Use of Cartilage Extracellular Matrix and Bone Marrow Aspirate Concentrate in Treatment of Osteochondral Lesions of the Talus

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Abstract: Osteochondral lesions of the talus are generally the result of trauma and often result in persistent pain and disability. Various treatment options have evolved to treat these challenging problems, ranging from conservative management to marrow stimulation and cartilage or chondrocyte transplantation. Microfracture is the first line of treatment for many of these lesions. However, there is concern that microfracture results in fibrocartilage, which has inferior wear characteristics when compared with native hyaline cartilage. We describe the use of cartilage extracellular matrix and bone marrow aspirate to augment this procedure in hopes of producing a more hyaline-like cartilage with improved wear characteristics.

Key Words: talus, osteochondral lesion, microfracture, cartilage scaffold, bone marrow aspirate

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HISTORICAL PERSPECTIVE

The term osteochondritis dissecans was first used by König in the 1880s to describe loose bodies within the knee joint.1 Kappis later applied this same term to similar lesions of the ankle.2 These lesions have been called numerous things as time has passed and are now referred to as osteochondral defects (OCDs) or, in the ankle, osteochondral lesions of the talus.3 History of trauma is implicated in 70% of medial and 98% of lateral lesions of the talus.3 A common mechanism of trauma is ankle sprains, with approximately 23,000 ankle injuries per day and 2 million ankle sprains per year in the United States.4,5 Cartilage damage can occur in up to 50% of ankle sprains and 73% to 80% of acute ankle fractures.6,7 Therefore, this diagnosis must be strongly considered in patients with persistent ankle pain and disability following such injuries.

An osteochondral lesion of the talus left untreated is a significant risk factor for degenerative changes and subsequent osteoarthritis (OA).8,9 Canale and Belding9 found degenerative changes in up to 50% of cases. Ankle arthritis is primarily post-traumatic with some 70% to 78% being the result of trauma, such as fractures or ligamentous injuries.10,11 Numerous treatment options have been developed for osteochondral lesions of the ankle.12–14 Nonoperative management consists of immobilization with casts, boots, or braces, activity modification, NSAID therapy, corticosteroid injections, as well as hyalurone and platelet-rich plasma (PRP) injections.15 Conservative management has been associated with poor success rates. In the landmark study by Berndt and Harty,16 there was a 75% rate of poor outcomes with conservative treatment. In a systematic review of 52 studies completed in 2009, meta-analysis of nonoperative management revealed a success rate of 45% to 53%.17 Because of poor outcomes with nonoperative management, numerous operative techniques have been developed including marrow stimulation such as drilling and microfracture, osteochondral autograft/allograft transfer (OATs), and autologous chondrocyte implantation (ACI).18,19 However, controversy regarding the best surgical treatment remains. Procedures requiring an open approach and malleolar osteotomy, as OATs and ACI often do, can pose an increased risk of wound complications and malunion or nonunion of the osteotomy site.20–22 Other risks include donor site pain and morbidity following autologous tissue harvest.23,24 For osteochondral allograft transplantation, there is risk of infection transmission as well as host immune response; for ACI, there is a need for 2 separate procedures and the possibility of cell dedifferentiation.5,22

Microfracture surgery has developed into the first-line treatment for most osteochondral lesions under 15 mm in diameter25,26 or 150 mm² in surface area.27,28 There have been numerous studies completed, with good to excellent outcomes reported in 65% to 90% of cases.13 Advantages of this procedure are that it is cost-effective; there are low morbidity and complication rates; it is minimally invasive; and the procedure is not technically complicated or complex, although it is not without its own disadvantages.28 One particular downfall of the microfracture technique is that the repair tissue is rich in fibrocartilage composed primarily of type I collagen, whereas native articular cartilage is hyaline cartilage composed primarily of type II collagen.29,30 This new repair tissue is inferior to hyaline cartilage in terms of stiffness, resilience, and wear characteristics.31 The addition of PRP and bone marrow aspirate concentrate (BMAC), which serves as a source of mesenchymal stem cells (MSCs), has been shown to possibly improve the healing or repair potential for OCDs.32,33 This is because of the numerous growth factors, including platelet-derived growth factor, transforming growth factor-β and vascular endothelial growth factor, which may have chondrogenic effects on the MSCs.33,34 Downfalls of these mediums are that PRP is merely injected into the joint space and is not concentrated to where the osteochondral defect is and with the BMAC, it relies on formation of a fibrin clot to form and hold the MSCs in the defect. This clot may potentially become dislodged and ineffective in treating the defect.

More recently, there has been the development of various extracellular matrix (ECM) scaffolds, which are used in conjunction with microfracture surgery. One such product is BioCartilage (Arthrex, Naples, FL), which contains cartilage ECM derived from native articular cartilage and is rich in type

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II collagen and proteoglycans. These cartilage products are mixed with autologous blood or BMAC, which serves as a source of MSCs, and are injected into the prepared osteochondral defect. This provides a scaffold for the mesenchymal cells to adhere to versus relying on the development and adherence of the marrow clot to the defect. Cartilage ECM with BMAC can also be used in cystic lesions of the ankle in which the cartilage dome has been violated. Previous research has demonstrated that human MSCs cultured in decellularized osteoblast-derived ECM were driven toward osteogenic lineage with increased type I collagen production. However, human MSCs cultured in decellularized chondrocyte-derived ECM were driven toward a chondrogenic phenotype with increased type II collagen production. This may lead to a more hyaline-like cartilage, similar to that of native articular cartilage, when compared with type I collagen.

**INDICATIONS AND CONTRAINDICATIONS**

As previously stated, microfracture technique has become the first-line treatment for osteochondral lesions <15 mm in diameter or 150 mm² in surface area. When lesions are larger than this or there is a cystic component to the lesion, treatment methods become more controversial. When lesions are >1.5 cm, several authors have advocated for various transplantation techniques such as ACI or osteochondral allograft/autograft transfer (OATS). These various transplantation techniques have yielded good to excellent outcomes for the treatment of larger osteochondral lesions.

These same transplantation techniques, particularly the OATs procedure, have also been indicated in instances of cystic lesions. We provide an alternative in that of bone grafting cancellous bone chips soaked in BMAC, which is subsequently covered with cartilage ECM and BMAC. This allows for adequate debridement and filling of the cystic defect with bone graft, while still providing a cartilage scaffold on which repair cartilage can develop.

The addition of the cartilage ECM does not change the general indications and contraindications from the standard microfracture technique. Indications include: failure of nonoperative treatment, displaced fragments, small cystic or noncystic lesions, size <1.5 cm², age below 50 years, body mass index (BMI) < 30, and presence of ankle instability. Contraindications include: size >1.5 cm², 2 prior conventional surgical treatments, large cystic lesion, inadequate nonoperative treatment if indicated, and acute lesion with attached subchondral bone >7.5 mm in diameter. Relative contraindications include: 1 prior conventional surgical treatment, age above 50 years, BMI >30, and kissing lesion on the tibia.

**PREOPERATIVE PLANNING**

All patients undergo thorough history taking and physical examination. Adequate examination of the ankle including determination of malalignment and instability must be completed. Abnormalities in these areas will require correction before or at the time of treatment of the osteochondral lesion(s) to reduce exposure of the ankle joint to abnormal stresses. The anterior drawer and talar tilt tests should be performed to evaluate the ATFL and CFL, respectively. Physical examination findings consistent with an osteochondral lesion are dependent on location of the lesion. Patients with lateral lesions are generally tender to palpation over the anterolateral joint line, while the foot is in plantarflexion. Patients with medial lesions are often tender to palpation over the postero medial joint line with the foot in dorsiflexion. There may also be an effusion present and patients may complain of catching, popping, or clicking with ankle range of motion.

Patients then undergo weight-bearing x-rays, including anteroposterior, lateral, and mortise views. This may identify any bony pathology or defects but magnetic resonance imaging (MRI) and computed tomography scans are much more sensitive in detecting osteochondral lesions, especially if the lesion is purely cartilaginous. Several authors have demonstrated that there is close correlation between MRI findings and visual findings seen during arthroscopy. For this reason, recent or current MRI studies are generally obtained as well as computed tomography scans to further evaluate any osteochondral lesions and delineate precise location and size to aid in planning of arthroscopic portals. These studies also evaluate whether there may be a cystic component to the lesion, which can change operative procedures and techniques.

**TECHNIQUE**

The procedure is typically started by placing the patient in a supine position with subsequent prepping and draping of the operative foot as well as the ipsilateral iliac crest. BMAC collection is performed by a bone marrow aspiration from the ipsilateral iliac crest. This is completed by making a small skin nick over the ipsilateral anterior iliac crest. Blunt dissection is performed to cortical bone and then a trocar and three 20 mL syringes are used to obtain the bone marrow aspirate. This is then centrifuged to obtain the BMAC, which is used as a source of MSCs. While the BMAC is being prepared, attention is directed to the operative ankle.

All patients undergo standard diagnostic ankle arthroscopy beginning with introduction of the 2.9 mm, 30-degree arthroscope though an anterolateral portal followed by placement of a probe through an anterolateral portal. Special care must be taken with placement of the anterolateral portal to avoid injury to the medial and intermediate dorsal cutaneous nerves. Systematic evaluation of the entire ankle joint through direct arthroscopic visualization is undertaken and notation is made of any significant loose bodies, synovitis, scar tissue, joint laxity, osteophytes, or osteochondral lesions (Fig. 1). The ankle joint is then debrided using an arthroscopic shaver, grasper, or bur and attention is subsequently directed toward any osteochondral lesions that may be present. The articular cartilage is thoroughly examined for the presence of fissuring, looseness, softness, or fraying (Figs. 2, 3). Using a curette (Fig. 4) and arthroscopic shaver (Fig. 5), any abnormal cartilage is debrided down to the level of subchondral bone (Fig. 6), with care being taken to ensure a stable cartilage rim around the defect (Fig. 7) while avoiding creation of an overly large defect from excessive debridement. It is also imperative that any calcified cartilage that may be present deep in the defect yet superficial to the subchondral bone plate be debrided (Fig. 8). This calcified cartilage serves as a potential barrier and has been shown to impede growth of repair tissue in the knee and is likely to negatively impact outcomes if not debrided. Once debridement has been completed, a series of holes or “microfractures” are placed in the exposed subchondral bone to a depth of at least 2 mm using 30-, 45-, or 60-degree awls (Fig. 9). The microfracture holes should be placed throughout the defect with approximately 3 to 4 mm between each microfracture to ensure that there is a stable bone bridge present (Fig. 10). The joint space is then cleared of any further loose bodies or debris. The pressure in the joint is reduced exposing the ankle joint to abnormal stresses. The anterior drawer and talar tilt tests should be performed to evaluate the ATFL and CFL, respectively. Physical examination findings consistent with an osteochondral lesion are dependent on location of the lesion. Patients with lateral lesions are generally tender to palpation over the anterolateral joint line, while the foot is in plantarflexion. Patients with medial lesions are often tender to palpation over the posteros medial joint line with the foot in dorsiflexion. There may also be an effusion present and patients may complain of catching, popping, or clicking with ankle range of motion.

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FIGURE 1. Initial arthroscopic view of an unprepared osteochondral lesion with significant fissuring of the articular cartilage.

FIGURE 2. Osteochondral lesion demonstrated down to the level of subchondral bone through use of a probe.

FIGURE 3. Articular cartilage flap with exposed subchondral bone.

FIGURE 4. Articular cartilage being prepared through use of a curette.

FIGURE 5. Articular cartilage being prepared through use of an arthroscopic shaver.

FIGURE 6. Osteochondral lesion prepared for microfracture with subchondral bone exposed in the bed of the lesion.
FIGURE 7. Arthroscopic probe testing for stability of the peripheral rim of articular cartilage surrounding the defect.

FIGURE 8. Calcified cartilage being removed with a curette in preparation for microfracture.

FIGURE 9. Microfracture being performed in the exposed subchondral bone of the osteochondral lesion with extrusion of a fat droplet visible.

FIGURE 10. Osteochondral lesion following microfracture with microfracture holes visible in the center and upper left aspect of the lesion.

FIGURE 11. Bleeding demonstrated from the microfracture holes following decrease in pump pressure indicating adequate depth of penetration into the subchondral bone has been reached.

FIGURE 12. Osteochondral lesion following microfracture and evacuation of fluid from the ankle joint.
FIGURE 13. Osteochondral lesion being dried in preparation for cartilage extracellular matrix (ECM) and bone marrow aspirate concentrate (BMAC) mixture application.

FIGURE 14. Cartilage extracellular matrix (ECM) and bone marrow aspirate concentrate (BMAC) mixture being applied to the osteochondral lesion.

FIGURE 15. Osteochondral lesion filled with cartilage extracellular matrix (ECM) and bone marrow aspirate concentrate (BMAC) mixture.

FIGURE 16. Cartilage extracellular matrix (ECM) and bone marrow aspirate concentrate (BMAC) mixture being smoothed within defect by a Freer elevator.

FIGURE 17. Cartilage extracellular matrix (ECM) and bone marrow aspirate concentrate (BMAC) mixture, shown slightly recessed within the defect to allow for application of fibrin glue.

FIGURE 18. Osteochondral lesion with fibrin glue being applied over cartilage extracellular matrix (ECM) and bone marrow aspirate concentrate (BMAC) mixture.
FIGURE 19. Final product of the osteochondral lesion following microfracture and application of cartilage extracellular matrix (ECM) and bone marrow aspirate concentrate (BMAC) mixture demonstrating the fibrin coat to be flush with the surrounding articular cartilage.

(Fig. 11). This ensures that the microfracture holes have reached an adequate depth.

If there are no cystic lesions identified, application of the cartilage ECM is initiated after evacuation of the fluid from the joint (Fig. 12) and drying of the defect (Fig. 13). Should there be any large cystic lesions identified during debridement of the osteochondral lesion or while performing the microfracture, this is treated with bone grafting. The cystic cavity must be thoroughly debrided with use of curettes to ensure adequate preparation. The ankle joint is again thoroughly examined and if no additional abnormalities are noted, the fluid is evacuated from the joint and the defect is dried with pledgets. Cancellous bone allograft chips are then mixed with the previously obtained BMAC preparation. This is then packed into the cavity to the level of the subchondral bone plate and a fibrin coat is applied and allowed to solidify for 5 minutes. The next step is application of the cartilage ECM.

The cartilage ECM is mixed with previously prepared BMAC in a 1:1 ratio in the supplied mixing syringe. A Tuohy delivery needle is then used to deliver the cartilage ECM mixture into the dried defect (Figs. 14, 15) and a Freer elevator is used to smooth out the mixture (Fig. 16). Care must be taken at this time to ensure that the mixture is slightly recessed within the defect to ensure that the final product does not sit proud within the joint space (Fig. 17). Once the mixture has been smoothed within the defect, a fibrin coat is applied to the cartilage ECM mixture using the supplied dual lumen applicator tip (Fig. 18). Again, care must be taken to avoid applying excessive fibrin causing the final product to sit proud within the joint space. Once the fibrin has been applied, the ankle is not to be manipulated for at least 5 minutes to allow the fibrin to solidify and the final product to set (Fig. 19). The ankle is then ranged to assure that the cartilage ECM has adhered to the defect. If so, the equipment is withdrawn and the arthroscopic portals are closed with suture and a sterile compressive dressing is applied. Posterior and stirrup splints are also applied to immobilize the ankle at neutral temporarily.

If the osteochondral lesion cannot be sufficiently accessed arthroscopically, debridement and application of the cancellous bone soaked in BMAC and cartilage ECM may be completed in open manner. This is generally performed through a medial malleolar osteotomy for medial lesions as they tend to be central or posterior and are more common. For lateral lesions, access is generally obtained through a standard anterolateral approach medial to the fibula. Simple plantarflexion of the foot is usually sufficient to visualize the lesion given that the lesions are generally located more centrally. Division of the lateral ligaments allows further exposure. Lateral malleolar osteotomy is less commonly required for lateral lesions.

If the patient is to have any other open procedure or ligamentous reconstructions or repairs, this is completed after the arthroscopic or open microfracture with cartilage ECM and BMAC augmentation.

RESULTS

This study was approved by the Institutional Review Board. All patients who were at least 18 years or older, at least 6 months out from index surgery, and underwent microfracture with cartilage ECM and BMAC augmentation for the treatment of an articular cartilage lesion of the talus, by a single surgeon, were included from this study. All patients completed a preoperative and postoperative subjective questionnaire, which included the Foot and Ankle Disability Index (FADI) activities of daily living subscale (ADL), FADI sports subscale, and FADI total score. FADI scores were calculated as a percentage, with a total possible score of 100. There were 7 patients (5 females, 2 males) with a mean age of 43.7 years available for preliminary follow-up. Mean BMI was 25.8 (range, 21.3 to 30.0). Mean follow-up was 8.4 months (range, 6.3 to 12.6 mo). One patient underwent subsequent ankle arthroscopy at 7 months following index surgery for pain and arthrobrosis. Initial and second-look arthroscopic images from this patient can be seen in Figures 20A–D. Mean preoperative FADI ADL subscale was 64 (range, 39 to 89), which improved to 83 (range, 62 to 100) postoperatively. Mean preoperative FADI sport subscale was 29 (range, 0 to 47), which improved to 53 (range, 22 to 100) postoperatively. Mean preoperative FADI total score was 56 (range, 33 to 79), which improved to 76 (range, 52 to 100) postoperatively. Overall, patients showed improvements in all subscales and total score.

COMPLICATIONS

Complications that may be encountered during this procedure are largely related to ankle arthroscopy itself. There may be damage to branches of the superficial peroneal nerve, the intermediate and medial dorsal cutaneous nerves, as they course through the area of the anterolateral portal placement. If the talar osteochondral lesion is posterior and requires placement of posterior portals, extreme caution must be taken when making the posteromedial portal. The incision in this area is very close to the neurovascular bundle running posterior to the medial malleolus and risk of damage to these structures is increased. There is also the chance that the cartilage ECM and BMAC mixture does not adhere to the prepared defect while testing range of motion before closure. Should this be the case, the dislodged product should be removed from the joint space to clear joint of any loose bodies. The defect should again be debrided and dried followed by a reattempt at placement of the cartilage ECM mixture with fibrin coating. There should be minimal manipulation of the ankle joint following placement of the fibrin coat on the cartilage ECM mixture to allow for sufficient time for the final product to adhere and set-up. For this reason, the microfracture technique with cartilage ECM and BMAC augmentation should be the final arthroscopic procedure performed before withdrawal of the arthroscopic equipment.
POSTOPERATIVE MANAGEMENT

Patients participate in a postoperative rehabilitation protocol that was developed by the surgeon and the physical therapist. The postoperative management can vary quite significantly depending on other confounding injuries or procedures performed in addition to the microfracture surgery with cartilage ECM and BMAC augmentation. Weight-bearing status and length of time for the rehabilitation process are also dependent on the location of the osteochondral lesion(s) and whether or not it is a weight-bearing surface. Although each rehabilitation protocol is patient-specific, the general protocol is as follows. A sterile compressive dressing with posterior and stirrup splints are applied in the operating room and continued for 1 to 2 weeks. The patient is instructed on use of crutches and to be non–weight-bearing in the postoperative splint until his/her follow-up appointment. At the initial postoperative visit, surgical dressings are removed, incisions are examined for signs of infection, and range of motion is tested. At that time, the patient is provided with a walking boot, which can be removed 4 to 5 times per day to work on range of motion of the ankle joint, but the patient continues to be non–weight-bearing. Patients start home range of motion exercises on their own in addition to formal physical therapy with goals of increasing range of motion beginning 1 to 2 weeks after surgery. At 6 weeks postoperatively, progressive weight-bearing is initiated over a 2- to 4-week period. Once full weight-bearing without pain has been achieved, weaning of the walking boot over the following 2 weeks takes place. If not already done, formal physical therapy is prescribed for the patient around the 6-week time frame, with goals of improving range of motion, strength, and proprioception. Patients can gradually return to normal activities over the 3- to 6-month postoperative period, starting with low-impact activities such as swimming, walking, or biking.

POSSIBLE CONCERNS, FUTURE OF THE TECHNIQUE

Although we provide preliminary outcomes for a small subset of patients, short-term outcomes are necessary to determine whether use of cartilage ECM is a viable treatment option for patients with osteochondral lesions of the talus. This technique follows sound orthopedic principles of treating pathologic defects with repair or restoration. This is carried out through the use of tissue that can provide a scaffold for growth, in addition to cells capable of producing the desired tissue. Bone grafting of cystic defects is a well-documented treatment method in the knee and has also been reported to be a successful method of treatment for OCDs of the talar dome. These techniques are problematic in that accompanying articular cartilage defects are ignored and the accepted result is that the repair tissue will comprise fibrocartilage, that is primarily type I collagen. Combining a cartilage scaffold surface with MSCs, from BMAC, capable of forming type II collagen is intuitively logical, and it is expected that adding a scaffold and additional MSCs will only improve the results from microfracture alone.

REFERENCES


