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OSTEOCHONDRAL LESIONS OF THE TALUS TREATED WITH AUTOLOGOUS MATRIX-INDUCED CHONDROGENESIS: LONG-TERM RESULTS

E. DELMASTRO[1], M. JORDAN[2], W. FISCHER[3], S. HERZ[4], M. THOMAS[5]

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[1]UOSD Centro Patologia del Piede, ASST Gaetano Pini-CTO, Milan, Italy
[2]Department of Foot and Ankle Surgery, Hessingpark Clinic, Augsburg, Germany
[3]Department of Radiology, Hessingpark Clinic, Augsburg, Germany
[4]Radiologie Augsburg-Friedberg, Augsburg, Germany
[5]Department of Foot and Ankle Surgery, Diakonissenkrankenhaus, Augsburg, Germany

Corresponding Author
Elena Delmastro, MD; e-mail: delmastro.elena@gmail.com

ABSTRACT – ***Objective:*** The purpose of this study is to evaluate long-term outcomes following surgical treatment of osteochondral lesions of the talus (OLT) *via* autologous matrix-induced chondrogenesis (AMIC).

Patients and Methods: Patients who had presented with symptomatic OLT and who had been treated *via* AMIC, in a single surgical center, were included in this study. Patient-reported outcome measures were the European Foot and Ankle Society (EFAS), the Manchester Oxford Foot Questionnaire (MOXFQ), and the Foot Function Index (FFI). The Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) score was determined from an immediate post-operative magnetic resonance imaging (MRI) and then from a 10-year post-operative MRI.

Results: 19 patients were included in the study. At a follow-up of 10 years, the mean scores for EFAS, FFI, and MOXFQ were 31.9±9.1, 16.2±20.9, and 9.6±12.9, respectively. The total MOCART score was 46.5±13.3. There was no significant correlation between radiological and patient-reported outcomes.

Conclusions: These long-term outcomes are consistent with studies of shorter duration; AMIC can be considered a reliable method to deliver positive patient outcomes for the surgical treatment of OLT.

KEYWORDS: AMIC, Autologous matrix-induced chondrogenesis, Cartilage, Talus, Ankle.

INTRODUCTION

Osteochondral lesions of the talus (OLT) are a common occurrence, which can stem from acute ankle trauma as well as chronic ankle instability[1,2], while other patients may present with OLTs without a history of trauma[3]. Regardless of the origin, these lesions are likely to lead to ankle pain and can limit mobility, with serious sequelae including progression to osteoarthritis[4]. Indeed, a cascade of events can lead to progressive, incremental cartilage damage at the ankle joint[5]. Unfortunately, adult cartilage has exceptionally low repair potential due to low vascularity and high stiffness[6]. New tissue formation at a lesion site can usually occur *via* fibrocartilage formation, with fibrotic scarring likely responsible for patients' persistent complaints[1]. Consequently, surgery is often required to treat symptomatic lesions.

There are many surgical options for treating OLTs. Among these are microfractures, which are often considered a first-line treatment as they are easy to perform and have a low cost[7], but their durability is questionable[8]; furthermore, microfractures alone are not recommended in lesions bigger than 100 to 150 mm^2 or in lesions without a stable cartilaginous rim[9,10]. For lesions bigger than 100 mm^2, other surgical techniques are recommended. Osteochondral autograft transplant (OAT) is an option, but it can lead to comorbidity at the harvest site[11]. Matrix-induced autologous chondrocyte implantation (MACI) has shown positive clinical outcomes, but it requires 2 surgeries, usually a few weeks apart, and is limited by the expense of the procedure[12]. As an alternative to multiple procedures, comorbidity, or short-term benefits, autologous matrix-induced chondrogenesis (AMIC) has been shown to provide durable positive outcomes[13]. All these techniques can benefit from additional therapies such as stem cell infiltration or platelet-rich plasma (PRP), but the role of these additional therapies is not yet well defined compared to the use of a scaffold alone.

The AMIC technique includes OLT debridement, bone marrow stimulation, and the coverage of the OLT site by a bilayer collagen I/III membrane. In a recent consensus[14], it was the only membrane showing consistent evidence. In the most recent systematic reviews[15,16], AMIC provided significant improvements in patient outcome scores. Longer-term results, however, are lacking from most clinical studies concerning the repair of OLT. Therefore, the aim of this study was to conduct a clinical and radiological follow-up at 10 years in a series of patients treated with the AMIC technique for OLTs.

PATIENTS AND METHODS

Study Design

This study has an ambispective design, combining a retrospective and a prospective component. Patients were retrospectively recruited from those treated with the AMIC technique by 2 foot and ankle surgeons between 2011 and 2015. OLTs were diagnosed clinically and radiologically with magnetic resonance imaging (MRI). The inclusion criteria for the patients were: osteochondral lesions of the talus types III and IV, according to Berndt and Harty's classification[17], having reached skeletal maturity, and the ability to give informed consent. Exclusion criteria were osteoarthritis of the ankle joint, kissing lesions, active infections, and vascular-nervous lesions. Of 24 patients screened for eligibility, 19 satisfied the inclusion criteria and were enrolled in the study. Clinical (PROMs) and radiological (MRI) assessments were then prospectively collected during a dedicated follow-up visit conducted by the authors in 2023 at Hessingpark-Clinic in Germany, after approval from the Ethics Committee had been obtained on January 31st, 2023.

Operative Technique

The surgical technique involved two phases; the first was arthroscopic and was needed for diagnostic confirmation and microfracture. Microfractures were performed systematically with a Chondro Pick (Arthrex, Naples, FL) with a depth of 4 mm and a distance of 3-4 mm between the perforations. The entire surface of the lesion was covered with perforations. The second phase included the arthrotomy, medial or lateral, based on the localization of the lesion (Figure 1), and the subsequent preparation and positioning of a bilayer collagen I/III membrane (Chondro-Gide, Geistlich Pharma AG, Wolhusen, Switzerland) (Figure 2), which was fixed with a synthetic fibrin glue (Figure 3). In two patients, due to the posterior location of the OLT, a medial malleolar osteotomy was required, which was subsequently fixed using two cannulated screws. Following these procedures, a drain was placed, layered suturing was performed, the surgical dressing was applied, and the limb was positioned in a 90° half-cast. The operation was generally carried out under spinal-general anesthesia with a tourniquet applied at the root of the limb. Ankle mobilization according to pain tolerance was allowed starting from the third postoperative day in order to recover the range of motion (ROM). The physiotherapy program aimed for full ROM recovery by the sixth postoperative week.

Postoperative radiographs of the ankle were obtained immediately after surgery, and at 2 and 6 weeks postoperatively. A follow-up MRI was performed between 6 and 10 weeks after the procedure.

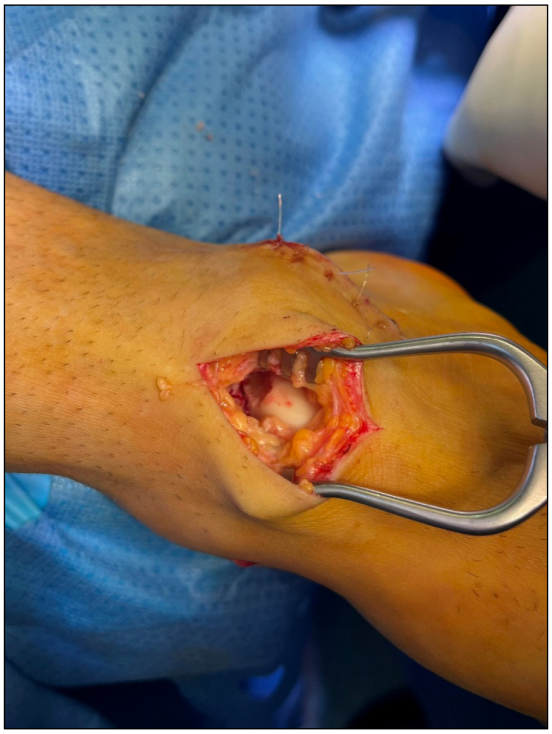


Figure 1. Intraoperative view of the osteochondral lesion after arthrotomy.

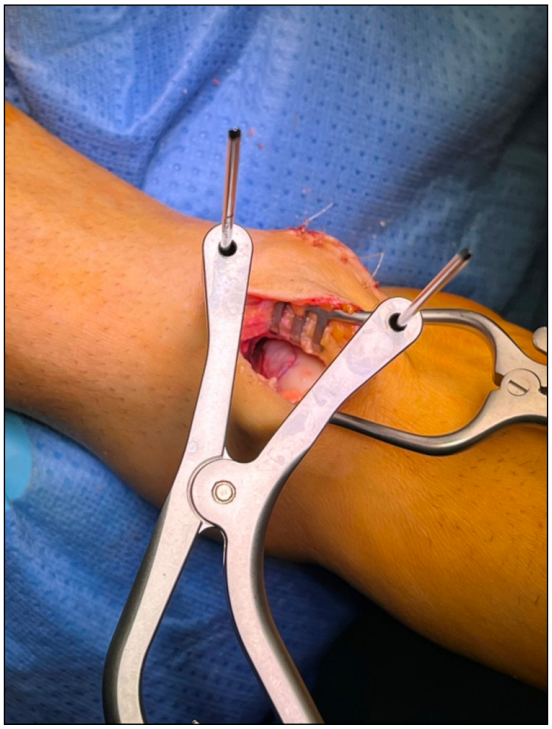


Figure 2. Positioning of the collagen membrane.

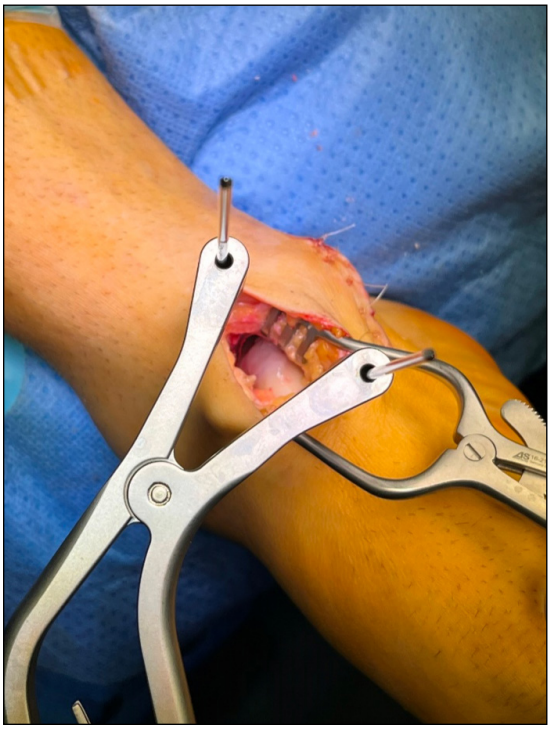
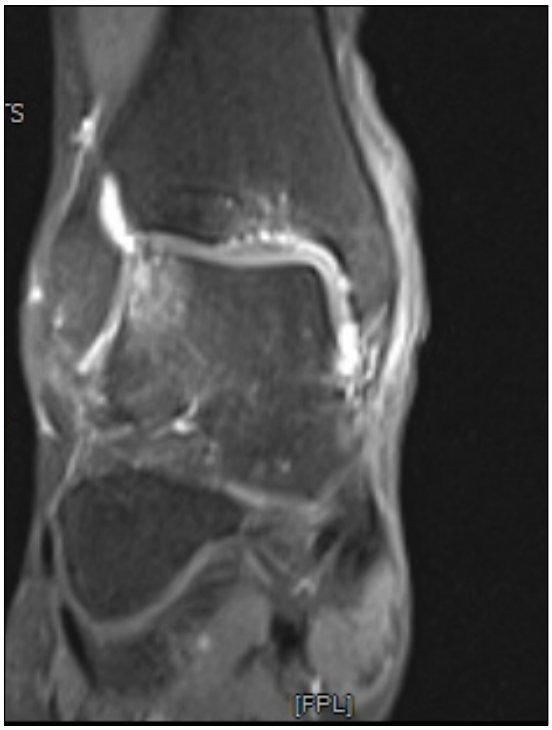


Figure 3. Fixation of the membrane with fibrin glue.

Outcome Measures

The clinical evaluation was performed by clinical examination and 3 patient-reported outcome measures (PROMs): the European Foot and Ankle Society (EFAS)[18], Foot Function Index (FFI)[19], and Manchester Oxford Foot Questionnaire (MOXFQ)[20]. All 3 were recorded at a mean of 10 years post-operatively. Radiologic follow-up was conducted using MRI and was performed with a 3T MRI unit. The MRI was performed post-operatively at 2 months follow-up (Figure 4), and approximately 10 years after surgery on average (Figure 5). In the final MRI, the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) 2.0[21] score was evaluated independently by two radiologists specialized in musculoskeletal tissue analysis.

Figure 4. Preoperative MRI of the osteochondral lesion.



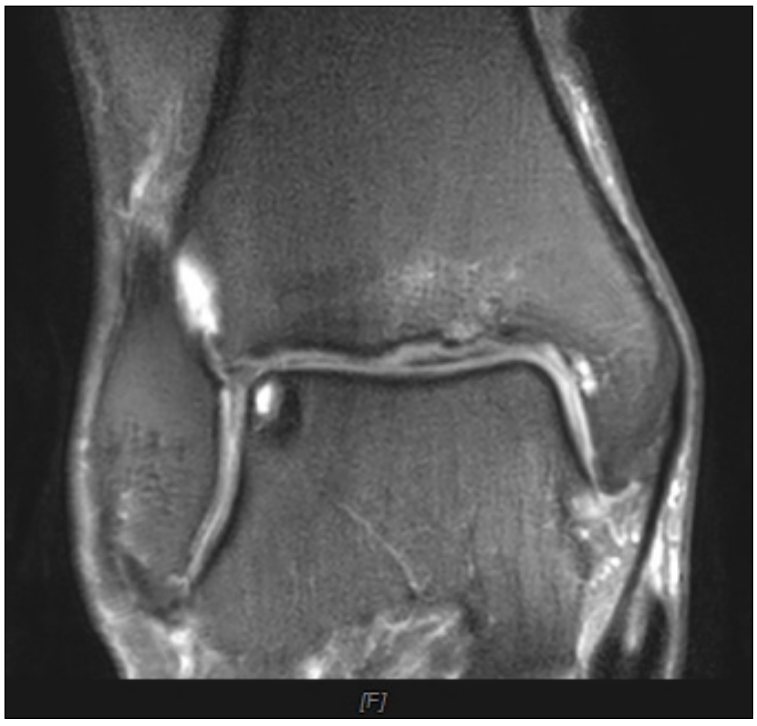


Figure 5. 10-year follow-up post-operative MRI of the lesion treated with AMIC.

Statistical Analysis

Descriptive statistics for the PROMs and the MOCART 2.0 parameters are presented as means and standard deviations. Inter-observer reliability between the two radiologists for the MOCART 2.0 score was assessed using Pearson's correlation coefficient. To evaluate the relationship between the MOCART 2.0 score and the PROMs, both Pearson's and Spearman's rho correlation coefficients were calculated, given the small sample size. A p-value < 0.05 was considered statistically significant. The statistical analysis was conducted using JASP software version 0.19 (Amsterdam, Netherlands).

Ethics Approval

The Ethics Committee of the Review Board of Hessingpark Clinic approved the study protocol on January 31st, 2023 (Study Protocol: 01-INT-2023).

RESULTS

The study included 19 patients (20 lesions) who had undergone AMIC for the treatment of OLT. The demographic data of the entire cohort are presented in Table 1.

Table 1. Demographic data of the patients.

Gender	Female: 7 - Male: 12
Age at surgery (years)	47.3±10.4
Lesion area (mm²)	109.5±50.4
BMI	26.0±2.8

Imaging Results

Two radiologists separately examined the MRI performed 10 years after surgery and evaluated the MOCART 2.0 score. The values for the parameters of the MOCART 2.0 score are presented in Table 2. An analysis was therefore first conducted to evaluate the possible homogeneity of the values obtained by the observers. The Pearson correlation highlighted the significance of this correlation for most of the subcategories of the MOCART 2.0 score and, in particular, for the final result of the MOCART 2.0 score (Table 3). The categories filling, integration of adjacent cartilage, bone defect/overgrowth, subchondral changes, and total reported a significant correlation in the Pearson analysis.

Table 2. Descriptive statistics of the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) 2.0 score parameters, evaluated separately by two examiners.

	Reviewer 1 **Mean ± SD (range)**	**Reviewer 2** **Mean ± SD (range)**
Volume of cartilage defect filling	14±5.5 (0-20)	13.5±7.9 (0-20)
Integration into adjacent cartilage	12.8±3.8 (5-15)	11.5±4.9 (0-15)
Surface of the repair tissue	5.5±3.2 (0-10)	5.5±3.6 (0-10)
Structure of the repair tissue	0.5±2.2 (0-10)	0.0±0.0 (0-0)
Signal intensity of the repair tissue	4.0±5.0 (0-10)	8.5±3.6 (0-10)
Bone defect/overgrowth	2.5±2.6 (0-5)	3.8±2.2 (0-5)
Subchondral changes	3.3±6.1 (0-20)	3.8±6.3 (0-20)
Total	46.5±13.3 (20-60)	44.8±12.1 (20-65)

Table 3. Pearson's correlation of the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) 2.0 score analyzed by two examiners.

MOCART 2.0 parameters	Pearson's r	*p*	Sig.
Volume of cartilage defect filling	0.622	0.003	*
Integration into adjacent cartilage	0.475	0.034	*
Surface of the repair tissue	0.320	0.169	
Structure of the repair tissue	-	-	*The variance was equal to 0
Signal intensity of the repair tissue	0.343	0.139	
Bone defect/overgrowth	0.577	0.008	*
Subchondral changes	0.935	<0.001	*
Total	0.616	0.004	*

Subsequently, for the correlation analysis, a MOCART 2.0 value was defined by averaging the observed values from each reviewer.

In addition to the MOCART 2.0 score, the radiologists separately assessed the presence of edema: in 3 patients, both radiologists reported the presence of this finding, while in 4 patients, this finding was assessed by only one radiologist. We therefore did not evaluate this parameter due to the discrepancy in the observations.

Clinical Results

With regard to the clinical outcomes, 3 PROMs were administered to the patients to evaluate their return to normal daily activities. These are summarized in Table 4.

Table 4. Descriptive statistics of PROMs results.

	Mean ± SD (range)
EFAS	19.8±4.6 (9-24)
EFAS sport	12.1±4.9 (1-16)
EFAS total	31.9±9.1 (12-40)
MOXFQ walking standing	4.5±6.4 (0-21)
MOXFQ pain	3.2±3.8 (0-10)
MOXFQ social interaction	1.9±3.3 (0-11)
MOXFQ total	9.6±12.9 (0-37)
FFI pain	5.9±8.2 (0-23)
FFI function	10.3±13.6 (0-39)
FFI total	16.2±20.9 (0-59)

European Foot and Ankle Society (EFAS), Manchester Oxford Foot Questionnaire (MOXFQ), Foot Function Index (FFI).

Correlations

The relationship between the MOCART 2.0 score and the various PROMs was assessed, and these are presented in Table 5. While the outcome scores as well as MOCART are parametric data, which would typically call for a Pearson's correlation, with the small sample size, we also calculated a Spearman-rho correlation coefficient. As shown in Table 5, there was no relationship between the MOCART scores and any of the PROMs.

Table 5. D.Correlations between the Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) 2.0 and the PROMs.

	Pearson		Spearman	
	r	*p*	r	*p*
MOCART 2.0 - EFAS	0.283	0.226	0.226	0.339
MOCART 2.0 - FFI	0.329	0.157	0.325	0.163
MOCART 2.0 - MOXFQ	-0.302	0.195	-0.233	0.323

European Foot and Ankle Society (EFAS), Manchester Oxford Foot Questionnaire (MOXFQ), Foot Function Index (FFI), Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART).

Revisions and Reoperations

Among the 19 patients of the study, no revision or major or minor complication was reported at the follow-up.

DISCUSSION

Clinical Outcomes

The results of all 3 PROMs indicate that patients treated with AMIC for OLT showed good clinical results up to 10 years post-operatively. The scores for MOXFQ, EFAS and FFI, along with their subscales, demonstrate that patients experienced durable, positive outcomes with regard to both pain and function. While the radiological evaluations yielded a fairly low score, no correlation was found between any of the PROMs and the MOCART scores.

The outcome scores in this study were comparable to what has been reported elsewhere for surgical repair of OLT. Although the EFAS is a relatively recent assessment tool, its relation to well-established outcome scores has already been demonstrated[22]. Furthermore, the scores we have documented in this study are apparently slightly better than those published[22-24]. The EFAS scores, along with the specific subscales, that we presented show slightly better results compared with published data, with a similar comparison of our FFI results[23,24], while the MOXFQ outcomes that we have measured are notably lower (indicating a better outcome) than those reported in the literature[22]. The sample size in this study is small, but the length of follow-up in our data supports the durability of the AMIC technique for the surgical repair of chondral defects.

The utility of this surgical technique in the repair of OLT has been reported previously, in various surgical approaches[25,26]. Regardless of the specific surgical techniques, positive outcomes have been reported in studies that have documented medium-term follow-up of 5 years[23,27,28]. In terms of patients treated, these positive results have been reported in a study that included a large number of patients (n=129) with a 5-year follow-up[23]. Additionally, a study[29] with 8 years of follow-up concluded that the AMIC procedure led to a significant reduction of pain, a recovery of ankle function, and a successful return to sports. While not an exhaustive list of data concerning AMIC, the length of follow-up and the number of successfully treated patients support the use of this technique, and the data we have presented further underscore the procedure's potential to provide lasting, positive outcomes for patients.

Radiological Evaluations

Regarding MRI evaluations, the utility of this imaging modality for evaluating outcomes has already been questioned. It has been succinctly stated that clinical outcome does not correlate with any MRI parameter, even though the patients had positive outcomes as measured by the American Orthopedic Foot & Ankle Society (AOFAS)[30]. To further question the utility of this imaging modality, it was noted

that there was no relationship between the MOCART score and any of the PROMs[31], which was also a conclusion of a study that presented 8 years of follow-up after OLT repair *via* the AMIC procedure[29]. As our data show, there is no correlation between the PROMs and the MOCART 2.0. This should be kept in mind, especially by colleagues who do not frequently deal with the repair of OLT. An MRI performed for simple follow-up may show a MOCART/MOCART 2.0 score that is concerning enough to warrant another surgery. However, the clinical and anamnestic evaluation of the subject is much more important, as it can indicate the success or failure of the primary surgical intervention. The importance of MRI in post-operative routine check-ups should thus be reconsidered, as it does not seem to provide any real benefit to patients or physicians.

Limitations

It is important to acknowledge the limitations of this study. Firstly, the small sample size precluded a statistical analysis that could have considered covariates such as age, body mass index (BMI), or defect size and whether these variables had an impact on the measured outcomes. Another limitation is the lack of preoperative data, as this would have given a precise value of the clinical improvement of the patients, and allowed an assessment of the positive response rate in comparison to established values for minimal clinically important difference.

CONCLUSIONS

The observational results that have been presented in this study, both clinical and radiological, are comparable with other AMIC studies in the literature, and this data extends the documented follow-up to 10 years[22-24]. The data presented, although with the limitations mentioned above, show good long-term results for the AMIC technique. Larger datasets and multicenter studies are needed to provide more robust evidence supporting the conclusions of this study.

Ethics Approval:
This study was conducted in accordance with the Declaration of Helsinki of 1975 (as revised in 2013), and the protocol was reviewed and approved by the Review Board of Hessingpark Clinic (Study Protocol: 01-INT-2023, date of approval: January 31st, 2023).

Informed Consent:
All subjects provided written informed consent for inclusion before they participated in the study.

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Authors' Contributions:
E.D. and M.T. participated in the drafting and critical revision of the manuscript. M.J. contributed extensively to the study's methodology development and was instrumental in the acquisition of data. W.F. and S.H. played a key role in obtaining the radiological data and their interpretation. E.D. provided substantial input in the writing and editing of the manuscript and was also deeply involved in the data analysis and interpretation. M.T. contributed significantly to the drafting of the manuscript, particularly in the discussion and conclusion sections.

ORCID ID:
Elena Delmastro: 0000-0003-1710-8635

Conflict of Interest:

The authors declare that they have no conflict of interest to disclose.

Data Availability:

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

AI Disclosure:

Artificial intelligence or assisted technologies were not used in the preparation of this study.

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