Original Article

Arthroscopic Rotator Cuff Repair with a Fibrin Scaffold Containing Growth Factors and Autologous Progenitor Cells Derived From Humeral cBMA Improves Clinical Outcomes in High Risk Patients

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Purpose: To report the clinical outcomes after biologically augmented rotator cuff repair (RCR) with a fibrin scaffold derived from autologous whole blood and supplemented with concentrated bone marrow aspirate (cBMA) harvested at the proximal humerus. **Methods:** Patients who underwent arthroscopic RCR with biologic augmentation using a fibrin clot scaffold ("Mega- Clot") containing progenitor cells and growth factors from proximal humerus BMA and autologous whole blood between April 2015 and January 2018 were prospectively followed. Only high-risk patients in primary and revision cases that possessed relevant comorbidities or physically demanding occupation were included. Minimum follow-up for inclusion was 1 year. The visual analog score for pain (VAS), American Shoulder and Elbow Surgeons (ASES), Simple Shoulder Test (SST), Single Assessment Numerical Evaluation (SANE), and Constant-Murley scores were collected preoperatively and at final follow-up. In vitro analyses of the cBMA and fibrin clot using nucleated cell count, colony forming units, and live/dead assays were used to quantify the substrates. **Results:** Thirteen patients (56.9 ± 7.7 years) were included. The mean follow-up was 26.9 ± 17.7 months ($n = 13$). There were significant improvements in all outcome scores from the preoperative to the postoperative state: VAS (5.6 ± 2.5 to 3.1 ± 3.2; $P < .001$), ASES (42.0 ± 17.1 to 65.5 ± 30.6; $P < .001$), SST (3.2 ± 2.8 to 6.5 ± 4.7; $P = .002$), SANE (11.5 ± 15.6 to 50.3 ± 36.5; $P < .001$), and Constant-Murley (38.9 ± 17.5 to 58.1 ± 26.3; $P < .001$). Six patients (46%) had retears on postoperative MRI, despite all having improvements in pain and function except one. All failures were chronic rotator cuff tears, and all were revision cases except one (1.6 ± 0.5 previous RCRs). The representative sample of harvested cBMA showed an average of 28.5 ± 9.1 × 10^6 nucleated cells per mL. **Conclusions:** Arthroscopic rotator cuff repairs that are biologically augmented with a fibrin scaffold containing growth factors and autologous progenitor cells derived from autologous whole blood and humeral cBMA can improve clinical outcomes in primary, as well as revision cases in high-risk patients. However, the incidence of retears remains a concern in this population, demanding further improvements in biologic augmentation. **Level of Evidence:** IV, therapeutic case series.

Introduction

Despite the advancements in arthroscopic surgery with procedure-specific devices, variable healing rates between 13% and 94% prevail for rotator cuff repairs.[1-3] This is due to poor tendon quality with degenerative changes, massive rotator cuff tears, and

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chronic tears with fatty infiltration of the muscle and concomitant muscle atrophy.[1,3,4] Age, smoking, diabetes mellitus, and hypercholesterolemia are important biological factors and comorbidities, respectively.[3] One fundamental factor of rotator cuff healing is that instead of a physiological enthesis, scar tissue is formed.[1,3] The scar tissue formation during healing results in an inferior construct compared to normal tendon tissue.[4]

A promising advancement in orthopaedic surgery is the combination of novel devices with cell-based therapies, which is further expanding and is becoming more relevant.[5] In order to reduce the rerupture rate, improve tendon healing, and decrease morbidity, biological augmentation of rotator cuff repair (RCR) with autologous bone marrow aspirate (BMA) has been introduced.[6,7] The bone marrow aspirate can be intraoperatively concentrated (cBMA), and a fibrin scaffold—a carrier for mesenchymal stem cells (MSCs), as well as growth factors—can be applied at the repair site.[6,8]

MSCs, also referred to as progenitor cells, show long-term proliferation, high self-renewal rates, and the ability to differentiate toward specific cell lineages, which makes them excellent candidates for cell-based therapies.[5] Currently, there is no consensus about the ideal carrier construct for MSCs.[5] A fibrin scaffold has important advantages, including U.S. Food and Drug Administration approval, viability of suspended cells, and lack of adverse effects on tendon healing.[5]

There is a high demand for clinical studies to investigate the significance of biological augmentation during rotator cuff reconstruction.[3,9] The purpose of this study was to report the clinical outcomes after biologically augmented RCR with a fibrin scaffold derived from autologous whole blood and supplemented with cBMA harvested at the proximal humerus. Our hypothesis was that RCR augmented with autologous cBMA and platelet-rich plasma delivered in a fibrin scaffold will lead to the improvement of shoulder function, the reduction of pain, and decreased failure rates in high-risk patients.

Methods

Patients

Patients who received biologic augmented RCR in primary and revision cases between April 2015 and January 2018 in our department by a single surgeon (ADM) were prospectively followed. Institutional review board approval was obtained (IRB no. 21X-200-1). Ethical approval was obtained via the Human Research Determination Form to the Institutional Review Board (IRB) of the University of Connecticut (IRB no. 21X-200-1). Patients with primary rotator cuff tears with relevant comorbidities are associated with non-healing (i.e., diabetes, cancer, rheumatoid arthritis, and smoking), those with a history of failed RCR, or patients with the need for a return to a physically demanding occupation (e.g., firefighters, policemen) were included to identify patients at high risk of failure. Those who did not fulfill this criteria were not considered for biologic augmentation. Severe osteoarthritis, nerve injuries, prior surgery with tendon transfers, and severe fatty infiltration of the rotator cuff muscles with high-grade tendon retraction that resulted in a non-reconstructable condition were excluded. Patients who were unable or unwilling (e.g., imprisonment, incompliance) to complete a thorough preoperative and postoperative evaluation were not included in this study.

Surgical Technique

RCR Repair

All surgeries were performed by a single, shoulder fellowship-trained surgeon (ADM). Each patient was placed in the beach chair position, and following an interscalene block and successful induction of general anesthesia, a diagnostic arthroscopy was completed to confirm the presence of a rotator cuff tear. In revision cases, loose suture material and/or anchors were removed. Torn rotator cuff tendons were mobilized and repaired arthroscopically using a double-row technique. First, the medial row repair was completed at the articular margin using two double-loaded suture anchors (PEEK Corkscrew FT Suture Anchor, 5.5 mm × 14.7 mm, with two no. 2 FiberWire, Arthrex). To follow, the fibrin scaffold "Mega-Clot" was delivered to the repair site, and the lateral row repair was completed thereafter, using two additional suture anchors tied in a horizontal mattress fashion (PEEK SwiveLock, 4.75 mm × 19.1 mm; Arthrex). Any remaining clot was placed on top of the repair site in the subacromial space.

The current technique for fibrin scaffold creation and BMA processing is based on the publications of Voss et al. and Mazzocca et al.[6,8] Here, the principle was to biologically enhance the rotator cuff healing process by delivering progenitor cells, as well as growth factors to the repair site.[6] Therefore, a fibrin clot was designed as a scaffold that contained progenitor cells and growth factors.[6] In the current study, cBMA was the source of progenitor cells, while platelet-rich plasma (PRP) and platelet-poor plasma (PPP), processed from autologous whole blood, provided growth factors and high concentrations of fibrinogen to serve as the scaffold matrix.[6] Bovine thrombin was used to activate and stabilize the clot.[6]

PRP and PPP Preparation

Preoperatively, 60 mL of venous peripheral blood was drawn using a 60-mL syringe prefilled with 8 mL of acid citrate dextrose anticoagulant (ACD-A) (Citra Labs, LLC, Braintree, MA) to prepare autologous PRP and

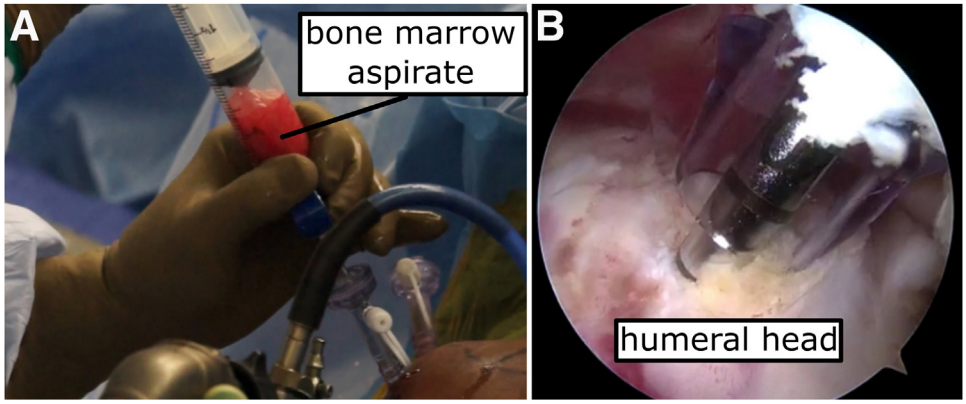

Fig 1. Bone marrow aspiration (A) of the proximal humerus at the location of the medial row anchor (B).

PPP.[6] The blood was then transferred and processed using an Angel-System (Arthrex, Naples, FL) with a hematocrit setting of 7%.[6]

Bone Marrow Aspiration

BMA was harvested from the humeral head at the designated position of the first anchor for RCR, as previously published.[6,8] An 11-gauge heparin-flushed (1,000 IU/mL) nonfenestrated bone marrow aspiration trocar (Arthrex, Naples, FL) was used. The trocar needle was inserted 25 to 30 mm below the cortex level into the cancellous bone near the bone cartilage junction.[6] The needle was connected to a heparin-flushed (1,000 IU/mL), 60-mL syringe containing 3 mL of ACD-A, and the syringe was pulled back to maximize suction (Fig 1).[6] This standardized aspiration method was repeated two to four additional times, for a total aspiration volume of 60 to 120 mL.[6] The BMA was further processed in the Angel-System™.[6] To achieve the highest number of progenitor cells in the concentration process of the BMA, the hematocrit was set to 15%.[6] To create the fibrin scaffold, the cBMA was then moved onto the sterile field with the autologous PRP and PPP.[6]

Fibrin Scaffold ("Mega-Clot") Creation

The biologic scaffold, containing progenitor cells and growth factors, was created using 1 mL of a stable fibrin clot composed of 0.1 mL of cBMA, 0.1 mL of PRP, 0.6 mL of PPP, and 0.2 mL of bovine thrombin (5,000 IU/mL) reconstituted in $CaCl_2$.[6] The final volume of the clot was dependent upon the maximal available volume of the processed cBMA.[6] In general, the fibrin scaffold was scaled up, according to the volumes of cBMA, PPP, PRP, and bovine thrombin mentioned previously to produce a clot $\leq$30 mL in a customary 30-mL syringe.

Fibrin Scaffold ("Mega-Clot") Implantation

Prior to "Mega-Clot" delivery, the arthroscopic fluid flow was turned off.[6] The previously used 11-gauge nonfenestrated bone marrow aspiration trocar was connected to the 30-mL syringe containing the autologous fibrin scaffold and was inserted through an arthroscopic portal to the repair site. Then, the autologous biologically enhanced fibrin clot was evenly distributed below the repair site (Fig 2), and the lateral row repair was completed. Finally, arthroscopic visualization of both the repair and injected scaffold was performed to evaluate stability. Any remaining clot was distributed over the rotator cuff repair site (Fig 3).

In Vitro Laboratory Processing

Nucleated Cell Count

The volume of BMA and cBMA was documented for every case by the total amount of intraoperatively harvested and processed aspirate, respectively. Additionally, the volume of fibrin clot was recorded. Immediately following the surgery, samples of cBMA and fibrin clot were taken to the research laboratory for processing. For each patient, the total number of nucleated cells in the cBMA was counted using a Z1 Coulter® Particle Counter (Beckman Coulter Life Sciences, Indianapolis, IN), calibrated to detect particles >8 µm, after adding 10 µL of cBMA to a transparent cuvette containing 9.9 mL of 0.9% NaCl solution. The nucleated cell count per 1 mL of cBMA was then calculated by multiplying the Coulter Counter output by 100.

Colony Forming Units

For each patient, 1.0 mL of cBMA was cultured with 9.0 mL of complete -Minimal essential medium (MEM) containing 10% of fetal bovine serum (Thermo Fisher Scientific, Waltham, MA) and 0.1% penicillin/streptomycin in a Primaria (Fisher Scientific, Agawam, MA) 100-mm culture dish. Cells were grown at 37°C in a 5% humidified CO_2 incubator.[10,11] After 48 hours, the medium was changed to remove nonadherent cells. Cultures were checked daily for the appearance of colony forming units (CFUs), defined as a cluster of 8 or

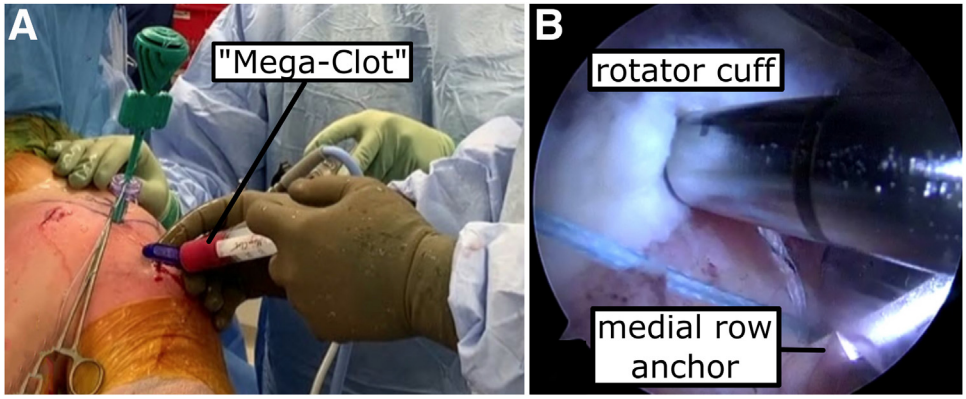

Fig 2. Implantation of "Mega-Clot" (A) beneath the rotator cuff repair (B) prior to completing lateral row fixation.

more cells.[12] CFUs were counted, as soon as colonies formed, in one representative quadrant of the dish by a single trained technician using a microscope (Nikon® Eclipse TS 100, Nikon Corporation, Tokyo, Japan) at 10× magnification. The total number of CFUs in 1 mL of cBMA was then calculated by multiplying by 4.

Live/Dead Assay

Additionally, 1.0 mL of the intraoperatively created fibrin clot from each case was immediately taken to the laboratory for culture in complete medium to detect the cellular viability of the MSCs contained within the scaffold. After 1, 2, and 4 weeks, each clot was incubated in sterile phosphate-buffered saline (PBS) with 2 μM calcein-AM and 4 μM ethidium homodimer-1 (ThermoScientific, Molecular Probes, Eugene, OR) for 30 minutes. After staining, clots were washed twice with PBS, removed from wells, and examined for cellular viability and cytotoxicity on a glass slide using a fluorescence microscope (Leica DMI 6000B, Leica Microsystems, Buffalo Grove, IL) at 10× magnification. Viable cells fluoresced green, while dead cells were red.

Postoperative Rehabilitation

All patients underwent a standardized postoperative protocol in three phases with limitations of range of motion and activities. Immediately after surgery until the 6th postoperative week, patients wore a sling and passive range of motion was allowed between 0° and 180° for flexion, 0° and 30° of external rotation, and 0° and 45° of abduction. Starting in the 7th postoperative week, patients weaned off the sling and active range of motion was allowed in all planes except for internal rotation above 0°. Thereafter, active range of motion was allowed in all planes and periscapular strengthening was intensified.

Clinical Outcomes

Outcomes scores were collected prospectively prior to surgery and at a minimum of 12 months postoperatively. The visual analog scale for pain (VAS), American Shoulder and Elbow Surgeons (ASES), Simple Shoulder Test (SST), Single Assessment Numeric Evaluation (SANE), and Constant-Murley scores were recorded. The changes in reported ASES and SANE clinical outcome scores were compared to the minimal clinical important difference (MCID) and substantial clinical benefit (SCB) by Cvetanovich et al. to assess the clinical relevance of these scores in the rotator cuff tear population.[13] Additionally, final postoperative outcome scores were compared to the patient acceptable symptomatic state (PASS) score, which provides the minimum score that is associated with patient satisfaction.[14] For ASES, Cvetanovich et al. reported an 11.1-point change and 17.5-point change for MCID and SCB, respectfully. The ASES PASS score was 86.7. For SANE, these authors reported a 16.9-point change and 29.8-point change for MCID and SCB, respectfully, while the PASS score was 82.5.[13] Additionally, the range of motion (flexion, abduction, and external rotation) and comorbidities were documented.[15,16] Postoperatively, the integrity of the repair was evaluated with MRI in patients with recurrence of symptoms, and the incidence of surgical failure requiring revision surgery was documented.

Statistical Analysis

Continuous variables were presented as means and standard deviations (SDs), and categorical variables were summarized using frequencies and proportions. Differences in preoperative and postoperative outcome scores were examined using the nonparametric Wilcoxon sign rank test. Differences in the amount of change in patient-reported outcomes were compared using a linear mixed effects model with a random intercept to account for repeated measures on the same individual. Differences in the frequency of categorical covariates between failures and nonfailures were examined with the Fisher's exact test. A P value of <0.05 was considered statistically significant. All

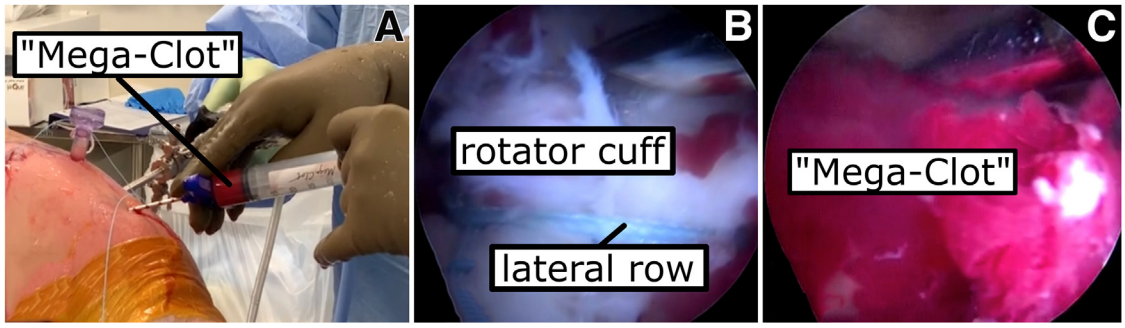

Fig 3. Implantation of remaining mega-clot on top of the completed rotator cuff repair (A–C).

analyses were performed with Stata Statistical Software (StataCorp LLC, College Station, TX).

Results

A total of 17 high-risk patients received the intervention in the study period. There were four patients lost to follow-up, resulting in a final cohort of 13 patients with mean age of 56.9 ± 7.7 years and mean follow-up of 26.9 ± 17.7 months (n =13). There were 10 male and 3 female patients. Surgery was performed on 9 right and 4 left shoulders, which affected 12 shoulders on the dominant side (92.3%). The mean body mass index (BMI) was 31.3 ± 4.5 kg/m^2. Three patients were smokers, and four patients had diabetes mellitus. All included patients suffered from atraumatic rotator cuff tears, and the majority of patients (76.9%) were chronic cases. No prior history of a rheumatic disease or cancer for the included patients was documented. Eight patients (61.5%) were revision rotator cuff repairs. In 10 cases (76.9%), surgery was conducted in chronic (≥6 weeks) rotator cuff lesions. In detail, four cases received an isolated repair of the supraspinatus tendon, while in three cases a combined supraspinatus and infraspinatus tendon repair was performed. In two patients, subscapularis and supraspinatus tendon were combined and repaired. Four patients received a combined repair of subscapularis, supraspinatus and infraspinatus tendon. Two patients received a tenodesis of the long head of the biceps. Patient demographic data are shown in Table 1.

An average volume of 92.2 ± 30.2 mL of BMA was processed to a mean volume of 3.9 ± 0.6 mL of cBMA. After removal of 1 mL of cBMA for analysis in our laboratory, the resulting average volume of 2.9 ± 0.6 of cBMA was further processed to a fibrin clot with an average volume of 29.3 ± 5.7 mL.

In Vitro Laboratory Processing

The representative 1 mL of cBMA collected and processed from the intraoperatively derived humeral BMA showed an average of 28.5 ± 9.1 × 10^6 nucleated cells/mL. There was an estimated average of 1,671.1 ± 1132.2 CFUs/mL in the processed fibrin clot aliquot.

A representative sample of the live/dead assay results of the fibrin "Mega-Clot" at 1, 2, and 4 weeks is shown in Fig 4 (top row) at 10× magnification. After 1 week in culture, a significant majority of cells remained viable, and the appearance of colonies could be noted (arrows). At 2 weeks, cells still remained viable, and the appearance of cellular processes could be seen (arrows). By 4 weeks, cells began to form a cellular network, with mostly live cells populating the clot (arrows). The bottom row shows representative brightfield images of these cellular colonies after 1, 2 and 4 weeks in culture at 10× magnification.

Clinical Outcomes

Patients showed a significant reduction of the mean VAS score from 5.6 ± 2.5 to 3.1 ± 3.2 at final follow-up (P < .001). There was a significant improvement for ASES (42.0 ± 17.1 to 65.5 ± 30.6; P < .001), SST (3.2 ± 2.8 to 6.5 ± 4.7; P = .002), SANE (11.5 ± 15.6 to 50.3 ± 36.5; P < 0.001), and Constant-Murley (38.9 ± 17.5 to 58.1 ± 26.3; P < .001) scores from the preoperative to the postoperative state. Range of motion improved significantly for forward elevation (112.3° ± 52.3° to 151.9° ± 39.6°; P = .007), abduction (103.8° ± 52.7° to 141.9° ± 49.1°; P = .018) and external rotation (40.8 ± 19.8 to 66.2 ± 40.3; P = .032).

At final follow-up, six patients (46%) with an average age of 60.0 ± 9.4 years showed an MRI confirmed retear of the rotator cuff. All of these patients had chronic rotator cuff tears. Additionally, the majority (5 of 6) were revision cases with an average of 1.6 ± 0.5 rotator cuff surgeries prior to the current operative treatment. No single patient demographic or preoperative factor was found to have a statistically significant association with failure (Table 2). The etiology of the repair failure was variable with two cases of insidious/atraumatic onset; one patient was involved in a motor vehicle accident, one patient injured the shoulder lifting a heavy object; one patient complained of too aggressive physical therapy, and another had a fall and landed

Table 1. Patient Demographic Data

Characteristic	
	Mean ± SD
Age, yr	56.9 ± 7.7
BMI, kg/m^2	31.3 ± 4.5
Length of follow-up, m	26.9 ± 17.7
	N (%)
Sex	
Male	10 (76.9%)
Female	3 (23.1%)
Type	
Primary	5 (38.5%)
Revision	8 (61.5%)
Previous RCR	
0	5 (38.5%)
1	3 (23.1%)
2	3 (23.1%)
3	2 (15.4%)
Chronic tear (≥6 weeks)	
Yes	10 (76.9%)
No	3 (23.1%)
Tear Grade (Goutallier)	
1	1 (7.7%)
2	4 (30.8%)
3	8 (61.5%)
Laterality	
Left	4 (30.8%)
Right	9 (69.2%)
Dominant arm	
Yes	12 (92.3%)
No	1 (7.7%)
Diabetes	
Yes	4 (30.8%)
No	9 (69.2%)
Inflammatory arthropathy	
Yes	0
No	13
Smoker	
Yes	3 (23.1%)
No	10 (76.9%)
Cancer	
Yes	0
No	13 (100%)

BMI, body mass index; RCR, rotator cuff repair.

onto the affected arm. Despite the MRI-confirmed failure, all patients had improvements in pain and function scores at final follow-up except one. These cases showed a reduction of the mean VAS score from 6.0 ± 2.6 to 3.8 ± 3.2. Clinical outcomes scores improved in this subgroup for ASES (39.3 ± 16.8 to 56.3 ± 25.5), SST (2.8 ± 2.6 to 4.3 ± 3.4), SANE (16.2 ± 22.6 to 37.7 ± 33.5), and Constant-Murley (34.2 ± 11.5 to 49.7 ± 22.0) scores from preoperative to the postoperative state. Interestingly, there were no differences in the change in preoperative to postoperative outcome scores for those with and without surgical failure. Range of motion improved for forward elevation (85.0 ± 53.9 to 136.7 ± 43.7), abduction (76.7 ± 42.3 to 121.7 ± 45.4), and external rotation (41.7 ± 22.3 to 56.7 ± 22.5) in these cases as well.

The majority of patients reported clinically relevant improvements in pain and function, as evidenced by the majority of patients meeting the MCID and SCB thresholds with respect to the ASES and SANE scores, including those with repair failures (Table 3). Despite improvements in patient-reported outcome scores for the majority of patients, only four patients (30.8%) met the ASES PASS criteria for the minimum score indicating patient satisfaction. Moreover, no patients with surgical failure reached this threshold.

Of the patients with RCR failure, only one patient underwent subsequent revision surgery. This patient was involved in a motor vehicle accident and was the only patient in the cohort to report worsened pain and clinical outcome scores. However, for the majority of cases (83%) with repair failure, patients chose against further operative intervention due to subjective improvements in pain and function.

Discussion

The most important finding of the current study was that arthroscopic rotator cuff repairs biologically augmented with a fibrin scaffold containing growth factors and progenitor cells derived from autologous whole blood and humeral cBMA showed clinical improvement in primary as well as revision cases. Interestingly, improvements in clinical outcomes were seen in the majority (83%) of surgical failures as well, which may help illustrate the beneficial effect of biologic augmentation in these patients. Nonetheless, there was a 46% failure rate in this cohort, indicating that the treatment of these high-risk patients remains a challenge and advancements on biologic augmentation is required.

Biologic augmentation of rotator cuff repairs has increased in popularity, as many investigations have identified the limited healing potential of these injuries as a biologic problem.[17,18] In particular, the supplementation of mesenchymal stem cells, also known as connective tissue progenitor cells, for rotator cuff repairs has garnered increased interest.[7,19-22] Ellera Gomes et al. biologically augmented 14 cases of open primary rotator cuff repairs with progenitor cells derived from the ilium.[23] This lead to improved clinical outcomes and no retears after 12 months.[23] Hernigou et al. also observed a reduced re-tear rate after augmented arthroscopic rotator cuff repair with MSCs derived from cBMA of the ilium compared to the control group.[7] Documented re-tears were correlated with significantly lower numbers of MSCs.[7] Further, Hernigou et al. observed that the number of transplanted cells was the most relevant parameter for outcomes, and patients without biologically augmented repairs were four times more likely to experience a poorer result.[7] In the current study, all patients but one showed clinical improvement, and only one retear was

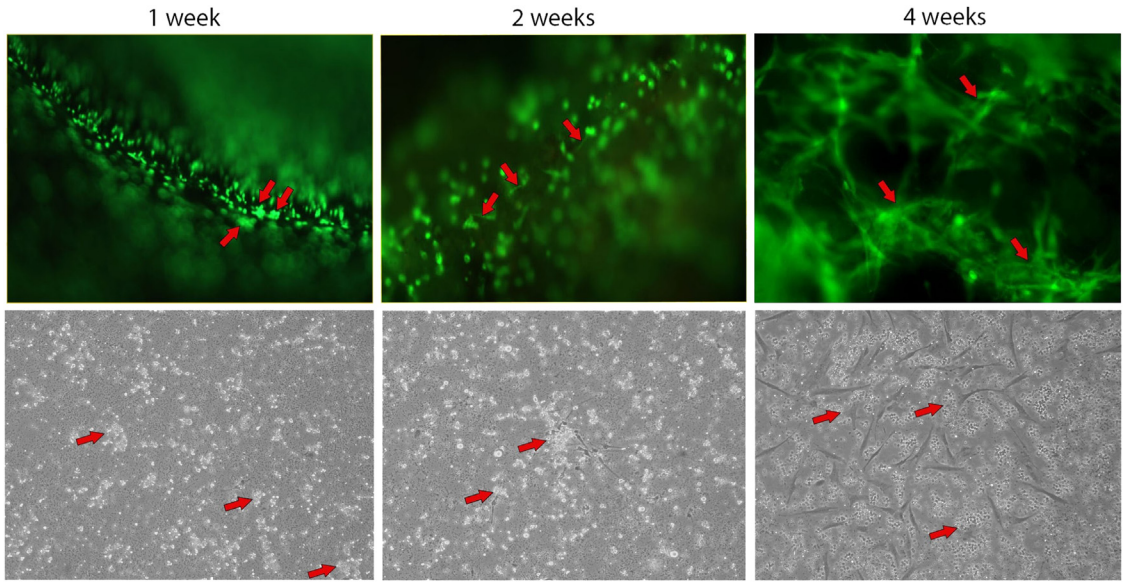

Fig 4. Live/dead assay (top row) of fibrin "Mega-Clot" after 1, 2, and 4 weeks in culture, showing excellent cellular viability (green fluorescence) In the bottom row, brightfield images of colony forming units are shown at its respective culture time. At 1 week, colonies were identifiable (arrows). At 2 weeks, the appearance of cellular processes was seen (arrows). At 4 weeks, cellular networks were identified (arrows). All images were taken at 10× magnification.

reported in primary cases. Unfortunately, there is limited published clinical outcomes data investigating biologically augmented RCR and a comparison between our study and the results of Hernigou et al. and Ellera Gomes et al. is limited due to methodological differences.[7,23] In particular, the patient populations were significantly different in these studies, with only primary repairs performed, as well as excluding high-risk patients based on medical comorbidities and tear size, unlike the patients in the current study. Contrarily, we included primary and revision cases of RCR, because, in our opinion, both situations should be evaluated for the beneficial effects of biologic augmented repair techniques. These differences may account for the higher failure rate in the current study.

Ellera Gomes et al. reported that the median concentration of progenitor cells was 3.81×10^8 in an aliquot of cBMA from the ilium.[23] Hernigou et al. found an average number of MSCs in cBMA to be 4,300 ± 1,800 per mL of BMA harvested from the ilium.[7] The reported average concentration of progenitor cells of Ellera Gomes et al.,[23] and the number of CFUs of Hernigou et al.[7] were higher than in the current study, although methodical differences limit the comparison of humerus- and ilium-derived cBMA. Each BMA was processed in different devices by another technician, according to the standards of the corresponding lab. Without a standardized method for the processing of BMA and counting CFUs, a comparison between cBMA from the humerus and ilium

Table 2. Possible Risk Factor Associations for Failure

Factor	*P* Value
Age	0.174
BMI	0.391
Sex	0.559
Revision	0.266
Previous RCR	0.353
Tear grade	0.999
Chronic	0.192
Dominant arm	0.999
Diabetes	0.999
Inflammatory arthropathy	N/A
Smoker	0.559
Cancer	N/A

BMI, body mass index; RCR, rotator cuff repair.

Table 3. Number of Patients Obtaining Clinically Relevant Improvements in ASES and SANE Scores

Score	Success		Failure		Total		*P* Value
Criteria Fulfilled?	Yes	No	Yes	No	Yes	No	
ASES							
MCID	5	2	4	2	9	4	.999
SCB	4	3	4	2	8	5	.999
PASS	3	4	1	5	4	9	.559
SANE							
MCID	6	1	4	2	10	3	.559
SCB	6	1	4	2	10	3	.559
PASS	3	4	0	6	10	3	.192

ASES, American Shoulder and Elbow Surgeons; MCID, minimal clinical important difference; PASS, patient acceptable symptomatic state; SANE, Single Assessment Numerical Evaluation; SCB, substantial clinical benefit.

regarding the effect on rotator cuff healing is very limited. This was supported by a recent systematic review by Murray et al., concluding that the reported information on cBMA protocols, as well as composition is inadequate and precludes the comparison across the limited number of available studies.[24]

Biologically augmenting the rotator cuff during surgery with PRP is another approach that has been increasingly used in orthobiologics.[25] However, there is an ongoing controversy regarding the effect of PRP on rotator cuff healing and clinical outcomes.[25] Recently, Hurley et al. showed in a meta-analysis, including 18 randomized controlled trials that the use of PRP in rotator cuff repair resulted in improved pain levels, functional outcomes, and healing rates for certain tear sizes.[26] In another study, Kim et al. observed that adipose-derived MSCs loaded in a fibrin glue for arthroscopic rotator cuff repair significantly improved the retear rate.[27] Hernigou et al. also observed a lower retear rate with 87% intact rotator cuffs in cases where the repair was augmented with cBMA from the ilium.[7] Teng et al. showed in an in vitro study that the expression of collagen I, osteocalcin, and osteopontin was higher in the coculture of bone marrow-derived MSCs with PRP.[28] These results are encouraging, especially if the BMA for rotator cuff repair can be harvested locally and an additional procedure with concomitant risks at the ilium can be avoided.[8,29] It bears the additional advantage that the same patient positioning can be applied, and surgical time can be minimized.

Despite literature promoting the use of cBMA and/or PRP to augment rotator cuff repairs, the lead author has since modified his biologic augmentation technique based on the high failure rate from this cohort along with the results of several recent biologic studies investigating the subacromial bursa. Utsunomiya et al. identified the highest potency of MSCs to be present in the subacromial bursa compared to the glenohumeral synovium, margin of the ruptured supraspinatus tendon, and the entheses.[10] Morikawa et al. demonstrated that cells from the subacromial bursa had greater differentiation ability and gene expression over time compared to concentrated bone marrow aspirate from the proximal humerus.[30] As such, for similar high-risk patients, the lead author has since added minced subacromial bursa to the biologic clot as an additional source of MSCs. Muench et al. reported the clinical results of 16 high-risk patients with rotator cuff repairs at a minimum 1-year follow up using a fibrin clot containing subacromial bursa, cBMA, and PRP.[22] By combining these biologic adjuncts, it was believed the maximum biologic effect could be obtained. In this cohort, using the ASES score, the MCID was achieved in 93.8% of patients, SCB in 93.8%, and the PASS threshold was met in 62.5% of patients.[22] This compared to 69.2%, 61.5%, and 30.8%, respectfully, in the current study. Moreover, Muench et al. reported only one failure (6%) secondary to a traumatic fall, compared to six failures (46%) in the current cohort.[22] Consequently, the lead author now uses minced subacromial bursa in all rotator cuff repairs indicated for biologic augmentation.

Limitations

There were limitations to this study that need to be considered. The sample size was small, we did not have a control group, and we had relatively short follow-up.[3,9] Patients as well as clinicians in the current study were not blinded, which could have generated bias. Finally, the surgical procedure was performed by the same orthopaedic surgeon, and the cBMA was processed according to a standardized protocol.

Conclusions

Arthroscopic rotator cuff repairs that are biologically augmented with a fibrin scaffold containing growth factors and autologous progenitor cells derived from humeral cBMA can improve clinical outcomes in primary, as well as revision cases in high-risk patients. However, the incidence of retears remains a concern in this population, demanding further improvements in biologic augmentation.

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