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Topical Review: MACI as an Emerging Technology for the Treatment of Talar Osteochondral Lesions

Article by Dekker TJ, Erickson B, Adams SB and Gross CE.
Foot Ankle Int. 2017 Sep; 38(9):1045-1048.

Commentary by **Lawrence A. DiDomenico, DPM and Mohammed K. Hassan, DPM**

The authors certify that they have no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

CONDENSATION

Approach

“Talar osteochondral lesion” is a collective term used for multiple pathological lesions of the talus which include osteochondral defects, chondral defects, osteochondritis dissecans and osteochondral fractures, over 75% of which are due to a traumatic event. With the talus receiving tenuous blood flow, an injury to the subchondral plate followed by repetitive loading could result in localized osteonecrosis of the subchondral plate. The chondral defect leads to pain, decrease in activity, mechanical symptoms and morbidity. Various operative treatment modalities have been used for addressing the difficult pathologies of the talus osteochondral lesions. Matrix-induced autologous chondrocyte implantation (MACI) is a modified technique of autologous chondrocyte implantation (ACI) that attempts to point out the possible pitfalls of the original technique. Unlike ACI, MACI obviates the need for periosteal patch retrieval and the theoretical leakage of chondrocyte cells, which could compromise the integrity and overall outcome of the original ACI technique by utilizing a biodegradable scaffold to retain chondrocytes. The evidence for its use is limited to level IV case series and more comparative studies are needed in the future prior to definitive recommendations in the use of MACI for talus osteochondral lesion.

The FDA has approved MACI for the knee and laid certain contraindications to its use like history of hypersensitivity to aminoglycoside or porcine

material, malalignment which would result in stress on the graft, advanced osteoarthritis, history of inflammatory arthritis or uncorrected blood coagulation disorder. The creation and processing of the graft occurs by harvesting articular cartilage. The therapeutic approach used a thorough diagnostic arthroscopy for identifying all intra-articular pathology before addressing the known osteochondral lesions by debriding the lesion and evaluating the surrounding cartilage and subchondral bone. The MACI scaffold filled with autologous chondrocytes delivered arthroscopically has yielded excellent clinical results. The subchondral bone was removed until healthy bone could be visualized, then the lesion was measured followed by the transferring of the dimension and shape to the scaffold of choice. The joint was then dried if performed arthroscopically, and the remainder of the case was performed through a dry arthroscopic technique.

Some studies have recommended the use of splinting for the postoperative course until the incision site has healed, followed by removal of the splint with passive range of motion with non-weightbearing or partial weightbearing precautions up to six weeks. Studies have also advocated for continuous passive motion for an average of six to eight hours per day, maintained for three weeks to facilitate an increase in range of motion and time to return to sport varies from six months to one year, postoperatively.

What Investigators Accomplished

- There was a statistically significant ($p < .05$) improvement in American Orthopaedic Foot and Ankle Society (AOFAS) scores and a decrease in visual analog scale (VAS) scores. Some patients returned and undertook second-look arthroscopy, all of whom demonstrated healed articular surfaces at that time
- Patients showed improvements in both AOFAS and VAS scores which were consistent for more than five years from MACI surgery with an average lesion size of 1.94 mm², good-to-excellent results have been reported in multiple case series in lesions that range from 50 mm² to 600 mm². The MACI technique is mostly used for patients with 0 to 5-mm deep lesions considered as type II, or type IIA having lesion greater than 5 mm deep. Graft hypertrophy was the only notable complication reported among the case series.
- The healing response was evaluated based on a variety of MRI sequences as well as calculating magnetic resonance observation of cartilage repair tissue (MOCART) score among patients with an average lesion size of nearly 2.5 cm² and compared with the healthy controls. Disparities were observed between T2 and T2* sequences in the MACI group at a short-term follow-up, but eventually they became equivalent to healthy controls at long-term follow-up. Diffusion weighted imaging demonstrated differences between MACI and control patients at short and long-term follow-up, although short-term follow-up showed remarkable differences. It was concluded that 12 months are required for achieving cartilage maturation postoperatively. This was supported by another author reporting that 30 ankles treated with MACI demonstrated improved AOFAS score and

an improved MOCART score from 6.3 preoperatively to 3.8 at final follow-up, nearly four years after the index procedure.

- Diffused immunostaining of type II hyaline-like collagen similar to that of a normal articular surface was observed in cartilage graft biopsy done on patients who underwent second-look arthroscopy. Those grafts were further utilized in both primary and revision procedures. The patients who underwent prior surgery demonstrated statistically lower AOFAS scores. It was concluded that an all-arthroscopic procedure is not only feasible, but also safe and effective.
- Studies by Anders et. al and Giza et. al showed that there were no marked difference in outcomes due to the etiological differences of the lesions (traumatic or non-traumatic) between groups at one and two-year follow-up with an increase in AOFAS scores and a significant ($p > 0.05$) improvement in physical function scores of the SF-36 questionnaire. MACI yielded stable and effective improvements in function at a minimum two-year follow up.

Investigators' Observations

Matrix-induced autologous chondrocyte implantation can be an effective treatment option for both primary or revision cartilage regenerative procedures in physically active individuals without tibiotalar arthritis. Although cost remains a concern, improvements in the durability of repair with type II cartilage replacement might offer long-term benefits.

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COMMENTARY

The authors provided the definition of and pathology for osteochondral lesions, and discussed the emergent treatment options. For a lesion smaller than 150 mm², micro-fracture or marrow stimulation is a gold standard. However, micro-fracture leads to the formation of fibrocartilage in the defect area, which is biomechanically weaker than hyaline cartilage. Such information is valuable to the reader because it provides an idea as to why matrix-induced autologous chondrocyte implementation – a modified technique of autologous chondrocyte implantation, which is harvested from the host and cultured in a laboratory and later implanted into the chondral defect site – is a viable alternative to micro-fracture, which has traditionally been the “go-to” procedure.

The authors specify the process and time it takes for the chondrocytes to grow in the laboratory setting. In addition, they cover some positive aspects to utilizing MACI, including the lack of requirement for a periosteal patch retrieval process, which leads to a high likelihood of the chondrocytes' leakage from the implantation site and a poor outcome.

On the negative side, the authors cite that there is a high cost associated with using such a technique. Given the cost-contained medical environment, such a procedure may not be for everyone, notably as insurance companies will not approve this treatment unless there is enough evidence to show that the procedure outperforms the current standard of practice. Time also adds to costs, as MACI requires increased time it takes to harvest and perform in vitro expansion of the chondrocytes in the lab, which require special monitoring and handling. Further, the outcomes and success of MACI are based on many case series that have no long-term follow-ups and there are no randomized control trials available to prove its efficacy. The authors comment that this procedure is not indicated for patients with advanced osteoarthritis, which leaves only a small fraction of the patient population as candidates with the appropriate indications.

This article is relevant to the foot and ankle field because it allows the reader to review the topic related to the etiology of osteochondral defects and new treatment modalities. However, in terms of therapeutics and efficacy, it is unclear whether MACI provides better outcome than the traditional treatment. Therefore, it may not be accessible to all patients when there is no FDA approval and insurance coverage for foot and ankle surgery. If so, we believe that only a small segment of the patient population who do not have advanced osteoarthritis may benefit from such a procedure. That may include healthy, young, athletic individuals. With all of this in mind, it would be difficult to persuade patients to try this procedure when they will ultimately be responsible for 100% out-of-pocket expense. Given the pace of progress in medicine, it may take some time before MACI becomes a mainstream treatment. Educating patients regarding MACI may help to spread the treatment more swiftly.