Particulated autologous cartilage transplantation for the treatment of osteochondral lesion of the talus: can the lesion cartilage be recycled?

Cite this article:
Bone Jt Open 2023;4(12):
942–947.

DOI: 10.1302/2633-1462.
412.BJO-2023-0097.R1

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Aims

Osteochondral lesions of the talus (OLT) are a common cause of disability and chronic ankle pain. Many operative treatment strategies have been introduced; however, they have their own disadvantages. Recently lesion repair using autologous cartilage chip has emerged therefore we investigated the efficacy of particulated autologous cartilage transplantation (PACT) in OLT.

Methods

We retrospectively analyzed 32 consecutive symptomatic patients with OLT who underwent PACT with minimum one-year follow-up. Standard preoperative radiography and MRI were performed for all patients. Follow-up second-look arthroscopy or MRI was performed with patient consent approximately one-year postoperatively. Magnetic resonance Observation of Cartilage Repair Tissue (MOCART) score and International Cartilage Repair Society (ICRS) grades were used to evaluate the quality of the regenerated cartilage. Clinical outcomes were assessed using the pain visual analogue scale (VAS), Foot Function Index (FFI), and Foot Ankle Outcome Scale (FAOS).

Results

All patients had ICRS grade IV cartilage lesions, except for one (ICRS grade III). The paired MOCART scores significantly improved from 42.5 (SD 1.53) to 63.5 (SD 22.60) ($p = 0.025$) in ten patients. Seven patients agreed to undergo second-look arthroscopy; 5 patients had grade I (normal) ICRS scores and two patients had grade II (nearly normal) ICRS scores. VAS, FFI, and all subscales of FAOS were significantly improved postoperatively ($p \leq 0.003$).

Conclusion

PACT significantly improved the clinical, radiological, and morphological outcomes of OLT. We consider this to be a safe and effective surgical method based on the short-term clinical results of this study.

Take home message

- Particulated autologous cartilage transplantation significantly improved the clinical, radiological, and morphological outcomes of osteochondral lesions of the talus.
- We consider this to be a safe and effective surgical method based on the short-term clinical results of this study.

Bone & Joint Open

Introduction

Osteochondral lesions of the talus (OLT) are a common cause of disability and chronic ankle pain. Initial nonoperative management includes rest, immobilization, and anti-inflammatory drugs. Tol et al[1] demonstrated a 45% success rate of nonoperative management for the treatment of OLT. If conservative treatment is ineffective, operative treatments, such as bone marrow stimulation (BMS), osteochondral autograft transplantation (OAT), autologous chondrocyte implantation (ACI), or osteochondral allograft transplantation can be considered.[2-5] However, these treatment strategies have disadvantages, such as inconsistent clinical and biological outcomes, donor site morbidity, poor integration, and high cost.

Surgical treatment strategies for OLT have advanced significantly over the past decade. Lesion repair using autologous cartilage chips is an emerging treatment method. The surge in interest in this novel strategy has been stimulated by both credible clinical and preclinical studies and the need for a more cost-effective treatment for articular cartilage lesions.[6-10] A method was first introduced by Lu et al[11] in 2006, in which autologous cartilage was minced and transplanted into an animal chondral defect model. They reported consequent chondrocyte migration and outgrowth, indicating that fragmented cartilage chips could be an abundant source of cartilage for redistribution. In a subsequent study, Christensen et al[8] compared autologous cartilage chip transplantation with BMS, finding that autologous cartilage chip transplantation resulted in superior regeneration of hyaline cartilage, less fibrous tissue components, and improved histological scores. This technique uses autologous hyaline cartilage harvested from the trochlear border or intercondylar notch in a knee joint for transplant to the curetted lesion site.

Another possible donor for autologous cartilage transplantation is the detached cartilage from OLT. Previous studies have specified that chondrocytes from the lesion itself are viable and could be used for further transplantation.[12,13] However, the clinical outcomes of particulate autologous cartilage transplantation using lesion cartilage are lacking.

In this retrospective study, we investigated the efficacy of autologous cartilage chip transplantation using cartilage derived from OLT. We hypothesized that autologous cartilage chip transplantation would improve clinical and morphological outcomes in patients with OLT.

Methods

We retrospectively analyzed 32 consecutive symptomatic patients with OLT who underwent PACT between August 2020 and December 2021. All surgeries were performed by a senior surgeon (BSK) and all patients had a minimum of one year follow-up. The inclusion criteria for the study were chondral or osteochondral lesions of the talus, no previous surgical treatment for OLT, and pain or functional impairments despite a minimum of six months of conservative treatment. The exclusion criteria were the presence of osteoarthritis (Kellgren-Lawrence grade ≥ 1),[14] malalignment of ankle joint, and a history of previous surgical treatment or ankle fracture. Standard preoperative radiography and MRI were performed for all 32 patients. A previously reported method for the measurement of the area and volume of the ellipse which uses the width and length of the lesion on MRI was used.[3,15] Follow-up second-look arthroscopy or MRI was performed with patient consent approximately one year postoperatively. An independent radiologist evaluated the images, and the Magnetic resonance Observation of Cartilage Repair Tissue (MOCART) score[16] was used (100 best; 0 worst) in the analysis. Pre- and postoperative International Cartilage Repair Society (ICRS) grades[17] were used to evaluate the quality of the regenerated cartilage by an independent orthopaedic surgeon.

Pre- and postoperative clinical outcomes were assessed using the pain visual analogue scale (VAS), Foot Function Index (FFI),[18] and Foot Ankle Outcome Score (FAOS).[19] The translational and transcultural adaptation of both functional outcome measures into the domestic version were validated.[20,21]

Surgical technique

All arthroscopic procedures were performed using the same technique. The patient was placed in the supine position, and two anterior portals (anteromedial and anterolateral) were used for the arthroscope and working instrument. Non-invasive traction (15 pounds) was applied using a footstrap for gentle ankle distraction. The joint was examined arthroscopically and the site and stability of the lesion were assessed. The cartilage was detached from the lesion using a grasper (Figure 1), and a small fragment of the cartilage was sent to the pathology department to check the viability. The remaining cartilage was then particulated into an approximately 1 mm^3 cube using a scalpel by an operating assistant. During fragmentation, the cartilaginous subchondral bone was examined by the senior author (BSK); unstable fragments were removed, and microfractures were performed to create a stable, smooth articular surface. Associated intra-articular lesions were assessed during surgery and debrided, removed, or excised. After removing the saline, the particulate cartilages were placed on the lesion under direct visualization using a dry scope (Figure 1). A freer elevator was used to shape the packed cartilage to align with the surrounding articular surface. Fibrin glue (GC Biopharma, Korea) was applied over the minced cartilage for stabilization.

An active range of motion exercises were encouraged two to three days postoperatively. The patients were placed in a splint for two weeks. After removal of the stitches, the patients wore firm walker boots, and partial weightbearing was permitted using crutches until postoperative six weeks.

Statistical analysis

SPSS version 25.0 (IBM, USA) was used for all statistical analyses. Patient demographics and clinical outcomes are presented as mean ± standard deviation (SD) or number. We performed Kolmogorov-Smirnov and Shapiro-Wilk normality tests to check the normality of the data. We used paired *t*-test to assess pre- and postoperative outcomes and Mann-Whitney test to compare subcategories. Pearson's correlation analysis was used to analyze correlations between patient characteristics and outcomes. The level of statistical significance was set at $p < 0.05$.

Results

Patient characteristics are presented in Table I. A total of 16 patients (50%) had a BMI > 25 kg/m^2, three patients had

Table I. Patient characteristics (n = 32).

Variable	Data
Mean age, yrs, (SD; range)	37.3 (16.5; 17 to 63)
Male, n (%)	18 (56.3)
Right, n (%)	17 (53.1)
Mean BMI, kg/m^2 (SD; range)	25.3 (3.9; 19.2 to 36.9)
Mean area, mm^2 (SD; range)	79.7 (40.7; 21.2 to 173.1)
Mean volume, mm^3 (SD; range)	226.8 (184.9; 15.3 to 993.2)
Mean preoperative MOCART score (SD; range)	38.3 (14.0; 5 to 75)
Mean follow-up duration, mnths (SD; range)	17.1 (5.3; 12 to 30)

MOCART, Magnetic resonance Observation of Cartilage Repair Tissue; SD, standard deviation.

Table II. Intra-articular lesions and accompanying procedures in arthroscopy.

Intra-articular lesions	Procedure	N (%)
Synovitis	Debridement	28 (87.5)
Soft-tissue impingement	Debridement	21 (65.6)
Ossicle	Removal	4 (12.5)
Osteophyte	Excision	3 (9.4)
Loose body	Removal	3 (9.4)
Os trigonum	Excision	3 (9.4)
Ganglion	Excision	1 (3.1)

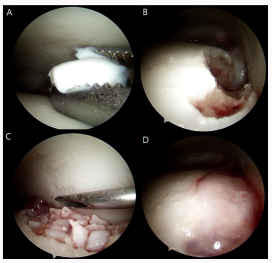

Fig. 1
a) Detached cartilage of the osteochondral lesion was harvested using a grasper. b) Subchondral bone defect was curetted and microfracture was performed to create a sufficient bleeding surface. c) After saline drainage, under direct visualization using a dry-scope, the particulated cartilages were transplanted to fill the lesion. d) Fibrin glue was applied over the cartilage fragments for stabilization.

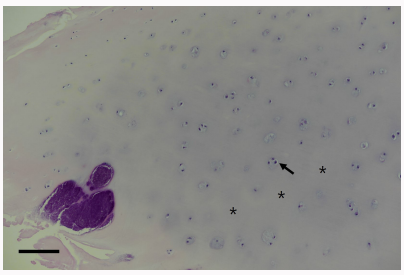

Fig. 2
Representative of the histological examination of a detached lesion cartilage. Hematoxylin and eosin staining was performed to check cell viability. Live chondrocytes within the lacunae (arrow) and the hyaline matrix (asterisk) were confirmed in all specimens (n = 32) (scale bars 200 μm).

a large lesion surface area (> 150 mm^2), and seven patients had a large cyst (> 300 mm^3). Chronic lateral ankle instability (CLAI) was diagnosed in 14 patients; therefore, a concomitant modified Broström operation was performed.

Intra-articular lesions observed in arthroscopy are presented in Table II. All patients had ICRS grade IV cartilage lesions, except for one (ICRS grade III). A small piece of the cartilage fragment was biopsied from each patient. Pathologists confirmed the viability of the lesion cartilage on the basis of live chondrocytes (mean 31.4 cells/high power field; 26 to 39) and live hyaline matrix from all specimens (Figure 2).

The clinical outcomes are shown in Table III. All parameters, including the pain VAS, FFI, and FAOS scores, showed significant postoperative improvements. Age, BMI, lesion area, and lesion volume were not significantly correlated with clinical outcomes according to Pearson's analysis (p ≥ 0.133). Risk factors including BMI > 25 kg/m^2 (n = 16), large lesion area > 150 mm^2 (n = 3), large lesion volume > 300 mm^3 (n = 7), and presence of CLAI (n = 14) were assessed using nominal scales to determine whether they influenced the clinical outcomes. Subgroup analysis was performed to compare clinical outcomes according to lesion size, volume, BMI, and presence of CLAI. There were no significant differences among the subgroups according to the VAS, FFI, and FAOS scores (p ≥ 0.081, Mann-Whitney test).

Follow-up MRIs were performed in ten patients after mean 12.0 months (SD 2.6; 11 to 19). The paired MOCART scores significantly improved from 42.5 (SD 1.53) to 63.5 (SD 22.6) (p = 0.025, paired *t*-test) (Figure 3). Seven patients agreed to undergo second-look arthroscopy after mean 11.4 months (SD 2.0; 11 to 14). Five patients had grade I (normal) ICRS scores, and two patients had grade II (nearly normal) ICRS scores (Figure 4). There were no reported complications related to any of the surgeries.

Discussion

The present study is the first to investigate PACT using lesioned cartilage for the treatment of OLT. The cartilage detached from the lesion was particulated and recycled to serve as a scaffold for live chondrocytes to enhance the healing process. The primary finding of this study was improved clinical and morphological outcomes. Biological healing response, examined via MRI or second-look arthroscope, was characterized with favourable cartilage repair.

The use of autologous cartilage chips for repair was first described in 1983 and has been further investigated in recent years.[7,8,11,22] Animal models have demonstrated that articular chondrocytes from cartilage chips are not notably damaged if the cartilage is cut using a sharp scalpel and can

Table III. Clinical outcomes of arthroscopic particulated autologous cartilage transplantation.

Variable, mean (SD)	Preoperative	Postoperative	p-value*
VAS	6.6 (0.9)	2.3 (2.0)	< 0.001
FFI	46.5 (18.7)	15.4 (12.6)	< 0.001
FAOS			< 0.001
Symptom	53.2 (15.8)	79.9 (13.1)	< 0.001
Pain	53.6 (13.5)	83.2 (13.1)	< 0.001
Active daily living	70.0 (15.1)	90.7 (9.4)	< 0.001
Sports	49.7 (17.0)	64.0 (24.3)	0.003
Quality of life	36.7 (15.4)	71.8 (20.2)	< 0.001
Sum	52.6 (11.5)	77.9 (13.6)	< 0.001

*Paired *t*-test.
FAOS, Foot and Ankle Outcome Scale; FFI, Foot Function Index; VAS, visual analogue scale.

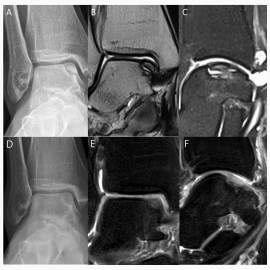

Fig. 3
a, b, and c) Preoperative standing anteroposterior radiograph and MRI scans of a 20-year-old female patient showing a completely detached osteochondral lesion (10 mm width, 20 mm length) on the medial talar dome. d, e, and f) 11-month postoperative images showing restoration of the lesion with homogenous cartilage well integrated with the surrounding cartilage. Note the reduced joint fluid in the postoperative MRI (f) compared to the preoperative image (c).

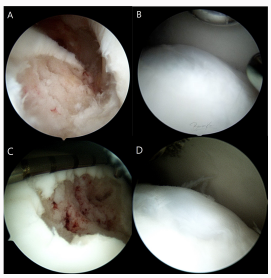

Fig. 4
a, c) Initial arthroscopic findings of two patients after microfracture and their corresponding second-look arthroscopic findings (b,d). a, b) A 21-year-old male patient with preoperative and 11-month postoperative arthroscopic findings with grade I International Cartilage Repair Society (ICRS) score. c, d) A 25-year-old female patient with preoperative and 12-month postoperative arthroscopic findings with grade I ICRS score.

migrate from their initial matrix to form a novel extracellular matrix.[23–27] Chondrocytes that are brought to the surface of their surrounding matrix start to proliferate again as part of a natural healing process, which has been shown to spontaneously heal small cartilage lesions in animal models.[28] In addition, PACT has shown significant cartilage repair results without bone graft in the shallow osteochondral lesion in a recent preclinical study.[29] Moreover, the degree of fragmentation is important. When cartilage chips are too large, a limited number of chondrocytes are activated. Bonasia et al[30] reported that the paste-like appearance of cartilage chips would provide an optimal environment for the regeneration of high-quality tissue.[30]

Is the detached cartilage from an osteochondral lesion viable? Can damaged cartilage be recycled and used to enhance regeneration? Previous studies have reported that chondrocytes from the lesion itself are viable and could be used for further transplantation.[12,13] Chaipinyo et al[13] showed that lesion articular cartilage was comparable to normal articular cartilage in morphology, cell density, ability to proliferate, and protein synthesis.[13] Biant et al[12] showed that mean concentration of glycosaminoglycan and the quantity of DNA in cell pellets from lesions and normal cartilage were not significantly different. Furthermore, the contents were comparable to those of chondrocytes from autologous bone marrow derived cells.[12] These findings are comparable with our result that the fragments from the lesion are alive with healthy chondrocytes and hyaline matrix (Figure 2).

Previous studies using minced cartilage transplantation for osteochondral knee lesions have reported promising short-term outcomes. Christensen et al[9] showed significant clinical and radiological improvements using autologous bone graft and cartilage chips in eight patients with a one-year follow-up. All parameters according to International Knee Documentation Committee (IKDC) score[31] (from 35.9 to 68.1; $p < 0.01$), Tegner score[32] (from 2.6 to 4.7; $p < 0.05$), 4/5 subscales of Knee injury and Osteoarthritis Outcome Score (KOOS)[33] ($p < 0.05$), and MOCART score (from 22.5 to 52.5; $p < 0.01$) increased significantly. Massen et al[10] reported significant improvements in pain (from 7.2 (SD 1.9) to 1.8 (SD 1.6); $p < 0.001$), function (from 7.2 (SD 2.0) to 2.1 (SD 2.3); $p < 0.001$), and MRI findings in osteochondral lesions of 27 patients treated with a minced cartilage procedure with a two-year follow-up.[10]

In addition, several studies compared the results of PACT with BMS. PACT showed more hyaline cartilage (17.1%) and less fibrous tissue (23.8%) compared to BMS (2.9% and 41.1%, respectively) in a preclinical study ($p < 0.01$ and $p < 0.01$, respectively).[8] Also, PACT was superior to BMS in ICRS II scores and type II collagen staining after six months ($p < 0.05$ and $p < 0.05$, respectively). Cole et al[34] prospectively compared the effect of BMS and cell-based cartilage repair using the Cartilage Autograft Implantation System (CAIS) with two-year follow-up, and concluded that IKDC score and most subdomains on the KOOS were significantly higher in the CAIS group. Moreover, higher incidence of intralesional osteophyte formation was observed in the BMS group (70%) than in the CAIS group (25%) at one-year follow-up. Although it is not discussed in this study, the superior clinical and histological results of PACT to BMS are expected to be similar in the ankle which should be investigated subsequently.

Allogenous particulate juvenile cartilage has been widely used in ankle joints. Ryan et al[35] concluded that

particulated juvenile allografts were effective whether by arthroscopy or open arthrotomy. However, Saltzman et al[36] showed that three out of six patients (50%) had persistent subchondral bone oedema and an uneven repaired tissue surface. Coetzee et al[37] concluded that clinical outcomes diminished when the lesion was larger than 150 mm^2. Similarly, Dekker et al[38] found that larger defects more than 125 mm^2 were prone to clinical failure (6/15 patients; 40%). Although limited in numbers, the current study has shown promising outcomes in patients with large lesion areas over 150 mm^2 or large lesion volume over 300 mm^3. Longer follow-up periods are required to confirm the promising clinical outcomes of PACT in patients with large lesions.

This study has several limitations. First, this was a retrospective study with a short follow-up period. Thus, we were unable to deduce any possible interactions between clinical and radiological outcomes and risk factors, including high BMI, large lesions, and large volume. Long-term deterioration of the regenerated cartilage cannot be ruled out. Second, the absence of a control group, such as BMS or OAT, is another limitation, although the results of the current study were consistent in all patients. Third, the lack of postoperative pathology could have weakened the correlation between the histological and the clinical or radiological outcomes. However, previous preclinical studies have shown a superior quality of regenerated cartilage in PACT, which could explain the improved outcomes.

In conclusion, PACT significantly improved the clinical, radiological, and morphological outcomes of OLT. We consider this to be a safe and effective surgical method based on the short-term clinical results of this study. Larger, controlled, long-term studies are needed to validate this procedure.

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H. Hong: Formal analysis, Investigation, Software.
J. W. Lee: Formal analysis, Methodology, Supervision, Visualization.
B. S. Kim: Data curation, Investigation, Methodology, Project administration, Validation, Visualization, Writing – review & editing.

Funding statement

The author(s) disclose receipt of the following financial or material support for the research, authorship, and/or publication of this article: This work was supported by Inha University Research Grant (67945-1).

Data sharing

The data that support the findings for this study are available to other researchers from the corresponding author upon reasonable request.

Ethical review statement

This study was approved by the Inha University Hospital Institutional Review Board (INHAUH 2023-01-030).

Open access funding

The authors report that the open access funding for this manuscript was supported by Inha University Research Grant (67945-1).