Bone Marrow Aspirate Concentrate Augmentation May Accelerate Allograft Ligamentization in Anterior Cruciate Ligament Reconstruction: A Double-Blinded Randomized Controlled Trial

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Purpose: To assess the effect of bone marrow aspiration concentrate (BMAC) augmentation on clinical outcomes and magnetic resonance imaging (MRI) findings in anterior cruciate ligament (ACL) reconstruction (ACLR) with bone−patellar tendon−bone (BTB) allografts. **Methods:** A double-blinded, randomized controlled trial was conducted on 80 patients undergoing ACL reconstruction using BTB allografts. Patients were randomized to 2 groups: (1) bone marrow aspirate was collected from the iliac crest, concentrated, and approximately 2.5 mL was injected into the BTB allograft, or (2) a small sham incision was made at the iliac crest (control). MRI was performed at 3 months and 9 months postoperatively to determine the signal intensity ratio of the ACL graft. **Results:** Seventy-three patients were available for follow-up at 1-year postoperatively (36 BMAC, 37 control). International Knee Documentation Committee (IKDC) scores were significantly greater in the BMAC group versus the control at the 9-month postoperative period (81.6 ± 10.5 vs 74.6 ± 14.2, $P = .048$). There was no significant difference in the proportion of patients who met the minimal clinically important difference for IKDC between the BMAC and control groups at 9 months (89% vs 85%; $P = .7$). Three months

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postoperatively, signal intensity ratio of the inferior third of the ACL graft was significantly greater in the BMAC group versus the control group (3.2 ± 2.2 vs 2.1 ± 1.5; $P = .02$). **Conclusions:** Patients who received BMAC augmentation of the BTB allograft during ACL reconstruction demonstrated greater signal intensity scores on MRI at 3 months, suggesting increased metabolic activity and remodeling, and potentially accelerated ligamentization. Additionally, patients in the BMAC group had greater patient-reported outcomes (IKDC) at 9 months postoperatively when compared with those who underwent a standard surgical procedure. There was no significant difference in the proportion of patients who met the minimal clinically important difference for IKDC between the BMAC and control groups at 9 months, suggesting limited clinical significance at this time point. **Level of Evidence:** I, randomized control trial.

Although anterior cruciate ligament reconstruction (ACLR) is one of the most common orthopaedic procedures performed in the United States,[1,2] few advances have been made to reduce the healing time of the anterior cruciate ligament (ACL) graft and the subsequent development of degenerative joint disease.[3-5] ACLR quantitative imaging studies have demonstrated that knee homeostasis is only re-established 2 years after surgery.[6] In addition, 1 in 4 young athletic patients who sustain an ACL injury and return to high-risk sports have been reported to sustain a subsequent ACL injury early in the return-to-play period.[7]

Disruption of the ACL leads to altered knee joint function and significantly increases the risk for knee osteoarthritis, with 50% to 90% of patients demonstrating evidence of knee osteoarthritis 10 years after ACLR.[8-11] While current ACLR techniques are generally perceived to be successful, a recent study demonstrated altered knee kinematics that correlated with poor patient functional outcomes in 38% of patients who underwent ACLR.[12] These factors have led to an increased interest in discovering methods to augment the biological responsiveness of cartilage and ligamentous cells in ACLR. One promising regenerative approach is the use of bone marrow aspirate concentrate (BMAC). BMAC consists of several growth factors and progenitor cells (mesenchymal stem/stromal cells) that can be applied directly to the site of injury intraoperatively. The pluripotent potential of these progenitor cells has been demonstrated to positively impact healing, regeneration, and biomechanical strength of ACLR grafts.[13-15]

There is a critical need to develop novel strategies to enhance ACL healing, to reduce the failure rate, and to accelerate recovery time after ACLR. The purpose of this study was to assess the effect of BMAC augmentation on clinical outcomes and magnetic resonance imaging (MRI) findings in ACLR with bone−patellar tendon−bone (BTB) allografts. We hypothesized that BMAC augmentation would be associated with improved radiographic evidence of ligamentization and clinical outcomes.

Methods

Study Design

This study was approved by our institutional review board (Rush University, #17082504). A double-blinded, randomized control trial was conducted on patients undergoing ACLR using BTB allografts. BTB allograft for ACLR is favored in our institution for its excellent biomechanical profile and rapid bone-to-bone healing.[16,17] Patients suitable for enrollment in this study were candidates for primary unilateral ACLR, between 18 and 60 years old, and had a proven complete ACL rupture confirmed by means of physical examination, MRI, and arthroscopy. Exclusion criteria were as follows: (1) a history of previous surgery on the ipsilateral knee, (2) reinjury of the ipsilateral ACL graft, (3) associated ligamentous injuries of the ipsilateral knee, (4) ipsilateral cartilage procedures not including chondroplasty, (5) unhealthy or symptomatic contralateral knee by means of previous injury and/or surgery, (6) high risk of postsurgical bleeding (history of bleeding disorders or on blood thinners), (7) diagnosed musculoskeletal cancer or any cancer not in long-term remission (at least 5 years), (8) pregnant or breastfeeding women, and (9) patients who have received platelet-based products or investigational treatment 12 months before procedure. Before the procedure, patients were randomized to either the BMAC or control group and underwent clinical examination including KT-1000 arthrometer (MEDmetric Corp., San Diego, CA) testing, range of motion (ROM) evaluation, and MRI. Patients allocated to the control group received a small sham incision at the iliac crest to ensure proper blinding, and no BMA was harvested.

BMAC Preparation and Surgical Technique

The patient is positioned in the supine position and the bone marrow harvesting is performed as previously described.[18] The syringes, trocar, and filters used for BMAC processing are flushed with heparin (500 units/mL), and the syringes are each loaded with 1 mL of anticoagulant citrate dextrose solution. The anterior iliac crest is identified and sterilely prepped and draped. An #11 blade is used to make a 5-mm stab incision over the iliac crest. Next, a bone marrow aspiration trocar is centered between the outer and inner walls of the iliac crest and a mallet is used to advance the trocar through the dense cortical bone into the medullary cavity. Trocar trajectory should be perpendicular to the anterior superior iliac spine. Approximately 50 to 90 cc of BMA is collected. The BMA is then placed in a

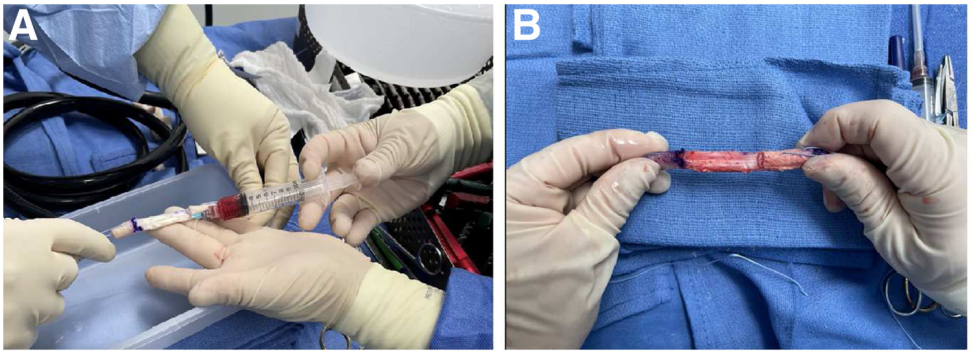

Fig 1. (A) BMAC injection of the tendinous allograft with a 25-gauge needle. (B) Allograft appearance minutes following injection of BMAC. (BMAC, bone marrow aspirate concentrate.)

centrifuging Angel Machine (Arthrex, Naples, FL) set up at 7% hematocrit. The final preparation of BMAC is automatically loaded into a sterile dual syringe system.

Biological Augmentation of the Graft

First, the patella and tibial bone plugs and tendinous graft are sized to ensure that the size of the graft is acceptable for the reconstruction tunnels. Patella bone plugs are typically 10 × 20 mm, and tibial bone plugs are typically 10 × 30 mm. The tendinous portion of the graft is harvested in continuity with the bone plugs.

The graft is then augmented with approximately 2.5 mL of BMAC (Angel System; Arthrex), which is injected throughout its intratendinous substance with a 25-gauge needle (Fig 1). A minimum of 15 minutes is allowed for the graft to soak with BMAC, following injection, to facilitate cell adhesion to collagen or extracellular matrix.[19]

Flow Cytometry

In total, 0.5 mL of BMA and BMAC was set aside before injection for postoperative enzyme-linked immunoassay, receptor testing, and flow cytometry. Testing was completed within 24 hours to verify presence of stem cells. Due to coronavirus disease 2019 restrictions, 33 of 37 BMAC samples were available for verification.

Surgical Technique

Anterolateral, anteromedial, and accessory transpatellar portals are created and diagnostic arthroscopy is performed to verify that the meniscus, femoral condyle and tibial plateau are stable and intact. The torn ACL is debrided with a full-radius resector. Attention is then turned to the femoral condyle where the intercondylar ridge and bifurcate ridge are outlined. On the tibial plateau, the anteromedial and posterolateral bundle center points are outlined to facilitate tunnel drilling. An anteromedial portal technique is used to drill the femoral tunnel, within the native footprint.

A 10- to 10.5-mm diameter femoral tunnel is drilled to a depth of 25 mm using a flexible curved (Versi-Tomic; Stryker, Kalamazoo, MI,) or straight drill bit. The anterior superior aspect of the tunnel is notched with a hexagonal screwdriver for interference screw placement. The femoral cortex is drilled with a 4.5-mm drill bit to facilitate suture passage.

Next, a 3-cm incision along the proximal anteromedial tibia is made. The tibial tunnel is then drilled with an ACL tip or elbow guide set at 65° followed by a 10-mm reamer. A rongeur is used to remove periosteum and soft tissue from the tibial orifice followed by a full-radius resector to remove debris intra-articularly.

The femoral bone plug sutures of the prepared allograft are passed through a loop of passing suture which is pulled though the tunnels. The graft is passed through a dry joint, without intra-articular saline, to prevent extravasation of BMAC cells from the graft (Fig 2). Fixation of the graft is established using 2 PEEK (polyether ether ketone) interference screws (Smith & Nephew, Andover, MA,) on the femoral and tibial sides,

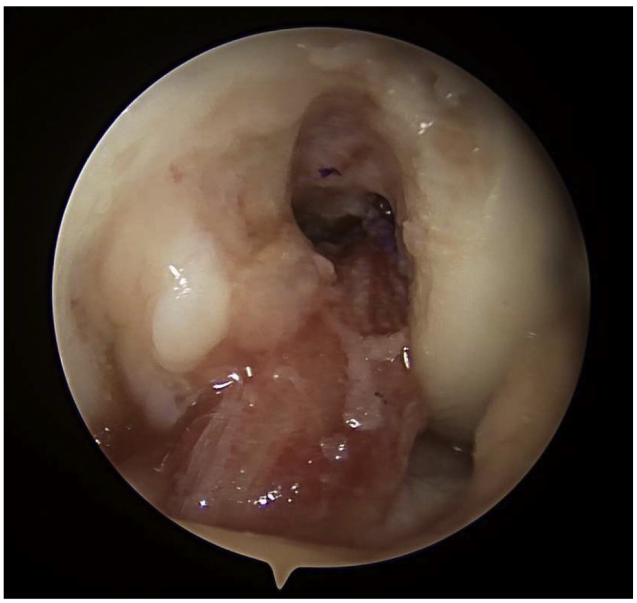

Fig 2. BMAC-augmented ACL allograft positioned in a dry left knee joint observed. through the anteromedial viewing portal. (ACL, anterior cruciate ligament; BMAC, bone marrow aspirate concentrate.)

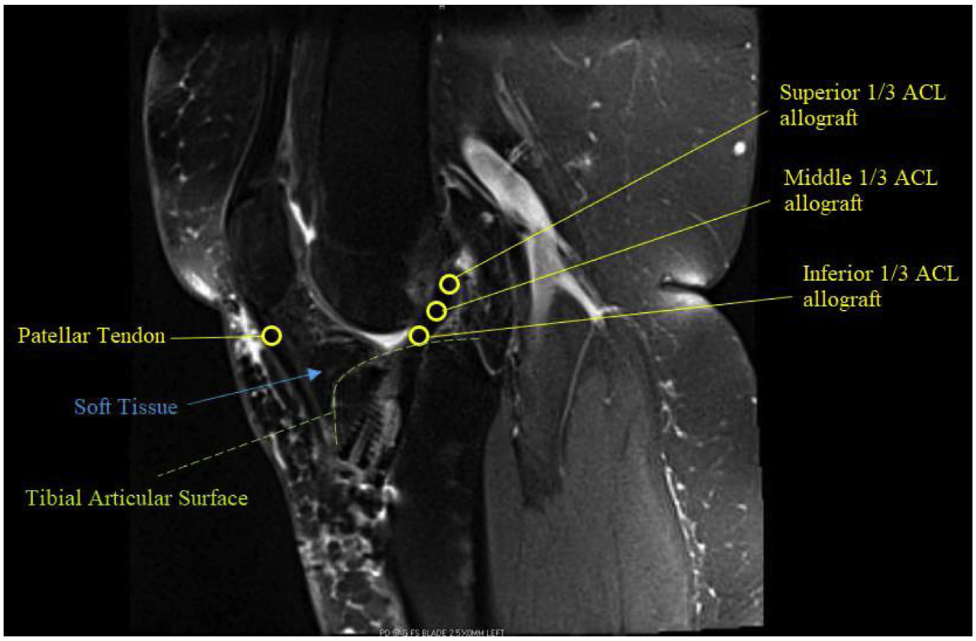

Fig 3. T2-weighted sagittal magnetic resonance imaging scan of a left knee labeled to highlight regions of the ACL graft and patellar tendon used to calculate signal intensity ratio. (ACL, anterior cruciate ligament.)

typically 8 and 10 mm in diameter, respectively. The knee is then tensioned in 5 to 10° of flexion, with a gentle posterior drawer force applied to reduce the tibiofemoral joint.

Rehabilitation Protocol

Following surgery, patients were allowed to bear weight immediately with no ROM restrictions. Patients with concurrent meniscal repair delayed full weight-bearing by 1 week. Crutches were used as needed for the first 2 weeks postoperatively, or until the patient was comfortable walking without assistance. A supervised physical therapy program was prescribed for 4 to 8 months following the concepts of periodization (ROM, muscular endurance, strength, and power phases could be developed based on the

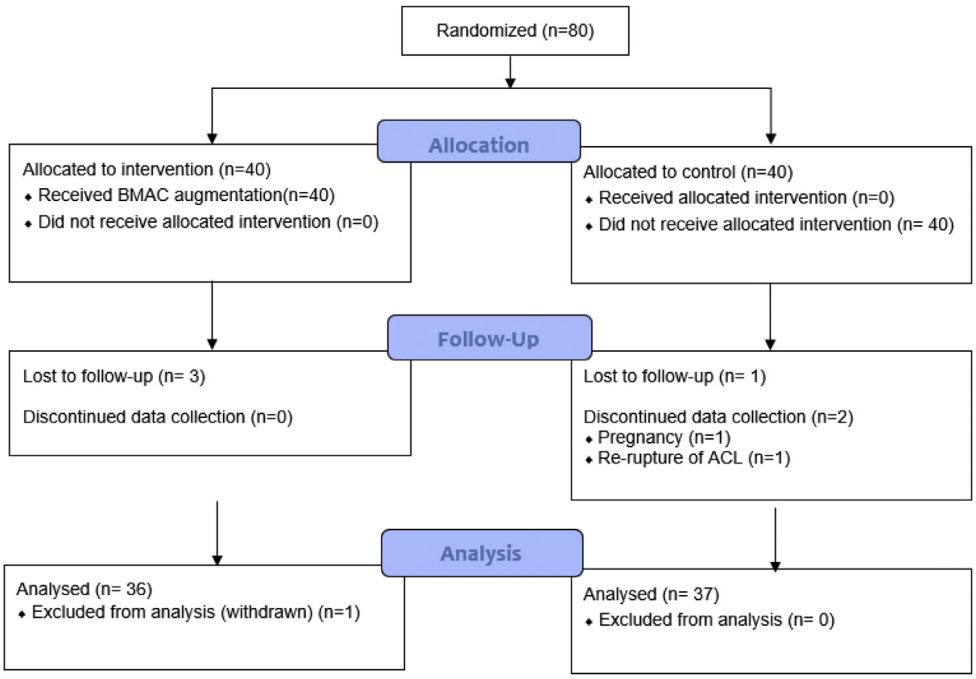

Fig 4. CONSORT diagram of randomized control study. (CONSORT, Consolidated Standards of Reporting Trials.)

Table 1. Patient Demographics, Concomitant Procedures and Preoperative PROs, Physical Examination

Characteristic	Control (n = 37)	BMAC (n = 36)	*P* Value
Mean age, y (SD)	36.6 (8.8)	36.3 (9.5)	.84
Sex, n (%)			.69
Male	18 (42.9)	15 (38.5)	
Female	24 (57.1)	24 (61.5)	
Laterality, n (%)			.17
Left	18 (42.9)	11 (28.2)	
Right	24 (57.1)	28 (71.8)	
Mean BMI (SD)	27.6 (4.6)	27.9 (7.1)	.83
Preoperative PROs (SD)			
KOOS	64.3 (16.5)	66.8 (13.6)	.59
Tegner	2.7 (1.6)	2.9 (1.4)	.64
IKDC	48.6 (16.4)	51.4 (14.7)	.47
Concomitant procedures, n (%)			
Meniscal repair	9 (24.3)	6 (16.7)	.52
Partial meniscectomy	11 (29.7)	13 (36.1)	.74
Patellar/femoral chondroplasty	4 (10.8)	1 (2.7)	.36
Preoperative surgical knee flexion, ° (SD)	124.7 (12.6)	122.2 (13.8)	.43
Preoperative KT difference* (SD)	2.04 (1.99)	2.01 (2.01)	.11

BMAC, bone marrow aspirate concentrate; BMI, body mass index; IKDC, International Knee Documentation Committee; KOOS, Knee Injury and Osteoarthritis Score; PROs, patient-reported outcomes; SD, standard deviation.

*KT difference: Surgical knee KT score − Nonsurgical knee KT score.

patients return to play timelines). For the first phase, after suture removal (1 week), patients transitioned to a stationary bike for 10 minutes per day with no resistance and slowly increasing the duration (by 1-2 minutes). Once the patient reached 30 minutes of continuous biking, he/she was allowed to increase resistance every 2 days. The length of each subsequent phase depended on the time frame of the rehabilitation program but was no shorter than 6 weeks. With ROM restored, the treatment emphasis shifted to the development of a muscular endurance base at week 8. Training emphasis transitioned to muscular strength development at week 15 before muscular power developed at week 21.

Clinical Evaluation

Clinical assessments occurred postoperatively at 6 weeks, 3 months, 6 months, 9 months, and 12 months by a blinded investigator. Flexion of both the nonsurgical and surgical knee was measured with the patient supine using a goniometer. Ligament stability was first evaluated via anterior drawer, Lachman, and pivot-shift tests. Direct anterior translation of the tibia of both the surgical and nonsurgical leg was then measured using the KT-1000 arthrometer (MEDmetric). International Knee Documentation Committee (IKDC) and Tegner scores were collected at 3 months, 6 months, 9 months, 12 months, and 24 months postoperatively. Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS-JR) scores were collected at 6 months, 12 months, and 24 months postoperatively.

MRI Assessment

The imaging protocol was standardized for both groups. Patients underwent MRI evaluation at 3 and 9 months' postoperatively. An abridged magnetic resonance protocol was performed with a T2-weighted (repetition time 3240 milliseconds/echo time 87 milliseconds) sagittal sequence, as well as intermediate-weighted (repetition time 3870 milliseconds/echo time 49 milliseconds) axial and coronal sequences. Additional imaging parameters included slice thickness/intersection gap at 4.0/1.0 mm and field of view at 15 cm as described in previous studies.[20,21] Regions of interest were standardized regarding area and placed at the proximal, middle and distal thirds of the ACL graft, as well as in the patellar tendon on a sagittal T2-weighted MRI scan. This was performed by a subspecialized musculoskeletal radiologist with 21 years of experience that was blinded to treatment group. Signal-intensity-ratios (SIRs) were calculated using the following formula: SIR = ACL region signal intensity/patellar tendon signal intensity.[20] An elevated SIR has been shown to be associated with increased graft revascularization at 3 months and decreased graft functionality at 6 to 12 months.[20,22-25] SIRs were compared between the 2 groups at both time points (Fig 3).[20]

Power Analysis and Statistical Analysis

As the primary end point of this study was MRI SIR, this was used to perform the power analysis. Hakozaki et al.[20] assessed the SIR of the double-bundle ACL graft 12 months after ACL reconstruction. At 12 months postoperatively, SIR was measured in 61 patients. The

Table 2. Patient-Reported Outcomes (PROs)

	Variables	Control, Mean (SD)	BMAC, Mean (SD)	*P* Value
Preoperative PROs	KOOS-JR	64.3 (16.5)	66.8 (13.6)	.59
	Tegner	2.7 (1.6)	2.9 (1.4)	.64
	IDKC	48.6 (16.4)	51.4 (14.7)	.47
3-month follow-up PROs	KOOS-JR	N/A	N/A	N/A
	Tegner	2.9 (1.1)	3.04 (1.0)	.72
	IDKC	54.8 (16.0)	55.5 (13.3)	.85
6-month follow-up PROs	KOOS-JR	82.8 (12.5)	78.7 (10.1)	.29
	Tegner	4.8 (1.5)	4.3 (1.2)	.29
	IDKC	72.9 (13.9)	70.9 (11.7)	.60
9-month follow-up PROs	KOOS-JR	N/A	N/A	N/A
	Tegner	5.1 (1.5)	5.4 (1.9)	.53
	IDKC	74.6 (14.2)	81.6 (10.5)	**.048**
1-year follow up-PROs	KOOS-JR	89.3 (9.3)	84.1 (10.7)	.15
	Tegner	5.5 (1.3)	6.2 (1.9)	.10
	IDKC	80.1 (13.0)	83.3 (11.5)	.31

NOTE: Bolded values are statistically significant.
BMAC, bone marrow aspirate concentrate; IKDC, International Knee Documentation Committee; KOOS-JR, Knee Injury and Osteoarthritis Score for Joint Replacement; N/A, not available; PROs, patient-reported outcomes.

mean SIR of the ACL graft was significantly greater ($P = .014$) in patients with positive pivot-shift test (SIR = 1.46) than in patients with negative pivot-shift test (SIR = 1.25). For this study, a difference of 20% was considered to be clinically relevant. To detect a difference of 0.25 in SIR (SD 0.21) with a power of 90% and an alpha of 5%, a sample size of 15 patients in each study group was required.

Descriptive statistics were used to report patient demographic characteristics and intraoperative data, and statistical analysis was performed with Excel (Microsoft, Redmond, WA) software. To determine whether the 2 groups were comparable in terms of number, age, and sex, an F test and Student's *t* test were used. Statistical analyses of the continuous variables were examined using Student's *t* test. For categorical variables, proportions were compared through χ^2 tests. Clinical relevance of statistically significant patient-reported outcomes (PROs) was evaluated using previously defined minimal clinically important difference (MCID) values (IDKC: 9.0, Tegner: 1.0, KOOS-JR: not available).[26,27]

Results

Study Sample Demographics

Eighty patients met inclusion criteria and were enrolled into this study. One patient asked to be withdrawn from the study. Another patient was excluded after she became pregnant shortly after enrolling. Four patients were lost to follow-up. Lastly, 1 patient in the control group was excluded from analyses due to a traumatic retear of her ACL graft secondary to a mechanical fall at 3 months postoperatively (Fig 4). Thus, 73 patients were included in this analysis of which the first author B.F. completed 57 procedures, A.Y. completed 5 procedures, and N.V. completed 11 procedures. The overall average follow-up rate for physical examination and PROs at 3, 6, 9, and 12 months' postoperatively was 84%, 73%, 74%, and 90%, respectively. The average follow-up rate for MRIs at 3 and 9 months was 97% and 90%, respectively. There were no significant differences in patient demographics, concomitant procedures, preoperative PROs and preoperative physical examination findings for each group ($P > .05$, Table 1). All 33 BMAC samples tested via flow cytometry were confirmed to contain stem cells at an average concentration of 900 cells/mL. No dose-dependent response with MRI SIR was observed ($P > .05$).

Patient-Reported Outcomes

Preoperatively, there was no significant difference in KOOS-JR, Tegner, or IKDC scores. At 9 months, patients who received BMAC had significantly greater IKDC scores when compared with the control group (81.6 ± 10.5 vs 74.6 ± 14.2, $P = .048$). Regarding clinical significance, 22 of 26 patients (85%) in the control group achieved a ΔIKDC score greater than 9.0 versus 25 of 28 patients (89%) in the BMAC group at 9

Table 3. MRI Signal Intensities at 3 and 9 Months' Postoperatively

Signal Intensity	Control, Mean ± SD
SIR superior third vs patellar tendon*	3.7 ± 1.9
SIR middle third vs patellar tendon*	2.6 ± 2.1
SIR inferior third vs patellar tendon*	2.1 ± 1.5
SIR superior third vs patellar tendon*	3.9 ± 2.4
SIR middle third vs patellar tendon*	3.3 ± 2.3
SIR inferior third vs patellar tendon*	3.5 ± 2.5

NOTE. Bone marrow aspirate concentrate containing mesenchymal stem cells.
MRI, magnetic resonance imaging.
*Signal intensity ratio (SIR) of allograft in comparison with ipsilateral patellar tendon.

Table 4. Physical Examination Findings

	Variables	Control, Mean (SD)	BMAC, Mean (SD)	*P* Value
Preoperative	Surgical knee flexion	124.7 (12.6)	122.2 (13.9)	.43
	Knee flexion difference	5.2 (5.4)	5.6 (5.4)	.48
	KT difference	2.0 (2.0)	2.0 (2.0)	.11
6 weeks' postoperative	Surgical knee flexion	113.3 (15.2)	115.9 (13.5)	.49
	Knee flexion difference	20.5 (14.2)	14.3 (14.0)	.10
	KT difference	0.3 (1.2)	0.4 (1.0)	.90
3 months' postoperative	Surgical knee flexion	125.4 (24.5)	124.1 (9.8)	.79
	Knee flexion difference	6.1 (9.0)	5.7 (7.0)	.82
	KT difference	0.2 (0.9)	0.3 (0.9)	.84
6 months' postoperative	Surgical knee flexion	130.74 (9.0)	130.2 (8.1)	.82
	Knee flexion difference	4.0 (5.7)	2.1 (7.4)	.32
	KT difference	0.2 (0.9)	0.4 (0.9)	.54
9 months' postoperative	Surgical knee flexion	129.4 (8.3)	133.2 (9.7)	.22
	Knee flexion difference	2.1 (5.9)	0.5 (3.5)	.29
	KT difference	0.2 (0.7)	0.3 (0.7)	.41
1-year postoperative	Surgical knee flexion	133.8 (9.5)	131.0 (11.1)	.36
	Knee flexion difference	1.1 (4.0)	2.1 (3.2)	.37
	KT difference	0.4 (0.9)	0.2 (0.7)	.27

NOTE. Knee flexion difference: Nonsurgical Knee Flexion − Surgical Knee Flexion; KT difference: Surgical knee KT − Nonsurgical knee KT.

months ($P = .70$). PROs were found to be nonsignificant at all other time points. Both groups demonstrated significant improvement in all PROs 1 year after ACLR ($P < .01$). PRO scores are summarized in Table 2.

MRI Assessment

The signal intensity ratio for the inferior third of the allograft was significantly greater in the BMAC group versus the control group (3.2 ± 2.2 vs 2.1 ± 1.5, $P = .023$) at 3 months (Table 3).

Physical Examination Assessment

There were no significant differences observed in surgical knee flexion, relative knee flexion difference, and relative KT-1000 difference between the BMAC group and control group at any time point ($P > .05$) (Table 4).

Discussion

The primary finding of this study is that BMAC augmentation of ACLR produced MRI evidence of increased signal intensity when compared with controls at 3 months. The greater SIR of the inferior allograft in the BMAC group may correlate with increased graft metabolic activity and remodeling and potentially accelerated revascularization and healing at 3 months. Additionally, while ACLR augmentation with BMAC yielded superior IKDC scores at 9 months, this difference was not found to be clinically significant.

The primary cell in the ACL is the fibroblast. Previous research has demonstrated that mesenchymal stromal/stem cells derived from bone marrow have the ability to differentiate into fibroblasts and connective tissue in ligaments.[28,29] The fibroblast also has receptors for many of the growth factors, including platelet-derived growth factor, transforming growth factor-beta, and basic fibroblast growth factor, that stimulate fibroblast growth, migration, and biosynthetic activity.[30] In light of such potential, applying BMAC to enhance ACLR presents an opportunity. BMAC may promote an improved ligamentization of the graft used for ACLR, reduce the proinflammatory factors released immediately after surgery, and contribute to better integration of the graft within the bone tunnels, thus avoiding their enlargement and failure over time.[31]

The increased SIR identified on MRI in the BMAC group at 3 months supports the theory of accelerated allograft ligamentization in ACLR with stromal/stem cell augmentation. The process of ligamentization is well described in the current literature. After an early phase of minimal remodeling, the ACL allograft undergoes a period of revascularization between 6 and 16 weeks. After 6 months, the allograft gradually gains strength before undergoing maturation from 9 to 24 months postoperatively.[22,23,32] During the process of revascularization, previous studies have shown increased SIR of both hamstring and patellar tendon grafts in ACLR.[22-25] Increased SIR in the BMAC group may be attributable to increased angiogenesis, a process accelerated by growth factors, such as vascular endothelial growth factor, present in the concentrate. This accelerated ligamentization process may play a role in reducing the risk of ACL rerupture in high-risk patients. The reported rate of ACL rerupture ranges from 1% to 11%, with the greatest risk occurring within the first 12 months of ACLR.[33-36] The impact of BMAC on the rates of ACL reinjury is a concept warranting further investigation.

Regarding ACL graft maturation, Hakozaki et al.[20] found significant correlations between SIR and KT-1000 arthrometer measurements 12 months

postoperatively, suggesting a lower SIR during the maturation phase may indicate increased ligament stability and strength. We found no significant differences between SIRs in the BMAC and control groups at 9 months. These results may be secondary to an incomplete and prolonged remodeling process highlighted by Sanchez et al.[37] In their study, Sanchez et al.[37] observed graft ligamentization in ACLR augmented with platelet-rich plasma in comparison with a control cohort. They found grafts treated with platelet-rich plasma had a synovial appearance in the early stage of ligamentization (6-12 months) whereas the control grafts lacked the formation of this synovial-like tissue. By 18 to 24 months, the authors showed that this tissue is eventually integrated into the remodeled tendon graft resembling the structure of a normal ACL. Given this prolonged timeframe, future research should aim to evaluate stem/stromal cell augmented ACL allografts during the late maturation phase.

Patients receiving BMAC augmented allografts had significantly greater IKDC scores than controls at 9 months (IKDC; 81.6 ± 10.5 vs 74.6 ± 14.2, $P = .048$). There was no statistical difference in PRO scores preoperatively between the 2 groups. Despite an average difference of 7.0 points in IKDC scores, this improvement in the BMAC group did not meet the threshold for previously established MCID. MCID is defined as the minimal change in score required for a patient to perceive a clinical difference. Nwachukwu et al.[26] found the MCID for IKDC in ACLR patients to be 9.0 points, suggesting that the greater IKDC scores found in our study at 9 months may not translate to improved patient functionality. In addition, there was no significant difference in the proportion of patients who met MCID for IKDC between the BMAC and control groups at 9 months (89% vs 85%; $P = .7$), suggesting limited clinical benefit for patients receiving BMAC at this time point. Still, as the ligamentization process can require up to 2 years to complete, further evaluation of clinical outcomes at 2 year follow up is necessary.[37]

There is promising evidence in the current literature that the addition of stromal/stem cell products to the graft or tunnels may accelerate graft ligamentization and improve graft strength and functionality. In a rabbit model, Lim et al.[38] showed that mesenchymal stem cell reinforced grafts demonstrate significantly greater load to failure versus nonaugmented controls, as early as 8 weeks following surgery. Other animal studies with modified grafts and injection of therapeutic native or recapitulated stem cells have also shown promise in reducing bone-tunnel enlargement, promoting graft maturation via mature fibrocartilage growth, and increasing graft strength.[13,14,21,39] While there is a paucity of translational human research, Silva et al.[40] performed a prospective randomized controlled trial evaluating the effect of injected BMAC on graft-to-bone healing in the femoral tunnel following hamstring ACLR. The authors concluded that BMAC had a limited role in graft-to-bone healing secondary to nonsignificant MRI signal intensity findings at the femoral interzone. However, this study was significantly limited by a small sample size of 40 patients and a failure to evaluate MRI signal intensity beyond 3 months. Previous studies have demonstrated a 6-to-12-month window for complete tendon-to-bone healing in ACLR.[41,42]

Limitations

This study had some limitations. First, 3 different surgeons enrolled patients in the study, allowing for slight variations in technique. Second, meniscal pathology was not an exclusion criterion for this study. Third, all participants in this study underwent BTB allograft ACLR, thereby limiting the applicability of these results to other allograft procedures. Fourth, the subjective nature of PROs is an inherent limitation of this study. Finally, due to COVID-19 restrictions, this study was unable to verify the presence of stem cells in the BMAC of 3 patients.

Conclusions

Patients who received BMAC augmentation of the BTB allograft during ALCR demonstrated greater signal intensity scores on MRI at 3 months, suggesting increased metabolic activity and remodeling and potentially accelerated ligamentization. Additionally, patients in the BMAC group had greater patient-reported outcomes (IKDC) at 9 months postoperatively when compared with those who underwent the standard surgical procedure. There was no significant difference in the proportion of patients who met MCID for IKDC between the BMAC and control groups at 9 months, suggesting limited clinical significance at this time point.

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