CHAPTER **28**

Human Amniotic Allograft Used on Talar Dome Lesions: A Comparative Study

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INTRODUCTION

Osteochondritis dissecans (OCD), or lesion of the talar cartilage and subchondral bone, is a common pathologic condition that is often painful and disabling. Kappis in 1992 and Rendu in 1932 first reported and described OCD relating specifically to talar fractures (1,2). Berndt and Harty later classified the injury in 1959 and experimentally proved the traumatic etiology of the lesion (3). However, nontraumatic lesions can also occur. These defects cause deep ankle pain with weight-bearing. Impaired function, limited range of motion, stiffness, catching, locking, and swelling may be present. Due to the functional demand of the ankle, even small lesions can become very symptomatic.

Numerous conservative modalities for treating this condition have been described in the literature, including rest, immobilization, nonsteroidal antiinflammatory drugs (NSAIDs), avoidance of high intensity activity, physical therapy, and injections. Results of nonoperative treatment are quite variable. A large meta-analysis of 52 studies that reviewed nonoperative treatment for OCD lesions, showed nonoperative treatment produced good or excellent results in only 45% of patients (4). This implies that symptomatic lesions often require surgical treatment. Conservative treatment is still a reasonable first choice for small stable lesions. Should nonsurgical treatment fail at controlling symptoms, an equally extensive list of operations has been advocated and this list has increase substantially over the last decade. Widely published surgical strategies include excision of lesions, primary internal fixation for large lesions, marrow stimulation, osteochondral autograft, and osteochondral allograft. Newer techniques include autologous chondrocyte implantation and juvenile cartilage allograft, with the common goal to diminish symptoms and improve function (5-7). Because of the weight-bearing function and the vascular status of the talus, it is generally believed that small lesions are best treated with a less invasive surgical approach.

Human amniotic allografts have been in widespread use in a variety of applications including burn care, dentistry, ophthalmic, ear, nose and throat, and spine surgery since the early 20th Century (8-15). Later, Vokov showed success in using these allografts for repairing hip joints, along with other joints (16). The versatility of amniotic allograft allows it to form few adhesions, which opened up the use to a larger field of modern study (17). The stem cells present in human amniotic allograft tissue are thought to have some level of immune privilege as well as being considered multipotent, meaning they can differentiate into various tissue types including muscle, tendon, bone, or cartilage (18). Additionally, the amniotic tissues are comprised of various types of collagen, hyaluronan, and glycosaminoglycan and are thought to be a reservoir for growth factors (18). Advances in technology have delivered a safe and consistent product over the last two decades and clinicians are beginning to learn the potential benefits that the undifferentiated tissues can have on the healing process. As a result, human amniotic allograft may compete with today's gold standard of allografts (19-25).

The authors have used amniotic or human allograft derived from amniotic tissue in several surgical applications with exceptional results (26). Therefore, it was felt that human amniotic allograft could be applied to arthroscopic treated talar lesions and positively enhance the long-term outcome. Secondarily, the authors evaluated the accuracy of preoperative size of the lesion on magnetic resonance imaging (MRI) versus intra-operative measurement.

PATIENTS AND METHODS

This research was designed as a prospective comparative study, Level II evidence. There were 488 patients with OCD lesions treated arthroscopically from August 2008 to March 2012. A total of 129 of those patients met inclusion criteria, which consisted of talar dome lesions less than 2 cm^2. Of these, any patient having had additional procedures such has peroneal tendon relocation, tibial, fibular, or talar exostectomies not done arthroscopically were eliminated. Two patients were lost to follow-up and not included in the results. This brought the final cohort to 101 patients. All patients received arthroscopic debridement and microfracture, but some patients were randomly selected to

also receive the liquid form of human amniotic allograft. The talar dome lesion was measured intra-operatively and correlated to size and location on the MRI. Modified ACFAS ankle scores were collected prior to any surgical treatment, and postoperatively at 3 months, 12 months, and at 24 months. Pain visual analog scores (VAS) were also taken prior to surgery and postoperatively at 24 months. Most patients had preoperative and postoperative physical therapy, measured in weeks. Demographic information was also collected on the patient, including sex and age, as well as comorbidities. Preoperative MRIs were manually reviewed to measure the size of the lesion as compared to the size measured intra-operatively.

Operative Technique

The ankle arthroscopy was performed with standard medial and lateral portals. All ankles were distracted with a standard uniform distraction technique. All limbs had a thigh tourniquet used at 300 mm Hg. A pre-emptive proximal ankle block was given to all patients. All ankles were inspected, and a generalized synovectomy was done as indicated. As needed, a medial to lateral debridement and exostectomy of the anterior lip of the tibia was performed. Care was taken to assure no residual kissing lesions remaining on the tibial-talar interface. The talar dome lesion was identified and correlated to size and location on the MRI (Figure 1). A circumferential debridement was done to the subchondral level. A micro-fracture awl was used to perform the microfracturing of the lesion (Figure 2). Liquid form human amniotic allograft (2 ccs liguid NuCel [NuTech Medical]) was used and applied directly to the lesion via needle technique and under direct visualization. Instruments were removed and portals were closed. Patients were then placed in an ankle stirrup splint until the first postoperative visit.

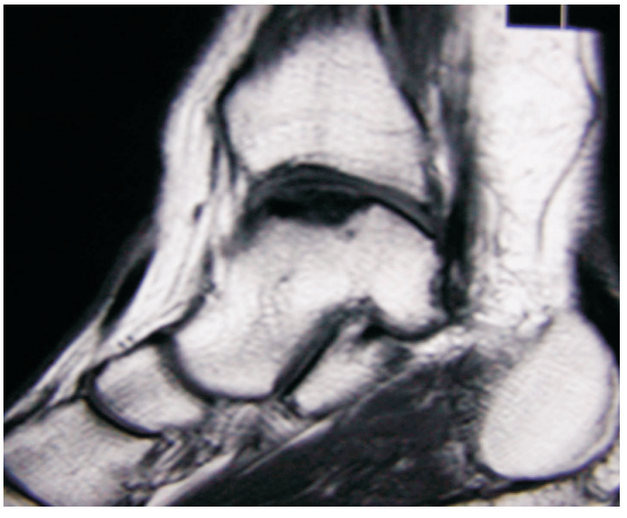

Figure 1. Preoperative magnetic resonance image of the talar dome lesion.

Human Amniotic Allograft Information

The human amniotic allograft used in this study is a commercial product that is composed of human amniotic membrane and cells from the amniotic fluid. The cells from the amniotic fluid include multipotent stem cells that have been shown to be capable of differentiation into a variety of tissue types including bone, muscle, cartilage, and tendon, among others. Additionally these tissues are rich in various growth factors including morphogenic proteins, hyaluronic acid, collagen precursors and proteoglycans (27-30). There is no antigenicity for the allograft due to the process of extracting amnion from the placental tissue (8,13,20,22,24,25). All harvested grafts are tested for human immunodeficiency virus, hepatitis, human T-cell lymphotropic virus type 1, and other diseases that are specific to processing. Each patient is also screened before donations can be collected.

RESULTS

A total of 47 patients were randomly selected to receive the allograft and 54 patients received the arthroscopic debridement and microfracturing alone. The patient characteristics are reviewed in Table 1. Patient characteristics were similar and there was no statistical significance between the 2 groups, except for the time of physical therapy. The group that did not receive the allograft had more physical therapy both prior to surgery and postoperatively. The average age was 47.3 years in the allograft group and 46 years in the nonallograft group. There were 24 females and

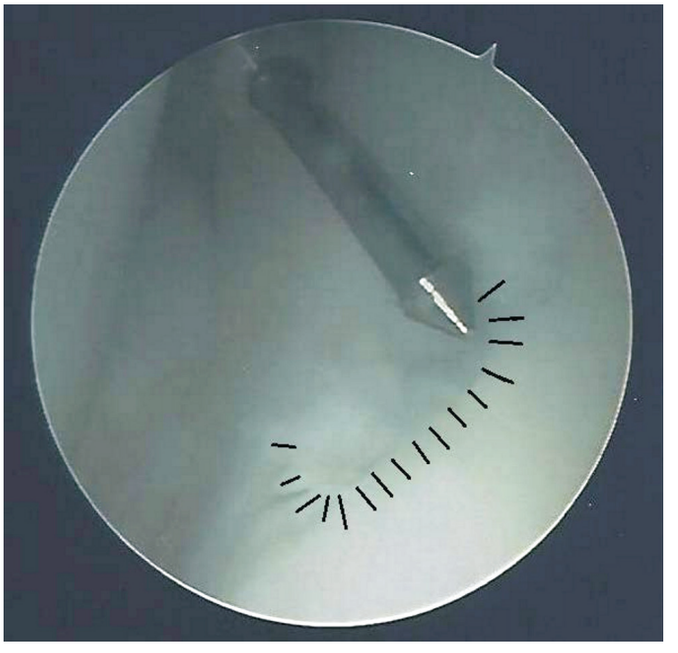

Figure 2. Typical osteochondritis dissecans with micro-fracture awl prior to application of liquid human amniotic allograft.

Table 1. Patient characteristics

	Allograft (n=47) n (%) or Mean (SD)	No Allograft (n=54) n(%)or Mean (SD)	*P**
Age (years)	47.3 (16.2)	46.0 (16.9)	0.70
Sex – Female	24 (51.1)	21 (38.9)	0.24
Diabetes	3 (6.4)	2 (3.7)	0.66
Hypertension	12 (25.5)	16 (29.6)	0.66
Obesity	3 (6.4)	4 (7.4)	0.99
Coronary artery disease	1 (2.1)	1 (1.9)	0.99
Thyroid disease	2 (4.3)	3 (5.6)	0.99
Injection prior to surgery	36 (76.6)	43 (79.6)	0.81
PT Pre-op (weeks)	3.9 (2.9)	5.1 (1.9)	0.01
PT Post-op (weeks)	4.7 (2.1)	5.7 (2.5)	0.02
Size of OCD			
MRI (cm)	1.8 (1.6)	1.8 (1.6)	0.83
Intraoperative (cm)	1.2 (0.4)	1.3 (0.4)	0.65

Table 2. Preoperative and postoperative visual analog scale scores

	Allograft (n=47)			No Allograft (n=54)			
	Pre	Post	Mean Change	Pre	Post	Mean Change	*P*
VAS	5.2 (1.8)	1.2 (1.4)	4.0 (1.8)	5.0 (1.9)	2.5 (1.3)	2.5 (1.4)	< 0.001

Table 3. Preoperative and postoperative ACFAS scores

	Allograft (n=47)				No Allograft (n=54)				
	Pre	3 mos	1 yr	2 yr	Pre	3 mos	1 yr	2 yr	*P* (change over time)
VAS	73.4	89.5	91.1	88.2	74.4	84.7	86.2	83.9	< 0.001
(4.3)	(3.9)	(3.4)	(4.7)	(5.0)	(4.5)	(4.1)	(5.9)		

23 males in the allograft group, compared to 21 females and 33 males in the nonallograft group. The average size of the lesion was the same for both groups. There were no identified postoperative complications in either group.

The average preoperative VAS in the allograft group was 5.2, which improved to 1.2 after surgery. In the nonallograft group, the average preoperative VAS score was 5.0, which improved to 2.5. The group that received the allograft had a mean change of 4.0 compared to the group that did not receive the allograft with a mean change of 2.5 ($P < 0.001$). The average ACFAS score for the allograft group was 73.1 preoperative, 89.6 at 3-months postoperative, 91.8 at 12 months postoperative, and 88.8 at 24 months postoperative ($P < 0.0001$ for each postoperative to preoperative score). The average ACFAS score for the nonallograft group was 74.4 preoperative, 84.7 at 3-months postoperative, 86.2 at 12 months postoperative, and 83.9 at 24 months postoperative ($P < 0.0001$ for each postoperative score to the preoperative score). The *P* value is for the overall trend over the 4 time points. Although both groups had improvement in the ACFAS score, the ACFAS scores were statistically higher for each time point in the allograft group (Tables 2, 3) (Figures 3, 4).

The average size of the defect or bone edema from MRI scans was 1.8 cm in both groups, 1.2 cm in the allograft group and 1.3 cm in the nonallograft group measured intraoperatively with a surgical ruler (Figure 5). There is moderate correlation, but not a perfect of strong correlation. This is something to consider when planning surgery.

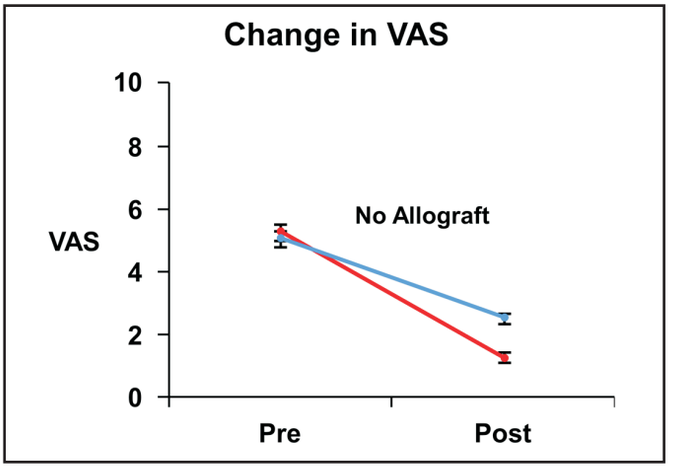

Figure 3. Mean ± SEM change in visual analog scale score.

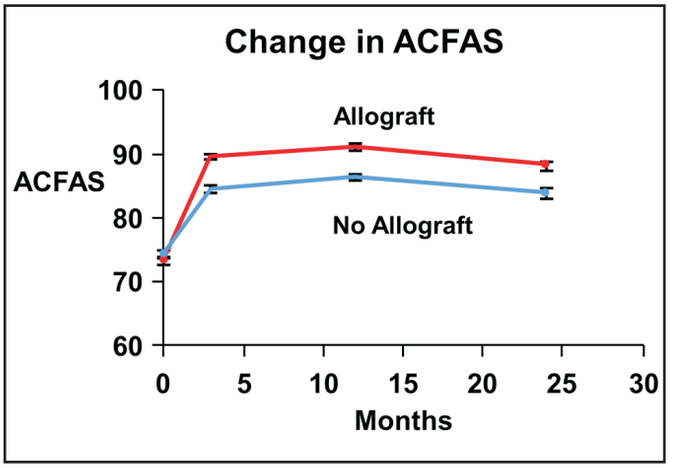

Figure 4. Mean ± SEM change in ACFAS score.

DISCUSSION

This prospective study shows that patients do significantly better overall from their preoperative status with arthroscopic-treated talar dome lesions less than 2 cm^2 using micro-fracture and adjunctive human amniotic allograft. While the use of human amniotic allograft has not been delineated as far as the techniques and applications in the ankle joint, it is accepted and has shown to be an effective allograft and a naive tissue in which its potential to differentiate can assist in healing (18). Possibly as an adjunct to further intervention, it is felt that this will allow hyaline cartilage development and the potential to develop into a more significant structural cartilage (27,29). The long-term efficacy and analysis cannot be derived based solely on this prospective application in the 37 patients. It would appear that there is a significant benefit in patient outcome, which may improve the long-term prognosis in these patients with progressive ankle joint arthrosis.

In conclusion, there will be continued application of human amniotic tissues within the role of allograft applications in the human body. The true role of this allograft tissue has not been fully ascertained; however, our data show that within the earlier postoperative years, there may be a use when applied to arthroscopically-treated talar dome lesions less than 2 cm^2.

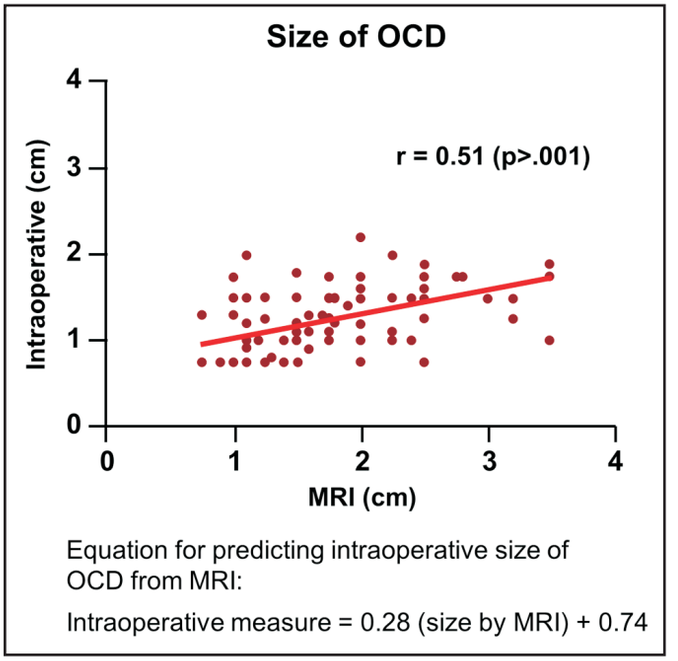

Figure 5. Correlation of lesion size preoperative versus intra-operative.

REFERENCES

1. Kappis M. Weitere Beiträgezur Traumatisch-Mechanischen Entstehung der Spontanen Knorpelablösungen (Sogen. Osteochondritis Dissecans). Deutsche Zeitschrift für Chirurgie 1992;171:13-29.
2. Rendu A. Fracture intra-articulaireparcellaire de la poûlieastraglienne. Lyon Médical 1932;150:220.
3. Berndt A, Harty M. Transchondral fractures (osteochondritis dissecans) of the talus. J Bone Joint Surgery 1959;41:988-1020.
4. Zengerink M, Tol JL, Struijs PA. Treatment of osteochondral lesions of the talus: a systematic review. Knee Surg Sports Traumatol Arthrosc 2010;18:238-46
5. Yvars MF. Osteochondral fractures of the dome of the talus. Clin Orthop Relat Res 1975;114:185-91.
6. Kelberine F, Frank A. Arthroscopic treatment of osteochondral lesions of the talar dome: a retrospective study of 48 cases. Arthroscopy 1999;15:77-84.
7. Angermann P, Jensen P. Osteochondritis dissecans of the talus: long-term results of surgical treatment. Foot Ankle 1989;10:161-3.
8. Hatch EL. Burns and bravery. In: Hatch EL, Médico E. My life as a country doctor in Mexico; 1999. p. 193-5.
9. Gwei-Djen L, Needham J. Medieval preparations of urinary steroid hormones. Int J Hist Med 1964;8:101-21.
10. Davis S. Skin transplantation: with a review of 550 cases at the Johns Hopkins Hospital. Johns Hopkins Hosp Rep Bat 1910;15:307-96.
11. Sabella N. Use of the fetal membranes in skin grafting. Med Reconciliation NY 1913;83:478-80.
12. Stern M. The grafting of preserved amniotic membrane to burned and ulcerated surfaces. substituting skin grafts. J Am Med Assoc 1913;60:973-4.
13. Douglas B. Homografts of fetal membranes as a covering for large wounds-especially those from burns: an experimental and clinical study (preliminary report). J Tennessee Med Assoc 1952;45:230-5.
14. DeRotth A. Plastic repair of conjunctival defects with fetal membranes. Arch Ophthal 1940;23:522-5.
15. Shimberg M. The use of amniotic-fluid concentrates in orthopaedic conditions. J Bone Joint Surg1938;20:167-77.
16. Volkov MV. Arthroplasty of joints using amniotic membrane. In: Chapchal G. Arthroplasty of the hip: 5th International Symposium 1972 in Nijmegen Netherlands, Georg Thieme, Stuttgart. 1973.
17. Trelford JD, Hanson FW, Anderson DC, Mendel VE. Amnion autografts, permanent structure. J Med 1975;6:243-7.
18. Sachs BP, Stern CM. Activity and characterization of a low molecular fraction present in human amniotic fluid with broad spectrum antibacterial activity. Brit J Obstet Gynaecol 1979;86:81-6.
19. Anderson JJ. bone grafting and orthobiologics for reconstruction of the diabetic lower extremity. In: Zgonis T. Surgical reconstruction of the diabetic foot and ankle. Lippincott Williams & Wilkins, Philadelphia; 2009. p. 192-3.
20. Cornell CN. Osteoconductive materials and their role as substitutes for autogenous bone grafts. Orthopedic Clin North Am 1999;30:591-8.
21. Weinraub GM. Orthobiologics: a survey of materials and techniques. Clin Podiatr Med Surg 2005;22:509-19.
22. Lane JM, Bromstrom MP. Bone grafting and new composite biosynthestic graft materials. AAOS Instructional Course Lectures 1998;47:525-34.
23. Martin RB, Chapman MW, Sharkey NA, Zissimos SL, Bay B, Shors EC. Bone ingrowth and mechanical properties of coralline hydroxyapatite 1 year from implantation. Biomaterials 1993;14:341-8.
24. Anderson JJ, Boone JJ, Hansen M, Brady C, Gough A, Fowler Z. Ankle arthrodesis fusion rates for mesenchymal stem cell bone allograft verses proximal tibia autograft. J Foot Ankle Surg 2014;53:683-6.
25. Anderson JJ, Jeppesen NS, Hansen M, Brady C, Gough A, Fowler Z. First metatarsophalangeal joint arthrodesis: comparison of mesenchymal stem cell allograft versus autogenous bone graft fusion rates. Surgical Science 2013;4.
26. Anderson JJ, Gough AF, Hansen MH, Swayzee Z. Initial experience with tricortical iliac crest bone graft and human amniotic allograft in evans calcaneal osteotomy. J Am Podiatr Med Assoc 2014.
27. Davitt JS, MacWilliams BA, Armstrong PF. Plantar pressure and radiographic changes after distal calcaneal legthening in children and adolescents. J Pediatr Orthop 2001;21:70-5.
28. NuTech Medical NuCel: Multipotential Cellular Matrix (HCT/P).
29. NuTech Medical NuCel: Product Overview; 2012.
30. Sato TA, Keelan JA, Mitchel MD. Critical paracrine interactions between TNF-α and IL-10 regulate lipopolysaccharide-stimulated human choriodecidual cytokine and prostaglandin E_2 production. J Immunol 2003;170:158-66.