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Yashas Reddy
Thomas Jefferson University, yashas.reddy@students.jefferson.edu

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Biologic Augmentation in Osteochondral Lesions of the Talus

By Yashas Reddy, Class of 2025
Faculty Advisor: Dr. David Pedowitz, MD

Introduction

Osteochondral lesions of the talus (OLT) are injuries involving damage to the cartilage and bone associated with the talar dome. They occur in up to 50% of ankle sprains and 73% of ankle fractures, varying in stability and severity.[1] Standard weight-bearing ankle radiographs may allow for visualization of the lesions if substantial bone fragmentation is involved but CT and MRI are more sensitive for subchondral bone damage and purely cartilaginous lesions, respectively (Figure 1). The majority of patients with OLT are active individuals in their 20s and 30s, and often present after sustaining an acute inversion injury.[2] Trauma to the talar dome creates an ischemic environment in the joint, which ultimately leads to disintegration of the subchondral bone in addition to damage to the overlying cartilage. This may lead to generalized ankle pain, weakness, and swelling. In addition to acute trauma, these lesions may develop as a result of osteochondritis dissecans (OCD). OCD lesions commonly present in patients between 10-20 years of age and have a multifactorial etiology, including genetic predisposition and loss of blood supply to a region of the joint.[3] Incidence of these lesions is higher in young athletes, suggesting that microtrauma also plays a role in OCD becoming symptomatic.

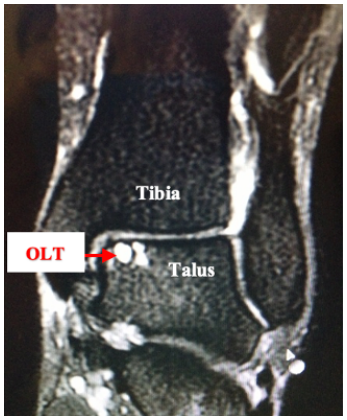

Figure 1. MRI of osteochondral lesion. Image obtained from Dr. David Pedowitz (Rothman).

Despite the prevalence of OLT, there is still a great deal of uncertainty regarding the best treatment option. Although non-operative management such as NSAIDs, rest, and immobilization is a viable option for some patients, these methods fail about 45-55% of the time.[4] Traditionally, bone marrow stimulation (BMS) through microfracture is often the treatment of choice for OLT. Microfracture involves drilling small holes through the subchondral plate (Figure 2), which releases mesenchymal stem cells and growth factors, in hopes of filling the lesion with fibrocartilage and vascular supply over time. This is a relatively simple and inexpensive surgical technique that yields about 85% good-excellent outcome scores for small to medium sized lesions.[5] However, the fibrocartilage produced as a result of microfracture is inferior to the body's native cartilage and susceptible to greater deterioration over time with compression shear and tension forces.[2] In addition, the fibrocartilaginous ingrowth does not always completely integrate with surrounding cartilage after microfracture.[5] Further challenges with this method include intra-lesion osteophytes, subchondral bone resorption, and fissures within the repaired lesion seen on long-term follow-up.[6,7] Lastly, regarding the unclear pain generator in OLTs, some are concerned that microfracture merely creates a painful lesion rather than a biological substrate for a new bearing surface.

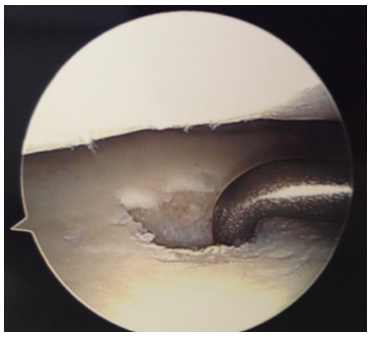

Figure 2. Arthroscopic Image of Lesion Created By Microfracture. Image obtained from Dr. David Pedowitz (Rothman).

Osteochondral autografts and allografts are an alternative treatment method (Figure 3). These grafts allow for the repair of subchondral bone through the transplantation of hyaline cartilage to the site of injury. However, poor incorporation between the graft and host leading to peripheral cell death and the formation of cysts remains a challenge of this technique.[8]

For skeletally immature patients, conservative treatment, BMS, and osteochondral autografts have been shown to be successful in about

44%, 77%, and 67% of children, respectively.[9] In addition, fixation of the fragment to underlying bone using Kirschner wires, screws, or bioabsorbable pins was clinically successful in about 80% of children.[9] This fixation method has also had significantly higher radiological success rates compared to other surgical methods due to the preservation of the natural architecture and hyaline cartilage.[9]

In recent years, biologic augmentation in OLT has emerged as an attempt to minimize the challenges posed by established treatments – most notably their limited durability and poor incorporation. Biologics have also been shown to decrease the action of osteoclasts and may minimize cyst formation, allowing them to be an effective adjunct to microfracture and osteochondral graft transfer.[10]

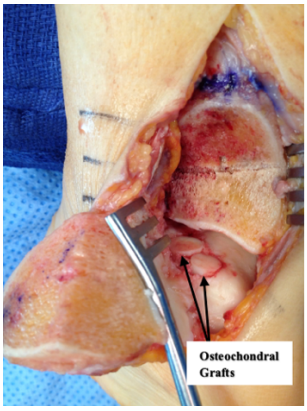

Figure 3. Implantation of osteochondral grafts at lesion site. Image obtained from Dr. David Pedowitz (Rothman).

Platelet-Rich Plasma Therapy

Platelet-rich plasma (PRP) therapy is a growing biologic augmentation method that utilizes a patient's own platelets and growth factors to stimulate the regeneration of injured ligaments and tendons. The injection is prepared by drawing a patient's blood, centrifuging the sample, and isolating the platelets from other components. This releases numerous factors from the broken platelets which can contribute to a healing cascade. Chondrocyte cultures in PRP have demonstrated increased chondrogenesis, type II collagen deposition, and proteoglycan synthesis, all of which are essential components of articular cartilage. These effects help prevent resorption of bone and degradation of cartilage.[11]

Initial in-vitro studies in sheep and rabbits showed that PRP allowed for improved osteochondral lesion healing when combined with microfracture, in comparison to microfracture alone.[12,13] PRP-treated lesions in rabbits also demonstrated an increase in type II collagen and proteoglycan content in the repaired tissue, along with improved histological scores.[14] Recent in-vivo research has shown that PRP, in conjunction with bone marrow stimulation, demonstrated greater improvements in functional outcome scores, joint function and decreased pain[15]. Benefits were most pronounced in smaller-sized lesions (<15 mm). However, sample sizes in each of these studies was small and the method/content of PRP preparation varied in each case.

Bone Marrow Aspirate Concentrate

Bone marrow aspirate concentrate (BMAC) has also been of great interest with regard to the management of OLT. Bone marrow aspirate is obtained from the patient's bone marrow, traditionally from the iliac crest, as shown in Figure 4. It contains both platelets and mesenchymal stem cells and possesses similar anti-inflammatory effects to PRP. Moreover, the mesenchymal stem cells within BMAC have the capacity to differentiate into chondrocytes, making it a useful biologic in conjunction with BMS.[16]

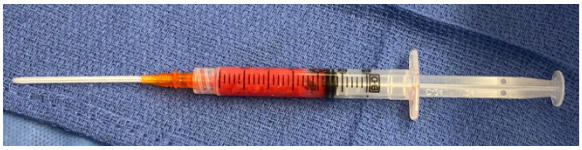

Figure 4. BMAC in syringe after harvesting from iliac crest. Image obtained from Dr. David Pedowitz (Rothman).

In the equine model, BMAC combined with microfracture was shown to improve histologic scores at the site of the lesion in comparison to microfracture alone.[17] MRI mapping also demonstrated improved healing in the experimental group.[17] In a human study, adding BMAC to BMS has been shown to improve articular cartilage repair, functional outcomes, and MOCART scores, the latter of which are used to grade the quality of repaired cartilage tissue after surgery.[18,19] The merits of BMAC have not only been demonstrated when implemented with microfracture, but also when used with osteochondral autograft transplantation.[20]

BioCartilage

Extracellular matrix cartilage allograft – marketed as BioCartilage (Arthrex, Naples FL) – is developed from dehydrated allograft cartilage and is composed of type II collagen, proteoglycans, and cartilage growth factors. BioCartilage enables chondrocyte synthesis and proliferation by acting as a tissue network to allow for greater cell interaction. After stimulation of mesenchymal cell migration by

microfracture, these cells mix with the matrix provided by BioCartilage leading to the formation of hyaline cartilage.[21] Figure 5 demonstrates insertion of BioCartilage at the lesion after microfracture has been performed.

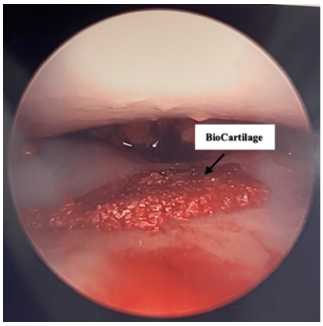

Figure 5. Microfracture site after BioCartilage implantation. Image obtained from Dr. David Pedowitz (Rothman).

When combined with BMS and BMAC, BioCartilage improves pain, functional outcomes, and MOCART scores.[22] In radiographic studies, the BMS + BioCartilage groups showed a greater infill, less edema, and fewer fissures compared to the groups receiving only BMS[23]. The decrease in fissures is especially noteworthy as this is a commonly encountered problem in long-term MRI follow-up of OLT's treated with microfracture. Support for BioCartilage has grown rapidly in recent years as long-term follow up outcomes have been favorable.[22]

DeNovo Natural Tissue Graft

DeNovo (Zimmer Biomet, Warsaw IN) is allograft composed of juvenile hyaline cartilage, which contains immature chondrocytes. Juvenile chondrocytes have much higher proteoglycan and collagen type II content and demonstrate significantly faster growth in monolayer cultures compared to adult cells.[24] Early clinical trials in patients with large OLT have also shown substantial improvements in pain, activity, and function.[25] Although DeNovo allograft implantation in conjunction with BMAC has demonstrated improved functional outcome scores, postoperative MRI of the tissue still showed similar composition to that of fibrocartilage.[26] Therefore, long-term follow up is still needed to determine the durability of this augmentation method.

Conclusion

Overall, PRP, BMAC, BioCartilage, and DeNovo have all had promising results in early in-vivo and in-vitro studies. However, the superiority of certain methods over others has not been studied in a randomized fashion. The utility of peripheral blood stem cells and adipose-derived stem cells are also being investigated with respect to the management of OLT. Rather than the superiority of certain biologic augments, it is likely that a combination of biologic augments must be utilized for increased durability and tissue incorporation in OLT. Harvesting the body's natural capability of restoring cartilage is a challenging, but potentially very fruitful endeavor in foot-and-ankle orthopaedics.

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