correlate with increasing tear size, tendon shortening and MTJ retraction. Initial stages of muscle-tendon unit retraction in the setting of rotator cuff tears with minimal fatty infiltration occurs through muscle shortening whereas tears with later stages of fatty infiltration shorten through tendon shortening[29]. Kim *et al*[30] reported similar results that showed with increasing tear size and tendon reaction, the tendon length shortens. These results support that initial retraction in smaller tears occur with muscle shortening but as tears enlarge and become more chronic the tendon shortens as well.

Meyer *et al*[31] also looked at the effect of MTJ shortening on rotator cuff repair healing. They determined that the muscle and tendon lengthened an average of 14 mm and 8 mm, respectively, after a successful rotator cuff repair. They also determined that a shorter preoperative tendon length correlated with worse overall healing rates although preoperative MTJ position had no effect[31]. Tashjian *et al*[32] evaluated MRIs of 51 patients after arthroscopic rotator cuff repair and did find a significant associate with preoperative MTJ position and postoperative tendon healing. If the preoperative MTJ was at the level of the glenoid or medial then 55% of tears healed whereas if the MTJ was lateral to the glenoid face then 93% of tears healed. Consequently, both greater preoperative MTJ retraction and greater preoperative tendon shortening negatively affect healing after rotator cuff repair.

#### *Other patient-related factors (smoking, osteoporosis, hypercholesterolemia, diabetes)*

Several other patient-related factors have been reported to affect rotator cuff tendon healing. Smoking not only increases the risk for rotator cuff tears, but has been reported to influence rotator cuff tear size as well[33]. Smoking has been shown to delay tendon-to-bone healing in a rat model and clinical studies have demonstrated inferior clinical outcomes after repair in smokers[34,35]. Finally, Neyton *et al*[36] evaluated healing after arthroscopic double-row suture bridge repair for the impact of smoking. The authors determined healing rates were significantly worse in smokers (78%) compared to non-smokers (93%) after single tendon repair.

Both bone mineral density and vitamin D deficiency have been shown to affect rotator cuff tendon healing following surgical repair. Chung *et al*[14], in a study of 272 patients after arthroscopic rotator cuff repair, found that bone mineral density was an independent predictors of rotator cuff healing. In a rat rotator cuff repair model, Angeline *et al*[37] demonstrated that vitamin D deficiency negatively affects the biomechanical and histological properties of rotator cuff repairs during the early phase of healing. This effect was found to be independent of bone mineral density[37].

Other system diseases have been associated with rotator cuff tearing as well as rotator cuff healing. Abboud *et al*[38] collected serum cholesterol and lipid profiles on patients with full-thickness rotator cuff tears and compared them to a control population. They determined that total cholesterol, triglycerides and low-density lipoprotein cholesterol concentrations were higher in patients with rotator cuff tears. Consequently, patients with cuff tears are more likely to have hyper-cholesterolemia compared to controls. Beason *et al*[39] evaluated the effects of hypercholesterolemia on tendon healing in a rat rotator cuff tear model. These authors determined that there was a significant reduction in rotator cuff repair stiffness in hypercholesterolemic rats compared with controls[40]. This data would support hypercholesterolemia likely plays a role not only in the development of rotator cuff tearing but also on the ability for a tendon to heal after repair. Similarly, diabetes has been found to have a detrimental effect on tendon healing using a rat rotator cuff tear model[39]. Modification of serum cholesterol levels and blood glucose levels may play a role in improving healing after repairs.

## SURGEON-RELATED FACTORS

### *Repair construct-single-row vs double-row*

A number of surgical techniques are available to the surgeon treating tears of the rotator cuff. An ideal rotator cuff repair construct would provide high initial fixation strength and minimize gap formation during healing[41]. Biomechanical studies of double-row repairs have shown increased load to failure, improved contact areas and pressures, and decreased gap formation when compared to single row repairs[42-46]. These biomechanical studies have led to a number of clinical studies comparing single-row with double-row repair techniques. These studies have, in general, failed to demonstrate significant differences in functional outcomes with single *vs* double-row techniques. Grasso *et al*[47] in a prospective randomized study of single-row *vs* double-row arthroscopic rotator cuff repairs reported that arthroscopic rotator cuff repair with the double-row technique showed no significant difference in clinical outcome compared with single-row repair. In contrast, Park *et al*[48] reported that in patients with large to massive tears (> 3 cm), the American Shoulder and Elbow Surgeons Score, Constant scores and Shoulder Strength Index were all significantly better in the group that had double-row repair.

Despite the fact that most studies have failed to demonstrate clinical differences with singe *vs* double row repairs at short term follow-up, there appears to be a lower re-tear rate for the double-row compared with the single-row repairs[49-51]. Lapner *et al*[49], in a multicenter randomized controlled trial comparing single-row with double-row fixation in arthroscopic rotator cuff repairs reported that although double-row fixation was associated with higher healing rates, no significant differences in functional or quality-of-life outcomes were identified between single-row and double-row fixation techniques. In contrast, Burks *et al*[52], in a prospective randomized clinical trial comparing arthroscopic single- and double-row rotator cuff repair reported no clinical or MRI differences between single-row or double-row techniques.

A modification of the double-row technique is the double-row suture bridge technique[36,53-56]. Gartsman *et al*[54], evaluated the repair integrity of single-row *vs* double-row suture bridge arthroscopic rotator cuff repairs in a prospective, randomized study. They demonstrated that double-row suture bridge repair resulted in a significantly higher tendon healing rate compared to arthroscopic single-row repair. Mihata *et al*[53] demonstrated that in the subcategory of large and massive rotator cuff tears, the re-tear rate in the double-row suture bridge group was significantly less than those in the single-row group and the non-suture bridge double-row group. Several techniques have been described for double row suture bridge repair. Kim *et al*[55] compared three different methods including knotted and knotless techniques and demonstrated equivalence between techniques with regards to functional outcomes and repair integrity.

An alternative to double row repairs for improving fixation and healing is to increase the number of sutures per anchor. Jost *et al*[57] evaluated the effects of increasing suture number on rotator cuff healing strength in a sheep model and determined that increasing the number of sutures decreased cyclic gap formation and increased load to failure. Barber *et al*[58] determined that single row repairs utilizing triple-loaded anchors were more resistant to cyclic displacement than double-row suture bridge repairs. Other authors have evaluated various suture configurations for rotator cuff repair. White *et al*[59], in a biomechanical study, reported no difference in biomechanical strength with 4 simple sutures, 2 mattress sutures, or 1 grasping suture. They concluded that this provides justification for the use of the simplest configuration with which the surgeon is comfortable.

Overall, the biomechanical data would support that double-row fixation is stronger than single row fixation using double-loaded suture anchors although increasing suture numbers per anchor (triple-loaded anchors) may offset any biomechanical advantage of double row repairs. Clinically, double-row repairs have improved healing rates compared to single row repairs using double-loaded suture anchors. Nevertheless, functional outcomes between double-row and single-row repairs are equivalent except in large and massive tears where double-row fixation may provide a functional advantage over single-row repairs.

### Rehabilitation

A number of rehabilitation protocols have been described for use following rotator cuff repair. While some surgeons recommend early, aggressive rehabilitation programs, others recommend a more conservative rehabilitation program. Data are conflicting on which, if any, of these programs provides superior results. Early aggressive rehabilitation programs have been shown to result in better early outcomes, pain relief, and range of motion however most studies show no difference with regard to these parameters with longer-term follow-up[60-66]. One concern with early aggressive rehabilitation programs is that they may be associated with a higher incidence of tendon re-tear.

Immobilization has been shown to affect tendon healing although the data is conflicted. Galatz *et al*[67] and Hettrich *et al*[68] have shown that complete removal of load is detrimental to rotator cuff healing. In contrast, Gimbel *et al*[69] demonstrated that long durations of immobilization in rats result in enhanced mechanical properties of the healing supraspinatus tendon insertion site.

Like the basic science literature, the clinical literature is also conflicting as to whether the rehabilitation program utilized affects clinical healing rates after rotator cuff repair. While some studies show higher re-tear rates with early, aggressive therapy protocols, others show a trend or no difference in re-tear rates[62,63]. In a prospective randomized study of early aggressive *vs* delayed rehabilitation protocols, Cuff *et al*[63] demonstrated a slightly higher but non statistically significant re-tear rate at 1 year in the early group (15%) compared to the delayed group (9%). Lee *et al*[62] evaluated re-tear rates at 6 mo comparing aggressive with conservative rehabilitation protocols. They found that the re-tear rate was significantly higher in the more aggressive group (23.3%) compared with the conservative group (8.8%). They found no difference, however, in long-term functional outcomes between the two groups[62]. In contrast, Kim *et al*[61] evaluated early and delayed range of motion protocols after rotator cuff repair and found no statistically significant difference in healing rates between the two groups with a trend toward lower re-tear rates in the early range of motion group (12% *vs* 18%).

In summary, the literature shows that early aggressive rehabilitation protocols may result in a slightly higher incidence of re-tear compared with more conservative protocols. The benefits of early aggressive therapy protocols seen in the early postoperative period on pain relief and range of motion, however, are not observed with longer term follow up. The risk, therefore, may outweigh the benefits of such protocols in the majority of cases supporting the use of a slower rehabilitation protocol.

## BIOLOGICS

### Platelet rich plasma

Biologic augmentation of rotator cuff repairs has gained significant interest over the past several years as biomechanically improvements in repair constructs have maximized. Numerous growth factors have been shown to improve proliferation and collagen secretion of tenocytes *in vitro* including basic fibroblast growth factor, vascular endothelial growth factor, and transforming growth factor-β[70-74]. Platelet-rich plasma (PRP) is a fraction of whole blood containing high platelet counts that release these various growth factors when activated. Because these growth factors have shown a positive effect on healing *in vitro*, a large interest exits in the application of PRP to augment rotator cuff repair healing.

Several studies have been performed evaluating the effect of PRP on rotator cuff healing. There is currently no consensus on PRP application during rotator cuff repair as several studies have shown a positive effect on healing while others have shown no effect or a negative effect. Weber *et al*[75] performed a prospective randomized study evaluating the effects of platelet rich fibrin matrix (PRFM) on tendon healing and found no differences in healing rates in PRFM treated repairs compared to controls. Rodeo *et al*[76] reported similar results for PRFM in a randomized control trial where healing rates in the PRFM group were 67% compared to 81% in the non-augmented repairs ($P$ = 0.2). Bergeson *et al*[77] actually reported significantly worse healing rates with PRFM application *vs* non-augmented repairs (38% *vs* 56%, $P$ = 0.024).

Contrary to the findings reporting no effect of PRP on tendon healing, several authors have found beneficial effect of PRP on rotator cuff healing[78,79]. Barber *et al*[78] reported on a matched group of rotator cuff repairs treated with PRFM and non-augmented repairs and reported healing rates of 70% with PRFM augmentation and 40% without augmentation. Jo *et al*[79] performed a randomized control trial comparing PRP repair augmentation of large and massive rotator cuff tears and reported re-tear rates in the PRP

**Table 1 Studies evaluating factors affecting healing after rotator cuff repair**

| Study | Study type | Number of patients/duration of follow up | Primary outcome | Conclusion | Level of evidence |
|---|---|---|---|---|---|
| Age | | | | | |
| Boileau *et al*[5] | Case series | 65 pts/29 mo | CT arthrogram, MRI | Healing rate significantly lower in patients > age 65 | IV |
| Tashjian *et al*[11] | Case series | 48 pts/16 mo | US | Older age associated with lower tendon healing rate | IV |
| Cho *et al*[12] | Case series | 120 pts/25.2 mo | MRI | Older age associated with lower tendon healing rate | IV |
| Oh *et al*[13] | Case series | 177 pts/29 mo | CT arthrogram | Older age was related to poor postoperative repair integrity | IV |
| Tear size | | | | | |
| Galatz *et al*[6] | Case series | 18 pts/36 mo | US | High rate of tendon healing failure | IV |
| Chung *et al*[15] | Case series | 108 pts/31.7 mo | CT arthrogram, US | High rate of tendon healing failure | IV |
| Fatty infiltration/atrophy | | | | | |
| Thomazeau *et al*[22] | Case series | 30 pts/21.1 mo | MRI | Supraspinatus atrophy was a strong risk factor for retear | IV |
| Liem *et al*[10] | Case series | 53 pts/26.4 mo | MRI | Higher degrees of muscular atrophy and fatty infiltration preoperatively are associated with tear recurrence | IV |
| Goutallier *et al*[23] | Case series | 220 shoulders/37 mo | CT arthrogram, MRI | The likelihood of a recurrent tear was greater for tendons whose muscle showed fatty degeneration greater than grade 1 | IV |
| Chung *et al*[15] | Case series | 108 pts/31.7 mo | CT arthrogram, US | Higher FI of the infraspinatus was the single most important factor negatively affecting cuff healing | IV |
| Tendon retraction | | | | | |
| Meyer *et al*[31] | Retrospective cohort | 33 shoulder/24 mo | MRI | The combination of Goutallier grading and preoperative tendon length appears to be a more powerful predictor for the reparability of a tendon tear than Goutallier grading alone | III |
| Tashjian *et al*[32] | Case series | 51 pts/25 mo | MRI | The position of the MTJ with respect to the glenoid face can be predictive of healing, with over 90% healing if lateral and 50% if medial to the face | IV |
| Other patient factors | | | | | |
| Neyton *et al*[36] | Case series | 105 pts/16.1 mo | MRI | Smoking was detrimental to healing | IV |
| Chung *et al*[14] | Retrospective cohort | 408 pts/37.2 mo | CT arthrogram, US | Bone mineral density, as well as FI of the infraspinatus and amount of retraction, was an independent determining factor affecting postoperative rotator cuff healing | III |
| Abboud *et al*[38] | Case-control | 147 pts/NA | NA | Patients with rotator cuff tears were more likely to have hypercholesterolemia when compared with the control group | II |
| Repair construct | | | | | |
| Lapner *et al*[49] | RCT | 90 pts/24 mo | MRI, US | Smaller initial tear size and a double-row fixation technique were associated with higher healing rates | I |
| Burks *et al*[52] | RCT | 40 pts/12 mo | MRI | No clinical or MRI differences found between patients repaired with a SR or DR technique | I |
| Mihata *et al*[53] | RCT | 201 pts/38.5 mo | MRI, US | Retear rate in the compression double-row group was significantly less than in the single-row group and the double-row group | I |
| Gartsman *et al*[54] | RCT | 90 pts/10 mo | US | Arthroscopic double-row suture bridge repair resulted in a significantly higher tendon healing rate compared to single-row repair | I |
| Kim *et al*[55] | Case series | 79 pts/30.6 mo | MRI, US | The re-tear rate after suture-bridge repair was 15% | IV |
| Rehabilitation | | | | | |
| Lee *et al*[62] | RCT | 64 shoulders/7.6 mo | MRI | More patients in the aggressive early passive rehabilitation group (23.3%) had retears compared to the limited early passive group (8.8%) although not statistically significant | II |
| Kim *et al*[61] | RCT | 105 pts/12 mo | MRI, CT arthrography | Early passive motion did not negatively affect cuff healing | I |
| Biologics (PRP/MSCs) | | | | | |
| Weber *et al*[75] | RCT | 60 pts/12 mo | MRI | Healing rates did not differ between groups | I |

| | | | | | |
|---|---|---|---|---|---|
| Rodeo *et al*[76] | RCT | 79 pts/12 wk | US | No differences in tendon-to-bone healing between the PRFM and control groups | II |
| Bergeson *et al*[77] | Prospective cohort | 37 pts/27 mo in control group and 13 mo in PRFM group | MRI | No differences in retear rates between the PRFM and control groups | III |
| Barber *et al*[78] | Case-control | 40 pts/31 mo | MRI | PRFM group had lower retear rates than control group | III |
| Jo *et al*[79] | RCT | 48 pts/15.9 in PRP group and 17.3 in control group | MRI | Retear rate in the PRP group was significantly lower than in the control group | I |
| Hernigou *et al*[86] | Case-control | 90 pts/10 yr | MRI | Higher rate of healing and reduced number of re-tears over time in the MSC groups compared to the control group | III |

CT: Computed tomography; MRI: Magnetic resonance imaging; PRFM: Platelet rich fibrin matrix; MSC: Mesenchymal stem cell; PRP: Platelet-rich plasma; US: Ultrasound; MTJ: Muscle-tendon junction; DR: Double row; SR: Single row; FI: Fatty infiltration; NA: Not applicable; RCT: Randomized controlled trial.

augmentation group (20%) significantly lower than in the non-augmented group (56%) ($P$ = 0.023).

At this point in time, it is unclear why certain studies have performed well with augmentation and others have found no improvement. Potential factors may be preparation mechanisms, timing of application and technique of repair to name only a few. Until further research is performed to elucidate which patients and through which technique PRP application may be beneficial, the use of PRP as an augmentation to rotator cuff repair to improve healing is experimental and of questionable utility.

### Mesenchymal stem cells

Mesenchymal stem cells (MSCs) have been explored as an option for biologic augmentation of rotator cuff repairs. Mazzocca *et al*[80] have demonstrated that MSCs can be isolated from the proximal humerus through the anchor tunnels created during arthroscopic rotator cuff repair. Utsunomiya *et al*[81] investigated multiple potential sources of MSCs that can be harvested during arthroscopic rotator cuff repair. They demonstrated that synovial cells harvested from the subacromial bursa are a good potential source of MSCs[81]. Gulotta *et al*[82] evaluated MSCs in an animal rotator cuff repair model and found that the addition of MSCs to the healing rotator cuff insertion site did not improve the structure, composition, or strength of the healing tendon attachment site despite evidence that they are present and metabolically active[82]. In a subsequent publication, however, the authors reported that bone marrow-derived MSCs transduced with scleraxis (a transcription factor that is thought to direct tendon development during the embryonic period) improved rotator cuff healing in a rat model[83]. Similarly, Mazzocca *et al*[84] have demonstrated that bone marrow-derived MSCs treated with insulin differentiated into tendon-like cells. Kim *et al*[85], in an animal model, demonstrated that MSCs increase type Ⅰ collagen production at the site of rotator cuff repair. Finally, Hernigou *et al*[86] evaluated forty-five patients that received concentrated bone marrow derived MSCs as an adjunct to single row rotator cuff repair compared to a matched control group and found that the healing rate at 6 mo was significantly higher in the MSC group. Furthermore, the authors found that at a mean follow-up of ten years there was a significantly higher re-tear rate in the control group compared to the MSC group[86]. Although use of MSCs demonstrates promise for biologic augmentation of rotator cuff repair, further clinical studies are necessary before their use can be recommended in clinical practice.

## CONCLUSION

In summary, multiple factors have been shown to influence rotator cuff healing. Table 1 provides a summary of these factors and the relevant studies. Older age, larger tear size, worse muscle quality, greater muscle-tendon unit retraction, smoking, osteoporosis, diabetes and hypercholesterolemia have all shown to negatively influence tendon healing. Smoking cessation and blood glucose and cholesterol control are methods to potentially improve healing rates. Double-row rotator cuff repairs are biomechanically stronger and have better overall healing rates when compared to single-row repairs although clinical outcomes are equivalent between both repair constructs. Delayed rehabilitation after arthroscopic repair of most full thickness tears may improve healing rates with no negative effect on final range of motion therefore slower early rehabilitation can be recommended. Finally, no definitive evidence supports the use of platelet rich plasma regarding improvement of healing rates after rotator cuff repair therefore routine use is not currently recommended. Further research is required to identify effective biologically directed augments that will improve healing rates and clinical outcomes after rotator cuff repair.

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