



# Mid-term results of autologous matrix-induced chondrogenesis surgery with or without scaffolds for arthroscopic treatment of deep talus osteochondral lesions: A comparative study

Ahmet Fevzi Kekeç, MD<sup>1</sup>, Ahmet Yıldırım, MD<sup>2</sup>

<sup>1</sup>Department of Orthopedics and Traumatology, Necmettin Erbakan University, Meram Faculty of Medicine, Konya, Türkiye

<sup>2</sup>Department of Orthopedics and Traumatology, University of Health Sciences, Konya Health Application and Research Center, Konya, Türkiye

An osteochondral lesion of the talus (OLT) is a talar cartilage pathology commonly accompanied by bone damage of the subchondral region and it usually requires surgical treatment, if symptomatic. It can cause deep ankle pain after weight bearing and is associated with limitation of range of motion (ROM), locking, swelling, and joint stiffness.<sup>[1]</sup> Although microfracture, abrasion chondroplasty, curettage, drilling, mosaicplasty, and cellular or noncellular scaffolds have been used in the treatment of OLT, the most optimal treatment method is often determined based on the lesion size and depth.<sup>[2,3]</sup>

Osteochondral lesion of the talus was first classified by Berndt and Harty<sup>[4]</sup> in 1959. The Bristol classification has been more frequently used in recent years to

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**Correspondence:** Ahmet Fevzi Kekeç, MD. Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi, Ortopedi ve Travmatoloji Kliniği, 42080 Meram, Konya, Türkiye.

E-mail: afkekec@hotmail.com

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## ABSTRACT

**Objectives:** This study aims to investigate the effectiveness of arthroscopic autologous matrix-induced chondrogenesis (AMIC) procedure with or without polyglycolic acid-hyaluronic acid (PGA-HA)-based cell-free scaffold (CFS) in Bristol E4 and E5 osteochondral lesion of the talus (OLT) ranging between 1.5 and 3 cm<sup>2</sup>.

**Patients and methods:** Between March 2018 and March 2021, a total of 47 patients with OLTs (29 males, 18 females; mean age: 22.8±2.3 years; range, 18 to 65 years) were retrospectively analyzed. The patients were divided into two groups based on the procedures applied. Patients in the first group (Group 1, n=23) underwent the AMIC procedure alone (curettage, microfracture, and grafting), while patients in the second group (Group 2, n=24) underwent AMIC procedure with PGA-HA-based CFS. The localization of the lesions was evaluated. All OLTs were diagnosed with preoperative radiography and magnetic resonance imaging (MRI). During the preoperative period, lesion stages were evaluated based on the Bristol staging system, and the postoperative results were evaluated based on the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) scoring system.

**Results:** The mean follow-up was 36.2±5.6 months. In the early period, the three-month functional scores were comparable between the groups. While a significant increase was observed in the American Orthopaedic Foot and Ankle Society (AOFAS) scores from the mean preoperative of 62.71±4.44 points to the postoperative of 86.00±6.58 points in Group 1, a significant increase in the AOFAS score was observed from 65.28±7.91 points to 95.42±4.41 points in Group 2 at 12-month follow-up (p=0.016, p=0.011, respectively). The functional scores tended to progress after 12 months. Radiologically, a complete defect filling was observed in a mean of 10.5±2.7 months. No graft hypertrophy was recorded in any patients. The AOFAS and MOCART scores in Group 2 were found to be statistically significantly higher than that in Group 1 (p=0.034 for AOFAS 1/AOFAS 2 and p=0.006 for MOCART 1/MOCART 2). Overall, there was a positive, but weak, significant correlation between the final AOFAS scores and MOCART scores (r=0.347, p<0.001).

**Conclusion:** Arthroscopic AMIC procedure in deep OLTs between 1.5 cm<sup>2</sup> and 3 cm<sup>2</sup> can yield a statistically significant improvement both clinically and radiologically; however, the use of a PGA-HA-based CFS in addition to this procedure can improve the clinical and radiological recovery.

**Keywords:** American Orthopaedic Foot and Ankle Society, magnetic resonance observation of cartilage repair tissue, osteochondral lesion, scaffold, talus.

predict prognosis and patient management, with displaced detached lesions classified as Stage 4 and accompanying subchondral cystic lesions as Stage 5.<sup>[5]</sup> Although the arthroscopic microfracture technique is still considered the most ideal method in terms of both cost-effectiveness and prognosis in the OLT of up to 1 cm<sup>2</sup>, no consensus has been reached upon for the treatment for larger and deeper lesions.<sup>[6-8]</sup>

Autologous matrix-induced chondrogenesis (AMIC), a novel procedure that uses collagen or hyaluronic acid (HA) containing membrane on the lesion after debridement and microfracture (bone marrow stimulation) in OLT, with or without bone grafting, has been shown to be associated with favorable outcomes.<sup>[9-11]</sup> Recently, several studies have focused on the treatment of osteochondral lesions using tissue engineering and scaffold implantation to restore the articular surface;<sup>[12]</sup> however, arthroscopic treatment of deep and wide lesions has been an important problem in the literature due to difficulties in the supply of industrial products after the novel coronavirus disease 2019 (COVID-19) pandemic and economic restrictions using scaffolds in developing countries. In the present study, we, therefore, aimed to investigate the effectiveness of arthroscopic AMIC procedure with or without polyglycolic acid-HA (PGA-HA)-based cell-free scaffold (CFS) in Bristol E4 and E5 OLT ranging between 1.5 and 3 cm<sup>2</sup>.

## PATIENTS AND METHODS

This two-center, retrospective study was conducted at the Department of Orthopedics and Traumatology of two tertiary care centers between March 1<sup>st</sup>, 2018 and March 1<sup>st</sup>, 2021. A total of 47 patients with OLTs (29 males, 18 females; mean age: 22.8±2.3 years; range, 18 to 65 years) were included in this study. Inclusion criteria were as follows: age between 18 and 65 years; 1.5 to 3 cm<sup>2</sup> lesion area with a cyst, having no concomitant ligament injury, no diagnosed bone disease, no history of rheumatic disease, no history of concomitant fracture, having at least one-year follow-up data, and isolated talus medial or lateral Bristol Stages 4 and 5 symptomatic full-thickness chondral or osteochondral lesions. Exclusion criteria were as follows: having a history of concomitant rheumatic and neuromuscular diseases, a history of irregular diabetes (glycated hemoglobin [HbA1c >7]), a history of infection and septic arthritis, a body mass index (BMI) of >30, and a history of heavy smoking.

The patients were divided into two groups based on the procedures applied. Patients in the first group

(Group 1, n=23) underwent the AMIC procedure alone (curettage, microfracture, and grafting), while patients in the second group (Group 2, n=24) underwent AMIC procedure with PGA-HA-based CFS. All patients had a history of unsuccessful conservative treatment or previous surgery. A total of five patients underwent ankle arthroscopy in external clinics: three from the first group and two from the second group. All surgeries performed were diagnostic interventions that did not use autografts and scaffolds and none of the patients underwent adequate cartilage and necrotic bone debridement. The second surgery was performed in all patients at least six months after the initial surgery.

The lesions were evaluated in two different groups based on their localization, medial, and lateral. All OLTs were diagnosed with preoperative radiography and magnetic resonance imaging (MRI). During the preoperative period, lesion stages were evaluated based on the Bristol staging system, and the postoperative results during follow-up were evaluated based on the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) scoring system.<sup>[13,14]</sup>

Clinical evaluation was performed based on the American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot score. Based on this clinical rating system developed by Kitaoka et al.,<sup>[15]</sup> subjective pain and function scores are combined with objective scores obtained during the surgeon's physical examination (i.e., for assessing sagittal motion, hindfoot motion, ankle-hindfoot stability, and ankle-hindfoot alignment). The maximum score is 100 points, indicating no symptoms or impairments.

The MRI was evaluated in coronal and sagittal planes (T1 and T2 sequences, 1.5 T, Magnetom Symphony, Siemens, Germany) at 6, 9, 12, 18, and 36 months postoperatively, and the final follow-up MRI was interpreted using the MOCART scoring system, a scoring system created to identify cartilage repair tissues post-treatment. While the total score varies between 0 (worst) and 100 (best), each variable is given one point.<sup>[14]</sup>

### Operative technique

The patients were operated and followed by two different orthopedic surgeons with similar experiences in foot and ankle surgery in two tertiary clinics. Following the completion of preoperative anesthesia preparations, surgery was performed under spinal or general anesthesia with the help of a tourniquet in supine position without using a special technique



**FIGURE 1.** Arthroscopic images of ankle. (a) Microfracture application after debridement of lesion. (b) Osteochondral lesion which is filled with autologous bone graft. (c) Application of cell-free scaffold on lesion site.

for traction. The graft was harvested from a 0.5 to 1 cm<sup>2</sup> window opened on the medial malleolus in the same area as the lesion. An image was obtained from the medial standard arthroscopic portal using a 30° 4-mm optic for ankle arthroscopy, straight and angled mini curettes, 70° and 90° angle microfracture device, and a 3.5-mm-diameter shaver. Once the lesion was identified, arthroscopic curettage and microfracture were performed through the appropriate portal, and autograft was performed to fill the defective area and accelerate bone consolidation. The same procedures were combined with PGA-HA-based CFS, Cartilago® MATRIX (Biolot Medical, Ankara, Türkiye) to identify adhesion points for mesenchymal stem cells and to

promote optimal proliferation and regeneration in Group 2 (Figure 1).

Short leg splints were applied to the patients postoperatively, and crutches without weight were used for mobilization for 1.5 months. At the end of three weeks, the splint was terminated, and ankle plantar and dorsi flexion exercises were started. Partial weight-bearing was allowed at the end of 1.5 months, and full weight-bearing at the end of two months.

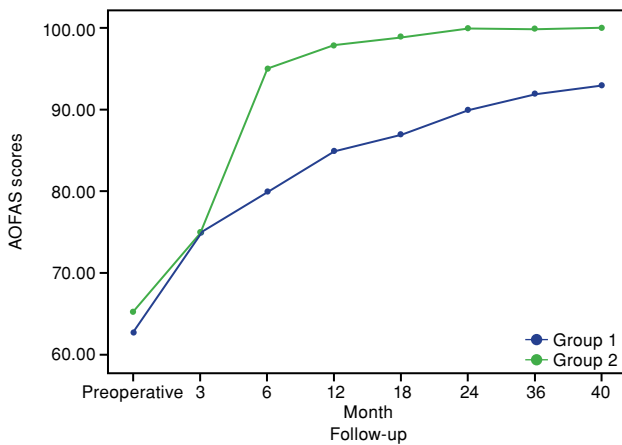
#### Statistical analysis

Statistical analysis was performed using the SPSS for Windows version 24.0 software

**TABLE I**  
Patient demographics, lesions characteristics, and AOFAS scores

	Group 1 (n=23)		Group 2 (n=24)		Total		p
	n	Mean±SD	n	Mean±SD	n	Mean±SD	
Age (mean)		23.6±2.1		24±2.3		22.8±2.3	0.537
Sex							
Male	14		16		29		
Female	9		8		18		
Body mass index (kg/m <sup>2</sup> )		23.4±4.5		24.2±5.1		23.7±4.8	0.572
Localization							0.785
Right	14		15		26		
Left	11		10		21		
Localization							0.825
Medial	19		20		39		
Lateral	4		4		8		
Lesion surface area (cm <sup>2</sup> )		2.05±0.34		2.18±0.26		2.12±0.32	0.260
Lesion depth (mm)		11.7±3.7		11.4±4.4		11±4	0.759
Follow-up (months)		37.2±6.1		34.9±5.1		36.2±5.6	0.169
Preoperative AOFAS scores		62.71±4.44		65.28±7.91		64±9.1	0.179
Postoperative AOFAS score		86.00±6.58		95.42 ±4.41		90.8±7.9	<b>0.034</b>

AOFAS: American Orthopaedic Foot and Ankle Society; SD: Standard deviation.



**FIGURE 2.** Graph of the statistical analysis of AOFAS scores at preoperative period, 3-6-12-18-24-36-40 months after surgery in both groups.

AOFAS: American Orthopaedic Foot and Ankle Society.

(IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean  $\pm$  standard deviation (SD), median (min-max) or number and frequency, where applicable. The Student t-test and rank-sum test were used for the analysis of non-normally distributed variables. The age of the patients, BMI, size of the defect, and factor analysis of the onset of complaints were calculated using the Pearson's product-moment correlation coefficient ( $r$ ). A  $p$  value of  $<0.05$  was considered statistically significant.

## RESULTS

Of a total of patients included in the study, the mean BMI was  $23.7 \pm 4.8$  (range, 18 to 29)  $\text{kg}/\text{m}^2$ . The lesion was located at the medial talus in 39 patients and

at the lateral talus in eight patients. The lesion was located at the right ankle in 26 patients and at the left ankle in 21 patients. A total of 33 patients suffered from ankle pain with unknown etiology, whereas 14 reported a major trauma; i.e., sprain. The onset of symptoms ranged from one to 26 months. The mean size and depth of the lesions were  $2.12 \pm 0.32 \text{ cm}^2$  and  $11 \pm 4 \text{ mm}$ , respectively.

The mean follow-up was  $36.2 \pm 5.6$  (range, 30 to 43) months. In the early period, the three-month functional scores were comparable between the groups. While a significant increase was observed in the AOFAS scores from the mean preoperative of  $62.71 \pm 4.44$  points to the postoperative of  $86.00 \pm 6.58$  points in Group 1, a significant increase in the AOFAS score was observed from  $65.28 \pm 7.91$  points to  $95.42 \pm 4.41$  points in Group 2 at 12-month follow-up ( $p=0.016$  and  $p=0.011$ , respectively) (Table I). The functional scores tended to progress, *albeit* slightly, after 12 months (Figure 2).

No restrictions on walking distance were reported in the study. Only two patients had dorsiflexion restriction ( $<10^\circ$ ). Supportive insoles were provided to 11 patients postoperatively. Only three patients preferred ankle bandage. Two patients reported temporary hypoesthesia related to superficial nerve dermatome. No other significant complications were reported in any of the patients.

Radiologically, a complete defect filling was observed in a mean of  $10.5 \pm 2.7$  (range, 7 to 14) months. No graft hypertrophy was recorded in any patients. When the AOFAS and MOCART scores of both groups were compared, the scores in Group 2 were found to be statistically significantly higher

**TABLE II**  
Evaluation of MOCART scores between groups

MOCART scoring system	Group 1	Group 2	$r$	$p$
	Mean $\pm$ SD	Mean $\pm$ SD		
Volume fill of cartilage defect	10.5 $\pm$ 2.7	19.2 $\pm$ 4.7	0.624	<0.001
Integration into adjacent cartilage	13.2 $\pm$ 3.4	14.1 $\pm$ 2.3	0.874	<0.001
Surface of the repair tissue	5.8 $\pm$ 3.2	6.9 $\pm$ 3.5	0.756	<0.001
Structure of the repair tissue	1.6 $\pm$ 2.4	2.7 $\pm$ 3.8	0.978	<0.001
Signal intensity of the repair tissue	15.2 $\pm$ 6.5	9.7 $\pm$ 2.4	0.298	0.056
Bony defect or bony overgrowth	0.7 $\pm$ 1.4	3.9 $\pm$ 3.9	0.478	<0.001
Subchondral changes	0.3 $\pm$ 1.7	8.9 $\pm$ 5.7	0.574	0.002
Adhesion	2.6 $\pm$ 2.1	-	-	-
Effusion	2.7 $\pm$ 2.3	-	-	-
Total	53.0 $\pm$ 13.2	67.4 $\pm$ 11.3	0.883	<0.001

MOCART: Magnetic Resonance Observation of Cartilage Repair Tissue scoring system; SD: Standard deviation.

TABLE III

Correlation analysis of the last recorded AOFAS score and the MOCART scores

	MOCART score	
	r	p
AOFAS score	0.347	<0.001

MOCART: Magnetic Resonance Observation of Cartilage Repair Tissue scoring system; AOFAS: American Orthopaedic Foot and Ankle Society.

than that in Group 1 ( $p=0.034$  for AOFAS 1/AOFAS 2 and  $p=0.006$  for MOCART 1/MOCART 2) (Table II). Overall, there was a positive, but weak, significant correlation between the final AOFAS scores and MOCART scores ( $r=0.347$ ,  $p<0.001$ ) (Table III).

## DISCUSSION

The novel procedure known as AMIC which uses collagen or HA containing membrane on the lesion after debridement and microfracture (bone marrow stimulation) in OLT, with or without bone grafting, has been well documented to have positive outcomes.<sup>[9-11]</sup> All previous studies in this field reported that this procedure is absolutely necessary to cover the lesion area with a membrane cover after the procedure and to keep the possible stem cell migration from the bone marrow in the lesion area for healing. However, in recent years, increasing global economic problems have caused serious difficulties in reaching such implants in low- and middle-income and developing countries. In addition, after the COVID-19 pandemic, disruptions began to be experienced in the supply of featured implants worldwide.<sup>[16-18]</sup> Therefore, alternative arthroscopic solutions were started to be considered in the treatment of OLTs larger than 1 cm<sup>2</sup>. Although non-osseous grafting of the peroneus longus tendon was used in a limited number of patients in the literature,<sup>[19]</sup> AMIC is still the most commonly used treatment method, after osteochondral autologous transfer surgery (OATS).<sup>[10,11,20]</sup>

In our study, we present the experiences of two different surgeons who are experienced in the treatment of arthroscopy lesions and OLTs in tertiary care centers with >200 arthroscopic AMIC procedures using many types of scaffolds. The patients with inaccessible scaffold (Group 1) and those who underwent the same procedure combined with the scaffold (Group 2) were compared both functionally and radiologically. To the best of our knowledge, this is the first study performed without using scaffold in medium-width lesions between 1.5 cm<sup>2</sup> and

3 cm<sup>2</sup> and only used grafting in addition to isolated microfracture.

The consensus statements on Scaffold-Based Therapies developed at the 2017 International Consensus Meeting on Cartilage Repair of the Ankle<sup>[21]</sup> and many studies in the literature have shown that isolated microfracture (bone marrow stimulation) without any membrane application in lesions <1.5 cm<sup>2</sup>, particularly 1 cm<sup>2</sup>, is an adequate, ideal method with favorable clinical results for OLTs.<sup>[21-23]</sup> Although there is no gold-standard treatment method for lesions between 1.5 cm<sup>2</sup> and 3 cm<sup>2</sup> in the literature, the most accepted methods are OATS and AMIC.<sup>[9,10,24]</sup>

In the present study, we evaluated medium-sized OLTs with the AOFAS clinical scoring and MRI-based MOCART radiological scoring, the most frequently used evaluation methods in terms of functional and radiological results.<sup>[12,25-27]</sup> Kubosch et al.<sup>[26]</sup> reported that AOFAS scores and Gottschalk et al.<sup>[27]</sup> revealed that the European Foot and Ankle Society (EFAS) scores were found to be compatible and correlated with MOCART scores. In our study, a statistically significantly positive, but weak correlation was found between the two scores. Therefore, the clinical progression of the patients included in this study was also reflected in the radiological improvement.

Although a statistically significant improvement was observed in both clinical and radiological terms in both groups with or without a scaffold and although the same procedures were performed, the clinical and radiological improvements were statistically significantly better in Group 2, in which the scaffold named Cartilago<sup>®</sup> MATRIX, a synthetic PGA-based biomaterial enriched with HA was used. By providing three-dimensional support, biomaterials also ensure the mechanical stability of mesenchymal stem cells.<sup>[28]</sup> In contrast to two-dimensional support, current evidence demonstrates that three-dimensional support preserves the chondrocyte structure, facilitates chondrocyte transformation, and produces a tissue structure that mimics native tissue characteristics, thereby improving repair.<sup>[28-30]</sup>

The effectiveness of HA-based scaffolds in terms of stem cell migration occurring after bone marrow stimulation and holding the cancellous autograft together has been shown in previous studies with a high level of evidence.<sup>[31,32]</sup> In this study, better clinical and radiological improvements were demonstrated in the scaffold group, supporting

the hypotheses mentioned in *in vivo* and *in vitro* studies.

Cell-free scaffolds have been shown to induce chondrogenesis due to its HA-based structure in addition to being an easy one-step arthroscopic procedure to treat talus osteochondral lesions without arthrotomy.<sup>[33]</sup> Kanatlı et al.<sup>[34]</sup> reported that cell-free PGA-HA scaffolds provided successful clinical results in the treatment of OLTs of  $\geq 2.5$  cm<sup>2</sup>. The scaffold content used in this study was similar to the product we used and the participants were similar in terms of lesion size and depth. In parallel with our study, a significant increase and correlation with AOFAS and MOCART scores was also found in their study.

A recent systematic review by Shimozono et al.<sup>[35]</sup> showed that scaffold-based therapy for the treatment of OLT could produce favorable clinical outcomes, but the low level of evidence, low quality of evidence, and variability of data confuse the efficacy of scaffold-based therapy for OLT. Although almost all of the 28 studies included in this review consisted of Level IV case series, only three were comparative studies and one was a randomized-controlled study. In addition, only one-third of the studies evaluated the outcomes with MRI, and no study analyzed the correlation of MOCART and AOFAS scores. We believe that our study would contribute to the deficiency and uncertainty in the literature.

Two studies from the same group in the literature showed that the use of PGA-HA-based CFS resulted in a high (57.5% *vs.* 62.5%) hypertrophic repair in talus osteochondral lesions (TOLs).<sup>[34,36]</sup> In another clinical study using PGA-HA-based CFS, much less than these two studies, hypertrophic defect repair was observed in approximately 12.5% of the patients.<sup>[37]</sup> Contrary to these studies, hypertrophic recovery was not observed in any of the patients in our study, as the CFS has the same content, but different scaffold microstructures compared to their counterparts in other studies.

The main limitations of this study are that it is retrospective study and includes a relatively small-to-medium-sized patient group. Subgroup analyses were not performed due to the small number of patients. More precise results may be obtained with larger patient numbers and prospective studies in the future. In addition, tissue repair was unable to be evaluated with cartilage-specific MRI evaluation techniques, such as delayed gadolinium-enhanced MRI and T2 mapping or biopsies for histological review.

In conclusion, arthroscopic AMIC procedure in deep OLTs between 1.5 cm<sup>2</sup> and 3 cm<sup>2</sup> can yield significant improvements both clinically and radiologically; however, the use of a PGA-HA-based CFS in addition to this procedure can improve the clinical and radiological recovery.

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**Ethics Committee Approval:** The study protocol was approved by the Necmettin Erbakan University Pharmaceutical and Non-Medical Device Research Ethics Committee (date: 22.07.2022, no: 2022-3904). The study was conducted in accordance with the principles of the Declaration of Helsinki.

**Patient Consent for Publication:** A written informed consent was obtained from each patient.

**Data Sharing Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Author Contributions:** Idea/concept: A.F.K., A.Y.; Design: A.F.K., A.Y.; Control/supervision: A.F.K., A.Y.; Data collection and/or processing: A.F.K., A.Y.; Analysis and/or interpretation: A.F.K., A.Y.; Literature review: A.F.K., A.Y.; Writing the article: A.F.K., A.Y.; Critical review: A.F.K., A.Y.

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