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The Role of Magnetic Resonance Imaging in Autologous Matrix-Induced Chondrogenesis for Osteochondral Lesions of the Talus: Analyzing MOCART 1 and 2.0

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Abstract

Objective. To determine the role of magnetic resonance imaging (MRI) MOCART (Magnetic Resonance Observation of Cartilage Repair Tissue) 1 and 2.0 scores in the assessment of postoperative outcome after autologous matrix-induced chondrogenesis (AMIC) for the treatment of osteochondral lesions of the talus (OLTs). It was hypothesized that preoperative patient factors or OLT morphology are associated with postoperative MOCART scores; yet postoperative clinical outcome is not. *Study Design*. Cohort study; Level of evidence, 4. This study evaluated isolated AMIC that were implanted on the talus of 35 patients for the treatment of symptomatic OLT. Tegner and AOFAS (American Orthopaedic Foot and Ankle Society) scores were obtained at an average follow-up of 4.5 ± 1.8 years and postoperative MRI scored according to the MOCART 1 and 2.0. *Results*. OLT size showed significant correlation with postoperative MRI scores (MOCART 1: $P = 0.006$; MOCART 2.0: $P = 0.004$). Bone grafting was significantly associated with a MOCART 1 subscale (signal intensity of repair tissue; $P = 0.038$). Age and defect size showed significant correlations with MOCART 2.0 subscales ($P < 0.05$). Patients with shorter follow-up had a significantly higher MOCART 1 score and a trend toward better MOCART 2.0 scores than patients with longer follow-up (64.7 vs. 52.9 months, $P = 0.02$; 69.4 vs. 60.6 months, $P = 0.058$). No MOCART score was associated with postoperative patient-reported outcomes (n.s.). *Conclusion*. Osteochondral lesion size is associated with postoperative MOCART scores in patients treated with AMIC for OLTs, with decreasing MOCART scores over time. Yet clinical outcome does not correlate with any MOCART score. Thus, MOCART assessment seems to have no significant role in the postoperative treatment of asymptomatic patients that underwent AMIC for OLTs.

Keywords

autologous matrix-induced chondrogenesis, osteochondral lesion, talus, MOCART, osteoarthritis, cartilage repair, AMIC

Introduction

Osteochondral lesions of the talus (OLTs are defined as damage to the coating cartilage and subchondral bone due to repetitive microtrauma or traumatic injury to the ankle joint[1-3] whether through direct trauma (i.e., sports)[4-6] or joint instability.[7-9] Native hyaline cartilage is rich in collagen type II and maintains nutrition through physiologic loading and unloading.[10] Once joint congruency is disturbed, however, successive joint degeneration results in osteoarthritis (OA) as adult cartilage has limited regenerative potential.[2] To prevent further degeneration and to improve clinical symptoms, numerous surgical treatment options for cartilage repair have been proposed.[11] Cell-based treatments such as autologous chondrocyte transplantation (ACI)[12-15] and matrix-induced autologous chondrocyte implantation (MACI)[16,17] require a 2-step procedure to initially harvest chondrocytes for incubation in the laboratory followed by implantation in a second surgery. Conversely, available 1-step procedures include osteochondral allograft implantation (OCA), which is limited in its availability of suitable allografts,[18-20] bone marrow stimulation (microfracturing) for smaller OLTs,[21-23] and autologous matrix-induced chondrogenesis (AMIC).[24]

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The AMIC technique comprises bone marrow stimulation of the subchondral bone with subsequent augmentation of a collagen type I/III bilayer membrane to contain the subchondral bleeding and provide a matrix for repair tissue maturation. Numerous studies reported good clinical improvement with high return to sport in the treatment of symptomatic OLTs,[25-30] superior to simple bone marrow stimulation.[24]

Postoperative magnetic resonance imaging (MRI) is the most important noninvasive method for evaluation of surgical procedures for cartilage repair.[10,31-33] In 2004, Marlovits et al.[31] introduced the MOCART score (Magnetic Resonance Observation of Cartilage Repair Tissue) based on a standard knee MRI protocol including intermediate-weighted sequences for cartilage evaluation. Originally, the score was designed for the evaluation of cartilage repair tissue after microfracturing, ACI, or MACI in the knee. The score considers 9 radiologic variables (degree of repair and defect filling, integration to border tissue, surface of repair tissue, structure of repair tissue, subchondral lamina, subchondral bone, adhesions, synovitis) and its use has found broad implementation for AMIC assessment in OLT.[25,28,29,34,35]

While postoperative MRI assessment provides valuable information regarding structural integrity of the joint, the role of the MOCART score as a follow-up tool in cartilage repair of the ankle remains controversial.[28,36,37,40] Recently, Schreiner et al. presented an updated version of the original MOCART score, the MOCART 2.0 score,[33] to mirror recent progressions in surgical and imaging techniques. The updated version overworked the variables, degree of defect filling from 50% into 25% increments, the integration to neighboring native cartilage, surface repair assessment in reference to repair length in place of depth, subchondral bone was changed to subchondral changes, which now includes signal intensity for edema in the bone marrow, cysts, or osteonecrosis. Meanwhile, the variables subchondral lamina, adhesions, and synovitis were excluded from the score with its points being reallocated to the new variable bony defect or bony overgrowth. While the purpose of this update was to enhance validity of postoperative MR imaging in cartilage repair, its clinical relevance is still to be determined.

Thus, the goal of the current study was to determine the role of MR imaging, namely, MOCART 1 and 2.0 scores, in the assessment of postoperative outcome after AMIC for the treatment of OLTs at a follow-up between 2 and 8 years. It was hypothesized that preoperative patient factors or OLT morphology are associated with postoperative MOCART scores, yet postoperative clinical outcome is not.

Materials and Method

Our ethics review board approved this study before initiation. Data are regularly collected and stored for patients undergoing elective surgery at our institution. This database was used to identify patients who underwent isolated cartilage repair with AMIC for focal osteochondral defects in the talus between October 2009 and August 2015. The surgical treatment with AMIC was indicated for symptomatic focal full-thickness chondral and OLTs. AMIC was contraindicated in patients with inflammatory arthritis and/or advanced osteoarthritis.

Patients were included in this study if they underwent isolated AMIC to the talus with postoperative MR imaging and had clinical outcome available, namely, the American Orthopaedic Foot and Ankle Society (AOFAS; 0-100 points) score[38] for ankle function and the Tegner score[39] (0-10 points) for sports activity. Exclusion criteria comprised any prior ankle joint surgery or concomitant ankle procedure, and if patients did not have MRI acquisition performed at the same date as clinical scores were obtained.

Clinical notes and operative reports were reviewed to determine patient's age at the time of surgery, sex, body mass index (BMI), smoking status, duration of symptoms, concomitant bone grafting, defect size, and location.

Surgical Technique

All patients' OLT were accessed via an open approach through a medial ($n = 32$) or lateral ($n = 3$) malleolar osteotomy.[25,28,30]

Undermined cartilage and flaps were sharply excised using a scalpel or curettage and cystic or necrotic bone lesions were debrided until vital bone tissue was visible. Next, the bone surface was microfractured by drilling with a K-wire (Ø 1.2 mm, DePuy Synthes, Oberdorf, Switzerland). When the extent of bone defect was cavernous or impressed the congruency, the semi-cylindrical joint surface of the talus was reconstructed with cancellous bone from the osteotomized tibia. Subsequently, the bilayer type I/III collagen matrix (Chondro-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) was cut to fit the defect and placed on the lesion with the smooth side facing up. After checking if the lesion is filled up sufficiently, surgical fibrin glue was utilized to secure the membrane to the adjacent cartilage (Tissucol Duo S, Baxter International Inc., Deerfield, IL). Last, the joint was brought through full range of motion to ensure proper graft fixation, followed by open reduction and internal fixation of the malleolar osteotomy with two 2.5-mm titanium screws (medial) or compression plating (lateral) and standard wound closure.

MRI Assessment

Postoperative MRIs were performed on a 1.5 T MAGNETOM Avanto Fit system (Siemens Healthcare, Erlangen, Germany) with a dedicated 8-channel foot and ankle coil using a musculoskeletal protocol incorporating coronal, sagittal and axial turbo spin-echo (TSE) intermediate-weighted sequences
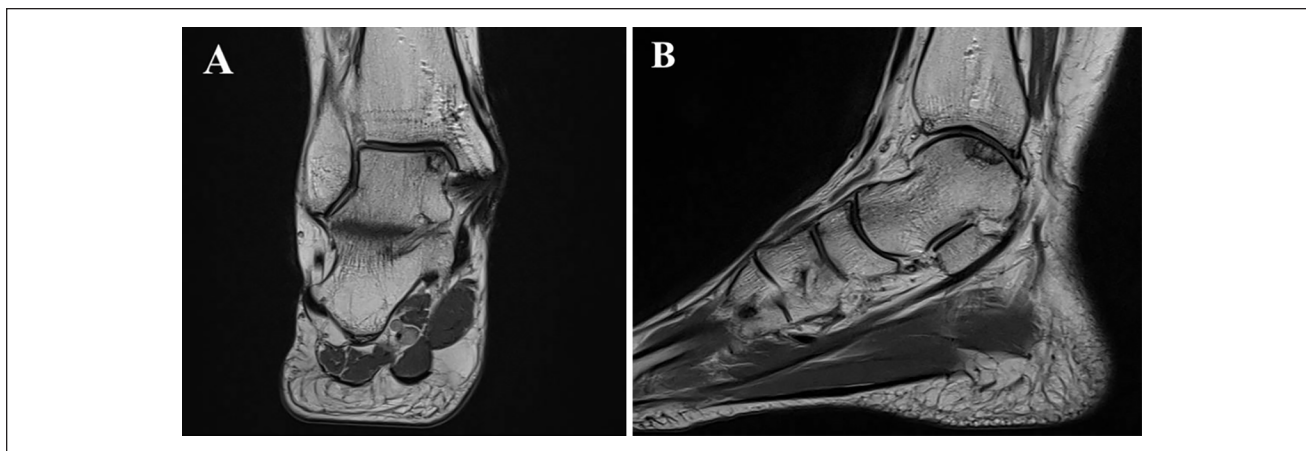
Figure 1. Postoperative intermediate-weighted coronal (**A**) and sagittal (**B**) MRI depicting an osteochondral lesion on the medial talar dome accessed via a medial malleolar osteotomy.

with and without fat saturation, using the Dixon technique, and a 3-mm slice thickness (**Fig. 1**).

For the present imaging study, the previously published and validated comprehensive MOCART[31] and MOCART 2.0[33] were utilized ranging from 0 to 100 points. Based on the original MOCART[31] scoring system comprising 9 radiologic variables, renewals of the MOCART 2.0 score[33] were the following: the degree of repair and defect filling is hypertrophic when exceeding 150% of the defect depth and incomplete filling is now assessed in 25% increments. The integration only accounts ingrowth into the neighboring native cartilage. Instead of regarding the depth of repair, the grading of surface irregularities is now referenced to the repaired length. The signal intensity division was retitled to normal signal, minor abnormal, and severely abnormal signal alterations. The subchondral bone score was revised to subchondral changes and added osteonecrosis as monitor. Last, the variables subchondral lamina, adhesions, and synovitis were removed and replaced by bony defect or bony overgrowth, reflecting a more detailed assessment of the bony lesion compared to the original score, which just rated the subchondral lamina as intact or not.

All MRIs were evaluated by a fellowship-trained musculoskeletal radiologist.

Statistical Analysis

Descriptive statistics were used to determine patient and lesion characteristics. All data were assessed for normality utilizing the Shapiro-Wilk test. Accordingly, continuous variables were analyzed with the independent *t* test. Point biserial and Pearson correlation, chi-square, and Fisher's exact test were used to assess the relationship of MOCART subscales with patient's age, sex, smoking status, BMI, duration of symptoms, bone grafting, lesion size and location, follow-up, and postoperative AOFAS and Tegner scores. Lesion size

Table 1. Patient and Lesion Demographics.

Patient and Lesion Characteristics	Patients ($n = 35$)
Age, years, mean $\pm$ SD	34.4 $\pm$ 10.7
Female sex, n (%)	14 (40)
BMI, kg/m^2, mean $\pm$ SD	28.7 $\pm$ 5.4
Smoker, n (%)	17 (48.6)
DOS >12 months, n (%)	27 (77.1)
Defect size, cm^2, mean $\pm$ SD	0.9 $\pm$ 0.6
Defect location, medial/lateral	32/3
Bone grafting, yes/no	27/8

SD = standard deviation; BMI = body mass index; DOS = duration of symptoms.

was calculated utilizing the ellipse formula for OLTs (sagittal length $\times$ coronal length $\times$ 0.79).[41] All statistical analyses were performed in SPSS for Mac (Version 23.0, SPSS Inc., Chicago, IL). Significance was set at $P < 0.05$.

Results

Thirty-five patients that underwent isolated AMIC for OLT at our institution with postoperative MRI and patient-reported outcomes were identified and included in this study. Mean postoperative MRI and clinical follow-up was obtained at 4.5 $\pm$ 1.8 years. Patient and lesion characteristics are presented in **Table 1**.

At final follow-up, mean AOFAS score was 92.63 $\pm$ 8.3 and patients reported a mean Tegner score of 5.1 $\pm$ 1.8, which significantly increased from 3.7 $\pm$ 2.0 ($P = 0.002$) preoperatively. Both MRI assessments were significantly associated with each other with a mean MOCART 1 score of 59.0 $\pm$ 14.9 compared to a mean MOCART 2.0 score of 65.1 $\pm$ 13.9 ($r = 0.885$; $P < 0.001$). In fact, subscales of both MOCART scores were strongly correlated with each

Table 2. Bivariate Correlations of Postoperative MOCART 1 and MOCART 2.0 Subscales and Total Score.

MOCART 1	Mean ± SD	MOCART 2.0	Mean ± SD	r	P Value
Filling of defect	16.9 ± 3.4	Volume fill of cartilage defect	19.1 ± 2.8	0.693	<0.001
Integration to border zone	13.0 ± 4.1	Integration to border zone	13.9 ± 2.5	0.946	<0.001
Surface of repair tissue	6.4 ± 3.1	Surface of repair tissue	6.9 ± 3.0	0.813	<0.001
Structure of repair tissue	1.4 ± 2.3	Structure of repair tissue	2.9 ± 4.5	1	<0.001
Signal intensity of repair tissue	14.1 ± 7.2	Signal intensity of repair tissue	10.0 ± 3.2	0.286	0.096
Subchondral lamina	0.9 ± 1.9	Bony defect/bony overgrowth	3.7 ± 3.7	0.575	<0.001
Subchondral bone	0.4 ± 1.4	Subchondral changes	8.7 ± 5.9	0.510	0.002
Adhesion	3.1 ± 2.5	—	—	—	—
Effusion	2.7 ± 2.5	—	—	—	—
Total	59.0 ± 14.9	Total	65.1 ± 13.9	0.885	<0.001

other, except "signal intensity" ($P < 0.001$ and $P = 0.096$, respectively; **Table 2**).

Analyzing the influence of preoperative factors on postoperative MRI assessment, osteochondral lesion size was the only preoperative factor that showed significant correlation with postoperative MOCART 1 and 2.0 total scores ($P = 0.006$ and $P = 0.004$, respectively). Bone grafting was the only preoperative factor significantly associated with a MOCART 1 subscale ("signal intensity"). Both age and defect size showed significant inverse correlations with MOCART 2.0 subscales ($P < 0.05$; **Table 3**).

Stratifying patients based on their follow-up, patients with a shorter follow-up (less than 4.5 years) showed a significantly higher MOCART 1 score than patients with a follow-up longer than 4.5 years ($64.7 ± 10.8$ vs. $52.9 ± 16.6$, $P = 0.02$). Patients with a shorter follow-up also exhibited a trend toward better MOCART 2.0 scores than patients with longer follow up ($69.4 ± 12.4$ vs. $60.6 ± 14.3$, $P = 0.058$). Specifically, MOCART 1 and 2.0 "signal intensity" subscale was significantly better in patients with shorter follow-up ($P = 0.016$ and $P = 0.031$, respectively). Furthermore, MOCART 1 and 2.0 "structure of repair tissue" subscale showed a trend toward better results in patients with shorter follow-up (both, $P = 0.06$).

When correlating postoperative MRI scores with clinical outcome, neither MOCART 1 nor 2.0 total or subscale scores were related to AOFAS or Tegner scores (n.s.).

Discussion

The key finding of the study presented herein is that MOCART and MOCART 2.0 scores strongly correlate with each other but do not show a statistically significant association with clinical outcome after isolated AMIC for the treatment of symptomatic OLTs. Interestingly, defect size was the only preoperative factor that was correlated with both postoperative total MOCART scores, which both seem to decline with prolonged follow-up.

While no direct comparison between the MOCART scores or an evaluation of the relationship between MOCART 2.0

and postoperative clinical outcome after cartilage repair in the ankle has been established yet, some studies have assessed postoperative MR imaging after AMIC and have investigated its association with patient-reported clinical outcome. Kubosch et al.[28] presented a case series of 17 patients treated with the open AMIC procedure for medial OLTs. At a mean follow-up of $39.5 ± 18.4$ months, postoperative MOCART scores averaged $52.7 ± 15.9$ with AOFAS scores averaging $82.6 ± 13.4$. Conversely to the presented results, the authors observed a statistically significant correlation between postoperative MOCART and AOFAS score (rho = 0.574, $P = 0.04$). Moreover, osteochondral lesion size ≥ 3 cm^3 was significantly associated with inferior AOFAS scores in the studied cohort, a factor that was inversely correlated with MOCART and MOCART 2.0 scores in the current study.

In a recently published study by Weigelt et al.,[25] the authors reported good to excellent clinical outcome with high return to sport after AMIC for OLTs in 33 patients with a mean MOCART score of $60.6 ± 21.2$. Correlating solely total MOCART scores, and not its subscales, to postoperative clinical outcome, no significant association was found. A similar finding was reported by Albano et al.,[34] who evaluated 16 patients at a mean follow-up of $30 ± 16.9$ months after AMIC for OLT. MRI acquisition was obtained at 12 and 24 months postoperatively and correlated with clinical outcome, assessed by VAS and AOFAS. Though MOCART scores increased significantly from $41.9 ± 14.6$ at 12 months to $51.9 ± 11.6$ at 24 months, their change did not show any significant association with the clinical improvement measured by the AOFAS.

While none of these studies investigated the relationship between MOCART subscales and clinical outcome, they do partially reflect the findings of the current study that neither MOCART total nor subscale scores are related with clinical outcome after AMIC for OLT. In a report published by de Windt et al., the authors systematically reviewed the evidence whether morphological MRI is reliable in predicting clinical outcome after cartilage repair in the knee. Assessing a total of 32 studies, they concluded that a majority of MRI parameters including the MOCART score did not show a significant correlation with clinical outcome, yet highlighting

Table 3. Significant Bivariate Correlations of Preoperative Patient and Lesion Parameters With Postoperative MOCART 1 and 2.0 Total Scores and Subscales.

	Correlation Coefficient	P Value
Total MOCART 1		
Defect size	−0.453	0.006
Signal intensity of repair tissue		
Bone grafting	0.530	0.038
Total MOCART 2.0		
Defect size	−0.477	0.004
Volume fill of cartilage defect		
Age	−0.401	0.017
Surface of repair tissue		
Defect size	−0.421	0.012
Signal intensity of repair tissue		
Defect size	−0.354	0.037

the fact that developing more advanced imaging techniques are warranted in the field of cartilage repair.[42]

On the other hand, the absence of correlation between MOCART and clinical outcome might be rooted in the particular postoperative time period MRI examinations were obtained. Ackermann *et al.*[43] presented a cohort study of 67 patients treated with ACI for cartilage defects in the knee. Analyzing the effect of chondrocytic gene expression on postoperative MR imaging and clinical outcome, the authors did not see any effect of increased chondrocytic gene expression on MOCART scores at final follow-up. When evaluating postoperative MRIs that were obtained at a follow-up between 12 and 30 months, however, increased gene expression was significantly associated with greater degree of defect filling, better integration at the border zone, and decreased effusion. It was theorized that 12 to 30 months might be the ideal time period for MRI evaluation of the repair tissue after ACI to the knee. They reasoned that ACI graft maturation requires 12 to 24 months to complete,[44] but graft aging with decreasing MOCART scores and general deterioration of the joint starts approximately after 30 months of follow-up.[45] Hence, 12 to 30 months represents a time period were a reliable evaluation of the repair tissue could be determined. Projecting this finding to the AMIC procedure, Gobbi *et al.*,[46] in a histological study, investigated the repair tissue after AMIC for OLTs. The study found that AMIC produced hyaline-like repair tissue in patients at 13.5 months postoperatively, suggesting complete maturation of the repair tissue. In the study presented herein, MRIs were obtained at a mean follow-up of 4.5 years with decreasing MOCART scores over time. This follow-up might explain the generally rather low overall MOCART scores as well as the absent association between MR findings and clinical outcome. Yet, follow-up did not affect the association between MOCART and clinical outcome in this study. However, future longitudinal studies are warranted to investigate if the clinical effect of early low MOCART scores might just occur at later time points

postoperatively. Until then, it remains questionable if timing plays a role in evaluating repair tissue of OLT treated with AMIC as the minimum follow-up was 2 years and graft deterioration might have already begun. Consequently, postoperative MR assessment with MOCART seems to not provide any further valuable information regarding clinical outcome after 2 years in patients that underwent isolated AMIC for OLTs who do not experience any symptoms that require further MR imaging evaluation to assess joint integrity.

However, the more detailed increments of the MOCART 2.0 might have slightly increased some subscale sensitivity. In fact, volume fill of cartilage defect inversely correlated with patient's age, meaning that younger patients presented with a more sufficient filling of the defect than patients of older age. This finding matches the report of Pestka *et al.*,[47] who analyzed cell quality in an *in vitro* examination of ACI cell cultivations. A total of 252 ACI patient samples were assessed for the cartilage relevant surface marker CD44 and the cartilage-specific differentiation markers aggrecan and collagen type II. The study revealed that patients younger than 20 years showed significantly higher expression rates of all 3 markers compared to older patients suggesting better cell quality. This might have contributed to the result seen in the current study; however, it will be of interest to see if similar observations can be made in cell-based therapies such as ACI and MACI utilizing the MOCART 2.0.

Last, defect size was the only preoperative factor that correlated with postoperative MOCART and MOCART 2.0 scores. While microfracturing is still referred to as the gold standard for lesions sizes up to 1.5 cm²,[48] AMIC has shown to result in favorable outcome in smaller as well as larger lesions without defect size being correlated with the postoperative clinical outcome.[25] Becher *et al.* treated 15 patients with microfracturing for OLTs and, similar to the results seen in the current study, found defect size to be a factor significantly associated with postoperative MOCART scores with higher scores found in patients with smaller lesions, yet this did not translate into improved clinical outcomes.[49]

The authors acknowledge the limitations of this study. The study was retrospective in its design with unavailable preoperative clinical scores. Thus, clinical improvement can only be assumed with a postoperative AOFAS score averaging over 92 points and postoperative Tegner scores showing a significant improvement compared to the retrospectively collected preoperative Tegner scores. Furthermore, both MOCART scores were originally designed for evaluating cartilage repair in the knee, yet its application in the assessment of cartilage repair in the ankle is widely accepted.[25,28,29,34,35,37,50]

Conclusion

In summary, osteochondral lesion size is associated with postoperative MOCART scores in patients treated with

AMIC for OLTs, with decreasing MOCART scores over time. Yet, clinical outcome does not correlate with any MRI parameter assessed by MOCART or MOCART 2.0. Thus, assessment of either MOCART score seems to have no significant role in the postoperative treatment of asymptomatic patients that underwent AMIC for OLTs.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

Ethical approval for this study was obtained from the cantonal ethics committee of Zurich (BASEC-Nr. 2019-02025).

Informed Consent

Written informed consent was obtained from all subjects before the study.

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