Concentrated Bone Marrow Aspirate May Decrease Postoperative Cyst Occurrence Rate in Autologous Osteochondral Transplantation for Osteochondral Lesions of the Talus

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Purpose: To clarify if the use of concentrated bone marrow aspirate (CBMA) would affect both postoperative functional outcomes and magnetic resonance imaging (MRI) outcomes compared with those of autologous osteochondral transplantation (AOT) alone; in addition, to assess the efficacy of CBMA reducing the presence of postoperative cyst formation following AOT in the treatment of osteochondral lesions of the talus. **Methods:** Fifty-four (92%) of 59 eligible patients who underwent AOT between 2004 and 2008 were retrospectively assessed at a minimum of 5-year follow-up. Twenty-eight patients were treated with AOT and CBMA (AOT/CBMA group) and 26 patients were treated with AOT alone (AOT-alone group). Clinical outcomes were evaluated using the Foot and Ankle Outcome Scores (FAOS) and Short-Form 12 (SF-12) preoperatively and at final follow-up. Postoperative MRI was evaluated with the modified Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) scoring system. Cyst formation was also evaluated on postoperative MRI. **Results:** The mean FAOS and SF-12 significantly improved in both the AOT/CBMA and AOT-alone groups, but there were no statistical differences between groups in FAOS (80.5 vs 75.5, $P = .225$) and SF-12 (71.1 vs 69.6, $P = .756$) at final follow-up. Additionally, there was no difference in the mean MOCART score (80.4 vs 84.3, $P = .484$); however, AOT/CBMA did result in a statistically lower rate of cyst formation (46.4% vs 76.9%, $P = .022$). No significant differences were found in the mean postoperative FAOS and SF-12 between patients with and without cysts postoperatively. **Conclusions:** CBMA reduced postoperative cyst occurrence rate in patients treated with AOT; however, CBMA did not result in significant differences in medium term functional outcomes and MOCART score in patients who underwent AOT. **Level of Evidence:** Level III, retrospective comparative trial.

Osteochondral lesions of the talus (OLTs) are a common ankle cartilage injury. OLTs are frequently associated with sports-related injuries, occurring in up to 50% of acute ankle sprains and fractures.[1] A recent systematic review reported that conservative treatment fails in approximately 50% of patients with OLT.[2] Surgical treatment for OLT includes autologous osteochondral transplantation (AOT). This procedure is typically indicated for patients who have failed conservative treatment, whose lesion size is >100 mm^2 to 150 mm^2, who have cystic lesions, or who have undergone failed bone marrow stimulation (BMS).[3,4]

Previous studies have shown that AOT provides excellent clinical outcomes for OLT; however, high rates of postoperative subchondral cyst formation of up to 75% at short-term follow-up have been reported.[5,6] The presence of subchondral bone cysts has been previously shown to be correlated with graft failure[7-9]; therefore, the high rate of cyst formation at the bone interface following AOT has prompted surgeons to look for a method of improving graft integration and reducing interface cyst production.[5,10]

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Concentrated bone marrow aspirate (CBMA) has been investigated as a source of both mesenchymal stem cells and growth factors for cartilage regeneration.[11] Several in vivo and in vitro studies have shown a potential for CBMA to improve both bone regeneration and cartilage repair tissue following BMS.[11,12] CBMA may also have the potential to reduce interface cyst formation by improved integration between the graft and native articular cartilage and bone.[13] The use of CBMA with BMS procedure in the treatment of OLT has been shown to improve border repair tissue integration on magnetic resonance imaging (MRI) compared with BMS alone in a case-control study.[14] Little is known however about the effect of the use of CBMA on the clinical and radiological outcomes of AOT in the treatment of OLT.

The purpose of the current study is to clarify if the use of CBMA would affect both postoperative functional outcomes and MRI outcomes compared with those of AOT alone, and, in addition, to assess the efficacy of CBMA reducing the presence of postoperative cyst formation following AOT in the treatment of OLT. The hypothesis of the current study was that the use of CBMA would result in better functional and MRI outcomes than those of AOT alone and reduce the presence of postoperative cyst formation.

Materials and Methods

Patients

This retrospective comparative study was approved by the hospital's institutional review board. All patients treated with AOT for the treatment of OLT between 2004 and 2008 by the senior author (J.G.K.) were identified via the institutional review board–approved Foot and Ankle Registry at the author's institution. Surgical intervention was indicated for patients who failed a minimum of 3 months nonsurgical management, including physiotherapy, immobilization, and nonsteroidal anti-inflammatory drugs. AOT was indicated for the patients whose lesion size was >10 mm or 100 mm^2, as well as following failed previous BMS or cystic lesions.[3,4] Patients between 2004 and 2005 were treated with AOT alone (AOT-alone group); patients between 2005 and 2008 were treated with AOT and CBMA (AOT/CBMA group). The inclusion criteria of the current study were age between 18 and 60 years at the time of surgery and a minimum 5 years of postoperative follow-up. Excluded were patients who did not have follow-up MRI.

Surgical Technique

After anesthesia, bone marrow aspirate was harvested from the ipsilateral iliac crest, as previously described.[15] Using a sharp trocar with a hollow aspiration sleeve, 60 mL of bone marrow was extracted. The aspirate was prepared and centrifuged using a standard commercially available CBMA centrifuge system (Arteriocyte Magellan Autologous Platelet Separator System; Arteriocyte Medical Systems, Cleveland, OH). Typically, it yielded up to 3 mL of CBMA.

The AOT procedures were performed using the Osteochondral Autograft Transfer System (OATS) system (Arthrex, Naples, FL). For medial talar lesion, a medial malleolar Chevron-type osteotomy was used, whereas an anterolateral tibial trapezoidal osteotomy was applied for lateral lesions if required for exposure of the osteochondral lesion.[16] After the damaged cartilage and bone were removed from the talus, the recipient site was inspected carefully to ensure that any cystic lesions were removed. Then, a 0.045-inch K-wire was used to create multiple small holes in the walls of the recipient site. If the lesion requires 2 grafts, a figure 8 "nested" technique, which minimizes the empty space that would be filled with fibrocartilage, was applied.[17] The donor osteochondral graft plug was harvested from the non-weight bearing portion of the lateral femoral condyle from the ipsilateral knee.[18] Once harvested, the authors soaked the graft in CBMA for at least 10 minutes, they were left to soak after the OAT donor plug was harvested while the talus was being prepared. Before implantation, 1.0 mL of CBMA was injected into the recipient site (Fig 1). The osteochondral graft plug was then transferred to the recipient site so that the topography matched the native cartilage.[19] Great care was taken to achieve congruency to avoid potential mechanical stress loading.[20] The osteotomy was finally reduced and fixed with 3 titanium screws. After wound closure, the remaining CBMA was injected into the ankle joint.

Postoperative Rehabilitation

The patients were kept non-weight bearing and in a postoperative short leg splint for 2 weeks postsurgery. At that time, the splint was switched to a Cam walker boot with continued non-weight bearing, and the patients started dorsi/plantarflexion exercises. At 4 weeks after surgery, patients began to bear 10% of their body weight and continued to increase until full weight bearing was achieved at approximately 6 weeks postoperatively. Formal physical therapy, including proprioception, strength, and range of motion, was then commenced. Sports-specific physical therapy began at 10 weeks after surgery. Patients were allowed to return to unrestricted activities typically at 12 weeks postoperatively.

Data Collection

Data on patient characteristics and clinical information were collected, including age, gender, duration of symptoms, lesion size, lesion location, the presence of cyst of the lesion, previous ankle procedures including

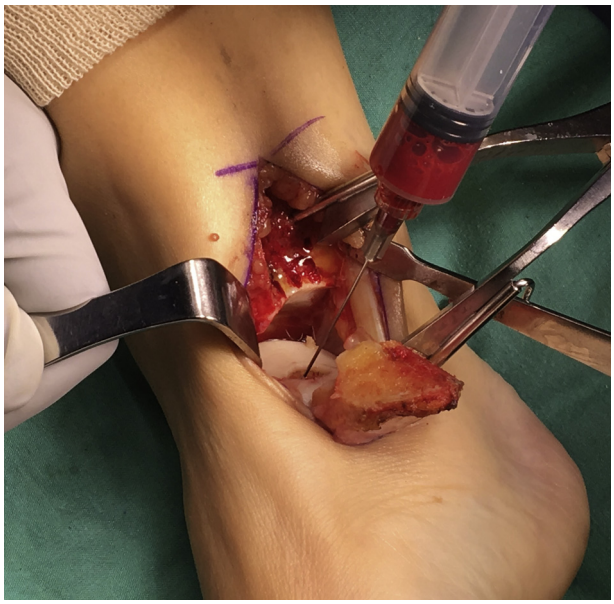

Fig 1. Medial malleolar osteotomy using a retractor was used to allow adequate visualization and access to the medial talar dome in the right ankle with the patient in the supine position. The damaged cartilage and bone were removed using the Osteochondral Autograft Transfer System. Concentrated bone marrow aspirate (CBMA) was then injected into the recipient site. Only 1.0 mL CBMA was injected into the recipient site, and the remaining CBMA was injected in the ankle joint after wound closure.

BMS, and concomitant procedures. As a part of our routine standard of care, we take MRI scans at 1, 2, and 5 years' follow-up. Lesion size and location were determined using preoperative MRI. Lesion size was calculated using the following ellipse formula: area = coronal length × sagittal length × 0.79.[4] Lesion location was determined using a 9-zone anatomic location scheme on MRI.[20] Any concomitant soft tissue pathology was identified on MRI and intraoperatively.

Clinical Outcome Analysis

Clinical outcomes were evaluated using the Foot and Ankle Outcome Scores (FAOS)[21] and Short-Form 12 (SF-12)[22] preoperatively and at final follow-up by an board-certified orthopaedic surgeon (Y.S.) who was blinded to the surgical procedures and the radiological analysis.

Radiological Analysis

Postoperative MRI was performed on a 3-T clinical imaging system (GE Healthcare, Milwaukee, WI) using fast-spin-echo proton density sequences to analyze articular cartilage. The image acquisition sequences were as follows: 2.5-mm-thick slice and 512 × 512 matrix in proton density, and 3-mm-thick slice and 512 × 512 matrix in fat-saturated proton density or short tau inversion recovery sequences. MRI scans were reviewed and graded by a board-certified musculoskeletal radiologist (T.D.) who was blinded to the surgical procedure and clinical outcome scoring. Assessment of the cartilage around the graft site was performed with the modified Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) scoring system.[23,24] Cyst formation was evaluated on postoperative MRI using fat-saturated proton density sequences in the axial, coronal, and sagittal planes. Cyst diameter was measured in 3 orthogonal axes, and the maximum diameter of those was applied. The cyst location was categorized relative to the osteochondral graft in the following categories: peripheral, inferior to the graft, or in the graft.[5]

Statistical Analysis

Descriptive statistics presented consist of mean and standard deviation for continuous variables and frequency and percentage for categorical variables. Obtained data of both groups were compared using the Student *t* test for continuous variables and the χ-square test for categorical variables. The paired *t* test was performed to compare preoperative and postoperative outcome scores. The Student *t* test was used to compare postoperative FAOS and SF-12 between patients with and without postoperative cyst formation. $P < .05$ was considered statistically significant. All statistical analysis was performed with SAS Software, version 9.3 (SAS Institute, Cary, NC).

Results

Clinical Characteristics

Review of the foot and ankle registry identified total 59 patients who underwent AOT procedure for OLT. Three patients were lost to follow-up because 2 had moved abroad and 1 did not respond to our attempts to contact him. Two patients who did not have postoperative MRI were excluded. A total of 54 patients were included in this study. Of those, 28 were treated with AOT and CBMA, and 26 were treated with AOT alone. Patient demographic data are summarized in Table 1. There were no significant differences of all patient demographic variables except for clinical follow-up time between the AOT-alone group and AOT/CBMA group. Concomitant procedures included lateral ankle ligament repair, debridement for anterior ankle impingement, and peroneal tendon repair. There were 3 complications postoperatively: 1 wound infection and 2 patients with knee stiffness. The wound infection was treated with arthroscopic lavage and antibiotic therapy. The 2 patients who had knee stiffness received a corticosteroid injection into the knee joint followed by physical therapy and reported relief of symptoms.

Table 1. Patient Demographics and Clinical Data

Clinical Characteristics	AOT Alone (N = 26)	AOT/CBMA (N = 28)	*P* Value
Age, yr, mean	33.6 ± 12.3	36.0 ± 15.3	.536
Male, N (%)	17 (65.4)	21 (75.0)	.439
Duration of symptoms, mo, mean	28.8 ± 17.9	23.0 ± 13.3	.278
Follow-up time, mo, mean	92.8 ± 13.8	84.2 ± 10.5	.036
Lesion size, mm^2, mean	102.5 ± 42.0	108.5 ± 43.3	.245
Cystic, N (%)	9 (34.6)	15 (53.6)	.161
Prior microfracture, N (%)	5 (19.2)	7 (25.0)	.61
Osteotomy site, N (%)	Medial: 16 (61.5) Lateral: 10 (38.5)	Medial: 22 (78.6) Lateral: 6 (21.4)	.171
Concomitant procedures, N (%)	5 (19.2) 3 ATFL repairs 2 debridements for AAIS	9 (32.1) 5 ATFL repairs 3 debridements for AAIS 1 peroneal tendon repair	.279
Number of grafts, N (%)	1: 24 (92.3) 2: 2 (7.7)	1: 25 (89.3) 2: 3 (10.7)	.702
Complications, N (%)	2 (7.7) 1 infection 1 knee stiffness	1 (3.6) 1 knee stiffness	.509
Subsequent procedures, N	6 (23.1) 5 arthroscopic debridements 1 distraction ankle arthroplasty	6 (21.4) 5 arthroscopic debridements 1 microfracture	.884

NOTE. Quantitative variables expressed as mean ± standard deviation.

AAIS, anterior ankle impingement syndrome; AOT, autologous osteochondral transplant; ATFL, anterior talofibular ligament; CBMA, concentrated bone marrow aspirate.

Clinical Outcomes

The mean follow-up times were 92.8 months in the AOT-along group and 84.2 months in AOT/CBMA group ($P = .036$). The mean FAOS and SF-12 significantly improved in both groups from before to after surgery ($P < .001$) (Table 2). No statistical differences were found between AOT-alone and AOT/CBMA groups at final follow-up (FAOS: AOT-alone vs AOT/CBMA, 75.5 vs 80.5, $P = .225$; SF-12: 69.6 vs 71.1, $P = .756$).

In both groups, there were 6 subsequent procedures. In the AOT- alone group, there were 5 procedures for arthroscopic debridement for anterior ankle impingement and 1 distraction ankle arthroplasty for progressive ankle arthritis at 34 months. In the AOT/CBMA group, there were 4 procedures for arthroscopic debridement for anterior ankle impingement in 4 patients, with 1 patient undergoing the procedure twice, and 1 microfracture for a new talar lesion, distinct from the original lesion, at 18 months.

MRI Outcome

The mean MRI follow-up time was 66.3 ± 28.4 months in the AOT-alone group and 60.8 ± 23.3 months in the AOT/CBMA group ($P = .594$). There was no statistical difference between the AOT-alone and AOT/CBMA groups in the mean MOCART score (84.3 vs 80.4, $P = .484$) (Table 2). At final follow-up of MRI, the rate of cyst occurrence in the AOT-alone group was significantly higher than that of the AOT/CBMA group (76.9% vs 46.4%, $P = .022$) (Table 3). No statistical differences were found between groups in cyst location and cyst diameter. Post hoc power analysis of proportions showed that power (1-β) was 0.693.

Based on postoperative cyst formation, the mean postoperative FAOS and SF-12 were 81.6 ± 13.1 and 70.2 ± 16.1 in patients with cyst formation and 75.8 ± 15.6 and 70.5 ± 17.4 in patients without cyst formation. There were no significant differences in postoperative FAOS and SF-12 between patients with and without cyst formation ($P = .175$ and .961, respectively).

Discussion

The primary finding from our study was that there were no significant differences in functional outcomes or in MOCART score in patients who underwent AOT alone vs AOT and CBMA for the treatment of OLT. The important finding in the current study, however, is that there was a significantly lower rate of postoperative cyst formation in patients treated with AOT with CBMA compared with AOT alone. This may suggest an improved graft−host integration should cyst formation occur from poor host−graft interface incorporation. Smyth et al.[13] found that platelet-rich plasma (PRP) resulted in improved AOT integration at the graft interface and resulted in reduced graft degeneration. Similarly, Boakye et al.[25] found PRP resulted in

Table 2. Clinical Outcome Scores and Modified MOCART Scores

	AOT Alone (N = 26)	AOT/CBMA (N = 28)	*P* Value
FAOS			
Preoperative, mean	52.3 ± 16.7	50.4 ± 15.5	.691
Postoperative, mean	75.5 ± 16.6	80.5 ± 12.8	.225
SF-12			
Preoperative, mean	40.7 ± 18.0	40.1 ± 15.0	.929
Postoperative, mean	69.6 ± 16.8	71.1 ± 17.1	.756
MOCART			
Postoperative, mean	84.3 ± 12.1	80.4 ± 15.9	.484
MRI follow-up time (mo), mean	66.3 ± 28.4	60.8 ± 23.3	.594

NOTE. Quantitative variables expressed as mean ± standard deviation.

AOT, autologous osteochondral transplant; CBMA, concentrated bone marrow aspirate; FAOS, Foot and Ankle Outcome Scores; MOCART, magnetic resonance observation of cartilage repair tissue; SF-12, Short-Form 12.

increased levels of transforming growth factor β1 compared with a saline control, which correlated to improved graft–host integration. It has been shown that PRP and CBMA have similar concentration of growth factors[26]; therefore, the use of CBMA in AOT should similarly improve integration of the graft and reduce cyst formation.

CBMA is bone marrow aspirate that can be harvested from several sites, including the iliac crest, sternum, and greater trochanter, and is prepared by centrifugation in a similar manner to PRP.[27] CBMA contains mesenchymal stem cells, growth factors, and cytokines that have the potential to improve both cartilage repair and bone formation.[11,28,29] The mesenchymal stem cells in CBMA, although a small percentage of total cells, have the ability to differentiate into osteoblasts and chondrocytes, which theoretically can improve the integration of the osteochondral plug. Additionally, CBMA has been shown previously to contain transforming growth factor β1 and bone morphogenic protein, which may increase graft/host interface integration.[26,28] Recently, CBMA has been shown to contain high concentrations of interleukin 1 receptor antagonist protein, which suggests that CBMA may be a potent anti-inflammatory agent.[26] This anti-inflammatory component may be advantageous in cartilage repair as it reduces the catabolic load on the joint as a whole.[30]

Several in vivo studies have evaluated the use of CBMA on BMS and shown improved cartilage repair tissue.[14,31] In a case control study, Hannon et al.[14] compared outcomes of patients who underwent BMS for OLT with and without CBMA and reported that BMS with CBMA resulted in comparably good mid-term clinical outcomes, but improved MOCART scores compared with BMS alone. Fortier et al.[11] reported that CBMA improved both histologic and radiological analysis in the repair of cartilage defects in an equine microfracture model compared with a control without CBMA. Their study demonstrated increased fill of defect and improved integration of repair tissue with surrounding cartilage.[11] Similarly, Saw et al.[32] found in a goat model that CBMA and hyaluronic acid improved cartilage repair compared with hyaluronic acid alone. Although current evidence suggests that CBMA as an adjunct to the treatment for OLT may improve cartilage repair and MRI outcomes, no such evidence was found in the current study using CBMA to augment AOT grafts.

The current study has shown that the functional outcome measures at final follow-up were similar; all patients in both groups had a significant improvement from baseline to final follow-up and both groups had excellent outcomes at final follow-up. There was a high survivorship rate in both groups, with only 1 patient being regarded as a clinical failure, requiring a distraction arthroplasty for progressive arthritis. Savage-Elliott et al.[5] previously found that postoperative cysts did not have any significant effect on short-term functional outcome measures following AOT; therefore, it would be expected that there would be no significant difference between the functional outcomes between the 2 groups at short-term follow-up. In the current study, the postoperative FAOS in patients without cyst formation was higher than those with cyst formation. The effect of cyst formation following AOT has not been fully elucidated on long-term outcome; however, several authors have shown poorer outcomes in patients with cysts in short- and medium-term outcomes.[7-9] Long-term consequences of subchondral cysts are concerning therefore.

The MOCART scores at final follow-up were similar between the patients treated with and without CBMA, whereas Hannon et al.[14] found that CBMA improved MOCART scores in patients undergoing BMS for OLT. This may be in part because of 2 different processes. In BMS, there is regeneration of new fibrous cartilage, but AOT replaces this cartilage and thus provides inherently

Table 3. Data of Cystic Change After AOT

	AOT Alone (N = 26)	AOT/CBMA (N = 28)	*P* Value
Patients with cysts, N (%)	20 (76.9%)	13 (46.4%)	.022*
Number of cysts, mean	1.3 ± 0.6	1.2 ± 0.2	.697
Cyst diameter, mean, mm	3.8 ± 1.9	4.9 ± 3.2	.225
Cyst location			
Graft	7 (26.9%)	4 (25.0%)	.891
Inferior	5 (19.2%)	5 (31.3%)	.888
Peripheral	14 (53.8%)	7 (43.8%)	.525

NOTE. Quantitative variables expressed as mean ± standard deviation.

*Statistically significant difference.

good MOCART scores ab initio. In the MOCART score system, there are only 5 points of 100 for the subchondral bone regeneration. The bone morphogenic protein contained in CBMA is theorized to increase the subchondral bone integration; thus, the MOCART score may be insufficient to detect a true difference between the groups when one exists.

Further study is required because little is known about the effect of the use of CBMA on the clinical and radiological outcomes of AOT in the treatment of OLT. The previous investigations have shown excellent outcomes with AOT and CBMA; however, the current study is the first to study the effect of CBMA with AOT compared with AOT alone.[18] Prospective randomized studies are needed to verify our findings because this is a retrospective review. Additionally, longer term follow-up studies are needed to assess survivorship. Although we did not have any revisions in our patients except for 1 distraction ankle arthroplasty, our outcomes were similar to Zengerink et al.,[2] who found that the overall success rate of AOT for OLT was between 74% and 100% in a systematic review at short-term follow-up. In a recent systematic review of patients treated with AOT in the knee however, a 72% survivorship rate at 10 years was found, suggesting that AOT grafts may decline over time.[33] The effect of postoperative cysts may play a role in the long-term degradation of this AOT procedure, which also warrants further study.

Limitations

Our study has some limitations and inherent bias. The biggest limitation is the retrospective nature of the study because it weakens the strength of our conclusions, although the majority of studies on cartilage repair in the ankle are low-level evidence.[34] There was a small sample size, which may introduce a potential for type II error; however, post hoc power analysis of proportions showed that power (1-β) was 0.693. As a result, we believe that it is reasonable to say CBMA may decrease postoperative cyst formation. Additionally, this study is of short- to mid-term follow-up, and it remains unclear whether these cysts may become symptomatic in the long term.

The study also lacked a component analysis of CBMA; therefore, there is a variability of characterization of the CBMA content. Although there was a small difference in the timeline of the 2 groups because of CBMA becoming part of our routine technique in 2005, we do not believe this affected the clinical outcomes because all of the procedures were performed by the same surgeon and there were no changes in intraoperative protocols or new instruments. There was no histologic analysis of the cartilage repair tissue because this is not feasible in our patient population; however, this remains an area of great interest as basic science studies have shown improved histologic scores with CBMA in BMS but no study has evaluated this in AOT.

Conclusions

CBMA reduced postoperative cyst occurrence rate in patients treated with AOT. CBMA did not result in significant differences in medium-term functional outcomes and MOCART score in patients who underwent AOT, however.

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