

# Osteochondral Lesions of the Talus and Autologous Matrix-Induced Chondrogenesis: Is Age a Negative Predictor Outcome?

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**Purpose:** To assess and evaluate healing and functional outcomes after arthroscopic talus autologous matrix-induced chondrogenesis (AT-AMIC) in 2 age groups: patients older than 33 years versus patients 33 years or younger. **Methods:** A total of 31 patients, of whom 17 were 33 years or younger ( $G_1$ ) and 14 older than 33 years ( $G_2$ ), were evaluated. All patients were treated with AT-AMIC repair for osteochondral talar lesion. Magnetic resonance imaging (MRI) and computed tomography (CT)-scan evaluations, as well as clinical evaluations measured by the visual analog scale (VAS) score for pain, American Orthopaedic Foot and Ankle Society Ankle and Hindfoot score (AOFAS), and Short Form-12, were performed preoperatively ( $T_0$ ) and at 6 ( $T_1$ ), 12 ( $T_2$ ), and 24 ( $T_3$ ) months postoperatively. **Results:**  $G_1$  consisted of 17 patients (mean age: 25 years, standard deviation:  $\pm 5$ ), whereas  $G_2$  consisted of 14 patients (mean age: 47 years, standard deviation:  $\pm 9$ ). In both groups, we found a significant difference for clinical and radiological parameters with the analysis of variance for repeated measures through 4 time points ( $P < .001$ ). In  $G_1$ , AOFAS improved significantly between  $T_0$  and  $T_1$  ( $P = .025$ ) and  $T_1$  and  $T_2$  ( $P = .011$ ); CT showed a significant decrease between  $T_1$  and  $T_2$  ( $P = .003$ ) and  $T_2$  and  $T_3$  ( $P < .0001$ ), whereas MRI reduced significantly at each follow-up. In  $G_2$ , AOFAS improved between  $T_0$  and  $T_1$  ( $P = .011$ ) and  $T_2$  and  $T_3$  ( $P = .018$ ); CT decreased between  $T_1$  and  $T_2$  ( $P = .025$ ), whereas MRI showed a reduction between  $T_1$  and  $T_2$  ( $P = .029$ ) and  $T_2$  and  $T_3$  ( $P = .006$ ). AOFAS in  $G_1$  was significantly higher at  $T_0$  ( $P = .017$ ),  $T_2$  ( $P = .036$ ), and  $T_3$  ( $P = .039$ ) compared with  $G_2$ . A negative linear correlation between AOFAS and VAS at  $T_1$  ( $R = -0.756$ ),  $T_2$  ( $R = -0.637$ ), and  $T_3$  ( $R = -0.728$ ) was found in  $G_1$ , whereas in  $G_2$ , AOFAS was negatively correlated with VAS at  $T_1$  ( $R = -0.702$ ). **Conclusions:** The study revealed that osteochondral lesions of the talus were characterized by similar sizes and features, both in young and old patients. We conclude that AT-AMIC can be considered a safe and reliable procedure that allows effective healing, regardless of age, with a significant clinical improvement; in particular, clinical results are related to starting conditions of the ankle. **Level of Evidence:** Level IV, therapeutic case series.

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An osteochondral lesion of the talus (OCLT) is a common defect involving the talar articular cartilage and the subchondral bone. One of the most common sources of OCLTs is injuries of the ankle, such as sprains, which are often recurrent, and fractures that can cause chronic instability. In these traumas, OCLTs occur in up to 70% of patients<sup>1,2</sup> and are mostly confined to the posteromedial or anterolateral talar dome.<sup>3</sup> Flick and Gould<sup>4</sup> found evidence of trauma in 98% of lateral and 70% of medial lesions. Nevertheless, nontraumatic causes of OCLTs have also been proposed, namely, congenital factors, ligamentous laxity, spontaneous necrosis, steroid treatment, embolic disease, and endocrine abnormalities.<sup>5</sup>

OCLTs either remain asymptomatic or progress to ankle pain due to various biological processes.<sup>6</sup> Pain relief and return to normal function are the main aims of OCLT

treatment. Debridement and subchondral bone microfractures are the most described surgical treatment for most small OCLTs, but lesions >1.5 cm have a poor outcome if only treated with this technique.<sup>7</sup> Surgical treatment is particularly advisable in patients with symptomatic, focal OCLTs that have failed nonoperative treatment, and in those with an acute, displaced fragment.<sup>8</sup> Arthroscopy in OCLTs, with both important diagnostic and therapeutic roles, allows direct visualization of all intra-articular structures with a limited surgical invasiveness. Other operative treatments to treat larger defects include osteochondral autograft transfer and autologous chondrocyte implantation (ACI).<sup>9,10</sup> Matrix-induced ACI is a derivative of the ACI method, where cultured chondrocytes are inoculated onto a 3-dimensional collagen scaffold, and then in a second intervention, implanted into the osteochondral defect.<sup>7</sup> Recent developments in the field include a matrix-assisted microfracture technique called autologous matrix-induced chondrogenesis (AMIC). This treatment allows stabilization and protection of the blood clot derived from the subchondral bone, providing a regeneration chamber to the bone marrow-derived mesenchymal stem cells, all in a single surgery.<sup>11</sup>

Independent prognostic factors such as age, size of the lesion, high body mass index, history of trauma, and presence of osteophytes have been shown by some authors to negatively affect the outcome of OCLT treatment by microfracture or ACI; however, there is currently no general consensus on the prediction of therapeutic success among the various OCLT treatment possibilities, although young age is considered to be an advantage in the healing of these lesions.<sup>12-14</sup> Patients younger than 18 years showed significantly better outcomes after microfracture and drilling,<sup>8</sup> whereas Cuttica et al.<sup>15</sup> assessed that increasing age up to 33 years was another variable that may have been associated with inferior outcomes. In contrast, Choi et al.<sup>16</sup> reported that increased age was not an independent risk factor for poor clinical outcome after arthroscopic marrow stimulation.

The purpose of our study was to assess and evaluate healing and the functional outcome after arthroscopic talus AMIC (AT-AMIC) in 2 age groups: patients 33 years or younger ( $G_1$ ) and patients older than 33 years ( $G_2$ ). We hypothesized that both groups would benefit from this procedure, that patients 33 years or younger would exhibit greater healing rates and would have a greater functional gain compared with patients older than 33 years.

## Methods

From January 2012 to January 2014, 52 patients underwent arthroscopic osteochondral talar reconstruction. The inclusion criteria were as follows: OCLT type III and IV according to Berndt and Harty's classification,<sup>17</sup> skeletal maturity, and ability to give informed

consent. The exclusion criteria were as follows: previous surgical treatment of the affected ankle, concomitant surgical procedure, arthritis of the ankle joint, kissing lesions, hemophilia, rheumatoid arthritis, severe metabolic disorders, autoimmune disease, ongoing chemotherapy, radiation treatment or immunosuppression, pregnancy, or lactation. Patients satisfying the inclusion and exclusion criteria were divided into 2 groups: patients 33 years or younger and patients older than 33 years. The 33-year cutoff was decided taking into account the existing literature on the topic.<sup>15,18</sup>

The surgical procedures were all performed by the senior author (F.G.U.). All surgical interventions were performed using the AT-AMIC technique previously described.<sup>11</sup> Briefly, surgery was characterized by 2 arthroscopic phases. First, after having achieved an adequate exposure through the use of a Hintermann spreader (Integra LifeSciences, Plainsboro, NJ) that allowed for sufficient joint distraction, the lesion was debrided and prepared to receive the regenerative treatment. Cancellous bone was harvested from the ipsilateral calcaneus with an accessory lateral approach on the calcaneus wall. The cancellous bone was introduced using the same cannula and impacted into the bony defect until complete fill was achieved. The second surgical step was performed in a dry condition, during which Chondro-Gide (Geistlich Surgery, Wolhusen, Switzerland), a porcine collagen type I/III matrix, was placed and fixed with synthetic fibrin glue (Tisseel, Baxter, Baxter) along the lesion edges. The Hintermann spreader was then removed and matrix stability within a normal ankle range of motion was verified.

All clinical assessments were performed by a clinician who was not involved in the treatment. The evaluation included clinical and quality of life parameters. Clinical evaluation consisted of subjective global pain assessment by the visual analog scale (VAS) pain score, whereas the intensity of pain, walking capacity, and activities of daily life were assessed by the American Orthopaedic Foot and Ankle Society Ankle and Hindfoot score (AOFAS) and Short Form-12 in its physical (PCS) and mental component score (MCS).<sup>19-21</sup> All imaging measurements were performed using the standard tools of the institution Picture Archiving and Communication System. The reading of all magnetic resonance imaging (MRI) and computed tomography (CT) scans was blinded and was performed by 2 orthopaedic surgeons (C.M., F.L.) not involved in the surgical procedure. The area of the lesions was defined and measured for each patient on the MRI and CT scan according to Choi et al.<sup>22</sup> using coronal length (horizontal extension measured from the coronal image), sagittal length (horizontal extension measured from the sagittal image), depth (vertical extension measured from the sagittal image), and area (calculated with the ellipse formula as coronal length  $\times$  sagittal length  $\times$  0.79). Each patient in both

groups was evaluated clinically and radiologically preoperatively ( $T_0$ ), as well as at 6 ( $T_1$ ), 12 ( $T_2$ ), and 24 ( $T_3$ ) months. All the evaluations were performed as part of the current study and are registered with an ethical institutional review board.

### Statistical Analysis

The statistical analysis was performed with Matlab statistical toolbox version 2008 (MathWorks, Natick, MA) for Windows at 32 bit, on a sample of 31 patients. Multicomparison tests were performed with the analysis of variance (ANOVA) test for repeated measures into groups (Total Group,  $G_1$ , and  $G_2$ ) and the Bonferroni correction was used in pairwise comparison into groups between 2 consecutive control points, whereas one-way ANOVA was used to test the difference between the means between  $G_1$  and  $G_2$ . In addition, Pearson's linear correlation coefficient  $R$  was calculated and the corresponding  $P$  values were computed with Student's  $t$ -test, under null hypothesis of Pearson's linear correlation coefficient  $R = 0$ . All statistical tests with  $P$  value less than .05 were considered as significant and all measures were expressed as mean  $\pm$  standard deviation.

### Results

The mean follow-up period was 27 months (range: 24–31 months). Of 52 patients screened for eligibility, 31 satisfied the inclusion and exclusion criteria and were enrolled in the study. Of the 21 excluded patients, 8 had already been subjected to interventions to the affected ankle, 5 patients had severe post-traumatic osteoarthritis of the ankle, 2 showed a kissing lesion, 3 had not reached skeletal maturity, 2 women were pregnant, and 1 was hemophilic. Thirty-one patients satisfying the inclusion and exclusion criteria, of whom 41.9% were females and 58.1% were males, aged between 16 and 65 years (mean 35, standard deviation [SD]  $\pm 13$ ). The young patients' group ( $G_1$ ) consisted of 17 patients, of whom 52.9% were females and 47.1% were males, aged between 16 and 33 years (mean 25, SD  $\pm 5$ ). The group of patients older than 33 years ( $G_2$ ) consisted of 14 patients, 28.6% females and 71.4% males, aged between 34 and 65 years (mean 47, SD  $\pm 9$ ). No patients were lost to the final follow-up of 24 months.

### Clinical Results

In both groups, we found a significant difference for AOFAS, VAS, PCS, and MCS with ANOVA for repeated measures through 4 time points ( $P < .001$ ). In particular, in  $G_1$ , AOFAS improved significantly between  $T_0$  and  $T_1$  ( $P = .0251$ ) and  $T_1$  and  $T_2$  ( $P = .0110$ ). In  $G_2$ , we noted a significant improvement for AOFAS between  $T_0$  and  $T_1$  ( $P = .011$ ) and between  $T_2$  and  $T_3$  ( $P = .0176$ ). In  $G_1$ , a significant improvement for VAS, PCS, and MCS was noted between  $T_0$  and  $T_1$  (VAS:  $P = .001$ , PCS:  $P < .0001$ , MCS:  $P < .0001$ ). In

$G_2$ , VAS improved between  $T_0$  and  $T_1$  ( $P = .0006$ ) and between  $T_2$  and  $T_3$  ( $P = .0212$ ), whereas PCS and MCS improved significantly only between  $T_0$  and  $T_1$  (PCS:  $P = .0025$ , MCS:  $P = .0048$ ). Clinical results are reported in Table 1.

### Radiological and MRI Evaluation

Both CT and MRI showed a significant difference with ANOVA for repeated measures through 4 time points ( $P < .001$ ). Particularly in  $G_1$  the size of the lesion measured by CT decreased significantly between  $T_1$  and  $T_2$  ( $P = .0029$ ) and between  $T_2$  and  $T_3$  ( $P < .0001$ ), whereas the lesion measured with MRI reduced significantly at each follow-up. In  $G_2$ , the size of the lesion measured by CT improved significantly between  $T_1$  and  $T_2$  ( $P = .0247$ ), whereas MRI showed a reduction of the lesion between  $T_1$  and  $T_2$  ( $P = .0294$ ) and  $T_2$  and  $T_3$  ( $P = .0062$ ) (Figs 1 and 2). Radiological results are reported in Table 2.

### Effect of Age

$G_1$  showed significantly higher scores on the AOFAS evaluation at  $T_0$  ( $P = .0175$ ),  $T_2$  ( $P = .0356$ ), and  $T_3$  ( $P = .0387$ ) compared with the corresponding follow-up evaluations of  $G_2$ . The Short Form-12 MCS at  $T_0$  was significantly higher in  $G_2$  with respect to  $G_1$  ( $P = .0465$ ). With regard to lesion size, there were no significant differences between the groups as evaluated by MRI and CT scans at each control point. Results are reported in Table 3.

### Correlations

In  $G_1$ , we found a positive linear correlation between the AOFAS and MCS at  $T_0$  ( $R = 0.694$ ). Moreover, the AOFAS evaluation was negatively correlated with VAS at  $T_1$  ( $R = -0.756$ ),  $T_2$  ( $R = -0.637$ ), and  $T_3$  ( $R = -0.728$ ), and positively correlated with PCS at  $T_1$  ( $R = 0.763$ ) and  $T_3$  ( $R = 0.751$ ). In  $G_2$ , the AOFAS were negatively correlated with VAS at  $T_1$  ( $R = -0.702$ ) and positively correlated with PCS at  $T_2$  ( $R = 0.631$ ) and  $T_3$  ( $R = 0.736$ ). Significant linear correlations are reported in Table 4.

### Complications

No complications were reported in both groups.

### Discussion

In our sample of patients, we noted a significant improvement in all clinical parameters over the time period examined. Also the lesion size reduced significantly by the 24-month follow-up. Comparing the 2 groups, we found that young patients had higher AOFAS before surgery and at  $T_2$  and  $T_3$ , showing a better ankle function before the surgical procedure, but also a faster healing. This finding confirms that AT-AMIC can be considered a safe and reliable procedure that allows

**Table 1.** Clinical Results for All Patients, G<sub>1</sub>, and G<sub>2</sub>, Respectively, at T<sub>0</sub>, T<sub>1</sub>, T<sub>2</sub>, and T<sub>3</sub>

Parameters	T <sub>0</sub>	T <sub>1</sub>	T <sub>2</sub>	T <sub>3</sub>	Multicomparison Test
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	P Value
All patients					
AOFAS	53.03 ± 15.60	73.64 ± 16.29	82.77 ± 14.37	88.97 ± 10.78	<.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : .0001 (B*) T <sub>1</sub> vs T <sub>2</sub> : .0069 (B*) T <sub>2</sub> vs T <sub>3</sub> : .0004 (B*) <.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : <.0001 (B*) T <sub>1</sub> vs T <sub>2</sub> : .136 (B) T <sub>2</sub> vs T <sub>3</sub> : .016 (B*) <.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : <.0001 (B*) T <sub>1</sub> vs T <sub>2</sub> : .436 (B) T <sub>2</sub> vs T <sub>3</sub> : .131 (B) <.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : <.0001 (B*) T <sub>1</sub> vs T <sub>2</sub> : 1.00 (B) T <sub>2</sub> vs T <sub>3</sub> : .977 (B)
VAS	7.84 ± 1.37	4.26 ± 2.54	3.13 ± 2.00	1.84 ± 1.46	
PCS	30.35 ± 4.80	44.38 ± 9.04	48.03 ± 8.04	50.57 ± 6.67	
MCS	42.47 ± 4.47	52.35 ± 5.29	51.72 ± 5.51	53.48 ± 6.24	
G <sub>1</sub>					
AOFAS	58.41 ± 15.73	78.06 ± 14.81	87.06 ± 13.11	92.12 ± 10.27	<.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : .0251 (B*) T <sub>1</sub> vs T <sub>2</sub> : .0110 (B*) T <sub>2</sub> vs T <sub>3</sub> : .0593 (B) <.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : .0001 (B*) T <sub>1</sub> vs T <sub>2</sub> : .603 (B) T <sub>2</sub> vs T <sub>3</sub> : .981 (B) <.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : <.0001 (B*) T <sub>1</sub> vs T <sub>2</sub> : 1.00 (B) T <sub>2</sub> vs T <sub>3</sub> : .405 (B) <.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : <.0001 (B*) T <sub>1</sub> vs T <sub>2</sub> : 1.00 (B) T <sub>2</sub> vs T <sub>3</sub> : 1.00 (B)
VAS	7.70 ± 1.48	4.00 ± 2.59	2.88 ± 2.25	2.06 ± 1.66	
PCS	31.02 ± 5.45	46.34 ± 8.83	48.69 ± 8.41	52.18 ± 6.37	
MCS	41.28 ± 5.27	53.02 ± 4.91	51.20 ± 4.85	53.29 ± 5.74	
G <sub>2</sub>					
AOFAS	46.50 ± 12.67	68.29 ± 16.40	77.57 ± 14.12	85.14 ± 10.13	<.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : .011 (B*) T <sub>1</sub> vs T <sub>2</sub> : .491 (B) T <sub>2</sub> vs T <sub>3</sub> : .0176 (B*) <.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : .0006 (B*) T <sub>1</sub> vs T <sub>2</sub> : .812 (B) T <sub>2</sub> vs T <sub>3</sub> : .0212 (B*) <.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : .0025 (B*) T <sub>1</sub> vs T <sub>2</sub> : .461 (B) T <sub>2</sub> vs T <sub>3</sub> : .773 (B) <.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : .0048 (B*) T <sub>1</sub> vs T <sub>2</sub> : 1.00 (B) T <sub>2</sub> vs T <sub>3</sub> : 1.00 (B)
VAS	8.00 ± 1.19	4.57 ± 2.44	3.43 ± 1.59	1.57 ± 1.12	
PCS	29.55 ± 3.72	41.99 ± 8.71	47.21 ± 7.47	48.61 ± 6.50	
MCS	43.91 ± 2.60	51.54 ± 5.61	52.35 ± 6.17	53.70 ± 6.79	

NOTE. Evaluations were performed preoperatively (T<sub>0</sub>) and at 6 (T<sub>1</sub>), 12 (T<sub>2</sub>), and 24 (T<sub>3</sub>) months postoperatively.

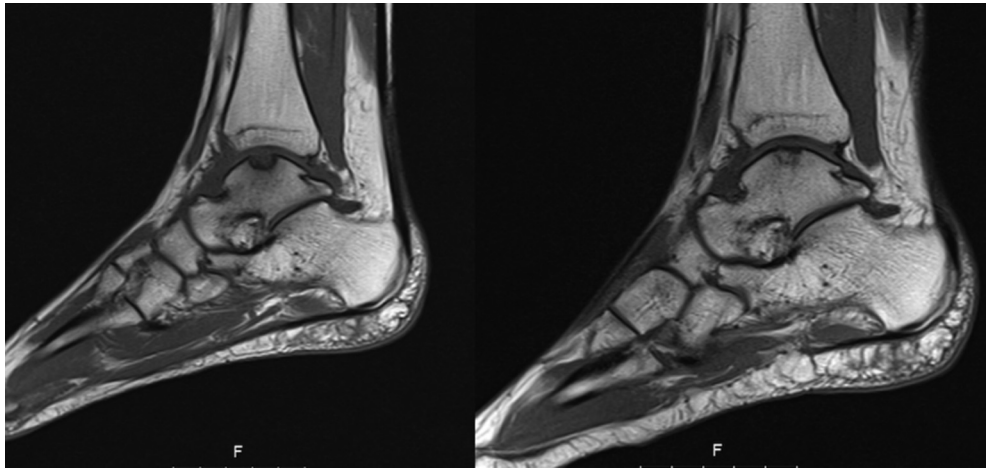
ANOVA, analysis of variance; AOFAS, American Orthopaedic Foot and Ankle Society Ankle and Hindfoot scores; B, Bonferroni corrected; G<sub>1</sub>, patients 33 years or younger; G<sub>2</sub>, patients older than 33 years; MCS, mental component score; PCS, physical component score; SD, standard deviation; VAS, visual analog scale for pain.

\*Significant test.

healing through cartilage repair. It is important, however, to take into consideration, especially for ankle functionality (AOFAS), that the rapid healing may be related to the condition of the ankle at T<sub>0</sub>.

The 33-year cutoff regarding age in the present study was arrived on by taking into account earlier published findings.<sup>15,17</sup> Specifically, Cuttica et al.<sup>15</sup> in their study showed that for patients 33 years of age or





**Fig 1.** Magnetic resonance imaging in a patient (age at surgery 19.6 years) from G<sub>1</sub>. Right ankle, sagittal view. In the image on the left, examination performed at T<sub>0</sub>: osteochondral lesion on the talar dome, extended from anterior to posterior for approximately 11 mm, characterized by full-thickness erosion of the cartilage with depression of the cancellous bone with sclerotic edges. On the right, examination performed at T<sub>3</sub>: evident reduction of the edema of the cancellous bone with good coverage of the osteochondral defect of the medial talar shoulder. (G<sub>1</sub>, group of patients 33 years or younger; T<sub>0</sub>, preoperative; T<sub>3</sub>, 24 months.)

younger, the change in the natural logarithm of the odds of a poor outcome increased 0.067 for each 1-year increase in age, whereas for patients older than 33 years, aging did not predispose patients to poor outcomes.

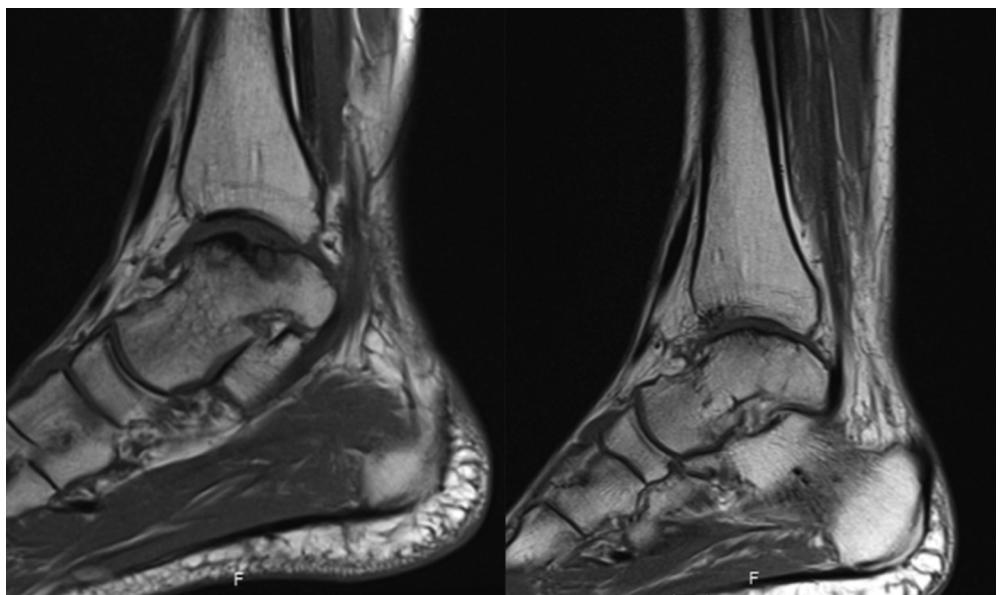
About aging and biomechanics, Menz<sup>23</sup> argues that aging in the ankle is associated with several changes in joint physiology, including a reduction in the water content of the cartilage, the synovial fluid volume, and the proteoglycans. The collagen fibers in the cartilage undergo a crosslinking process, resulting in increased stiffness.<sup>24</sup> These changes may contribute to the

reduced range of motion in lower extremity joints observed in older people, explaining lower magnitude of change between pre- and postoperative AOFAS values as compared with G<sub>1</sub>.

Several studies interestingly have reported a reduced range of motion of approximately 12% to 30% lower in older people.<sup>24,25</sup> This may explain the lower AOFAS in almost all follow-ups in G<sub>2</sub> and the lower preoperative values as compared with G<sub>1</sub>.

It is important to note that the initial area of the lesions was similar in the 2 groups and the reduction of the lesion showed no difference between young and

**Fig 2.** Magnetic resonance imaging in a patient (age at surgery 48.5 yr) from G<sub>2</sub>. Right ankle, sagittal view. In the image on the left, examination performed at T<sub>0</sub>: large osteochondral lesion on the medial shoulder of the talar dome with cystic-dystrophic resorption associated with edema of the cancellous bone. On the right, examination performed at T<sub>3</sub>: good restoration of the articular surface of the talus and minimal edema at the level of the anterior portion of the repair site. (G<sub>2</sub>, group of patients older than 33 years; T<sub>0</sub>, preoperative; T<sub>3</sub>, 24 months.)



**Table 2.** Radiological Results for All the Patients, G<sub>1</sub>, and G<sub>2</sub>, Respectively, at T<sub>0</sub>, T<sub>1</sub>, T<sub>2</sub>, and T<sub>3</sub>

Parameters	T <sub>0</sub>	T <sub>1</sub>	T <sub>2</sub>	T <sub>3</sub>	Multicomparison Test
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	P Value
All patients					
CT, mm <sup>2</sup>	118.28 ± 51.43	107.90 ± 43.98	89.83 ± 38.25	79.17 ± 35.90	<.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : .113 (B) T <sub>1</sub> vs T <sub>2</sub> : <.0001 (B*) T <sub>2</sub> vs T <sub>3</sub> : .0002 (B*) <.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : .0022 (B*) T <sub>1</sub> vs T <sub>2</sub> : <.0001 (B*) T <sub>2</sub> vs T <sub>3</sub> : <.0001 (B*)
MRI, mm <sup>2</sup>	153.65 ± 76.11	127.00 ± 60.51	97.89 ± 53.33	87.36 ± 47.26	
G <sub>1</sub>					
CT, mm <sup>2</sup>	121.14 ± 51.89	104.76 ± 40.32	86.39 ± 33.72	75.29 ± 30.07	<.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : .120 (B) T <sub>1</sub> vs T <sub>2</sub> : .0029 (B*) T <sub>2</sub> vs T <sub>3</sub> : <.0001 (B*) <.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : .0472 (B*) T <sub>1</sub> vs T <sub>2</sub> : .0001 (B*) T <sub>2</sub> vs T <sub>3</sub> : .0009 (B*)
MRI, mm <sup>2</sup>	148.67 ± 63.56	121.20 ± 48.09	90.21 ± 36.67	82.46 ± 36.27	
G <sub>2</sub>					
CT, mm <sup>2</sup>	114.80 ± 50.64	111.71 ± 47.77	94.00 ± 42.75	83.89 ± 41.41	<.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : 1.00 (B) T <sub>1</sub> vs T <sub>2</sub> : .0247 (B*) T <sub>2</sub> vs T <sub>3</sub> : .255 (B) <.001 (ANOVA test) T <sub>0</sub> vs T <sub>1</sub> : .150 (B) T <sub>1</sub> vs T <sub>2</sub> : .0294 (B*) T <sub>2</sub> vs T <sub>3</sub> : .0062 (B*)
MRI, mm <sup>2</sup>	159.70 ± 88.63	134.04 ± 72.17	107.21 ± 67.13	93.31 ± 57.30	

NOTE. Evaluations were performed preoperatively (T<sub>0</sub>) and at 6 (T<sub>1</sub>), 12 (T<sub>2</sub>), and 24 (T<sub>3</sub>) months postoperatively.

ANOVA, analysis of variance; B, Bonferroni corrected; CT, computed tomography; G<sub>1</sub>, patients 33 years or younger; G<sub>2</sub>, patients older than 33 years; MRI, magnetic resonance imaging; SD, standard deviation.

\*Significant test.

elderly patients, confirming the effectiveness of our technique that promotes rapid and similar healing independent of age.

It is also interesting to note that the AOFAS in young patients correlates linearly with the mental state (MCS), in contrast to older patients where we did not observe this correlation. Moreover, at the final follow-up, we noted a correlation between the AOFAS and the

physical health of patients, which shows that the ankle affects both the mental and physical states.

Presently, there is no consensus among peer-reviewed publications on what might be considered a cutoff age

**Table 3.** Clinical and Radiological Comparison Between G<sub>1</sub> and G<sub>2</sub>, Respectively, at T<sub>0</sub>, T<sub>1</sub>, T<sub>2</sub>, and T<sub>3</sub>

	G <sub>1</sub> vs G <sub>2</sub> (P Value)					
	AOFAS	VAS	PCS	MCS	CT, mm <sup>2</sup>	MRI, mm <sup>2</sup>
T <sub>0</sub>	.0175*	.284	.207	.0465*	.371	.350
T <sub>1</sub>	.051	.274	.097	.227	.337	.286
T <sub>2</sub>	.0356*	.232	.312	.289	.298	.211
T <sub>3</sub>	.0387*	.186	.074	.431	.261	.270

NOTE. Evaluations were performed preoperatively (T<sub>0</sub>) and at 6 (T<sub>1</sub>), 12 (T<sub>2</sub>), and 24 (T<sub>3</sub>) months postoperatively.

AOFAS, American Orthopaedic Foot and Ankle Society Ankle and Hindfoot scores; CT, computed tomography; G<sub>1</sub>, patients 33 years or younger; G<sub>2</sub>, patients older than 33 years; MCS, mental component score; MRI, magnetic resonance imaging; PCS, physical component score; VAS, visual analog scale for pain.

\*Significant test.

**Table 4.** Univariate Correlation Analysis: Significant Linear Correlations Among Clinical Parameters in G<sub>1</sub> and G<sub>2</sub>

Linear Correlations Into Groups	Pearson's Linear Correlation Coefficient (R)	P Value
G <sub>1</sub>		
AOFAS/MCS at T <sub>0</sub>	0.694	.0020
AOFAS/VAS at T <sub>1</sub>	−0.756	4.42 × 10 <sup>−4</sup>
AOFAS/PCS at T <sub>1</sub>	0.763	3.62 × 10 <sup>−4</sup>
AOFAS/VAS at T <sub>2</sub>	−0.637	.00596
AOFAS/VAS at T <sub>3</sub>	−0.728	9.32 × 10 <sup>−4</sup>
AOFAS/PCS at T <sub>3</sub>	0.751	5.12 × 10 <sup>−4</sup>
G <sub>2</sub>		
AOFAS/VAS at T <sub>1</sub>	−0.702	.0052
AOFAS/PCS at T <sub>2</sub>	0.631	.0154
AOFAS/PCS at T <sub>3</sub>	0.736	.0027

NOTE. Evaluations were performed preoperatively (T<sub>0</sub>) and at 6 (T<sub>1</sub>), 12 (T<sub>2</sub>), and 24 (T<sub>3</sub>) months postoperatively.

AOFAS, American Orthopaedic Foot and Ankle Society Ankle and Hindfoot scores; G<sub>1</sub>, patients 33 years or younger; G<sub>2</sub>, patients older than 33 years; MCS, mental component score; PCS, physical component score; VAS, visual analog scale for pain.

for repairing osteochondral talar lesions, and the aim of this study is to evaluate the age-dependent outcome after reconstruction with the AT-AMIC technique. Conversely, Deol et al.<sup>8</sup> found that age is one of the major factors that can influence the success of treatment for osteochondral lesions of the talus. In fact, several studies have shown that the chondrogenic potential of both chondrocytes and chondrogenic stem cells declines with aging in animal and human models. In patients treated for osteochondral lesions of the knee, youth has been associated with improved outcomes. Supporting this, Chuckpaiwong et al.<sup>12</sup> in their sample of 105 patients evaluated which factors might be considered predictors for success in arthroscopic debridement with osteochondral bone stimulation for OCLTs. After a mean follow-up of  $31.6 \pm 12.1$  months, they noted that increasing age negatively affected the success of this kind of surgery without specifying if it is possible to determine an ideal age for surgery. Ferkel et al.<sup>18</sup> retrospectively evaluated a total of 64 patients who underwent arthroscopic treatment for OCLTs with a cutoff age of 32 years and showed that the older age group had an AOFAS of 80, whereas the younger group had a score of 88 with no significant differences among the 2 groups.

The finding is similar to previously reported data by Deol et al.<sup>8</sup> in which all patients treated for an OCLT with marrow stimulation who were younger than 20 years had a good or excellent outcome. Deol et al.<sup>8</sup> ascribe this satisfying result to the rich microvascular supply within the subchondral zone in patients with open physes and in those recently achieving skeletal maturity.

Lee et al.<sup>13</sup> in 2010 evaluated a total of 38 patients who had ACI treatment for OCLTs and underwent a second look arthroscopy 1 year after the ACI operation. Patients were evaluated with a modified magnetic resonance observation of cartilage repair tissue scoring system to assess the outcome of the repaired cartilage. Factors that may affect cartilage repair after ACI treatment for OCLTs were evaluated. Of the different factors assessed, the authors noted how the size of the lesion and the patient's age were negative predictive outcomes.

In 2012, Choi et al.<sup>16</sup> first addressed the issue of the feasibility of arthroscopic surgery in older patients, usually by choosing an arbitrary age limit. Hypothesizing that patient age is not associated with poor clinical outcome after arthroscopic surgery for OCLTs, and other patient variables are the major determinants of clinical success and/or failure, 173 ankles underwent arthroscopic marrow stimulation treatment for OCLTs and were stratified into 6 age groups (20, 20-29, 30-39, 40-49, 50-59, and 60 years) to determine the effect of age on clinical outcome. No significant differences were found among the 6 age groups in the preoperative and postoperative VAS and AOFAS. There was a significant increase in the duration of symptoms and a significant

decrease in the incidence of trauma in the older group. The authors, in contrast to some of the previous studies on this topic, concluded that increased age was not an independent risk factor for poor clinical outcome after arthroscopic treatment for OCLTs.

Recently, Polat et al.<sup>26</sup> assessed the long-term clinical and radiographic outcomes of arthroscopic debridement and microfracture for osteochondral lesions of the talus in 82 patients with a minimum 5-year follow-up. The mean age of the patients was 35.9 years and they presented a mean defect size of  $1.7 \text{ cm}^2$ . The mean preoperative AOFAS was 58.7, and the mean postoperative AOFAS improved to 85.5. At the last follow-up, 35 patients had no symptoms and 19 patients had pain after walking more than 2 hours or after competitive sports activities. The authors concluded that arthroscopic debridement and microfracture provide a good option for the treatment of osteochondral lesions of the talus and mostly functional outcomes do not correlate with defect size or patient age. The study confirms that microfractures can be considered the gold standard for the small lesions ( $<1.5 \text{ cm}^2$ ), but we believe that the advantage of the AT-AMIC technique is linked to the fact of combining the functional principle of microfracturing, based on the release of multipotent mesenchymal progenitor cells, cytokines, and growth factors from the subchondral bone, with a suitable scaffold that enhances the chondrogenic differentiation of mesenchymal stem cells, and in combination with fibrin glue, stimulates chondrocytes to enhance proteoglycan deposition.<sup>27</sup> In this way, the clot formed as a result of hemorrhage is covered and hence stabilized. The matrix that covers the clot is composed of collagen type I and III that is the main structural protein of connective tissue and an important component of articular cartilage forming a unique bilayer matrix with a compact and a porous side. Further studies with longer follow-up will confirm the advantages linked to the technique also on larger sized lesions, exploiting the principle of microfractures.

### Limitations

The limitations of our study include the relatively small number of patients who did not allow for subpopulation analysis. Another limitation is represented by the lack of modified magnetic resonance observation of cartilage repair tissue assessment of the repair tissue, which could have given useful information about tissue quality in the 2 groups. Nonetheless, the combination of MRI and CT information provided a good evaluation of the neocartilage and subchondral bone after the AT-AMIC surgical procedure.

### Conclusions

The study revealed that osteochondral lesions of the talus were characterized by similar sizes and features, both

in young and old patients. We conclude that AT-AMIC can be considered a safe and reliable procedure that allows effective healing, regardless of age, with a significant clinical improvement; in particular, clinical results are related to starting conditions of the ankle.

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