Clinical Research

Atelocollagen-Induced Chondrogenesis Versus Microfracture Alone for Osteochondral Lesions of the Talus

Surgical Technique and a 1-Year Clinical Outcome Study

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Abstract: *Osteochondral lesions of the talus (OLTs) are a common cause of post-traumatic ankle pain and disability. Atelocollagen-induced chondrogenesis (ACIC) aims to encourage the development of hyaline cartilage, which is biomechanically superior to fibrocartilage. This single-center, retrospective database study assessed patients who underwent arthroscopic microfracture with or without atelocollagen scaffold augmentation for OLT. Between 2010 and 2019, 87 patients underwent microfracture only and 31 patients underwent ACIC. Propensity score matching was used to match the ACIC group in a 1:2 ratio to a corresponding microfracture-only group using logistic regression. American Orthopaedic Foot & Ankle Society (AOFAS) scores, 100-mm Visual Analog Scale (VAS), Short Form-36 (SF-36), and satisfaction were assessed at preoperative, 3-, 6-, and 12-month intervals. There were no differences in baseline characteristics between groups after matching ($P > .05$). Both groups had similar improvements to VAS, AOFAS, and SF-36 scores up to 12 months ($P > .05$). Both groups had significant 1-year improvements to physical functioning, physical limitations in usual role activities, pain, and social functioning domains, but the ACIC group additionally had significant improvements to general health, vitality, and mental health. Patients in the ACIC group were also more satisfied than the microfracture group at all time points. Patients with OLTs who underwent ACIC reported superior satisfaction and improvements to quality of life, although clinical outcomes were similar to those who underwent microfracture alone at 1 year.*

> “. . . patients who received an ACIC–augmented procedure were more satisfied and had significant 1-year improvements in more domains of the Short Form-36 than patients who had only received a microfracture alone.”

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Introduction

Osteochondral lesions of the talus (OLTs), characterized by a focal injury to talar articular cartilage and adjacent bone, are a frequent cause of ankle pain and disability.[1] Most patients have a history of trauma,[2] with OLTs occurring in up to 50% of patients with ankle sprains and fractures.[3,4] Ankle sprains are one of the most commonly encountered musculoskeletal injuries,[5] and a significant proportion may have chronic pain secondary to an associated OLT. Hence, effective treatments are essential to reduce morbidity and allow patients to return to function or sports expediently.

Conservative therapies, while the mainstay of initial treatment, are only for symptomatic relief, as OLTs heal poorly due to the limited regenerative potential of articular cartilage and a poor blood supply to the talus.[6] Bone marrow stimulation ([BMS] microfracture) is the most common surgical procedure performed for OLTs. Drilling into the subchondral bone underlying the OLT allows for the migration of mesenchymal stem cells from the bone marrow, which have the potential to differentiate into chondrocytes and regenerate articular cartilage. However, there are some drawbacks to this procedure. First, the resultant blood clot may be easily washed away by synovial fluid, and it also lacks sufficient structural integrity to resist sheering forces during movement.[7] Furthermore, microfracture typically results in the formation of fibrocartilage, which is biomechanically and biologically inferior to hyaline cartilage, raising concerns on the longevity of the regenerated cartilage.[8] In response, there has been a growing interest in scaffold-based repair techniques, with the aim of improving the quality of regenerated cartilage.[9]

Creating ideal conditions for the regeneration of hyaline articular cartilage is a challenge that has been faced by physicians both at the bench and at the bedside. Since the introduction of autologous chondrocyte transplantation in the 1990s,[10] various hyaluronic acid–based and collagen-based scaffolds have been developed, each with their own technical considerations.[9] With improvements in biomaterials, previously 2-staged procedures involving autologous cultured chondrocytes have evolved into single-staged cell-free scaffolds with bone marrow simulation techniques. One such technique consisting of a soluble collagen-based scaffold and fibrin glue was previously described by Shetty et al[7,11] for osteochondral lesions of the knee. It consists of atelocollagen, which is an acellular, highly purified form of type I collagen, itself a component of hyaline cartilage. The atelocollagen acts as a scaffold and substrate, encouraging Mesenchymal stem cells (MSCs) to differentiate into chondrocytes.[12] In our institution, we have moved toward soluble polymer-based scaffolds for its ease of deployment via arthroscopy. Unlike other mesh-based matrices that require suturing to adjacent hyaline cartilage, the atelocollagen scaffold can be injected with a fibrin glue arthroscopically into the osteochondral lesion after microfracture that solidifies after 5 minutes. The scaffold conforms to the shape of the OLT, resulting in a watertight construct retaining MSCs in the scaffold that is resistant to mechanical forces. This technique has demonstrated promising results *in vivo* and for clinical outcomes,[12-15] with a recent randomized controlled trial (RCT) demonstrating comparable outcomes at 2 years and histological evidence of superior cartilage regeneration.[13] However, not much is known on the short and intermediate improvements to clinical outcomes before 2 years, which is when most of the regeneration occurs.

Hence, the aim of this study is to compare the clinical outcomes of atelocollagen-induced chondrogenesis (ACIC) with microfracture for the treatment of OLT, specifically looking at the improvements in the immediate postoperative period to 1 year. We hypothesized that patients in the ACIC group would have superior clinical outcomes, quality of life, and satisfaction compared with those undergoing microfracture alone at 1 year.

Materials and Methods

This single-center, retrospective database study assessed the clinical outcomes of patients who underwent arthroscopic microfracture with or without atelocollagen scaffold application for OLT.

Data from our institutional foot and ankle surgery registry were reviewed. All patients who undergo foot and ankle surgery at our institution have their preoperative and postoperative outcomes recorded in this registry. These patients are followed-up at intervals of 3, 6, and 12 months postoperatively. The 3- and 6-month follow-ups were deemed valid only if they occurred within ±1 month, respectively, from the expected date of follow-up. The 1-year follow-up was also only deemed valid if they occurred within ±2 months from the expected date of follow-up.

In our study, we included adult patients with an isolated OLT, with an area less than 1.5 cm^2 as assessed by magnetic resonance imaging and had pain that was corresponding to the site of the OLT. All patients were initially treated with conservative measures for at least 3 months prior to surgery. We further identified patients who underwent either an arthroscopic microfracture (microfracture group) or an arthroscopic microfracture and application of an atelocollagen scaffold (ACIC group) between January 2010 and December 2019. All surgeries were performed by fellowship-trained foot and ankle surgeons. Our exclusion criteria were (1) patients with concurrent ligament reconstruction and (2) revision surgery. Each patient from the ACIC group was matched to 2 corresponding patients in the microfracture group using propensity score matching. The patients were matched for age, sex, body mass index (BMI), and preoperative function scores.

Both matched groups of patients were evaluated for pain, function, quality of life, and satisfaction at 3, 6, and 12 months postoperatively.

Surgical Technique

All surgeries were performed under general or regional anesthesia. Patients with an anterior or talar dome OLT were placed supine, while patients with posterior lesions were placed prone. A nonsterile pneumatic tourniquet was placed on the operated limb and inflated 10 minutes after standard antibiotic prophylaxis was administered.

All arthroscopy procedures were performed using a 4-mm, 30° scope (Smith & Nephew, London) via standard antero-medial or postero-medial and lateral portals. An inspection of tibial and talar articular cartilage was carried out before the identification of the OLT (Figure 1A). The denuded cartilage flap was debrided to healthy borders, and exposed bone was prepared with curettes and shavers till stable. Microfracture was performed with standard microfracture picks. An angled pick was used to penetrate the subchondral bone perpendicularly, with each hole a minimum of 3 to 4 mm apart (Figure 1B).

Patients in the ACIC group received atelocollagen augmentation using CartiFill (Regenerative Medicine System, Seoul). To facilitate the insertion of the atelocollagen matrix, dry arthroscopic conditions were achieved. The normal saline irrigation was stopped and remaining fluid in the ankle joint was removed using an angled suction tube. A carbon dioxide insufflator (UHI-3; Olympus Medical Systems Corp., Tokyo) was attached to the trocar and the joint was distended with carbon dioxide to a pressure of 20 mm Hg, at a maximum flow rate of 20 L/min. The positive pressure pushes the surrounding synovium and soft tissues away from the operative site. Dry scope conditions are essential to prevent damage to the insufflator (Figure 1C). The OLT was further dried using surgical patties inserted through the arthroscopic portal.

The CartiFill application system consists of two 1-mL syringes, one filled with 1 mL of fibrin glue (Tisseel; Baxter, Deerfield, Illinois), and one filled with 0.9 mL of atelocollagen and 0.1 mL of thrombin. The atelocollagen and thrombin mixture was combined with the fibrin glue in a 1:1 ratio using a double-barrelled syringe applicator device attached to an 18G non-beveled needle. The mixture was injected into the OLT until it was at the same level of the surrounding articular cartilage. The resulting gel mass was shaped using a McDonald dissector and allowed to polymerize for 5 minutes (Figure 1D). During this time, it was essential that the intra-articular space be kept dry with a combination of gentle suction and absorbent surgical patties. Subsequently, CO_2 inflow was shut off and fluid irrigation of the joint was restarted. To confirm that the mixture was stable and adherent to bone, the lesion was gently probed, and the ankle was mobilized through a full range of motion.

All patients underwent a standard postoperative rehabilitation protocol. Patients were placed on a backslab for a minimum of 2 weeks, before being allowed to wear a walker boot for 4 weeks. Patients were allowed mobilization exercises; however, no weight bearing was allowed until after 6 weeks postoperatively, where progressive weight-bearing exercises were subsequently allowed.

Clinical Outcomes

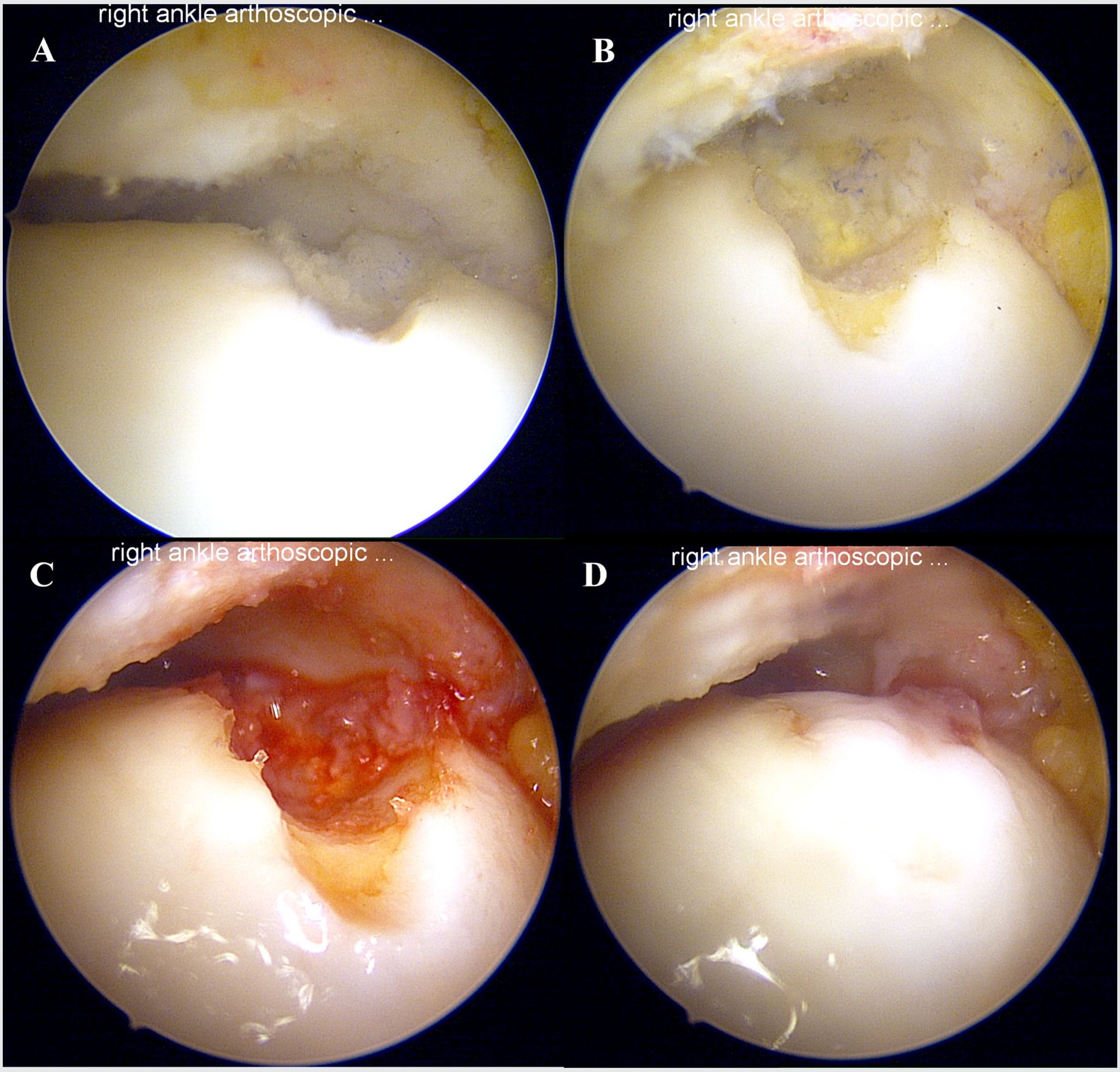
All clinical assessments were performed by an independent health care professional. The following data were collected: Visual Analog Scale (VAS), American Orthopaedic Foot & Ankle Society Ankle-Hindfoot Scale (AOFAS AHS), and Short Form-36 (SF-36). The patients were assessed preoperatively and were prospectively followed up at 3, 6 months, and 1 year postoperatively. Patients were also asked questions related to their satisfaction and whether their expectations were met at each timepoint postoperatively.

We used the AOFAS AHS, VAS, and SF-36 to evaluate functional outcomes, pain, and quality of life, respectively. These scores are widely used and have been validated for use in ankle pathology. The AOFAS AHS is a physician-based rating system, consisting of subjective assessments of pain, activity limitations, use of assistive devices, walking distance, and difficulties with walking surfaces. This is followed by an objective assessment of range of movement, stability, and alignment of ankle-hindfoot.[16] A goniometer was used to measure sagittal (tibiotalar) and hindfoot (subtalar) motion. The score ranges from 0 to 100 (best possible), with a breakdown of 50 points for function, 40 for pain, and 10 for alignment. Aside from the AOFAS AHS, the VAS is the second most common tool used in foot and ankle surgery.[17] It consists of a 10-cm line, with "no pain" and "extreme pain" marked at the left and right terminus, respectively. The distance from the left in centimeters at which the patient marks their level of pain is taken to be the VAS score, to the nearest 0.1 cm. To assess for health-related quality of life, we used the SF-36. The SF-36 evaluates the domains of physical functioning, role functioning limitations due to health problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and general mental health. Each domain consists of a score ranging from 0 to 100, with higher scores indicating a better quality of life.

Satisfaction and expectation fulfillment were also assessed at 3, 6 months, and 1 year postoperatively. Patients were asked 2 multiple-choice questions: (1) whether their expectations were met as a result of the surgery and (2) how they would rate the overall results of the surgery. A total of 6 or 7 possible responses, respectively, were assessed based on a Likert scale, with lower scores indicating better results. The questions are detailed in Figure 2. Responses for expectation fulfillment and satisfaction

Figure 1.

(A) Right ankle medial talar dome osteochondral lesion (OLT) as observed under a diagnostic arthroscopy. (B) Appearance of OLT after debridement and microfracture. (C) OLT in dry scope conditions, pneumatic tourniquet deflated to encourage subchondral bone bleeding. (D) Final appearance of OLT after application of CartiFill atelocollagen scaffold.



less than 5 were deemed to have expectations fulfilled and be satisfied, respectively.

Statistical Analysis

Prior to the initiation of our study, we used G*Power Version 3.1.9.6 (Franz Faul, Kiel) to conduct a power analysis.[18] A meta-analysis[19] on 25 studies and 1868 ankles previously found that the mean preoperative AOFAS for patients with OLT was 62.4 ± 7.9 points. We used the minimal clinically important difference (MCID) of the AOFAS to calculate the required power.[20] The MCID is the smallest change in an outcome score that is perceived by patients, and aids clinicians in determining if an intervention resulted in clinically significant improvements. We set our MCID as 9.9 points based on a distribution-based approach described for ankle arthroplasty,[21] as the MCID for arthroscopic treatment of OLT has not been previously calculated.[22] To reach a power of 0.8 with type I error was set at 0.05 for an enrolment ratio of 2:1, a minimum of 21 patients (7 in the ACIC

Figure 2.

Questions asked for satisfaction and expectation fulfillment at 3, 6 months, and 1 year postoperatively.

1) Has the surgery for your foot and ankle condition met your expectation so far?
1 = Yes, totally
2 = Yes, almost totally
3 = Yes, quite a bit
4 = More or less
5 = No, not quite
6 = No, far from it
7 = No, not at all

2) How would you rate the overall results of your treatment for your foot and ankle condition?
1 = Excellent
2 = Very good
3 = Good
4 = Fair
5 = Poor
6 = Terrible

group and 56 in the microfracture group) was required.

All statistical analyses were performed using SPSS Version 26 (IBM Corp., Armonk, NY). To control for confounders in the baseline covariates of age, sex, and BMI, we used a propensity score matching algorithm. Using the nearest-neighbor method, we matched the microfracture group in a 1:1 ratio to each patient in the ACIC group. Propensity scores generated using logistic regression were used to adjust for both groups' age, sex, and BMI. Differences between continuous variables (VAS, AOFAS, SF-36 domains) were evaluated using the *t* test for unpaired samples, while the Kruskal-Wallis *H* test was used for nonparametric variables (satisfaction and expectations met). We also conducted a subgroup analysis using linear regression to determine whether age, sex, or BMI had any influence on 1-year postoperative AOFAS scores for both procedures. Data were presented in standardized coefficients (*b*) and in level of significance.

Results

Between January 2010 and December 2019, there were a total of 243 patients who underwent arthroscopic microfracture for primary OLT and met our inclusion criteria. Of the 243, 86 had other simultaneous procedures done (such as ligament reconstruction or tendinoplasty) and 31 received biological resurfacing procedures with products other than an atelocollagen scaffold, leaving 126 patients who received either procedure of interest. Of the 126 patients, there were 34 in the atelocollagen-induced chondrogenesis (ACIC) group and 92 in the microfracture-only group. Of the 34 in the ACIC group, 3 were lost to follow-up, leaving 31 patients for analysis. Of the 92 in the microfracture-only group, 5 were lost to follow-up, leaving 87 patients for analysis. The recruitment of patients is detailed in Supplemental Appendix 1.

At baseline, there was a significantly smaller proportion of female patients (37.9% vs 61.3%, $P = .035$) who were younger (42.0 ± 13.0 vs 48.6 ± 15.1 years, $P = .022$) in the microfracture group. No differences were observed in the other covariates of age and preoperative outcome scores.

To control for these differences, propensity score matching was used to select a group of microfracture patients with similar baseline covariates to patients in the ACIC group. Sixty-two patients in the microfracture group were matched in a 2:1 ratio to the 31 patients in the ACIC group using logistic regression. After matching, there were no differences between both groups in terms of age, sex, and BMI. Preoperatively, there were also no significant differences in the VAS, AOFAS, and all 8 SF-36 domains (Table 1).

For ACIC and microfracture groups, the mean follow-up at 3, 6 months, and 1 year was 2.8 and 2.9, 6.5 and 6.1, and 12.7 and 13.1 months, respectively.

Both groups of patients experienced significant improvements to VAS and AOFAS from pre-operation to 3, 6, and 12 months postoperatively. The AOFAS increased from 48.40 ± 14.98 to 82.64 ± 18.52 in the microfracture group and from 48.40 ± 14.98 to 82.55 ± 18.12 in the ACIC group. The VAS improved from 6.02 ± 2.17 to 2.03 ± 2.51 in the microfracture group and from 6.03 ± 2.09 to 1.73 ± 2.35 in the ACIC group. The greatest improvements to VAS and AOFAS were observed in the first 3 months, whereas modest improvements were recorded up to 1 year postoperatively. There were no significant differences between both groups for pain and function at all time points (Figure 3).

Patients in either group experienced quality-of-life improvements over 1 year after their surgery, with no significant differences found between the SF-36 scores for all domains at all time points (Supplemental Appendix 2). We also compared preoperative and 1-year postoperative SF-36 results for each domain. While both groups had significant improvements to physical functioning, roles affected by physical impairments, pain, and social functioning, patients in the ACIC group additionally had significant improvements to general health, vitality, and mental health (Figure 4). We presented these data in comparison with known population norms in Supplemental Appendix 3.

Alongside superior improvements in quality-of-life scores were observed that patients in the ACIC group were more satisfied with their surgery. Patients in the ACIC group reported higher satisfaction at all time points, and more had their expectations met at 3 months (Table 2). A mean score of 2 for both satisfaction and expectation fulfillment indicated patients on average rated their surgery "very good" and had their expectations "almost totally" met (Figure 2).

We also performed a subgroup analysis to determine whether the outcomes of either procedure were affected by other covariates such as age, sex, or BMI. Using a linear regression model, we found that higher BMI was correlated with worse off AOFAS scores at 1 year for microfracture-only ($b = -0.946$; $P = .049$) but not for the ACIC group ($b = -0.428$; $P = .569$). Sex ($P = .342$ vs $P = .343$) and age ($b = -0.066$; $P = .722$ vs $b = -0.330$; $P = .138$) did not individually influence the AOFAS scores obtained at 1 year for microfracture and ACIC groups, respectively (Figure 5).

Table 1.

Preoperative Baseline and Post-PSM Covariates and Clinical Outcome Scores.

Baseline variables	Baseline: Microfracture (n = 87)	Baseline: ACIC (n = 31)	Baseline: *P* value	After PSM: Microfracture (n = 62)	After PSM: ACIC (n = 31)	After PSM: *P* value
Sex, female, No. (%)	33 (37.9)	19 (61.3)	.035	29 (46.8)	19 (61.3)	.271
Age, y	42.0 ± 13.0	48.6 ± 15.1	.022	44.04 ± 12.85	48.55 ± 15.11	.132
BMI, kg/m^2	27.28 ± 4.71	27.18 ± 4.40	.917	27.08 ± 5.01	27.18 ± 4.40	.929
VAS	5.8 ± 2.2	6.0 ± 2.1	.666	6.02 ± 2.17	6.03 ± 2.09	.973
AOFAS	50.8 ± 14.8	46.8 ± 15.9	.209	48.40 ± 14.98	46.81 ± 15.95	.635
SF-36 physical functioning	63.0 ± 24.1	54.0 ± 25.8	.084	60.73 ± 24.87	54.03 ± 25.77	.227
SF-36 role physical	22.7 ± 34.2	29.0 ± 40.4	.401	23.79 ± 35.19	29.03 ± 40.36	.519
SF-36 bodily pain	40.3 ± 18.5	40.6 ± 17.8	.947	40.82 ± 19.86	40.56 ± 17.77	.951
SF-36 general health	73.0 ± 21.9	67.0 ± 23.2	.200	71.61 ± 22.73	67.00 ± 23.23	.360
SF-36 vitality	67.8 ± 24.0	65.0 ± 19.5	.559	67.34 ± 23.86	65.00 ± 19.54	.637
SF-36 social functioning	68.5 ± 32.6	73.8 ± 28.4	.428	73.39 ± 31.24	73.79 ± 28.39	.952
SF-36 role emotional	86.2 ± 32.0	94.6 ± 21.3	.176	91.94 ± 23.90	94.62 ± 21.25	.596
SF-36 mental health	81.7 ± 17.0	81.0 ± 14.0	.834	81.74 ± 16.61	81.03 ± 14.05	.838

Abbreviations: PSM, propensity score matching; ACIC, Atelocollagen-induced chondrogenesis; BMI, body mass index; VAS, visual analog scale; AOFAS, American Orthopaedic Foot & Ankle Society; SF-36, Short Form-36.

There were no complications in the current study, including nerve injury, infection, or delayed wound healing. Over the follow-up duration of 1 year, there were no patients who required readmission for a related issue or revision surgery.

Discussion

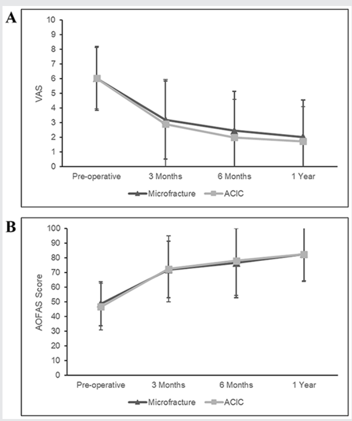
Our findings have demonstrated that patients who received an ACIC for the treatment of a symptomatic OLT had similar levels of pain and clinical outcomes to those who received a microfracture alone at up to 1 year. Nonetheless, our hypothesis was partially borne out by an increased quality of life and satisfaction experienced by these patients.

Bone marrow stimulation is an established treatment of OLTs, with good clinical results reported in the literature.[23,24] A systematic review by Zengerink et al[23] found that BMS resulted in a success rate of 85% in 326 patients. Excellent to good clinical results have been reported in between 83% and 89% of patients who underwent an OLT at up to 2 years postoperatively.[25-27] In a study comparing postoperative clinical outcomes and second-look arthroscopy, Lee et al found that 90% of patients who underwent a microfracture had excellent or good AOFAS scores at 12 months, but 40% of the same group had abnormal International Cartilage Repair System grade of cartilage healing. Alternatives, such as autologous chondrocyte implantation and osteochondral autograft transfer system (OATS), have been used by foot and ankle surgeons. The ACIC technique, first described by Brittberg et al,[10] is an effective technique in stimulating hyaline cartilage regeneration.[28] However, it is a staged and costly procedure, with associated risks of periosteal harvesting, limiting its widespread adoption.[24] The OATS technique is conducted via a malleolar osteotomy and is associated with donor site complications; hence it is generally reserved for large, uncontained lesions.

Autologous matrix-induced chondrogenesis (AMIC) has recently been proposed to address the limitations of BMS techniques, involving the implantation of a collagen membrane to augment BMS. Collagen is an important connective tissue protein

Figure 3.

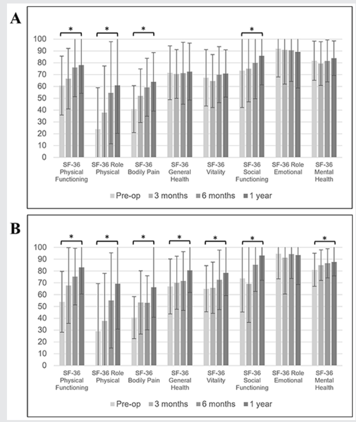
(A) VAS and (B) AOFAS Ankle-Hindfoot Scale at different time points. Abbreviations: ACIC, Atelocollagen-induced chondrogenesis; AOFAS, American Orthopaedic Foot & Ankle Society; VAS, visual analog scale.



that can act as a scaffold for MSCs to facilitate the regeneration of hyaline cartilage.[7] First described in the treatment of osteochondral lesions of the knee, it has recently been used in the treatment of OLTs.[12] In 2011, Wiewiorski et al[29] first described the use of a porcine-derived type I/III collagen membrane (Chondro-Gide, Geistlich Biomaterials, Wolhusen) to augment the microfracture and autologous bone grafting of a large OLT in a young male. In this case report, the patient reported no pain, had returned to sport, and had a maximum AOFAS score of 100 at 1 year follow-up. At 2 to 8 year follow-up, Weigelt et al[30] found that AMIC lead to significant pain reduction (VAS 6.4 ± 1.9-1.4 ± 2.0), recovery of ankle function (AOFAS 93.0 ± 7.5), and 79% of patients returned to sport. In addition, more than 88% of patients demonstrated filling of the defect on MRI. However, the main drawback of this procedure was the need for an open approach with a malleolar osteotomy to place the collagen membrane which is secured to the surface of the OLT using fibrin glue.

Figure 4.

SF-36 scores by domain at 1 year for the (A) microfracture group and (B) ACIC group. Abbreviation: SF-36, Short Form-36.



*Indicates statistically significant differences between preoperative and 1 year using a paired samples *t* test at $P < .05$.

The development of atelocollagen as an injectable form of collagen has allowed us to overcome these difficulties, allowing for the procedure to be fully conducted via an arthroscopic technique. Shetty et al[7] first described the ACIC technique in 2013 for osteochondral lesions of the knee, and several other authors have also recently applied this technique to OLTs.[12-15]

In vitro results of this technique have been promising in the treatment of OLTs. Volpi et al[12] seeded cultured human MSCs and articular chondrocytes on a atelocollagen scaffold, and found that there was a uniform distribution of MSCs within the polymerized atelocollagen matrix on histological analysis. Using a rabbit OLT model, Kim et al[15] found that subchondral bone and cartilage completely regenerated after microfracture and atelocollagen augmentation, with significantly increased histological scores compared with OLTs that received a microfracture alone at 12 weeks.

Clinical results of this technique are limited to small case series[12,14,15] and one RCT.[13] Volpi et al[12] conducted a 5-patient pilot study, finding that patients who underwent the ACIC procedure had improved VAS (6.6 ± 1.1 to 1.6 ± 1.5) and AOFAS (53.8 ± 15.1 to 86 ± 9) scores at 6 months. Similarly, Kim et al[15] reported on the results of ACIC in a series of 17 patients at a mean follow-up of 16 ± 4.2 months. They also found significant improvements of the AOFAS from 62 points to 88 points and VAS from 6.4 points to 1.8 points. Moreover, 15 of 17 patients (89%) reported good or excellent results. Usuelli et al[14] reported similar improvements to AOFAS (51.4 ± 11.6 to 71.8 ± 20.6) and VAS (6.9 ± 1.8 to 3.2 ± 1.9) in a case series of 9 patients. In the only available study comparing ACIC with the established microfracture technique, Lee et al[13] compared 22 patients who underwent ACIC with 23 patients who received a microfracture alone over 2 years. Similar to our study, the authors did not find any significant differences between 2-year AOFAS (91.2 ± 8.6 vs 86.9 ± 10.7, $P = .09$) and VAS (1.7 ± 2.0 vs 1.9 ± 1.9, $P = .72$). However, the authors did not report on satisfaction and quality-of-life scores. Nonetheless, none of the aforementioned studies examined outcomes at shorter intervals prior to 1 year. The results of our study highlight new evidence that most of the improvements to pain and function occur within 3 months of surgery for both techniques, and patients can expect gradual recovery thereafter (Figure 3). These findings will be useful for surgeons counseling patients with OLT, on the timeline of their expected recovery after surgery. As a newly investigated technique, outcome studies thus far have been limited to a maximum of 2 years postoperatively. We postulate that the purported in vitro benefits may manifest in better longevity of the regenerated cartilage. Hence, we await long-term outcome studies to determine these benefits are borne out superior longer term function and pain scores.

Our study also found that higher BMI exhibited significant correlation ($P = .049$) with worse 1-year AOFAS outcomes in the microfracture group,

Table 2.

Expectations Met and Satisfaction Recorded at 3, 6 Months and 1 Year Postoperatively.

Expectations Met and Satisfaction	Microfracture (n = 62)	ACIC (n = 31)	*P* value
Three months			
Expectations met	3.30 ± 1.32	2.49 ± 1.55	.010
Satisfaction	3.01 ± 1.04	2.29 ± 1.20	.005
Six months			
Expectations met	2.95 ± 1.61	2.31 ± 1.53	.058
Satisfaction	2.85 ± 1.30	2.24 ± 1.17	.026
One year			
Expectations met	2.87 ± 1.49	2.06 ± 1.29	.159
Satisfaction	2.74 ± 1.25	2.00 ± 0.97	.010

Abbreviation: ACIC, atellocollagen-induced chondrogenesis.

although the same was not observed in the ACIC group (*P* = .569). In the available literature, there has been conflicting evidence on the effect of BMI on clinical outcomes.[25,30-32] Nonetheless, we thought these findings would be interesting to report, showing preliminary evidence that ACIC may be more beneficial in patients with higher BMI, possibly related to the robust cartilage regeneration process previously observed in animal studies. However, larger studies are awaited before definite conclusions can be drawn.

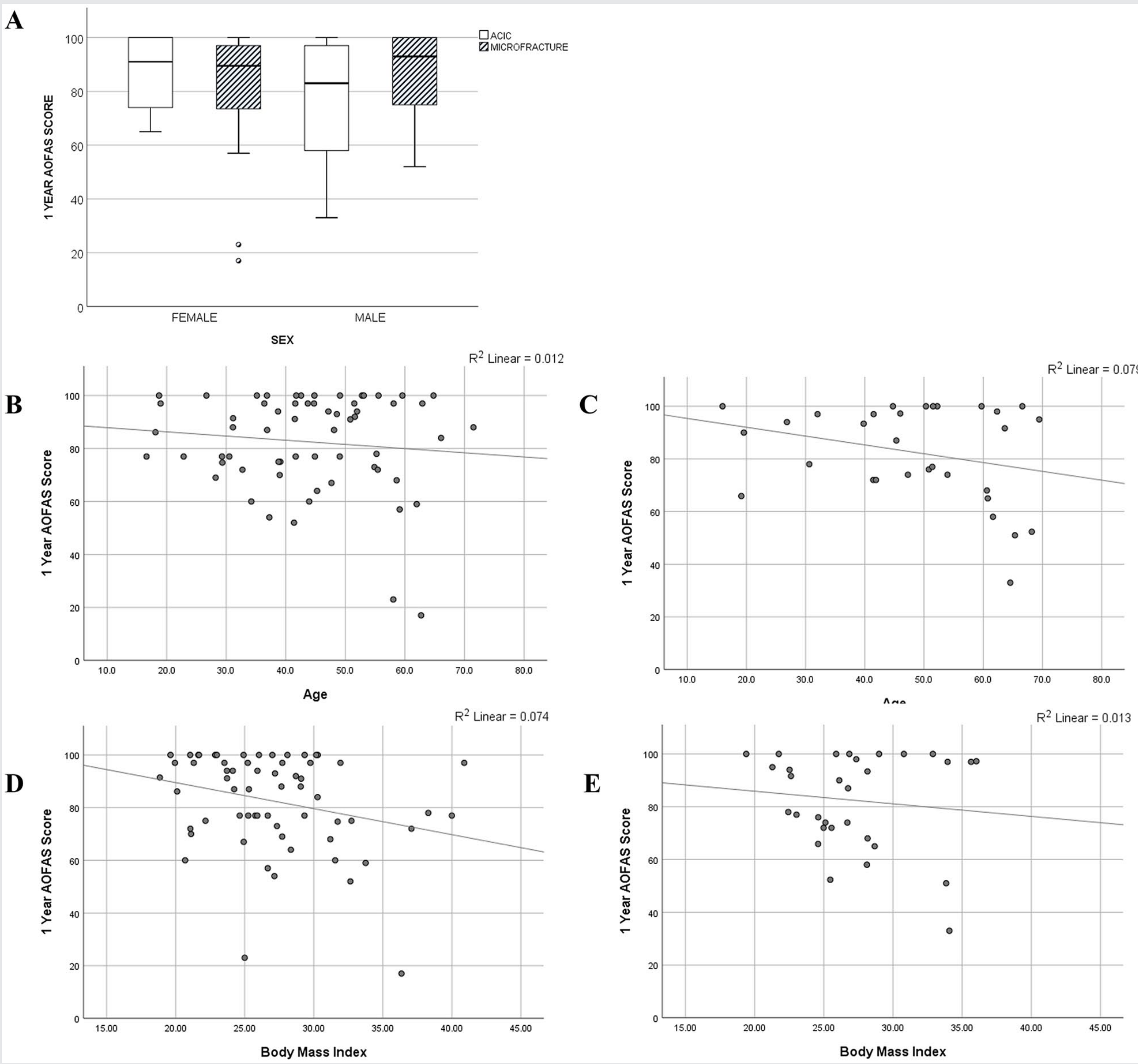
The impact of OLTs on quality of life has not been thoroughly investigated in the available literature. First reported by D'Ambrosi et al,[33] the authors found that patients with symptomatic OLTs reported worse Short Form-12 mental and physical component scores, worse than known national norms and similar to those reported by patients with other chronic medical conditions, such as osteoarthritis, lumbosciatalgia, and diabetes. Indeed, our study found that patients with OLTs suffered a reduction in quality of life compared with population norms,[34] most significantly in the domains of physical functioning, role physical, and bodily pain (Supplemental Appendix 3). While there have been no other studies that have reported on the individual domains of the SF-36 in OLT, the findings of our study indicate that surgical treatment is effective in improving patients' pain and physical function, with ACIC potentially offering further benefits to other domains of general health and vitality recovery postoperatively. The purported in vitro benefits of superior regeneration of articular cartilage in ACIC[12,13,15] could be related to a significantly higher satisfaction and expectation fulfillment reported by patients at various time points. Hence, foot and ankle surgeons can consider ACIC augmentation of routine microfracture for patients with symptomatic OLTs for a superior recovery of quality of life and consequently higher satisfaction.

To the best of our knowledge, our study is the first to report on quality of life and satisfaction, and we found that patients who underwent ACIC had a significant improvement to more SF-36 scores and had superior satisfaction and expectation fulfillment. Our findings may reflect the known limitations of the AOFAS scoring system, where it was found to be sensitive to changes in pain and function, it did not perform well as a tool to measure a patient's function within society, and whether the patient is able to remain as a productive individual.[35] In light of these limitations, Malviya et al[36] had proposed that a generic quality-adjusted life-year (QALY) score be used in conjunction with the AOFAS to reflect outcomes of foot and ankle surgery, which we have performed in this study.

The results of our study should be considered with its limitations. First, our study was conducted in a single institution, limiting the external validity of our results. Second, we did not evaluate radiographic severity, size, or cartilage recovery. We used 1.5 cm^2 for the upper limit in our inclusion criteria as larger OLTs had previously been found to have a poorer outcome when treated with BMS techniques.[37] Other authors have previously evaluated cartilage regeneration with the Magnetic

Figure 5.

Correlation between sex (A), age (B: microfracture, C: ACIC), and body mass index (D: microfracture, E: ACIC) on 1-year AOFAS scores. Abbreviations: ACIC, atellocollagen-induced chondrogenesis; AOFAS, American Orthopaedic Foot & Ankle Society.



Resonance Observation of Cartilage Repair Tissue score; however, many have also gone on to report that these scores do not correlate well with clinical outcomes.[13,15,24,30] Hence, our study investigated the patient-reported outcome measures of VAS, AOFAS, SF-36, and satisfaction, which are arguably more clinically relevant to the practicing foot and ankle surgeon. We are cognizant that a single year follow-up may not be sufficient to observe the purported benefits of longevity of the regenerated cartilage with ACIC. However, given our promising results, it was prudent for us to report our early outcomes, with the aim of following up these patients for their long-term outcomes. We anticipate that as more institutions adopt ACIC in the field of cartilage regeneration, higher powered, longer term studies comparing second-look arthroscopy or biopsy results will be published in the near future. With such data, definitive conclusions can be reached on the superiority of either technique especially with respect to specific patient groups.

Conclusion

Atelocollagen-induced chondrogenesis and microfracture alone are both an effective, single-stage procedures for the treatment of symptomatic OLT evidenced by clinical improvements experienced by both groups of patients. Despite similar VAS and AOFAS scores, patients who received an ACIC-augmented procedure were more satisfied and had significant 1-year improvements in more domains of the SF-36 than patients who had only received a microfracture alone.

Declaration of Conflicting Interests

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Ethical Approval

This study was approved by our institution's ethics committee (CIRB Reference Number: 2019/2679).

Informed Consent

Not applicable, because this article does not contain any studies with human or animal subjects.

Trial Registration

Not applicable, because this article does not contain any clinical trials.

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Supplemental Material

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