Foot and Ankle Surgery xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Foot and Ankle Surgery

journal homepage: www.journals.elsevier.com/foot-and-ankle-surgery

Autologous matrix induced chondrogenesis plus peripheral blood concentrate (AMIC+PBC) in chondral lesions of the ankle as part of a complex surgical approach – 7-year follow-up

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ARTICLE INFO

Article history:
Received 22 December 2024
Received in revised form 11 February 2025
Accepted 14 February 2025

Keywords:
Chondral lesion
Autologous Matrix Induced Chondrogenesis (AMIC)
Peripheral Blood Concentrate (PBC)
Ankle

ABSTRACT

Background: The aim of the study was to assess 7-year-follow-up (7FU) after Autologous Matrix Induced Chondrogenesis plus Peripheral Blood Concentrate (AMIC+PBC) in chondral lesions at the ankle as part of a complex surgical approach.

Methods: In a prospective consecutive non-controlled clinical follow-up study, all patients with chondral lesion at the ankle treated with AMIC+PBC from July 17, 2016 to May 31, 2017 were included. Size and location of the chondral lesions, the Visual-Analogue-Scale Foot and Ankle (VAS FA) and the EFAS Score before treatment and at 5FU were analysed and compared with previous 2-year-follow-up (2FU). Peripheral Blood Concentrate (PBC) was used to impregnate a collagen I/III matrix (Chondro-Gide, Wolhusen, Switzerland) that was fixed into the chondral lesion with fibrin glue.

Results: One hundred and twenty-nine patients with 136 chondral lesions were included in in the study. The chondral lesions were located as follows (n (%)), medial talar shoulder only, 62 (46); lateral talar shoulder only, 42 (31); medial and lateral talar shoulder, 7 (10); tibia, 18 (13). The average for lesion size was 1.8 cm^2, for VAS FA 45.7 and for EFAS Score 9.8. 2FU/5FU/7FU was completed in 105 (81 %)/104(81 %)/103(80 %) patients with 112/111/109 previous chondral lesions. VAS FA improved to 79.8/84.2/82.9 and EFAS Score to 20.3/21.5/20.8 (2FU/5FU). No parameter significantly differed 2FU/5FU/7FU.

Conclusions: AMIC+PBC combined with adjunctive procedures resulted in improved and high validated outcome scores, after 7 years, without deterioration in comparison to results after 2 and 5 years. No method related complications were recorded.

1. Introduction

Autologous Matrix Induced Chondrogenesis plus Peripheral Blood Concentrate (AMIC+PBC) in chondral lesions at the ankle as part of a complex surgical approach led to improved and high validated outcome scores at 2- and 5-year follow-up[1,2]. No method related complications were registered[1,2]. Longer follow-up was considered to be important[2]. Therefore, the initial study cohort was followed until 7-year follow-up (7FU). The aim of this study was to assess the 7FU of AMIC+PBC and comparison with earlier 2FU and 5 FU.

2. Material and methods[1]

In a prospective consecutive non-controlled clinical follow-up study, all patients with chondral lesion at the ankle that were treated with AMIC+PBC from July 17, 2016 to May 31, 2017 were included.

2.1. Inclusion criteria[1]

The only inclusion criterion was AMIC+PBC at the ankle. 141 patients were eligible for inclusion.

2.2. Exclusion criteria[1]

Exclusion criteria were bilateral treatment (n = 3 patients (2 %)) and AMIC+PBC at more than one joint surface, i.e. talus and tibia (n = 9 patients (6 %)). Patients undergoing revision procedures were not included.

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https://doi.org/10.1016/j.fas.2025.02.011

2.3. AMIC+PCB indication and techniques[1]

The indication for surgery as such with potential inclusion of AMIC+PBC was based on clinical symptoms as for example pain or instability and MRI-findings[1,3]. The definite indication for AMIC+PBC during the surgery was subjectively made by the surgeon during initial arthroscopy for unstable, fragmented or missing cartilage[1,4]. The other procedures included joint preserving measures such as synovectomy, lateral ligament reconstruction, peroneal tendon debridement/tenolysis, Gastrocnemius tendon lengthening and others[1,5,6]. The AMIC+PBC procedure was performed through a medial approach for medial chondral lesions and through a lateral approach for lateral or central lesions (Figs. 1a-1c)[1]. Malleolar osteotomies were performed when necessary to adequately reach the chondral lesion[7]. Medial malleolar and anterior tibial osteotomies were performed as single oblique saw cut[7]. Lateral malleolar osteotomies were performed as anterior window cut with the anterior syndesmotic ligament attached to the cut-out fragment and the central and posterior syndesmotic ligaments attached to the remaining main fragment[7]. The osteotomized fragments were later fixed with lag screws[7]. The chondral lesions were debrided to healthy cartilage margins. Subchondral cysts (MRI-stage 5, Hepple

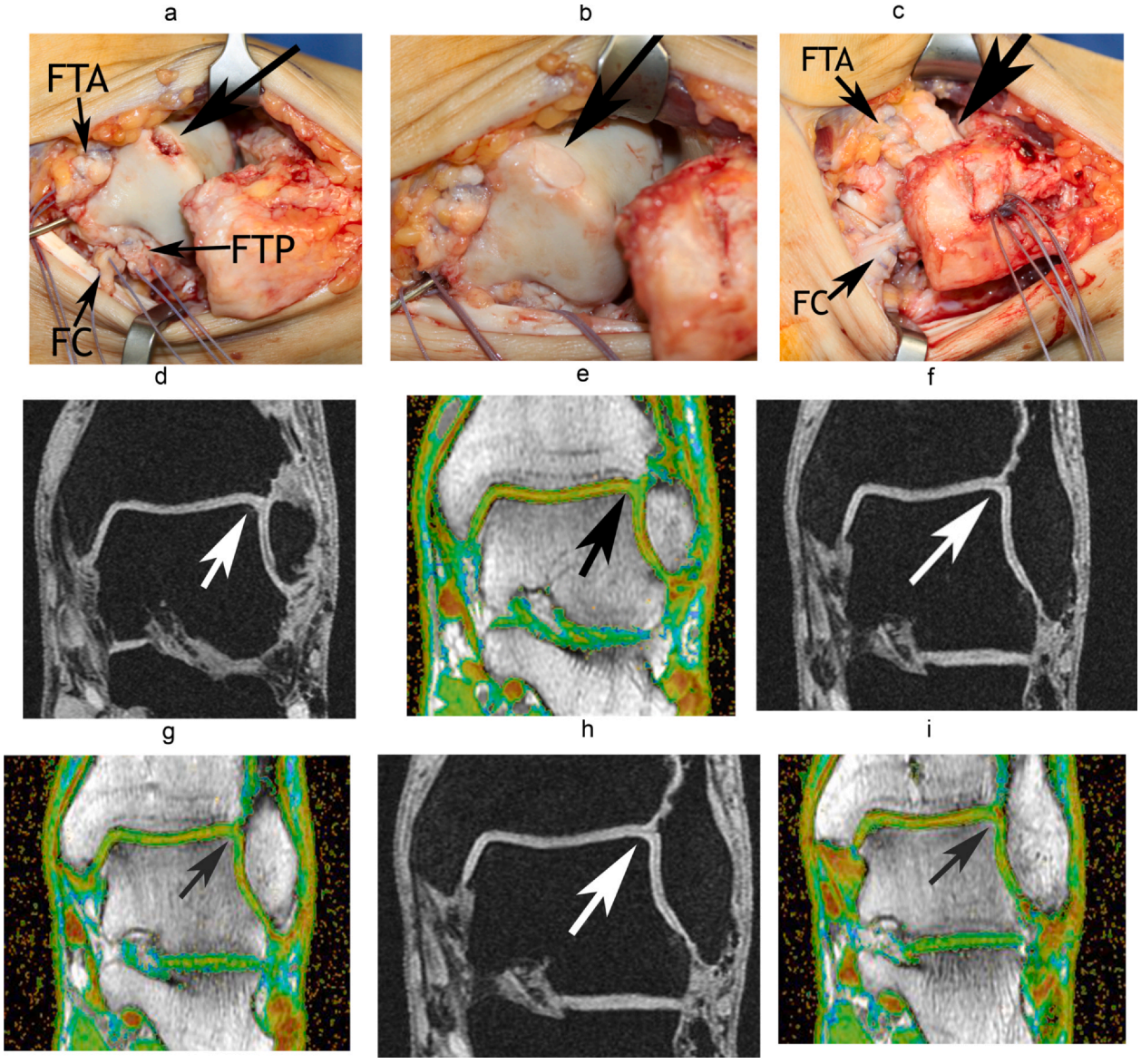

Fig. 1. a - i. AMIC+PBC at left lateral talar shoulder in a 43-year-old male patient[1,2]. The VAS FA/EFAS Score preoperatively was 52.6/12.6. Fig. 1a shows the chondral lesion (large black arrow). The size of the lesion was 1.4 × 1.8 cm (2.5 cm^2), and the maximal depth 0.8 cm. All three lateral ligaments (Fibulocalcaneal (FC), anterior and posterior tibiotalar (FTA and FTP) were elongated and partly dystopic. The ligaments were detached from the fibula, dystopic parts were debrided and remaining ligaments were sheathed with a suture (Orthocord, DepuySynthes, Raynham, MA, USA). A 2.0 mm Kirschner wire was inserted in the talus as joystick. Figure 2b shows the chondral lesion after AMIC+PBC (large black arrow) including autologous cancellous bone transplantation into the subchondral bone lesion, harvested from the distal tibia. Fig. 1c shows the situs after reinsertion of the lateral ligaments. 4.5 mm drill holes were drilled from the origins of the three ligaments (FTA, FC, FTP) towards proximal and lateral. The sheathed ligaments were pulled into these holes, and the sutures were knot at the proximal end of the holes. The patient completed follow-up at 24.2/60.3/86.1 months. The VAS FA/EFAS Score was 89.6/22.1 at 2FU, 90.1/22.5 at 5FU and 88.5/21.1 at 7FU. Fig. 1d shows a coronal MRI reformation of "Cartilage-mapping" T2 specification with 0.4 mm slice thickness at 2FU. At the lateral talar shoulder (arrow, location of earlier chondral lesion), the cartilage is clearly visible as well as the minimal joint gap between the tibial and talar cartilage despite minimal irregular surface of the subchondral bone. No subchondral bone oedema is visible (MRI-stage for chondral or osteochondral lesion negative)[3]. Fig. 1e shows a colour coded visualization of the cartilage at 2FU. At the lateral talar shoulder (arrow, location of earlier chondral lesion), the fluid percentage/content is not increased (green colour). An increased fluid percentage/content would be a sign for chondral damage which often precedes morphologically visible damage[1,7]. Fig. 1 f - g show MRI images at 5FU and Fig. 1 h - i at 7FU with similar technical specifications, interpretation and scoring as 2FU.

and Winson / Bristol classification) were cleared out[3,7]. Microfracturing with a 1.6 mm Kirschner wire was performed at intact subchondral bone, and at the ground and walls of subchondral bone defects[7]. Bone defects of more than 3 mm depth (cysts and others) were filled with autologous cancellous bone harvested from the distal tibia not exceeding the surrounding subchondral bone level. 15 cc peripheral venous blood was harvested with a special syringe (Arthrex-ACP, Arthrex, Naples, FL, USA)[7]. The syringe was centrifuged (10 minutes, 1500 rotations per minute)[1]. After centrifugation, the supernatant was aspirated including the entire fluid layer directly above the erythrocyte layer[7]. PBC is a modification of Platelet Rich Plasma (PRP) and Autologous Conditioned Plasma (ACP) [1,8–10]. PRP is also specified by addition of an anticoagulant, such as citrate dextrose A to prevent platelet activation prior to its use [1,10]. This addition is not included in PBC by definition[1]. The difference of PBC to ACP is that for PBC the aspirated supernatant (after centrifugation) included the entire fluid layer directly above the erythrocyte layer, whereas ACP includes the only the clear fluid above[1,8]. The supernatant was used to impregnate a collagen I/III matrix (Chondro-Gide, Geistlich, Wolhusen, Switzerland) by submerging the matrix completely into the supernatant for 3 minutes (impregnation)[1]. The matrix was cut to the size of the cartilage lesion roughly before and more exact after the impregnation[1]. The impregnated matrix was fixed into the chondral lesion with fibrin glue (Tissucoll or Tisseel, Baxter, Deerfield, IL, USA) (Fig. 1b)[1]. The matrix fixation was tested by moving the joint several times[1]. Adequate fixation was approved when the matrix stayed in place in the chondral lesion[1]. Closure was performed following the local standard with layer wise closure (joint capsule, subcutaneous, skin) [1]. The postoperative treatment included partial weight bearing with 15 kg with orthosis (Vacuped, Oped, Valley, Germany) for six weeks[1]. Motion of the joint was restricted for two days, and joint motion in the orthosis, i.e. approximately 10° range of motion, was started at day three after surgery[1]. Postoperative consultations were performed at 6 weeks, 3 months and then yearly[1].

2.4. Follow-up

Follow-up (FU) periods of 2years (2FU), 5 years (5FU) and 7 years (7FU), were performed between 22 and 26 months, 56–64 months and 80–88 months, respectively.

2.5. Assessment[1]

Before surgery and at follow-ups except at 3 months, radiographs (bilateral views (anteroposterior/Mortise and lateral with full weight bearing) or Weightbearing Computed Tomography (WBCT) scans were obtained. Magnetic resonance imaging (MRI) was obtained before surgery and at yearly follow-ups with so-called "Cartilage-mapping" with slice thickness of 0.4 mm was obtained, and Hepple and Winson / Bristol classification used (Figs. 1d - 1i)[3,11]. Visual Analogue Scale Foot and Ankle (VAS FA) and EFAS Score were registered[12,13]. The EFAS Score was available at the authors´ institution before official publication because the institution was included in the development and validation of the score[13]. The defect size and location were assessed intraoperatively. Complications and treatment failure were registered.

2.6. Statistical analysis

The data was analysed with SPSS software (IBM SPSS Statistics 25, IBM, Armonk, NY, USA). An unpaired *t*-test was used for statistical comparison of VAS FA and EFAS Score preoperatively and at follow-ups. Before using the paired *t*-test, the data were investigated regarding the distribution and the data were proven to be normally distributed. Chi2-test was used to compare the different MRI stages and ONEWAY-ANOVA (potential Scheffe Post Hoc test) was used to analyse differences of the follow-up scores for different lesion location, size (lesion size ≤2 cm or >2 cm) and MRI-stage. The significance level was defined as $p < 0.05$. A power analysis that was carried out before each specific statistical justified sufficient power (>0.8).

Table 1
Demographic parameter, preoperative VAS FA, EFAS Score, cause and suspected mechanism of chondral lesions (patient-based analysis, i.e. 129 patients in total for each group)[1,2].

Age (average, range)	35.6 (13–68)
Gender (male; n (%))	77 (60)
VAS FA (mean, range)	45.7 (17.5–78.9)
EFAS Score (mean, range)	9.8 (0–20)
Cause (n (%))	
Traffic accident	5 (4)
Sports-related trauma	62 (48)
Non-vehicular / sports-related trauma	43 (33)
Deformity without trauma	7 (5)
Hindfoot/ankle varus	4 (3)
Hindfoot/ankle valgus	3 (2)
Other	5 (4)
Unknown	5 (4)
Mechanism (n (%))	
Fracture	7 (5)
Single sprain	21 (16)
Multiple sprains	70 (54)
Other	3 (2)
Unknown	28 (22)

3. Results

3.1. Patients[1]

One hundred and twenty-nine patients with 136 chondral lesions were included in the study. Table 1 shows the demographic parameter, preoperative VAS FA, EFAS Score and suspected cause and mechanism of the chondral lesions.

3.2. Chondral lesions[1]

The chondral lesions were located as follows (n (%)), medial talar shoulder only, 62 (46); lateral talar shoulder only, 42 (31); medial and lateral talar shoulder, 7 (10) (7 lesions medial plus 7 lesions lateral = 14 lesions, i.e. 10 % of all lesions); tibia, 18 (13). The lesion size was 1.8 cm^2 on average (range, 0.6–4cm^2). Table 2 shows the MRI-stage of the lesions. Most common stages were 1 (cartilage lesion only) in 54 lesions (42 %).

Table 2
MRI based classification of 129 patients with 136 chondral lesions preoperatively and at 2FU/5FU/7FU[1,2].

Stage and stage description		Preop	2FU	5FU	7FU
		n (%)	n (%)	n (%)	n (%)
1	cartilage lesion only	54 (40)	40 (36)	42 (38)	41 (38)
2a	subchondral fracture with surrounding bone edema	43 (32)	19 (17)	16 (14)	16 (15)
2b	subchondral fracture with no surrounding bone edema	9 (7)	1 (1)	2 (2)	2 (2)
3	detached but undisplaced fragment	7 (5)	3 (3)	2 (2)	2 (2)
4	displaced fragment	7 (5)	1 (1)	2 (2)	2 (2)
5	subchondral cyst	16 (12)	6 (5)	6 (5)	5 (5)
	MRI-stage for chondral or osteochondral lesion negative	0 (0)	42 (38)	41 (39)	41 (38)

Preop, preoperatively; 2FU/5FU/7FU, 2-/5-/7-year follow-up
Lesion-based analysis, preop, n = 136; 2FU, n = 112; 5FU, n = 111; 7FU, n = 109.
Distribution preop versus 2FU/5FU/7FU; Chi2, $p < 0.01$.
Distribution 7FU versus 5FU Chi2, p = 0.88. Distribution 7FU versus 2FU Chi2, p = 0.78.

Table 3
Additional procedures performed during surgery[1,2].

Procedure	n (%)
Arthroscopy	129 (100)
Synovectomy	129 (100)
Debridement / tenolysis peroneal tendons	128 (99)
Lateral ligament reconstruction / augmentation	128 (99)
Gastrocnemius tendon lengthening	120 (93)
Medial malleolus osteotomy	17 (13)
Lateral malleolus osteotomy	1 (1)
Anterior tibial osteotomy	1 (1)
Autologous cancellous bone transplantation (under MAST)	34 (26)
Correction of malalignment	3 (2)
Correction above ankle	0 (0)
Correction below ankle	3 (2)

Patient-based analysis

3.3. Additional surgical procedures[1]

Table 3 shows the additional surgical procedures. Synovectomy was performed in all cases, lateral ligament reconstruction in 99 % and Gastrocnemius tendon lengthening in 93 %.

3.4. Complications / revisions

No complications (Neuropraxia, stiffness, wound healing delay, thrombosis, infection) were registered until latest follow-up. Three patients (2 %) underwent another joint preserving ankle surgery after 8, 13 and 16 months including another AMIC+PBC procedure. Each patient reported subsequent ankle sprains during sports activity before the second surgery. These 3 patients completed follow-up.

3.5. Follow-up

2FU/5FU/7FU was completed in 105 (81 %)/104(81 %)/103(80 %) patients with 112/111/109 previous chondral lesions after 23.8/60.2/84.1 months on average (range 22–25/55–63/81–87 months).

VAS FA improved to 79.8/84.2/82.9 and EFAS Score to 20.3/21.5/20.8 (2FU/5FU/7FU). Both scores differed between 2FU/5FU/7FU and preoperative (*t*-test, each $p < 0.05$). Both scores did not differ between 2FU, 5FU and 7FU (*t*-test, each $p > 0.6$)

The MRI stage improved between preoperative and 2FU/5FU/7FU (Table 2; Chi2, each $p < 0.01$), and did not differ between 2FU, 5FU and 7FU (Table 2, Chi2, $p = 0.88/0.78$)

In 42/41/41 of the previous lesion locations (38 %/39 %/40 %)(2FU/5FU/7FU), no lesion was visible in the MRI at follow-up (MRI-stage for chondral or osteochondral lesion negative)[3]. Different lesion location (medial/lateral talar shoulder, tibia), lesion size (≤2 cm or > 2 cm) or MRI-stage did not lead to different VAS FA or EFAS Score at follow-ups (ONEWAY-ANOVA, all $p > 0.05$, Post Hoc-test not applicable). Highest scores were registered in lesions located at the tibia, size ≤ 2 cm, and MRI-stage 1. The three patients with second surgery before follow-ups did not differ significantly regarding VAS FA / EFAS Score or other parameter from the remaining patients (data not shown).

4. Discussion

This is the first study analysing 7FU after AMIC+PBC in chondral defects of the ankle. An ongoing prospective data acquisition of all surgically treated patients including yearly follow-up at the authors´ institution is the basis for this ongoing analysis[1,2]. AMIC+PBC as part of a complex surgical approach allow for stable and favourable results after 2FU until 7FU. Still, No AMIC+PBC related adverse effects have been registered. The comparison with earlier published 5FU of MAST, confirms equivalency of MAST and AMIC+PBC over five years[7]. However, no 7FU of MAST has been published for comparison. The main difference of both procedures, i.e. using bone marrow aspirate concentrate (BMAC) or PBC has no influence on 2FU/5FU and probably also 7FU[1,2,7]. Consequently, the use of BMAC and PBC as adjunct might not have an effect on the tissue development and/or the clinical outcome[1,2,7]. AMIC alone (without BMAC or PBC) has been frequently used and numerous follow-up results have been published since our last publication for comparison[2,14–33]. From the different studies with up to 127 patients and up to 10-year follow-up, 2 studies included a validated outcome score for the ankle as our study[1,2,18,30]. For Magnetic Resonance Observation or Cartilage Repair Tissue (MOCART) score was exclusively used for MRI scoring in 5 other studies [19,21,22,25,28,34]. As discussed before, the MOCART score is not adequate for the ankle with cartilage thickness of 2 mm[2,35]. When facing the fact that typically a resolution of 3 mm is used for MRI and assessing cartilage thickness of 2 mm, we doubt that assessments like "cartilage interface" "demarcations border visible" or "defect visible" < 50 % or > 50 %, or "surface intact" or "damaged" < 50 % or > 59 % depth[2,35]. Finally, there is no score available for "cartilage interface" "defect visible" 50 % or "surface damaged" 50 % depth [2,35]. Therefore, we used the Hepple and Winson/Bristol score system which is focused on the subchondral bone in combination with MRI resolution of 04 mm[2,35]. Our study includes more cases than all other current studies[14–33]. Our results are best comparable with the results of the studies published by Gottschalk et al., Deiss et al. and Usuelli et al.[30,32,33,36]. Additional procedures such as corrective osteotomies, ligament reconstruction or Gastrocnemius tendon lengthening were less frequent or not performed in other studies[14–33]. Either, these pathologies were not present or were not registered[1,2]. The same is true for Gastrocnemius tendon lengthening which is not reported in any other study [1,7,37]. In our understanding deformity and above all instability is the most important and common prerequisite for chondral lesions at the ankle (see further below)[1,2]. As reported before, we observed a high percentage of lesions limited to the cartilage as before[1,2,7,37]. We still could not detect follow-up score differences between different location, size or MRI-stage of the chondral lesions, as reported before [1,2,7,37]. We observed only a trend and no significance to higher follow-up scores towards smaller lesions, located at tibia and lower MRI-stages[1,2,7,37]. The follow-up scores after MRI-stage V (subchondral cyst) were not the lowest as shown in other studies [1,3,7,17,37–40]. AMIC+PBC worked also for larger lesions and "higher" MRI-stages until 7FU[1,2,37]. The follow-up parameters did not significantly differ between 2FU, 5FU and 7FU including patient reported outcome measures (VAS FA / EFAS Score) and MRI stage of the chondral lesions (Tables 2 and 3)[1,2]. We conclude that the results are favourably stable between 2FU and 7FU.

4.1. Limitations

Limitations of the study are as reported before: incomplete follow-up, subjective indication for treatment, potential influence of associated procedures, missing control group, missing outcome parameter for the created cartilage, and using matched patient instead of a "real" control group[1,2]. 80 % of patients completed 7FU which is comparable to other clinical studies and is deemed satisfactory[1,2]. One patient that completed 2FU did not complete 5FU/7FU and one that did complete 5FU did not complete 7FU. The indication for AMIC+PBC was subjectively made by the surgeon during initial arthroscopy[1,2,7,37]. This is the typical decision-making process also in other studies that can be considered subjective[1,2,7,37]. Subjective "surgical" decision-making is considered to be superior to indication based on any kind of imaging-based staging with the described limitations[1,2,7,37]. The indication for AMIC+PBC was not similar to the indication for surgery as such which was based on clinical symptoms and radiographic findings[1,2,7,37]. The simultaneous

additional procedures may confound the results as in all other studies (Table 3)[1,2,18,19,21,25,27–30,32,33,37,38,41]. The additional procedures were considered to be necessary to restore joint function (for example lateral ligament reconstruction in 99 % or Gastrocnemius tendon lengthening in 93 %[1,2]. Other procedures were performed on a regular basis (for example synovectomy in 100 %)[1,2]. The percentage of Gastrocnemius lengthening is high and even increasing in comparison with earlier studies[1,2,7,37]. The indication for gastrocnemius lengthening is not clearly defined and debatable[1,2,7,37]. Studies have shown that decreased joint load after lengthening of shortened Gastrocnemius tendon is beneficial despite potentially decrease calf muscle strength [1,2,7,18,19,21,25,27–30,32,33,37]. In our experience isolated chondral lesions are extremely uncommon, additional pathologies co-exist and additional procedures are required[1,2,7]. This is reflected in our practice [1,2,7]. Thus, it is practically impossible to isolate the effect of the AMIC+PBC procedure, for the purposes of analysis of the results of treatment of cartilage lesions, which are usually associated with instability and/or joint stiffness[1,2,7].

In conclusion, AMIC+PBC combined with adjunctive procedures combined with adjunctive procedures resulted in improved and high validated outcome scores, after 7 years, without deterioration in comparison to results after 2 and 5 years. No method related complications were recorded.

Declaration of Competing Interest

Regarding the manuscript **Matrix Induced Chondrogenesis plus Peripheral Blood Concentrate (AMIC+PBC) in Chondral Lesions at the Ankle as Part of a Complex Surgical Approach - 7-Year Follow-up**, I state that none of the authors or the authors´ institution received funding in relation to this study. I am consultant of Curvebeam AI, Geistlich, Intercus and Implants International, shareholder of Curvebeam AI and proprietor of R-Innovation.

References

[1] Richter M, Zech S, Meissner S, Naef I. Comparison Matrix-Associated Stem Cell Transplantation (MAST) with Autologous Matrix Induced Chondrogenesis plus Peripheral Blood Concentrate (AMIC+PBC) in chondral lesions at the ankle-A clinical matched-patient analysis. Foot Ankle Surg 2020;26(6):669–75.
[2] Richter M, Zech S, Meissner S, Naef I. Autologous matrix induced chondrogenesis plus peripheral blood concentrate (AMIC+PBC) in chondral lesions at the ankle as part of a complex surgical approach - 5-year follow-up. Foot Ankle Surg 2022;28(8):1321–6.
[3] Hepple S, Winson IG, Glew D. Osteochondral lesions of the talus: a revised classification. Foot Ankle Int 1999;20(12):789–93.
[4] Richter M, Zech S. Matrix-associated stem cell transplantation (MAST) in chondral defects of foot and ankle is effective. Foot Ankle Surg 2013;19(2):84–90.
[5] Strayer LM. Recession of the gastrocnemius; an operation to relieve spastic contracture of the calf muscles. J Bone Jt Surg Am 1950;32-A(3):671–6.
[6] Pinney SJ, Sangeorzan BJ, Hansen Jr. ST. Surgical anatomy of the gastrocnemius recession (Strayer procedure). Foot Ankle Int 2004;25(4):247–50.
[7] Richter M, Zech S. Matrix-associated stem cell transplantation (MAST) in chondral lesions at the ankle as part of a complex surgical approach- 5-year-follow-up in 100 patients. Foot Ankle Surg 2019;25(3):264–71.
[8] Smith PA. Intra-articular Autologous Conditioned Plasma Injections Provide Safe and Efficacious Treatment for Knee Osteoarthritis: An FDA-Sanctioned, Randomized, Double-blind, Placebo-controlled Clinical Trial. Am J Sports Med 2016;44(4):884–91.
[9] Mei-Dan O, Carmont MR, Laver L, Mann G, Maffulli N, Nyska M. Platelet-rich plasma or hyaluronate in the management of osteochondral lesions of the talus. Am J Sports Med 2012;40(3):534–41.
[10] Dhurat R, Sukesh M. Principles and Methods of Preparation of Platelet-Rich Plasma: A Review and Author's Perspective. J Cutan aesthetic Surg 2014;7(4):189–97.
[11] Richter M, Mittlmeier T, Rammelt S, Agren PH, Hahn S, Eschler A. Corrigendum to 'Intramedullary fixation in severe Charcot osteo-neuroarthropathy with foot deformity results in adequate correction without loss of correction - Results from a multi-centre study' [Foot Ankle Surg 21 (2015) 269-276]. Foot Ankle Surg 2016;22(4):289.
[12] Richter M, Zech S, Geerling J, Frink M, Knobloch K, Krettek C. A new foot and ankle outcome score: Questionnaire based, subjective, Visual-Analogue-Scale, validated and computerized. Foot Ankle Surg 2006;12(4):191–9.
[13] Richter M, Agren PH, Besse JL, Coster M, Kofoed H, Maffulli N, Rosenbaum D, Steultjens M, Alvarez F, Boszczyk A, Buedts K, Guelfi M, Liszka H, Louwerens JW, Repo JP, Samaila E, Stephens M, Witteveen AGH. EFAS Score - Multilingual development and validation of a patient-reported outcome measure (PROM) by the score committee of the European Foot and Ankle Society (EFAS). Foot Ankle Surg 2018;24(3):185–204.
[14] Walther M, Gottschalk O, Aurich M. Operative management of osteochondral lesions of the talus: 2024 recommendations of the working group 'clinical tissue regeneration' of the German Society of Orthopedics and Traumatology (DGOU). EFORT Open Rev 2024;9(3):217–34.
[15] Waltenspul M, Meisterhans M, Ackermann J, Wirth S. Typical Complications After Cartilage Repair of the Ankle Using Autologous Matrix-Induced Chondrogenesis (AMIC). Foot ankle Orthop 2023;8(1). 24730114231164150.
[16] Viehofer AF, Casari F, Waibel FWA, Beeler S, Imhoff FB, Wirth SH, Ackermann J. Smoking Is Associated with Anterior Ankle Impingement After Isolated Autologous Matrix-Induced Chondrogenesis for Osteochondral Lesions of the Talus. Cartilage 2021;13(1_). 1366S-72S.
[17] Steele JR, Dekker TJ, Federer AE, Liles JL, Adams SB, Easley ME. Republication of "Osteochondral Lesions of the Talus: Current Concepts in Diagnosis and Treatment". Foot ankle Orthop 2023;8(3). 24730114231192961.
[18] Peras M, Bilichtin É, Choufani C, Caubère A, Barbier O. Results of the AMIC® method in patients operated on for an osteochondral lesion of the talar dome (OLTD) at a mean follow-up of 34 months. A retrospective multicenter study. Orthop Traumatol, Surg Res: OTSR 2024:104020.
[19] Migliorini F, Schenker H, Maffulli N, Eschweiler J, Lichte P, Hildebrand F, Weber CD. Autologous matrix induced chondrogenesis (AMIC) as revision procedure for failed AMIC in recurrent symptomatic osteochondral defects of the talus. Sci Rep 2022;12(1):16244.
[20] Migliorini F, Maffulli N, Eschweiler J, Götze C, Hildebrand F, Betsch M. Prognostic factors for the management of chondral defects of the knee and ankle joint: a systematic review. Eur J Trauma Emerg Surg: Publ Eur Trauma Soc 2023;49(2):723–45.
[21] Migliorini F, Eschweiler J, Maffulli N, Schenker H, Driessen A, Rath B, Tingart M. Autologous Matrix Induced Chondrogenesis (AMIC) Compared to Microfractures for Chondral Defects of the Talar Shoulder: A Five-Year Follow-Up Prospective Cohort Study. Life (Basel, Switz) 2021;11(3).
[22] Malahias MA, Kostretzis L, Megaloikonomos PD, Cantiller EB, Chytas D, Thermann H, Becher C. Autologous matrix-induced chondrogenesis for the treatment of osteochondral lesions of the talus: A systematic review. Orthop Rev 2020;12(4):8872.
[23] Maccario C, Barbero A, Indino C. Regeneration: AT-AMIC Technique: Limits and Indication. Foot Ankle Clin 2024;29(2):291–305.
[24] Klein L, Bode G, Wenning M, Behrens M, Schmal H, Kühle J. Medial malleolar osteotomy in the treatment of osteochondral lesions of the Talus - incidence and impact on functional outcome: a retrospective analysis based on data from the German Cartilage Register (KnorpelRegister DGOU). BMC Musculoskelet Disord 2024;25(1):427.
[25] Kekeç AF, Yıldırım A. Mid-term results of autologous matrix-induced chondrogenesis surgery with or without scaffolds for arthroscopic treatment of deep talus osteochondral lesions: A comparative study. Jt Dis Relat Surg 2023;34(3):613–9.
[26] Jiang N, Li H, Wang J, Shen L, Zeng X. The efficacy of autologous matrix-induced chondrogenesis (AMIC) for osteochondral lesions of the talus in the mid-long term: a systematic review and meta-analysis. J Orthop Surg Res 2024;19(1):373.
[27] Jantzen C, Ebskov LB, Johansen JK. AMIC Procedure for Treatment of Osteochondral Lesions of Talus-A Systematic Review of the Current Literature. J Foot Ankle Surg 2022;61(4):888–95.
[28] Götze C, Nieder C, Felder H, Peterlein CD, Migliorini F. AMIC for traumatic focal osteochondral defect of the talar shoulder: a 5 years follow-up prospective cohort study. BMC Musculoskelet Disord 2021;22(1):638.
[29] Götze C, Nieder C, Felder H, Migliorini F. AMIC for Focal Osteochondral Defect of the Talar Shoulder. Life (Basel, Switz) 2020;10(12).
[30] Gottschalk O, Kerschl FW, Mazet J, Suero E, Hörterer H, Altenberger S, Böcker W, Walther M. Evaluation of the new defined EFAS score (European foot and ankle society score) in relation to already established functional scores (FFI, MOXFQ) after cartilage reconstructive therapy (AMIC®) for osteochondral lesion of the talus. Foot Ankle Surg 2022;28(7):975–8.
[31] Gedikbas M, Ozturk T, Asci M, Erpala F, Sobay U, Güneş T. Comparison of autologous matrix-induced chondrogenesis and mosaicplasty in the treatment of osteochondral defects of the talus. Acta Orthop Et Traumatol Turc 2024;58(5):301–7.
[32] Efrima B, Barbero A, Maccario C, Indino C, Nocera C, Albagli A, Dahmen J, Usuelli FG. Significant Clinical Improvement After Arthroscopic Autologous Matrix-Induced Chondrogenesis for Osteochondral Lesions of the Talus: A 5-Year Follow-Up. Cartilage 2024. 19476035241240341.
[33] Deiss L, Walther M, Pfahl K, Hörterer H, Mehlhorn A, Röser A, Gottschalk O. Long-Term Results after Autologous Matrix-Induced Chondrogenesis for Osteochondral Lesions of the Talus: A 10-Year Cohort Study. Cartilage 2024. 19476035241301896.
[34] Lee KT, Choi YS, Lee YK, Cha SD, Koo HM. Comparison of MRI and arthroscopy in modified MOCART scoring system after autologous chondrocyte implantation for osteochondral lesion of the talus. Orthopedics 2011;34(8):e356–62.
[35] Albano D, Martinelli N, Bianchi A, Giacalone A, Sconfienza LM. Evaluation of reproducibility of the MOCART score in patients with osteochondral lesions of the talus repaired using the autologous matrix-induced chondrogenesis technique. La Radiol Med 2017;122(12):909–17.
[36] Gottschalk O, Mazet J, Kerschl F, Schenk H, Suero EM, Hörterer H, Böcker W, Walther M. Correlation between EFAS- and MOCART score and clinical outcome after AMIC(®)-procedure for osteochondral lesion of the talus. Arch Orthop Trauma Surg 2023;143(6):2895–900.

[37] Richter M, Zech S, Andreas Meissner S. Matrix-associated stem cell transplantation (MAST) in chondral defects of the ankle is safe and effective - 2-year-followup in 130 patients. Foot Ankle Surg 2017;23(4):236–42.
[38] Niemeyer P, Salzmann G, Schmal H, Mayr H, Sudkamp NP. Autologous chondrocyte implantation for the treatment of chondral and osteochondral defects of the talus: a meta-analysis of available evidence. Knee Surg Sports Trauma Arthrosc 2011;20(9):1696–703.
[39] Aurich M, Venbrocks RA, Fuhrmann RA. Autologe Chondrozytentransplantation am oberen Sprunggelenk. Rational oder irrational? Orthopade 2008;37(3). 188-5.
[40] Walther M, Valderrabano V, Wiewiorski M, Usuelli FG, Richter M, Baumfeld TS, Kubosch J, Gottschalk O, Wittmann U. Is there clinical evidence to support autologous matrix-induced chondrogenesis (AMIC) for chondral defects in the talus? A systematic review and meta-analysis. Foot Ankle Surg 2020;27(3):236–45.
[41] Giannini S, Buda R, Cavallo M, Ruffilli A, Cenacchi A, Cavallo C, Vannini F. Cartilage repair evolution in post-traumatic osteochondral lesions of the talus: from open field autologous chondrocyte to bone-marrow-derived cells transplantation. Injury 2010;41(11):1196–203.