Comparative Outcomes for the Treatment of Articular Cartilage Lesions in the Ankle With a DeNovo NT Natural Tissue Graft

Open Versus Arthroscopic Treatment

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Background: The treatment of osteochondral lesions of the talus (OLTs) with a juvenile cartilage allograft is a relatively new procedure. Although other treatment options exist for large OLTs, the potential advantage of a particulated juvenile allograft is the ability to perform the procedure arthroscopically or through a minimal approach. No previous studies have looked at the results of an arthroscopic approach, nor have any compared an arthroscopic technique with an open approach.

Purpose: To compare the outcomes of an arthroscopic transfer technique with the previously published open technique.

Study Design: Cohort study; Level of evidence, 3.

Methods: A total of 34 patients (mean age, 33 years) underwent treatment of talar cartilage lesions with a DeNovo NT Natural Tissue Graft. Of these treatments, 20 were performed arthroscopically and 14 were performed with open arthrotomy. There was no statistically significant difference between the groups with respect to age, lesion width, lesion depth, lesion length, or operative time. The mean lesion area was 107 mm^2. The scores from 6 different validated outcome measures were recorded for patients in each group preoperatively and subsequently at 6 months, 1 year, 18 months, and 2 years.

Results: Comparing outcome scores at each time point to baseline, there were no statistically significant postoperative differences found between open and arthroscopic approaches with regard to the visual analog scale (VAS) for pain ($P = .09$), American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot scale ($P = .17$), Foot and Ankle Ability Measure (FAAM)–sports subscale ($P = .73$), Short Form–12 (SF-12) physical health summary ($P = .85$), SF-12 mental health summary ($P = .91$), or FAAM–activities of daily living subscale ($P = .76$).

Conclusion: The treatment of talar articular cartilage lesions with a DeNovo NT Natural Tissue Graft demonstrated no significant differences in outcome at 2 years regardless of whether the graft was inserted with an arthroscopic or open technique.

Clinical Relevance: Our analysis demonstrated no significant difference between an arthroscopic versus open approach at any time point for the first 2 years after implantation of a juvenile particulated cartilage allograft for large OLTs. With that said, both groups demonstrated improvement from baseline. These findings indicate that surgeons with different levels of comfort utilizing arthroscopic techniques can offer this treatment modality to their patients without altering their planned surgical approach. In addition, this will be particularly helpful in counseling patients for surgery when the extent of the defect will be evaluated intraoperatively. Patients can be counseled that they will likely have the same incisions regardless of whether they require debridement, microfracture, or implantation of a particulated allograft.

Keywords: ankle; osteochondral defect; particulated allograft; arthroscopic surgery

Osteochondral lesions of the talus (OLTs) are common after ankle injuries, and it has been estimated that talar lesions are present in up to 40% and 70% of distal fibular fractures and acute lateral ankle inversion injuries, respectively.[3,12,17] While the natural history of these injuries can lead to good results in roughly half of cases, an operative intervention is usually utilized for large lesions or those that are refractory to conservative management.[4,16] Surgical interventions for smaller lesions often involve arthroscopic surgery with debridement and/or bone marrow stimulation. Larger lesions and revision surgery can involve cartilage restoration techniques such as autologous chondrocyte implantation (ACI), matrix-associated autologous chondrocyte implantation, autologous matrix-induced chondrogenesis, osteochondral

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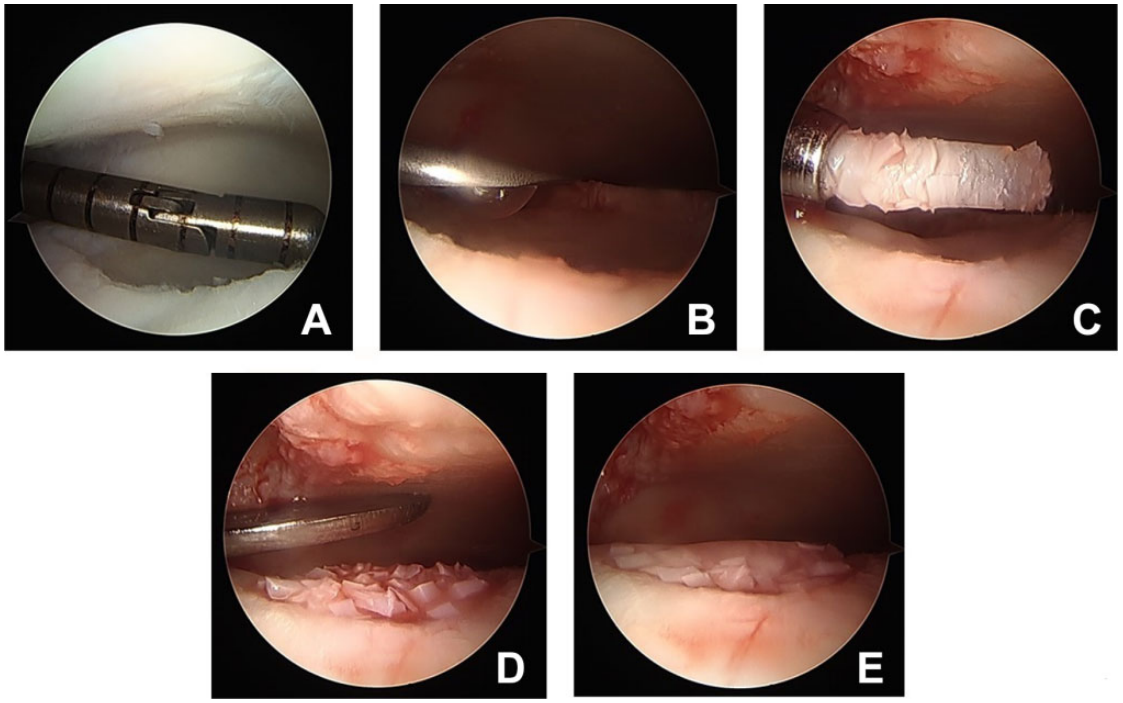

Figure 1. Arthroscopic images of particulated allograft insertion.

autograft or allograft transplantation (OATS), extracellular matrix cartilage allografts, matrix-associated stem cell transplantation (MAST), or implantation with a particulated juvenile cartilage allograft.[2,7,10,11,18]

The treatment of large OLTs with a particulated juvenile cartilage allograft is a procedure that has traditionally been performed through an open approach after an arthroscopic evaluation and preparation. The graft used is obtained from young donors up to 13 years of age. After minimal manipulation, it is prepackaged and designed to be implanted as a 1-stage procedure.[12,15] Arthroscopic implantation techniques have demonstrated promise in terms of preserving the anterior approach and removing the risk and possible morbidity associated with open medial malleolar osteotomy.[1,8,14] While the initial published outcomes of implantation of a particulated juvenile cartilage allograft appear promising, there are no studies comparing implantation approaches.[5,18]

The purpose of this study was to prospectively compare the outcomes of arthroscopic versus open implantation of a particulated juvenile cartilage allograft for the treatment of OLTs. It was hypothesized that at 2 years postoperatively, there would be no difference in outcomes between arthroscopic and open techniques.

METHODS

We performed a longitudinal prospective cohort study of 34 patients who underwent juvenile cartilage (DeNovo NT Natural Tissue Graft; Zimmer Biomet) implantation for OLTs performed by 2 fellowship-trained foot and ankle surgeons (P.M.R., A.T.G.) at 2 military facilities. This institutional review board–approved study was sponsored by Zimmer Biomet, and the patients were enrolled as part of a larger longitudinal study. Overall, 34 consecutive patients were enrolled in this arm of the study. To be included in the study, patients were required to be at least 18 years old and to have an osteochondral lesion confirmed by arthroscopic surgery. Patients with associated procedures or prior treatments for their osteochondral lesions were not excluded. There were no restrictions on minimum or maximum values for lesion size. Patients were not required to undergo previous surgery or previous attempts at nonoperative management. A total of 14 procedures were

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Ethical approval for this study was obtained from the institutional review board at Tripler Army Medical Center, Honolulu, Hawaii.

TABLE 1
Demographics of Patients[a]

	Open (n = 14)	Arthroscopic (n = 20)	*P* Value
Age, y	33 (19-45)	32 (20-52)	.94, .85, .76
Lesion width, mm	8.7 (5-16)	8.6 (4-15)	.72, .93, >.99
Lesion depth, mm	4.1 (1-10)	3.3 (0-10)	.81, .45, .48
Lesion length, mm	12.4 (7-15)	12.4 (6-20)	.06, .95, .89
Operative time, min	141 (83-253)	159 (64-304)	.19, .34, .32

[a]Data are presented as mean (range). *P* values are shown for folded *F* test, pooled *t* test, and Wilcoxon test, respectively.

performed through an open approach and 20 through an arthroscopic approach.

The surgical techniques for each arm of the study have been previously described.[5,14] In both groups, patients underwent diagnostic arthroscopic surgery utilizing a noninvasive ankle distractor. Once lesions were identified, all loose cartilage and/or bone was removed, and the borders were tested for stability. Once the lesions had been prepared, the technique varied based on the group. In the arthroscopic group, the entire procedure was performed through arthroscopic portals (Figure 1). The fluid was removed, and the ankle was dried utilizing a combination of felt pledgets and rolled gauze. A thin layer of fibrin glue was applied to the bed of the lesion, and particulated cartilage was delivered to the lesion via a cannula. Cartilage was formed with a surgical elevator and secured with a second layer of fibrin glue. In the open group, after preparation of the lesion, the fluid was removed, and the appropriate portal was extended to allow visualization of the lesion. A template of the lesion was formed with aluminum, and particulated cartilage was placed into the template with fibrin glue and then placed into the lesion under direct visualization. After placement, cartilage was secured with fibrin glue.

Both groups underwent the same rehabilitation protocol. Patients were nonweightbearing in a splint for 2 weeks, followed by transition to a controlled ankle motion walking boot for an additional 4 weeks. Range of motion was encouraged once patients were transferred to the controlled ankle motion walking boot. Patients were allowed to place weight on their ankles in stance but were instructed to use crutches for ambulation.

Patients were enrolled to be observed for a total of 5 years from graft implantation. All patients were evaluated preoperatively and then at 6, 12, 18, and 24 months. In addition to a physical examination, outcome measures at each interval were performed using 6 validated patient-reported surveys. These included the visual analog scale (VAS) for pain, American Orthopaedic Foot and Ankle Society (AOFAS) ankle-hindfoot scale, Foot and Ankle Ability Measure (FAAM)–sports subscale, FAAM–activities of daily living (ADL) subscale, 12-Item Short Form Health Survey (SF-12) physical health summary, and SF-12 mental health summary. Repeat imaging was not typically performed. Statistical analyses with a folded *F* test, *t* test (pooled), and Wilcoxon signed-rank test were performed.

RESULTS

Demographics for patients and lesions are shown in Table 1. The mean age for all patients in the study was 33 years (range, 19-52 years) and did not differ significantly between

TABLE 2
Outcome Scores[a]

	Open	Arthroscopic	*P* Value
VAS			
At 2 y	36.0 ± 23.8 (2.0 to 63.0)	19.3 ± 28.7 (0.0 to 62.0)	
Change from baseline	3.0 ± 11.9 (–18.0 to 10.0) [n = 5]	–25.0 ± 28.5 (–56.0 to 0.0) [n = 4]	.13, .09, .12
AOFAS			
At 2 y	85.0 ± 0.0 (85.0 to 85.0)	86.0 ± 19.1 (64.0 to 97.0)	
Change from baseline	7.0 ± 9.9 (0.0 to 14.0) [n = 2]	34.0 ± 15.6 (23.0 to 45.0) [n = 3]	.72, .17, .33
FAAM-ADL			
At 2 y	77.4 ± 15.8 (43.8 to 98.8)	79.9 ± 16.7 (54.8 to 100.0)	
Change from baseline	12.2 ± 21.4 (–25.0 to 49.3) [n = 11]	15.6 ± 25.1 (–23.6 to 56.0) [n = 11]	.66, .76, .61
FAAM-sports			
At 2 y	54.2 ± 28.0 (19.4 to 94.4)	60.5 ± 26.2 (19.4 to 100.0)	
Change from baseline	27.4 ± 33.4 (–19.0 to 78.0) [n = 10]	34.0 ± 41.3 (–41.0 to 97.0) [n = 9]	.59, .73, .72
SF-12 physical health summary			
At 2 y	44.6 ± 7.1 (33.2 to 55.1)	42.8 ± 11.0 (24.3 to 56.7)	
Change from baseline	6.5 ± 11.1 (–13.5 to 23.4) [n = 11]	7.6 ± 14.5 (–17.0 to 29.0) [n = 11]	.47, .85, .78
SF-12 mental health summary			
At 2 y	54.3 ± 12.0 (33.5 to 68.7)	59.1 ± 4.2 (50.0 to 63.5)	
Change from baseline	1.0 ± 18.9 (–33.2 to 23.7) [n = 11]	1.8 ± 7.0 (–9.0 to 12.9) [n = 11]	.01, .91, >.99

[a]Data are presented as mean ± SD (range). *P* values are shown for folded *F* test, pooled *t* test, and Wilcoxon test, respectively. ADL, activities of daily living; AOFAS, American Orthopaedic Foot and Ankle Society; FAAM, Foot and Ankle Ability Measure; SF-12, 12-Item Short Form Health Survey; VAS, visual analog scale.

TABLE 3
Change in Visual Analog Scale Scores[a]

	Open		Arthroscopic		
	Mean ± SD (Minimum, Median, Maximum)	95% CI	Mean ± SD (Minimum, Median, Maximum)	95% CI	*P* Value
6 mo	–15.7 ± 22.5 (–45.0, –17.0, 27.0) [n = 7]	–36.6 to 5.1	–27.3 ± 25.3 (–67.0, –18.0, 14.0) [n = 9]	–46.8 to –7.8	.7964, .3566, .5010
12 mo	–13.6 ± 29.6 (–52.0, –9.0, 26.0) [n = 5]	–50.3 to 23.1	–25.0 ± 28.1 (–64.0, –17.0, 15.0) [n = 7]	–51.0 to 1.0	.8673, .5133, .4340
18 mo	0.0 ± 21.9 (–19.0, –5.0, 24.0) [n = 3]	–54.5 to 54.5	–27.0 ± 19.8 (–41.0, –27.0, –13.0) [n = 2]	–204.9 to 150.9	>.9999, .2581, .4353
2 y	3.0 ± 11.9 (–18.0, 8.0, 10.0) [n = 5]	–11.8 to 17.8	–25.0 ± 28.5 (–56.0, –19.0, 0.0) [n = 3]	–95.7 to 45.7	.1345, .0916, .1150

[a]*P* values are shown for folded *F* test, pooled *t* test, and Wilcoxon test, respectively. Differences from baseline are depicted with a negative number when the patient's pain level improved.

TABLE 4
SF-12 Mental Health Summary Scores[a]

	Open		Arthroscopic		
	Mean ± SD (Minimum, Median, Maximum)	95% CI	Mean ± SD (Minimum, Median, Maximum)	95% CI	*P* Value
6 mo	1.0 ± 6.8 (–9.5, 2.3, 9.8) [n = 7]	–5.3 to 7.3	–2.0 ± 8.2 (–15.9, –2.8, 12.6) [n = 11]	–7.5 to 3.5	.6708, .4409, .4786
12 mo	–3.3 ± 14.7 (–20.9, –7.2, 13.2) [n = 7]	–16.8 to 10.3	–1.4 ± 11.1 (–19.2, –2.4, 16.2) [n = 11]	–8.8 to 6.1	.4159, .7585, .7215
18 mo	–11.2 ± 10.8 (–20.5, –13.7, 0.6) [n = 3]	–38.0 to 15.6	–1.0 ± 9.4 (–13.0, –2.1, 17.9) [n = 10]	–7.8 to 5.7	.6356, .1396, .2289
2 y	1.0 ± 18.9 (–33.2, 10.3, 23.7) [n = 9]	–13.5 to 15.5	1.8 ± 7.0 (–9.0, 0.6, 12.9) [n = 10]	–3.2 to 6.8	.0074, .9080,[b] >.9999

[a]*P* values are shown for folded *F* test, pooled *t* test, and Wilcoxon test, respectively. SF-12, 12-Item Short Form Health Survey.
[b]Satterthwaite *t* test.

TABLE 5
Concomitant Procedures[a]

	Open (n = 14)	Arthroscopic (n = 20)
Modified Broström	0/13	6/19
Synovectomy	12/13	9/19
Osteophyte removal	2/13	2/19
Impingement removal	2/13	2/13
Loose body removal	1/13	4/19

[a]Data are presented as No.

the 2 groups ($P = .85$). For the openly treated patients, the mean lesion width was 8.7 ± 2.9 mm (range, 5-16 mm), the mean lesion length was 12.4 ± 2.5 mm (range, 7-15 mm), and the mean lesion depth was 4.1 ± 3.0 mm (range, 1-10 mm). For the arthroscopically treated patients, the mean lesion width was 8.6 ± 2.7 mm (range, 4-15 mm), the mean lesion length was 12.4 ± 4.0 mm (range, 6-20 mm), and the mean lesion depth was 3.3 ± 2.9 mm (range, 0-10 mm). The lesion width, length, and depth were not significantly different between the 2 groups ($P = .93$, .95, and .45, respectively). The operative time for the open group was, on average, 141 ± 41 minutes (range, 83-253 minutes) and for the arthroscopic group it was 159 ± 59 minutes (range, 64-304 minutes). It should be noted that the operative time depicts the total time in the operating room rather than the surgical time. The difference in operative times was not statistically significant ($P = .34$).

The outcome scores in means, standard deviations, ranges, and changes from baseline at 2-year follow-up are shown in Table 2. Patients in both groups improved from baseline to 2-year follow-up. While the arthroscopic group had greater improvements in each area, the *P* values represent a comparison between the 2 groups and do not represent significant changes from baseline within each group with the numbers available. At 2-year follow-up, there were no statistically significant differences found between the open and arthroscopic approaches with regard to the VAS for pain ($P = .09$), AOFAS ($P = .17$), FAAM-ADL ($P = .76$), FAAM-sports ($P = .73$), SF-12 physical health summary ($P = .85$), or SF-12 mental health summary ($P = .91$).

With that said, patients in both groups showed improvement in their reported pain at each time interval, with the exception of the open group at 2-year follow-up (Table 3). Patients also showed improvements in their outcome scores for each measure at all time intervals, with the exception of the SF-12 mental health summary for both groups, which demonstrated a clinically insignificant fluctuation at the 12-month and 18-month marks postoperatively (Table 4).

Patients in both groups had concomitant procedures performed during the same operative setting. In the arthroscopic group, 14 of 20 patients had at least 1 concomitant procedure. In the open group, all 14 patients had at least 1 concomitant

procedure. For the most part, the procedures were synovectomy, loose body removal, or removal of osteophytes. It should be noted that 6 patients in the arthroscopic group were treated with a modified Broström procedure. The concomitant procedures are listed in Table 5.

DISCUSSION

Our analysis demonstrated no significant difference between an arthroscopic versus open approach at any time point for the first 2 years after implantation of a juvenile particulated cartilage allograft for large OLTs. The overall outcomes of both patient groups in our study compare favorably with the findings of a previous study by Coetzee et al.[5] In that study, the authors evaluated 24 patients at a mean follow-up of 16.2 months. The lesions were similar in size (125 mm^2 vs 107 mm^2 in our study). The AOFAS score at final follow-up was a mean of 85 (range, 77-93), the FAAM-ADL score was a mean of 82.4 (range, 76-89), the mean FAAM-sports score was 63.4 (range, 52-75), and the mean VAS score was 24 (range, 13-34). All of their scores are similar to those listed for our patients in Table 2. The implantation technique in their study was not standardized. An open approach was utilized in 21 patients, and an arthroscopic approach was utilized in 3 patients. Outcomes between techniques were not compared.

At 2-year follow-up, all outcome scores in both groups did improve at the 2-year mark compared with preoperative values, with the exception of the VAS in the open group and the SF-12 mental health summary in both groups. The differences between the groups were not significant with the numbers given, and statistical analysis was not performed on the differences between preoperative values and final outcomes within groups.

The postoperative AOFAS scores in our study are similar to those found in other published operative treatments for OLTs, including microfracture, OATS, and ACI.[6,7,9,13] A randomized trial was performed by Gobbi et al[9] comparing the outcomes of microfracture, chondroplasty, and OATS. The authors found no difference in outcomes between the 3 groups at 53-month follow-up, and all 3 groups demonstrated improvements at final follow-up. At 24-month follow-up, the AOFAS score was 82.7, 85.4, and 83.8 for the chondroplasty, OATS, and microfracture groups, respectively.[9] The mean AOFAS score for the arthroscopic and open groups in our study was 86.0 and 85.0, respectively, at 2-year follow-up. The study by Giannini et al[6] was not randomized but also provided a comparison of outcomes for microfracture, chondroplasty, OATS, and ACI. The technique performed varied based on the chronicity and size of the lesion. The authors also used the AOFAS and reported scores for the entire cohort that were similar to those from our study, with a mean of 90.5 at 12 months and 93.2 at 4 years.[6]

This study has limitations. While this is the largest comparative study published to date, the sample size was small. We were not able to obtain 100% follow-up at each time point, as the study was performed on a military population, which has planned change-of-station moves every 2 to 3 years. This mostly affected the AOFAS ankle-hindfoot scale, which requires a physician to be present. We were able to obtain better follow-up on subjective patient outcome measures, although we had less than 70% follow-up at every time point. We did not control for the size of the lesion or for associated procedures at the time of surgery. We evaluated the differences between the 2 treatment techniques but did not statistically evaluate the efficacy of the treatment within each group. Outside of clinical outcomes, no assessment of healing was performed in terms of repeat imaging or second-look arthroscopic surgery. In addition, 2-year outcomes are relatively short given the concern for the potential development of osteoarthritis in patients diagnosed with symptomatic OLTs.

CONCLUSION

The treatment of talar articular cartilage lesions with a DeNovo NT Natural Tissue Graft demonstrated no significant differences in outcome at 2 years regardless of whether the graft was inserted with an arthroscopic or open technique.

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