CHAPTER **10**

ANKLE ARTHRODESIS FUSION RATES FOR MESENCHYMAL STEM CELL BONE ALLOGRAFT VERSUS PROXIMAL TIBIA AUTOGRAFT

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INTRODUCTION

Historical literature views autograft as the gold standard for arthrodesis with the presumption that it yields a higher rate of fusion (1). Many times there is significant shortening, joint irregularity and bony voids often due to complications from previous trauma, malunion, and infection (2). Because of this, often during fusions, bone graft material interposition is needed as an adjunct to arthrodesis of the joint. The field of orthobiologics is rapidly expanding. There has been an explosion of scientific research behind bone grafting substitutes and materials. A growing consensus in the literature suggests that some bone graft materials perform equally well in comparison and even have shown improved clinical applications when compared to autograft as the gold standard for arthrodesis procedures (3-5).

Allogenic bone grafting material has been available and used as an adjunct for fracture and fusion repairs over the last hundred years (6). Autograft harvest and its applications have also been used for the last several hundred years (7). Over the last 10 years, allogenic bone graft material impregnated with precursor or mesenchymal stem cells (MSC) has expanded beginning in areas of the spine and is now being used in other areas of the body (8, 9). Mesenchymal stem cells are precursor cells that have potential to differentiate and proliferate into precursor cell lines. In the case of MSC allogenic bone graft, it has been implicated that they develop with increased potential as compared to nonimpregnated allograft bone. This in theory would be an improvement over allograft bone with only bone morphogenic proteins (BMPs) or like material and growth factors alone or in combination with allogenic bone. The BMPs are a group of over 20 naturally occurring, inducible proteins that are known to play a critical role in inducing osteogenesis. The most commonly used at this time are BMP-2 and BMP-7 as they have more osteo-selective properties (10).

The purpose of this retrospective cohort study was to assess outcomes subjectively and objectively in patients who had undergone ankle arthrodesis and received either MSC bone allograft or proximal tibia autograft as an adjunct. We report the results of 85 ankle arthrodeses performed utilizing a consistent surgical approach by the same surgeon.

MATERIALS AND METHODS

A total of 109 patients underwent ankle fusion surgery between January 2002 and May 2008. Inclusion criteria included >2 years of follow up, and patients who received either MSC bone allograft or autograft from the proximal tibia as an adjunct to ankle arthrodesis. Exclusion criteria included revision surgery, Charcot neuroarthropathy, fusion of adjacent joints, external fixation, and patients who received both autograft and MSC bone allograft with or without additional allograft. This excluded 24 patients leaving a total of 85 patients.

Of the included patients, bone autograft was taken from the proximal tibia medullary canal in 41 patients (Figures 1-3) and allogenic impregnated bone graft with MSC was used in 44 of the included patients (Figure 4). The fibula was also split into 2 parts and used as a strut onlay graft in all but 8 of the patients. We used the fibula as an onlay graft in both groups, this was not considered as an autograft harvest in either group. The decision to use proximal tibia autograft or MSC bone allograft was made preoperatively and perioperatively taking into account the patient's desire to avoid additional procedures, quality of bone, amount of degenerative change seen at the ankle joint, and availability of on-site MSC bone allograft. For example,

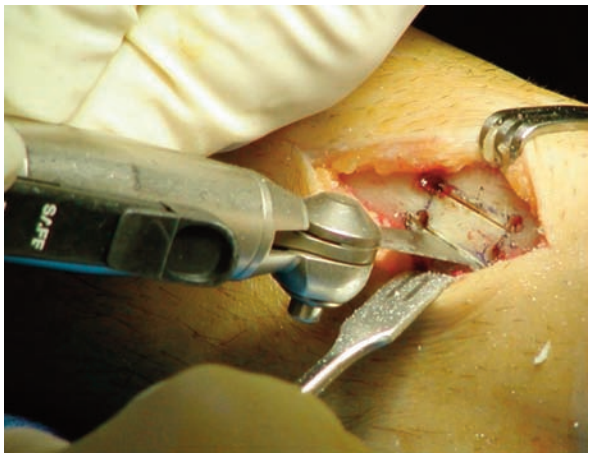

Figure 1.

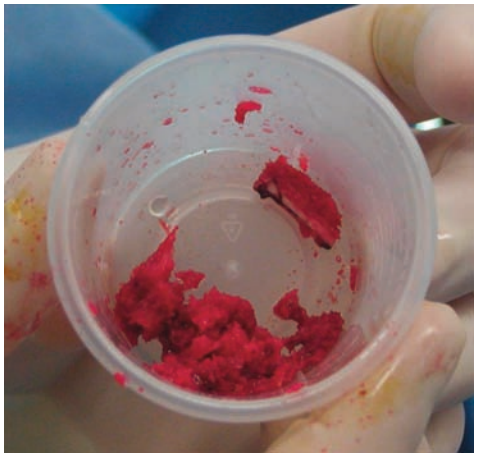

Figure 2.

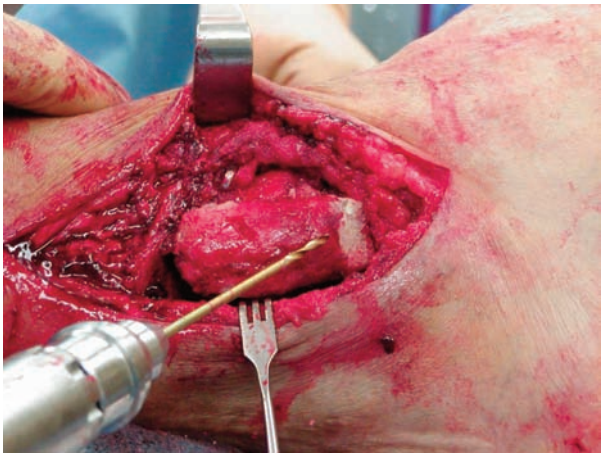

Figure 3.

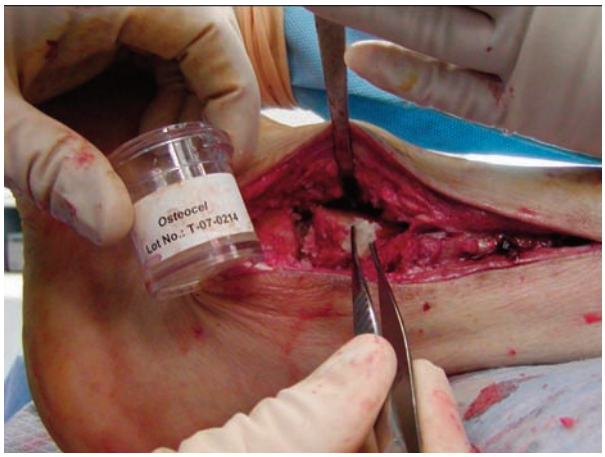

Figure 4.

if intraoperatively the patient needed a large amount of bone resected due to anatomy or soft bone, MSC bone allograft or autograft was used depending on the amount of bone needed. Also, if the patient had a preference for autograft versus MSC bone allograft, that was taken into consideration. Many of the MSC bone allograft preparations were not available during the first several years of fusion data collection.

The range of follow up was 2 to 8.5 years with a minimum of 2 years. The charts were reviewed thoroughly to determine the time to clinical fusion defined as the patient's cessation of pain, the ability to ambulate in regular shoe gear, and ability to return to previous activity. To determine patient satisfaction a modified and adjusted American College of Foot and Ankle Surgeons (ACFAS) ankle scale was used and the patient was also asked if they would undergo the same procedure again. They were radiographically analyzed by follow up films done at various intervals to determine the time to radiographic fusion. This was determined by 3 independent foot and ankle specialists with no knowledge of the time interval between fusion and the radiographic findings. Radiologic fusion was defined by bony trabeculation across the ankle and agreement between all 3 independent reviewers that fusion had taken place. When calculating time to radiologic fusion, malunions/nonunions were excluded in order to not skew the data. Postoperative complications to include nonunion/malunion were recorded. Fusion rates were also calculated and compared between both groups. The patient's contributing factors such as tobacco use, diabetes mellitus, rheumatoid arthritis, and underlying neurologic disorders were also noted.

RESULTS

A total of 85 consecutive ankle fusions in 85 patients met our inclusion criteria in our cohort. The cohort was divided into 2 groups, The MSC bone allograft group consisted of 44 patients and the autograft group was made up of 41 patients. The demographic description of the cohort can be seen in Table 1. The mean age was 62.4 ± 1.8 years and 64.0 ± 1.6 years in the MSC bone allograft group and the autograft group, respectively.

Radiographic fusion rate was 84.1% in the MSC bone allograft group and 95.1% in the autograft group ($P = 0.158$). The mean time to radiographic fusion was 13.0 ± 2.5 weeks and 11.3 ± 2.8 weeks ($P < 0.001$) in the MSC bone allograft group and the autograft group, respectively. The mean time to clinical fusion was 13.1 ± 2.1 weeks and 11.0 ± 1.5 weeks ($P < 0.001$) in the MSC bone allograft group and the autograft group, respectively. There was no difference between preoperative and postoperative ACFAS ankle scores when comparing MSC bone allograft and autograft groups ($P = 0.41$ and $P = 0.42$, respectively). A modified and adjusted ACFAS ankle score was used preoperatively and postoperatively. The MSC bone allograft score was 57.5 preoperatively and 78.75 postoperatively. The autograft group scores were 58.25 preoperatively and 80.25 postoperatively. There was statistical difference between the 2 groups when compared preoperatively ($P = 0.41$) and postoperatively ($P = 0.44$). Patients were asked if they would repeat the procedure 95.4% and 90.2% ($P = 0.42$) indicated they would do it again in the MSC bone allograft group and autograft group respectively (Tables 2, 3).

Complications were divided into moderate and minor complications. Moderate complications included nonuions/malunions and minor complications include superficial wound dehiscence. There were 7 nonunions in the MSC bone allograft group and 2 nonunions in the autograft group. There were 5 instances of superficial wound dehiscence in both groups, which healed uneventfully with local wound care in all cases. There were no complications in the autograft group from harvest from the proximal tibia site. Of the total 9 nonunions in the cohort, 6 of these were smokers. Unsurprisingly smokers had a higher incidence of nonunions than those who did not smoke ($P < 0.001$). There were 3 of the 9 smokers who went on to successful

Table 1

DEMOGRAPHIC DESCRIPTION OF COHORT (N = 85)

	MSC Allograft (N = 44)	Autograft (N = 41)
Age mean ± SD, years	62.4 ± 11.9	64.0 ± 10.3
Comorbidities (DM,RA,Neuro,Obese)	16	13
Smoker	7	2

MSC = mesenchymal stem cell; DM=diabetes mellitus; RA = rheumatoid arthritis; Neuro= peripheral neuropathy.

Table 2

RESULTS COMPARING MSC BONE ALLOGRAFT AND AUTOGRAFT IN ANKLE ARTHRODESIS

	MSC Allograft	Autograft	*P**
Rad FR	84.1%	95.1%	0.158†
Time to CU	13.1±2.1wks	11.0±1.5wks	< 0.001
Time to RU	13.0±2.5wks	11.3±2.8wks	< 0.001
Moderate Complications	7	2	0.158†
Minor Complications	5	5	

MSC = mesenchymal stem cell; rad = radiographic; fr = fusion rate; ru = radiographic union; cu = clinical union.
* By Student's t-test.
† By Fisher's exact test.

Table 3

MODIFIED AND ADJUSTED ACFAS SCORE AND LIKELIHOOD TO REPEAT PROCEDURE

	Preop	Postop	Likelihood to repeat procedure
MSC Allograft	57.5	78.75	42 (95.4%)
Autograft	58.25	80.25	37 (90.2%)
P*	0.41	0.44	0.42

ACFAS = American College of Foot and Ankle Surgeons; MSC = mesenchymal stem cell; preop = preoperative; postop = postoperative.
* By Student's *t*-test

clinical and radiographic union. It should be noted that preoperatively, the 9 smokers agreed to quit while 7 of the 9 started smoking again within 4-6 weeks following the surgery. There was no difference in healing rate in patients who had complications in regard to comorbidities ($P = 0.704$).

DISCUSSION

Ankle arthrodesis remains a viable option in treating ankle arthritis. We recognize that we have excluded complex revisional surgeries or surgeries including revision for nonunion, bone infections, patients with significant secondary deformity, Charcot neuroarthropathy, and those with external fixation in our cohort. In a majority of cases we used partial fibula onlay strut graft. Often the quality of this bone was not such that it could be used as a partial autograft, which is why we felt it necessary to harvest bone graft from the proximal tibia. There were no complications that have been recorded in the literature (11) such as tibial plateau fracture, wound and bone healing complications or dehiscence, or secondary tibial fractures from proximal tibia harvest in our study.

Although we recognize that no one ankle fusion is the same, we believe we have a significant number of ankle fusions with a similar surgical technique by the same surgeon that one may conclude that the overall surgical approach to ankle arthrodesis is consistent. By excluding the confounding or confusing nature of complex revisional surgeries, nonunions, and infections we felt we have a similar patient population to compare using MSC bone allograft and autograft use in ankle fusions.

There was not a statistical difference in the fusion rate between both groups although there was a difference between the groups in regard to time to clinical and radiographic fusion favoring autograft in both cases by approximately 2 weeks in each instance. This would suggest that autograft may allow earlier weight bearing and return to normal activities of daily living. However, patient satisfaction determined by using a modified and adjusted ACFAS ankle scale and willingness to repeat the procedure showed no difference statistically between the 2 groups.

Limitations in our study include lack of control group that received neither MSC bone allograft nor autograft, use of different MSC bone allograft preparations, using bony trabeculation as a definition of radiographic union. Also from a statistical standpoint, we did not perform regression type analysis and therefore were not able to determine the role that independent variables alone or in combination may have had on our outcomes.

Given the rapidly changing nature of the commercially available MSC bone allograft preparations, the same product was not always used. This could confound the data given that there is some variability in the minimal amount of viable MSCs per cc in the different preparations. It has been suggested in the literature that a higher concentration of MSCs may lead to enhancement of bony healing and this could lead to differences in terms of rate of bony healing (12). Although this is unfortunate, this represents the current climate of change in the rapidly expanding world of orthobiologics. Future studies would be helpful comparing the myriad MSC bone allograft preparations to each other. Also MSC bone allograft material was not readily available in the early stages of this study.

There is no clear gold standard in determining bony union. Controversy exists in the preferred modality to determine bony fusion (13). Radiographs alone are often insufficient in indicating the presence or absence of fusion, and more advanced modalities including computed tomography and nuclear medicine scans have been used. By using an independent panel of 3 experienced foot and ankle physicians, we felt this was an appropriate indicator in determining radiographic fusion given the high financial cost for advanced imaging modalities.

Even though we are aware of smoking and its relationship to nonunion, it should be noted that even when patients presumably have the requirement to quit 4 to 6 weeks prior to surgery, many of these patients resume smoking in the immediate postoperative period and incidentally in this study a majority of our nonunions did have smoking as a comorbidity. While this is well documented in the literature, this study underscores the deleterious effect smoking can have on bone healing as a majority of the nonunions were patients with a history of smoking (14).

Although we did not report on the additional cost of MSC bone allograft, this may be negated by the decrease in surgical time. Although the proximal tibia harvest for our patients added approximately 10 to 20 minutes to the total surgical time, there may be other surgeons who are less familiar with this technique and procedure in which case it may take up to 30 to 45 minutes. Many times this void was filled with a less expensive allograft proximally and this may also be taken into consideration in the overall cost of proximal bone graft harvesting. Although MSC bone allograft can be costly, it saves time and presumed morbidity although not seen in our study with a more proximal harvest site.

The overall conclusion in our study is that both the MSC bone allograft and autograft are equivalent in regard to patient satisfaction and fusion rates. Autograft showed shorter time to radiographic and clinical fusion. MSC bone allograft can be a useful adjunct in performing ankle arthrodesis and does not negate autograft as a gold standard.

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