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A Prospective, Randomized, Double-Blind Clinical Trial to Investigate the Efficacy of Autologous Bone Marrow Aspirate Concentrate During Arthroscopic Meniscectomy in Patients With Early Knee Osteoarthritis

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Background: Despite being recognized as a safe procedure with minimal reported complications, injecting autologous bone marrow aspirate concentrate (BMAC) as an adjuvant to arthroscopic partial meniscectomy (APM) for symptomatic patients with meniscal tears and concomitant knee osteoarthritis (OA) has not been studied in randomized controlled trials.

Purpose: To compare patient-reported outcome measure (PROM) scores and radiographic outcomes in symptomatic patients with meniscal tears and concomitant mild knee OA who underwent APM with and without an autologous BMAC injection administered at the time of surgery.

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

Methods: Enrolled patients aged ≥18 years determined to have a symptomatic meniscal tear with concomitant mild knee OA suitable for APM and meeting inclusion and exclusion criteria were randomized into 2 groups: BMAC and control (no BMAC). The primary endpoint of the study was the International Knee Documentation Committee (IKDC) score at 1 year postoperatively. Secondary endpoints included radiographic outcomes (Kellgren-Lawrence grade) at 1 year postoperatively and various PROM scores, including those for the IKDC, Knee injury and Osteoarthritis Outcome Score (KOOS), visual analog scale, and Veterans RAND 12-Item Health Survey, at 3 months, 6 months, 1 year, and 2 years after meniscectomy.

Results: Of the 95 enrolled patients, 83 (87.4%) were included for final analysis. No significant differences were found between the groups with regard to patient characteristics, intraoperative variables, concomitant procedures, preoperative PROM scores, or preoperative radiographic findings. At 1 year postoperatively, the BMAC group failed to demonstrate significantly better IKDC scores ($P = .687$) or radiographic outcomes ($P > .05$ for all radiographic measures) compared with the control group. Secondary PROM scores also did not significantly differ between the groups ($P > .05$ for all PROMs). However, there were higher achievement rates of the minimal clinically important difference for the KOOS Sport (100.0% vs 80.0%, respectively; $P = .023$) and KOOS Symptoms (92.3% vs 68.0%, respectively; $P = .038$) at 1 year postoperatively in the BMAC group than in the control group. All PROMs, excluding the VR-12 mental score, showed significant improvements compared with baseline at all postoperative time points for both the BMAC and control groups.

Conclusion: The addition of an autologous BMAC injection during APM did not result in significant changes in IKDC scores or radiographic outcomes at the 1-year postoperative mark. Secondary PROM scores were generally comparable between the 2 groups, but there was higher minimal clinically important difference achievement for the KOOS Sport and KOOS Symptoms at 1 year postoperatively in the BMAC group. In patients with symptoms consistent with a meniscal tear who had concomitant mild OA, the addition of BMAC to arthroscopic debridement did not affect the outcome.

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Osteoarthritis (OA) is a pervasive degenerative disease, impacting over 500 million people globally.[33] In the United States, more than 27 million people are affected by symptomatic radiographic OA, with over 9 million specifically experiencing knee OA.[32] Similarly, meniscal tears are commonly encountered injuries, with a prevalence of 35% in patients older than 50 years, and are a potential cause of mechanical symptoms and pain.[12,31,39] Of note, in patients with radiographically documented symptomatic knee OA, 75% exhibit evidence of a meniscal tear on magnetic resonance imaging (MRI).[2] Despite this high shared prevalence, previous studies have revealed that patients with symptomatic knee OA and a concomitant meniscal tear experience levels of pain similar to those of patients with knee OA and no meniscal tear, raising questions about the contribution of OA to the symptoms of meniscal tears in patients and how to best treat them.[2,12]

Arthroscopic partial meniscectomy (APM) serves as a primary intervention aimed at alleviating pain and mechanical discomfort by excising areas of the damaged meniscus, typically after an unsuccessful trial of nonoperative treatment.[6] Despite studies demonstrating short-term relief provided by APM, persistent concerns exist regarding the well-documented long-term progression of OA in knees after meniscectomy[1,13,17,22,31,39] as well as the overall utility of the procedure for symptomatic patients with meniscal tears and concomitant knee OA. In hopes of addressing this, the METEOR trial, a landmark, multicenter, randomized controlled trial involving symptomatic patients with meniscal tears and evidence of mild-to-moderate knee OA on imaging, failed to identify significant differences in pain and functional outcomes between patients who underwent APM compared with nonoperative therapy at 1 year and 5 years postoperatively. However, and equally important, 38% of patients from the nonoperative group crossed over to the operative group after failed therapy, and they largely benefited from the surgical intervention.[20,21] As such, this study furthers the consideration of the role of APM in treating symptomatic patients with meniscal tears and concomitant knee OA.

After meniscal damage, biological mediators of the proinflammatory cascade have been implicated in the development and progression of knee OA.[10] As such, there is growing interest in autologous biological interventions to alter this deleterious milieu within the joint.[7,27,28,30] Autologous orthobiological options, such as platelet-rich plasma (PRP) and bone marrow aspirate concentrate (BMAC), may contain concentrated marrow-derived mesenchymal stromal cells, white blood cells, platelets, and signaling molecules crucial to the processes of inflammation, chondrogenesis, and connective tissue healing while also standing out for their advantages over allogenic alternatives in terms of cost, availability, and regulatory considerations.[8] Despite being recognized as a safe procedure with minimal reported complications, injecting BMAC as an adjuvant to APM for symptomatic patients with meniscal tears and concomitant knee OA has not been extensively studied in randomized controlled trials.[3,5,23] Positive outcomes have been reported in the treatment of degenerative knee conditions with BMAC, either as a standalone treatment or as a surgical adjunct; however, these studies were largely uncontrolled, underpowered, and/or retrospective in nature.[4,11,15,26]

This study aimed to compare radiographic outcomes and patient-reported outcome measure (PROM) scores in symptomatic patients with meniscal tears and concomitant mild knee OA who underwent APM with and without an autologous BMAC injection administered at the time of surgery. To our knowledge, this study represents the first randomized controlled trial to prospectively investigate the effects of an autologous BMAC injection in patients with a concomitant diagnosis of mild knee OA after meniscectomy. We hypothesized that patients who received a concomitant BMAC injection would demonstrate significantly improved International Knee Documentation Committee (IKDC) scores at 1 year postoperatively compared with the control group. Furthermore,

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given the short-term follow-up, we anticipated no effect on the radiographic progression of knee OA at 1 year postoperatively but significantly improved scores on other PROMs up to 2 years postoperatively in the intervention group compared with the control group.

METHODS

This study obtained approval from the institutional review board (ORA No. 15090903-IRB01) at Rush University Medical Center before enrolling participants. Starting in 2017, patients presenting to our institution who were aged ≥18 years, determined to have a symptomatic meniscal tear with concomitant mild knee OA, met standard indications for APM, and provided consent for APM were considered for inclusion. Inclusion criteria involved the confirmation of a meniscal tear(s) on MRI as well as Kellgren-Lawrence (KL)[24] grade 1 to 2 changes on radiographic imaging or Outerbridge[38,40] grade ≤2 changes on MRI or an arthroscopic examination of tibiofemoral articular surfaces.

Exclusion criteria included the lack of decision-making capacity, unwillingness to participate in the necessary follow-up, those who were pregnant or planned to become pregnant during the duration of the study, a history of diabetes mellitus, rheumatoid arthritis or other autoimmune disorders, solid-organ or hematologic transplantation, a diagnosis of non–basal cell malignancy within the past 5 years, an infection requiring antibiotic treatment within the previous 3 months, previous surgery on the index meniscus, concomitant ipsilateral ligamentous or cartilage repair or restoration surgery, or therapeutic injection(s) to the affected knee within 6 weeks of surgery. Additionally, patients were excluded preoperatively if radiographic imaging revealed KL grade ≥3 changes or intraoperatively when arthritic changes were absent in the involved compartment.

Informed consent forms were signed on the day of surgery by patients who elected to enroll. After consent, patients were randomized in a 1:1 manner to the intervention (BMAC) or control (no BMAC) group. A diagnostic arthroscopic examination confirmed the eligibility criteria for both groups. Both groups then underwent standard APM. After APM, the surgeon was informed of the patient's group status. For the control group, a 1- to 2-mm sham incision was made over the ipsilateral anterior superior iliac spine (ASIS). For the intervention group, 60 mL of bone marrow was aspirated from the ipsilateral ASIS using the Angel System (Arthrex). The bone marrow aspirate was then passed off the sterile field and processed according to the manufacturer's instructions. Afterward, the processed BMAC (enriched with key components such as marrow-derived mesenchymal stromal cells, white blood cells, and platelets) was loaded into a sterile syringe. The surgeon then administered the injection into the operative knee, adjacent to the inferolateral portal, after portal closure at the conclusion of the case. Patients in both groups were advised to follow a standard postoperative protocol, including weightbearing as tolerated and graded activity progression over several weeks.

The primary endpoint of the study was the IKDC score at 1 year postoperatively. Secondary endpoints included radiographic outcomes (KL grade) at 1 year postoperatively and various PROM scores, including those for the IKDC, Knee injury and Osteoarthritis Outcome Score (KOOS), visual analog scale (VAS), and Veterans RAND 12-Item Health Survey (VR-12), at 3 months, 6 months, 1 year, and 2 years after meniscectomy. Complications and failures (defined as conversion to total knee arthroplasty [TKA]) were assessed by reviewing the electronic medical record at each follow-up. Electronic surveys were administered using Outcomes Based Electronic Research Database software (Universal Research Solutions) or PatientIQ software. Follow-up radiographic KL grading and analysis of other objective parameters were performed by a blinded fellowship-trained sports medicine surgeon (J.D.).

Statistical Analysis

Statistical analyses were conducted using SPSS software (Version 27; IBM). A power analysis based on previously published data on IKDC scores after APM by Koyonos et al[29] and the minimal clinically important difference (MCID) for the IKDC after APM as reported by Gowd et al[16] was performed. Utilizing these data, a sample size of 36 participants per group was calculated to achieve 80% power and an alpha level of 0.05, aiming to detect a clinically important difference of 10.6 points between the groups on the IKDC at 1 year after meniscectomy. To account for potential attrition, an enrollment goal of 50 participants per group was set.

Descriptive statistics, including absolute counts, percentages, means, standard deviations, and ranges where appropriate, were used to analyze patient characteristics and outcomes. The chi-square and Fisher exact tests were used to assess differences between nominal variables, the *t* test for parametric continuous variables, and the Mann-Whitney *U* test for nonparametric data to detect between-group differences. The Wilcoxon rank-sum test was employed for within-group differences in nonparametric data and the Friedman test for nonparametric repeated measures. Also, 2-way mixed analysis of variance determined between- and within-participant interactions for parametric continuous variables. An intention-to-treat analysis was performed for the primary outcome, the 1-year IKDC score, using mean imputation for missing data. Univariate and multivariate linear regression analyses were conducted to assess factors predictive of the 1-year IKDC score and 1-year KL grade. The criterion for inclusion in the multivariate model was a P value <.15 on univariate analysis. Statistical significance was set at $P < .05$.

RESULTS

Patient Characteristics, Intraoperative Variables, and Concomitant Procedures

Of 95 enrolled patients, 83 (87.4%) were included for final analysis. Of the 12 patients not included for analysis, 1 patient did not receive the allocated intervention (because of inadequate bone marrow withdrawal intraoperatively),

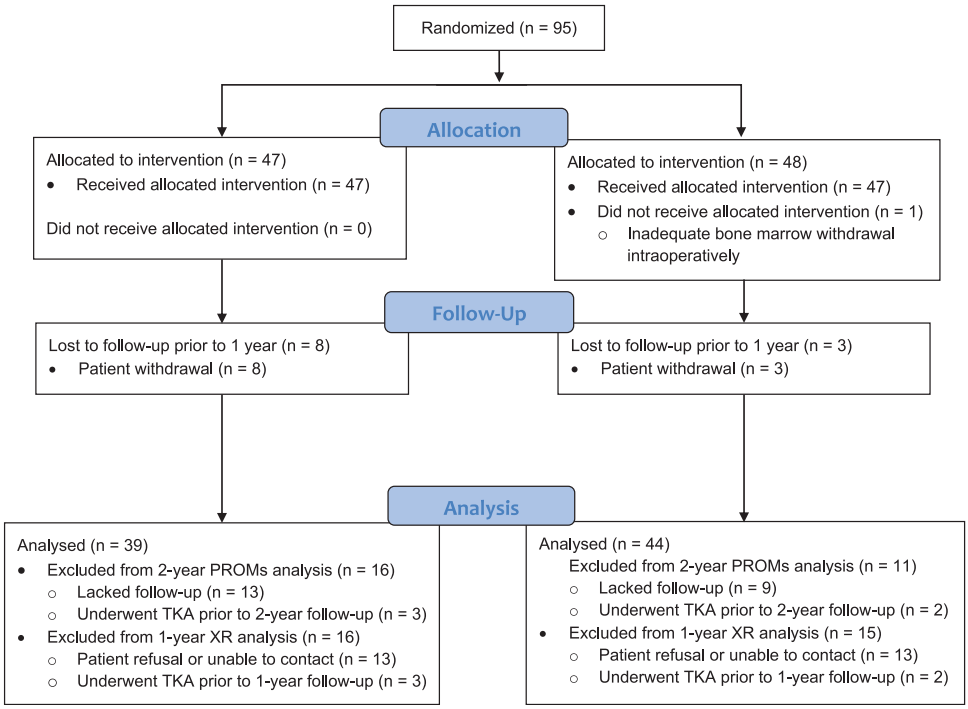

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) flow diagram. PROM, patient-reported outcome measure; TKA, total knee arthroplasty; XR, x-ray.

and 11 patients were lost to follow-up before 1 year (all because of patient withdrawal from the study) (Figure 1). Comparisons of patient characteristics, intraoperative variables (including the amount and location of APM), and concomitant procedures between the 2 groups (44 patients in the BMAC group and 39 patients in the control group) are found in Table 1. The BMAC group had a mean age of 55.2 ± 9.7 years and a mean body mass index (BMI) of 28.7 ± 5.2, while the control group had a mean age of 54.9 ± 7.9 years and a mean BMI of 30.5 ± 5.0. No significant differences were found between the groups with regard to age, sex, BMI, smoking status, knee laterality, meniscus laterality, meniscal tear type, percentage of meniscus removed, and concomitant procedures.

PROM Scores and MCID Achievement

No significant differences were found between the groups with regard to baseline IKDC, VAS pain, VR-12, and KOOS scores (Table 2). The mean IKDC score at 1 year after meniscectomy was 68.1 ± 22.9 for the BMAC group and 70.4 ± 22.7 for the control group, with no statistical difference found ($P = .687$). In addition, the mean change in the IKDC score from baseline to 1 year was 27.2 ± 21.0 for the BMAC group and 26.2 ± 21.4 for the control group, with no statistical difference found ($P = .695$). Likewise, secondary PROM scores (VAS pain, VR-12 mental, VR-12 physical, and KOOS subscales) at 3 months, 6 months, 1 year, and 2 years postoperatively did not statistically differ between the BMAC and control groups. Finally, no significant difference was observed between the groups for the 1-year IKDC score when performing an intention-to-treat analysis (Table 3).

In terms of within-group comparisons, all PROM scores at 3 months, 6 months, 1 year, and 2 years postoperatively were significantly improved compared with baseline for the BMAC group ($P < .05$), except for the VR-12 mental score in which no time points were statistically different compared with baseline. The same was true for the control group, except for the VR-12 mental score at 6 months, which was significantly improved compared with baseline ($P = .040$).

With regard to MCID achievement, the BMAC group was more likely to achieve the MCID for the KOOS Sport (100.0% vs 80.0%, respectively; $P = .023$) and KOOS Symptoms (92.3% vs 68.0%, respectively; $P = .038$) at 1 year postoperatively than the control group. Notably, the MCID for the IKDC at 1 year was achieved in 78.8% of patients in the BMAC group and 76.0% of patients in the control group ($P = .801$). Apart from the intergroup differences found for the KOOS Sport and KOOS Symptoms at 1 year, no statistical differences were found when comparing MCID achievement between the 2 groups for all other PROMs at 3 months, 6 months, 1 year, and 2 years postoperatively. Additional data regarding MCID achievement for each group is found in Table 4.

Radiographic Outcomes

Results from the radiographic analysis are found in Table 5. Baseline KL grades were comparable between the BMAC and control groups in both extension ($P = .738$) and flexion

TABLE 1
Patient Characteristics, Intraoperative Variables, and Concomitant Procedures[a]

	BMAC (n = 44)	Control (n = 39)
Patient characteristics		
Age, mean ± SD (range), y	55.2 ± 9.7 (36.1-77.0)	54.9 ± 7.9 (35.3-69.3)
Female sex	21 (47.7)	18 (46.2)
BMI, mean ± SD	28.7 ± 5.2	30.5 ± 5.0
Smoking status		
Current	2 (4.5)	1 (2.6)
Former	10 (22.7)	7 (17.9)
Never	32 (72.7)	31 (79.5)
Intraoperative variables		
Knee laterality		
Left	21 (47.7)	22 (56.4)
Right	23 (52.3)	17 (43.6)
Meniscus laterality		
Bilateral	14 (31.8)	7 (17.9)
Lateral	4 (9.1)	6 (15.4)
Medial	26 (59.1)	26 (66.7)
Tear type		
Complex	0 (0.0)	2 (5.1)
Degenerative	31 (70.5)	29 (74.4)
Flap	7 (15.9)	5 (12.8)
Flipped	1 (2.3)	0 (0.0)
Horizontal cleavage	0 (0.0)	1 (2.6)
Radial	4 (9.1)	1 (2.6)
Root	1 (2.3)	1 (2.6)
Amount of meniscus removed, mean ± SD, %	32 ± 22	39 ± 20
BMAC volume, mean ± SD, mL	2.87 ± 1.12	0.00 ± 0.00
Concomitant procedures		
Any concomitant procedure	22 (50.0)	22 (56.4)
Synovectomy	9 (20.5)	14 (35.9)
Articular cartilage debridement	11 (25.0)	11 (28.2)
Loose body removal	1 (2.3)	0 (0.0)
Plica excision	3 (6.8)	2 (5.1)
Baker cyst decompression	1 (2.3)	0 (0.0)

[a]Data are shown as n (%) unless otherwise indicated. BMAC, bone marrow aspirate concentrate; BMI, body mass index.

(P = .594). At 1 year postoperatively, mean KL grades were also found to be similar in extension (P = .771) and flexion (P = .940), with no significant difference found between the 2 groups in terms of the mean change in the KL grade in extension (P = .729) or flexion (P = .921). Additionally, the mean change in the joint space height did not statistically differ in extension (P = .715) or flexion (P = .676) between the BMAC and control groups. In terms of within-group comparisons, both groups experienced a significant progression of OA from preoperatively to 1 year postoperatively (BMAC: $P < .001$; control: P = .002).

Factors Predictive of 1-Year IKDC Score and 1-Year KL Grade

Factors predictive of the 1-year IKDC score and 1-year KL grade that were eligible for inclusion in the multivariate model are found in Table 6. On regression analysis of the entire cohort, the only baseline factors predictive of the 1-year IKDC score in both univariate and multivariate models were the preoperative IKDC score, which positively predicted postoperative scores (β coefficient = 0.347; standard error [SE] = 0.256; P = .017), and the 1-year KL grade, which negatively predicted postoperative scores (β coefficient = −0.355; SE = 3.004; P = .026). The overall multivariate model fit was R^2 = 0.334 (P = .002).

When considering the 1-year KL grade, baseline BMI (β coefficient = 0.391; SE = 0.031; P = .006) and baseline KL grade (β coefficient = 0.831; SE = 0.108; $P < .001$) positively predicted the outcome on univariate analysis, while the 1-year IKDC score negatively predicted the outcome (β coefficient = −0.435; SE = 0.007; P = .005). However, on multivariate analysis, only the preoperative KL grade (β coefficient = 0.762; SE = 0.121; $P < .001$) and 1-year IKDC score (β coefficient = −0.195; SE = 0.004; P = .032) maintained significance. The overall multivariate model fit was R^2 = 0.757 ($P < .001$).

Complications and Failures

No perioperative complications were reported in either group. In the BMAC group, there was 1 postoperative complication, with a participant developing septic arthritis

TABLE 2
Patient-Reported Outcome Measure Scores[a]

	Control	BMAC	*P* Value[b]
IKDC			
Preoperative	43.2 ± 15.5	40.5 ± 12.3	.541
3 mo	66.8 ± 18.5	69.2 ± 19.1	.568
6 mo	61.5 ± 24.1	63.9 ± 22.9	.606
1 y	70.4 ± 22.7	68.1 ± 22.9	.687
2 y	76.6 ± 14.2	70.1 ± 20.6	.276
KOOS Activities of Daily Living			
Preoperative	63.1 ± 18.2	62.3 ± 15.5	.752
3 mo	85.5 ± 16.7	85.9 ± 14.3	.848
6 mo	80.5 ± 21.7	83.5 ± 18.5	.707
1 y	84.8 ± 19.1	86.4 ± 18.7	.647
2 y	91.0 ± 11.1	86.1 ± 18.4	.650
KOOS Pain			
Preoperative	54.0 ± 17.7	55.0 ± 14.6	.561
3 mo	77.4 ± 18.4	82.3 ± 15.2	.342
6 mo	76.0 ± 19.1	76.7 ± 21.3	.805
1 y	81.8 ± 19.5	83.0 ± 20.3	.753
2 y	85.7 ± 10.4	81.0 ± 19.6	.775
KOOS Quality of Life			
Preoperative	27.9 ± 17.9	30.7 ± 15.9	.430
3 mo	63.9 ± 23.9	62.9 ± 25.2	.953
6 mo	58.8 ± 29.4	58.8 ± 29.0	.935
1 y	69.4 ± 24.2	70.8 ± 28.0	.595
2 y	72.7 ± 16.4	65.9 ± 25.7	.413
KOOS Sport			
Preoperative	32.1 ± 21.7	31.7 ± 21.4	.869
3 mo	66.2 ± 25.2	63.6 ± 26.4	.885
6 mo	58.9 ± 31.2	60.8 ± 26.8	.970
1 y	66.2 ± 24.7	69.3 ± 28.0	.515
2 y	75.3 ± 16.8	65.2 ± 30.8	.363
KOOS Symptoms			
Preoperative	59.2 ± 19.6	58.0 ± 16.4	.881
3 mo	77.1 ± 15.6	81.3 ± 12.4	.326
6 mo	74.2 ± 20.5	76.3 ± 19.8	.683
1 y	80.4 ± 19.4	82.0 ± 17.6	.917
2 y	82.3 ± 15.6	80.4 ± 20.9	.966
KOOS Joint Replacement			
Preoperative	55.1 ± 14.3	56.4 ± 10.4	.694
3 mo	75.2 ± 16.2	77.8 ± 14.4	.590
6 mo	72.2 ± 19.7	72.6 ± 18.3	.939
1 y	76.4 ± 21.2	77.7 ± 18.6	.974
2 y	80.5 ± 12.0	78.6 ± 19.4	.766
VAS pain			
Preoperative	4.6 ± 2.3	4.9 ± 2.5	.465
3 mo	2.4 ± 2.6	1.6 ± 1.7	.511
6 mo	3.0 ± 2.8	2.6 ± 2.4	.750
1 y	2.1 ± 2.4	1.3 ± 1.7	.447
2 y	1.3 ± 1.1	1.6 ± 2.1	.899
VR-12 mental			
Preoperative	54.6 ± 9.9	58.1 ± 9.1	.107
3 mo	57.6 ± 7.2	61.0 ± 5.8	.080
6 mo	58.6 ± 6.3	60.7 ± 6.1	.149
1 y	56.9 ± 9.5	62.0 ± 3.6	.090
2 y	59.9 ± 8.8	59.9 ± 9.8	.705
VR-12 physical			
Preoperative	38.3 ± 10.9	37.2 ± 9.0	.727
3 mo	47.0 ± 9.8	47.5 ± 9.7	.815
6 mo	46.6 ± 9.7	47.2 ± 8.8	.827
1 y	47.4 ± 10.3	48.9 ± 9.6	.481
2 y	49.5 ± 8.4	47.9 ± 10.0	.840

[a]Data are shown as mean ± SD. BMAC, bone marrow aspirate concentrate; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; VAS, visual analog scale; VR-12, Veterans RAND 12-Item Health Survey.
[b]Wilcoxon rank-sum test.

TABLE 3
Intention-to-Treat Analysis of 1-Year IKDC Score[a]

	Control	BMAC	*P* Value[b]
1 y	70.4 ± 18.4	68.1 ± 20.1	.318

[a]Data are shown as mean ± SD. Mean imputation was performed for missing data, yielding 47 patients in the control group and 48 patients in the BMAC group, corresponding to the total number of patients in each group who received their allocated intervention. BMAC, bone marrow aspirate concentrate; IKDC, International Knee Documentation Committee.
[b]Wilcoxon rank-sum test.

approximately 6 weeks after surgery in the index knee. This necessitated treatment through arthroscopic debridement, irrigation, and intravenous antibiotics. The control group had a higher percentage of participants (n = 3 [7.7%]) undergoing conversion to TKA during the follow-up period compared with the BMAC group (n = 2 [4.5%]). However, this difference did not reach statistical significance (P = .261). The mean time to TKA in the control group was 14.1 months (range, 11.8-18.6 months), while in the BMAC group, it was 13.5 months (range, 7.9-19.1 months).

DISCUSSION

The most important findings of this randomized controlled trial are that the addition of an autologous BMAC injection at the time of APM for symptomatic patients with meniscal tears and concomitant mild knee OA did not show significant differences in the IKDC score or radiographic outcomes at 1 year postoperatively compared with APM alone in such patients, thereby refuting our hypothesis for the primary clinical endpoint and supporting our hypothesis for the radiographic endpoint. Additionally, comparisons of most secondary PROMs yielded no significant differences between the 2 groups up to 2 years postoperatively. The 2 exceptions, MCID achievement for the KOOS Sport at 1 year (100.0% vs 80.0%, respectively; P = .023) and MCID achievement for the KOOS Symptoms at 1 year (92.3% vs 68.0%, respectively; P = .038), were found to be higher in the BMAC group than in the control group. This may be partially explained by higher, although not statistically significant, baseline scores in the control group, which has been previously associated with failure to achieve the MCID.[16] Nonetheless, further investigation into the effects of a concomitant autologous BMAC injection during APM on MCID achievement and PROM scores in this specific patient population is warranted.

In terms of within-group comparisons, all PROM scores at 3 months, 6 months, 1 year, and 2 years postoperatively were significantly improved compared with baseline for the BMAC group, except for the VR-12 mental score in which no time points were statistically different compared with baseline. The same was true for the

TABLE 4
MCID Achievement Rates[a]

	Control	BMAC	*P* Value[b]
IKDC			
3 mo	20/25 (80.0)	24/27 (88.9)	.458
6 mo	19/29 (65.5)	24/35 (68.6)	.796
1 y	19/25 (76.0)	26/33 (78.8)	.801
2 y	18/19 (94.7)	24/28 (85.7)	.635
KOOS Activities of Daily Living			
3 mo	22/25 (88.0)	22/26 (84.6)	>.999
6 mo	18/25 (72.0)	24/31 (77.4)	.642
1 y	21/25 (84.0)	24/26 (92.3)	.419
2 y	16/18 (88.9)	18/24 (75.0)	.431
KOOS Pain			
3 mo	18/25 (72.0)	22/26 (84.6)	.274
6 mo	20/26 (76.9)	26/32 (81.3)	.686
1 y	20/25 (80.0)	24/26 (92.3)	.248
2 y	16/18 (88.9)	22/24 (91.7)	>.999
KOOS Quality of Life			
3 mo	21/25 (84.0)	20/26 (76.9)	.726
6 mo	17/26 (65.4)	23/31 (74.2)	.469
1 y	20/25 (80.0)	22/26 (84.6)	.726
2 y	16/18 (88.9)	20/24 (83.3)	.685
KOOS Sport			
3 mo	20/24 (83.3)	23/26 (88.5)	.697
6 mo	18/26 (69.2)	25/31 (80.6)	.319
1 y	20/25 (80.0)	26/26 (100.0)	**.023**
2 y	16/18 (88.9)	20/24 (83.3)	.685
KOOS Symptoms			
3 mo	18/25 (72.0)	20/26 (76.9)	.687
6 mo	18/26 (69.2)	24/32 (75.0)	.625
1 y	17/25 (68.0)	24/26 (92.3)	**.038**
2 y	13/18 (72.2)	21/24 (87.5)	.256
KOOS Joint Replacement			
3 mo	20/25 (80.0)	21/27 (77.8)	.845
6 mo	19/26 (73.1)	23/33 (69.7)	.776
1 y	18/25 (72.0)	21/27 (77.8)	.631
2 y	14/17 (82.4)	23/27 (85.2)	>.999

[a]Data are shown as n (%). BMAC, bone marrow aspirate concentrate; IKDC, International Knee Documentation Committee; KOOS, Knee injury and Osteoarthritis Outcome Score; MCID, minimal clinically important difference.

[b]Fisher exact test and Pearson chi-square test.Bolded *P* values indicate statistical significance ($P < .05$).

TABLE 5
Radiographic Outcomes[a]

	Control	BMAC	*P* Value
KL			
Extension at baseline	0.75 ± 0.85	0.85 ± 0.91	.738
Flexion at baseline	0.70 ± 0.73	0.89 ± 0.93	.594
Extension at 1 y	1.41 ± 1.14	1.31 ± 1.16	.771
Flexion at 1 y	1.45 ± 1.26	1.42 ± 1.27	.940
Extension delta	0.50 ± 0.83	0.50 ± 0.65	.729
Flexion delta	0.55 ± 0.69	0.58 ± 0.70	.921
Joint space height, mm			
Extension delta	–0.36 ± 1.44	–0.92 ± 1.60	.715
Flexion delta	–0.95 ± 1.43	–0.76 ± 1.02	.676

[a]Data are shown as mean ± SD. BMAC, bone marrow aspirate concentrate; KL, Kellgren-Lawrence.

control group, except for the VR-12 mental score at 6 months, which was significantly improved compared with baseline. These significant PROM score improvements occurred despite participants in both groups experiencing a significant radiographic progression of OA. As such, these findings reinforce the results drawn from other authors that APM is frequently capable of providing symptomatic relief in the short term, although it is unable to affect the overall disease progression of tibiofemoral OA.[13,35,39]

Positive outcomes have been reported in the treatment of degenerative knee conditions with BMAC, either as a standalone treatment or as a surgical adjunct; however, injecting BMAC as an adjuvant to APM for symptomatic patients with meniscal tears and concomitant knee OA has not been studied in randomized controlled trials.[3-5,11,15,23,26] Nonetheless, our findings align with a 2021 retrospective cohort study presented as a conference abstract by Davila Castrodad et al, which reported no significant differences at 1-year follow-up in several PROMs when comparing APM alone and APM combined with a BMAC injection (unpublished data [Davila Castrodad IM, Kurowicki J, Doerr N, et al. Degenerative meniscal tears: a comparison of postoperative outcomes after meniscectomy with and without BMAC. e-Poster presented at: International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine 2021 Global Congress; November 27, 2021]). With regard to other orthobiological interventions, our findings are similar to those of a 2016 randomized controlled trial conducted by Filardo et al,[14] which demonstrated no significant differences in pain and functional outcomes at up to 6-month follow-up when comparing APM alone and APM combined with a hyaluronic acid injection. In contrast, our findings differ from a 2015 randomized controlled trial conducted by Duif et al,[9] which demonstrated favorable results for an adjuvant leukocyte-poor PRP (LP-PRP) injection with APM and/or cartilage debridement as opposed to APM and/or cartilage debridement alone for patients with cartilage or meniscal degeneration. Contrary to our findings, Duif et al reported significantly improved VAS pain scores at 6 months in the LP-PRP group compared with the control group. The observed discrepancy between our study and that of Duif et al could be attributed to the distinct biological composition of LP-PRP. Studies have demonstrated that LP-PRP reduces the expression of pro-inflammatory markers in cartilage and the synovium while increasing anti-inflammatory markers.[37] In contrast, BMAC, while also recognized for creating an anti-inflammatory milieu,[25] has a higher composition of white blood cells compared with LP-PRP.[8] Although evidence varies, several studies have reported that high white blood cell concentrations in biological preparations lead to the increased expression of inflammatory cytokines, resulting in inferior outcomes compared with leukocyte-poor preparations.[34,41]

Previous landmark studies, such as that by Moseley et al[36] and the METEOR trial, have investigated the efficacy of arthroscopic surgery compared with nonoperative therapy for patients with degenerative knees.[20,21] In both instances, the authors failed to identify significant differences in patients who underwent arthroscopic surgery as

TABLE 6
Associations of Patient Variables With Postoperative Outcomes[a]

	Univariate			Multivariate		
	β Coefficient	SE	*P* Value	β Coefficient	SE	*P* Value
1-year IKDC score						
Preoperative IKDC	0.437	0.197	**<.001**	0.347	0.256	**.017**
Postoperative KL	–0.435	2.820	**.005**	–0.355	3.004	**.026**
BMI	–0.297	0.520	**.021**	–0.129	0.631	.399
1-year KL grade						
Preoperative KL	0.831	0.108	**<.001**	0.762	0.121	**<.001**
Postoperative IKDC	–0.435	0.007	**.005**	–0.195	0.004	**.032**
BMI	0.391	0.031	**.006**	0.066	0.019	.474

[a]The criterion for inclusion in the multivariate model was a *P* value <.15 on univariate analysis. BMI, body mass index; IKDC, International Knee Documentation Committee; KL, Kellgren-Lawrence; SE, standard error. Bolded *P* values indicate statistical significance ($P < .05$).

opposed to nonoperative treatment, further bringing into question the role of APM in symptomatic degenerative knees. However, these studies have notable limitations. The trial by Moseley et al provided no clear indication regarding how severe the arthritic state was in each case, its statistical analysis and drawn conclusions have been strongly criticized by independent statisticians, and all patients included in the study were from the Veterans Affairs system, limiting the generalizability of the findings to the broader population.[19] As for the METEOR trial, the investigators limited their patient population to age ≥45 years, and the study adopted broad definitions of OA and the symptoms of a meniscal tear.[18] In addition, patients who failed nonoperative therapy in that study had still largely benefited from a surgical intervention.[20,21]

Considering the findings of these trials, our study sought to determine whether augmenting this procedure with an autologous BMAC injection would make a difference for this specific patient population, which may have a less predictable outcome compared with arthroscopically treated patients with isolated symptomatic meniscal tears. Despite significant improvements on a vast majority of PROMs for each group at 3 months, 6 months, 1 year, and 2 years postoperatively, our study was unable to find differences that could be attributed to BMAC augmentation, with the exceptions of higher MCID achievement for the KOOS Sport and the KOOS Symptoms at 1 year. Notably, however, high percentages of patients in both groups achieved the MCID for the IKDC (85.7%-94.7%) and KOOS (Activities of Daily Living: 75.0%-88.9%; Pain: 88.9%-91.7%; Quality of Life: 83.3%-88.9%; Sport: 83.3%-88.9%; Symptoms: 72.2%-87.5%, and Joint Replacement: 82.4%-85.2%) up to 2 years after APM, consistent with the positive outcomes demonstrated by both the METEOR trial and a 5-year follow-up of the trial's patients, which reflect a similar patient population that was treated with APM without a concomitant orthobiological injection.[20,21] As such, the clinical implications of these findings require further investigation in addition to a thorough dialog between patients and providers when discussing treatment options for symptomatic meniscal tears with concomitant mild knee OA.

Even though this study provides valuable insights into the use of autologous BMAC as an adjuvant to APM in patients with concomitant mild knee OA, several limitations need consideration. First, specific inclusion and exclusion criteria of the study restrict the generalizability of the findings to a broader population, particularly those outside the defined age range or with different comorbidities. In addition, this study was conducted at a single institution, which may limit the applicability of the results to other health care settings with potentially different patient demographics and clinical practices. Additionally, the number of patients eligible for study inclusion who declined to participate in the study, along with their reasons for doing so, was not recorded. Furthermore, the trial protocol was not published before initiation of the study. During the development of the study protocol, it was decided not to administer a placebo injection with saline into the knee joint and to only perform a sham incision at the ASIS for the control group. This decision was based on the eventual presence of residual saline in the knee joint after APM and the potential risks of administering an additional saline injection, such as joint infections. Finally, the study follow-up period may not capture and reflect longer term outcomes, which is a critical concern in the context of patients after meniscectomy, especially in those with preexisting OA.

CONCLUSION

No significant differences were found in either IKDC scores or radiographic outcomes at the 1-year postoperative mark when comparing the BMAC and control groups. Furthermore, most secondary PROMs showed no significant differences between the 2 groups up to 2 years postoperatively, with the exception of the BMAC group demonstrating higher MCID achievement for the KOOS Sport and KOOS Symptoms at 1 year postoperatively. Notably, patients with symptoms consistent with a meniscal tear who have concomitant mild OA may still benefit from arthroscopic debridement with or without BMAC.

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