CHAPTER **24**

# FIRST METATARSOPHALANGEAL JOINT ARTHRODESIS: COMPARION OF MESENCHYMAL STEM CELL ALLOGRAFT VERSUS AUTOGENOUS BONE GRAFT FUSION RATES

*John Joseph Anderson, DPM*
*Nathan S. Jeppesen, DPM*
*Myron Hansen, DPM*
*Chad Brady, DPM*
*Adam Gough, DPM*

## INTRODUCTION

Bone grafting is indicated for many surgical procedures. The first metatarsophalangeal joint (MPJ) in a large proportion of cases, does not need a bone graft interposition while attempting to achieve fusion. However, various situations and patient conditions may affect the quality of the bone that makes bone grafting necessary for optimum results for the patient. A consequence of some systemic diseases and end stage deformity of the first MPJ can be the formation of soft bone, bony voids, and bony cysts (1-4). In situations where excessive bone resection is necessary depending on the patient condition and in cases where secondary to variety of intraoperative techniques, a small amount of bone graft is necessary, the surgeon must decide where best to harvest or which graft source to use. These options range from the gold standard autograft (1), to allograft, to myriad other orthobiologic materials designed to facilitate bony fusion. Many times the resected portions of the first metatarsal head or bone from a secondary surgical procedure may provide sufficient autologous bone quality during the first MPJ fusion. This may be used to facilitate bony union at these sites.

Mesenchymal stem cells (MSC) that are impregnated in cancellous allograft are becoming more commonly used to aid in achieving adequate fusion rates. MSCs are multipotential adult stem cells that can differentiate into bone, cartilage, or fat cells depending on local needs and environment (5). MSCs in the arthrodesis setting will be exposed to cytokines and other local factors that will direct them in differentiation to the osteoblast cell line (5). Donor MSCs are also advantageous in that they elicit little to no immune response in host tissue and even aid in reducing local inflammatory response (6). The combination of MSCs with a cancellous carrier (available in several different varieties commercially) makes these grafts osteoinductive, osteoconductive, and osteogenic, theoretically closely resembling a patients autologous bone.

In the current health care age we realize the cost and impact of increased operative time to harvest bone graft elsewhere such as the proximal tibia, the distal tibia, the calcaneus, or surrounding areas. Likewise there is also an increased era of cost containment with the expense of operative materials, i.e., orthobiologics, bone allograft including demineralized bone matrix, bone allograft and MSC products. This study compares what the literature suggests is the "gold standard," (1) which is bone autograft to allogenic bone graft impregnated with MSCs in the context of first MPJ arthrodesis. There are no long term outcome studies comparing these two groups of patients requiring first MPJ fusions. Our primary hypothesis is that there will be very comparable times to fusion and union rates among autograft and allograft with MSC groups in the setting of a first MPJ arthrodesis. This should help the surgeon with additional information in the comparison of the use of these materials. A secondary endpoint of this study was to evaluate the number of nonunions in patients with higher risk co-morbid conditions. We hypothesize that the presence of diabetes, obesity, rheumatoid arthritis (RA), or smoking will increase the rate of nonunions within our patient population.

## PATIENTS AND METHODS

The study included 204 consecutive patients, from August 2003 to December 2008, undergoing first MPJ arthrodesis for end-stage deformity correction from the practices of all authors except NSJ. The patients were divided into 3 treatment groups consisting of first MPJ fusion with MSC impregnated allogenic graft, autologous bone graft, and end-to-end arthrodesis where no graft interposition was used or necessary. The end-to-end arthrodesis group was used

in this study as a similar but not necessarily equivalent "control" to the other groups. Data collection used for statistical analysis was patient age, patient sex, radiographic time to union, clinical time to union, nonunion rate, presence of comorbid conditions, and patient satisfaction compared between 3 treatment groups.

Radiographic union was determined by visualizing obvious bony bridging (7) across the arthrodesis site in a time blinded fashion by 3 independent podiatric surgeons. Clinical union was determined by 3 criteria (7); subjective resolution of pain about the operative site, lack of clinical motion, and full return to normal shoe gear. Patients were evaluated on a weekly basis for the first two weeks, clinically, and radiographically. Then, every 2 weeks, patients were evaluated until all conditions noted previously had been met. Multivariate analysis was performed to determine p values in all situations where possible. Data regarding additional procedures that were secondary procedures to the first MPJ fusion were not gathered in this study.

Patient satisfaction was determined via office visit survey. In this survey, patients were questioned about their satisfaction with the procedure and willingness to have the procedure again. Patients were also questioned about their timeliness of getting back into regular shoe gear, which was 1 of the 3 criteria for clinical union determination noted above.

The following were exclusionary criteria for this study; revisional first MPJ fusion secondary to malunion or previous nonunion, previously infected joint, history of Charcot neuroarthropathy, or history of first MPJ dislocation with sesamoidal fracture. A total of 39 patients were excluded based on these criteria making the total number of patients evaluated 165. A breakdown of these patients can be found in Table 1.

The allogenic MSC products utilized in this study were Trinity (Evolution) and Osteocel (Plus). Both of these products underwent changes in the amount of MSCs in their product through the duration of the study and both underwent name changes indicated in parenthesis above. The brand of MSC graft used was based on surgical site or hospital availability and was not designated in data collection for this study.

**Table 1**

**BREAKDOWN OF EXCLUDED PATIENTS**

| | |
|---|---|
| Malunion of first MPJ | 21 |
| Prior nonunion to first MPJ | 11 |
| History of Charcot deformity | 3 |
| History of first MPJ septic joint | 3 |
| First MPJ dislocation with sesamoid fracture | 1 |
| **Total** | **39** |

## SURGICAL TECHNIQUE

The arthrodesis techniques were similar in each case. All procedures were done under anesthesia with local adjunct. The primary operative procedure was a first MPJ fusion in each of the cases. The first MPJ joint was approached via dorsal medial approach and a linear dissection performed. The bone was curettaged on both sides of the joint down to the subchondral bleeding bone via rongeur, burr, and curettage technique. At that time a determination was made by the surgeon whether or not use of bone graft was necessary. It was deemed necessary in cases where there was soft bone, bone voids, or bone cysts about the fusion site (Figure 1).

If a secondary surgical procedure was done and excess bone of necessary quality was available or the dorsal medial first metatarsal bone had enough cancellous quality bone to use as a graft then this graft was used. If an adjunct procedure was performed and other graft elsewhere such as phalanx or metatarsal bone was available, this bone was used. The autogenous graft was reduced to cancellous bone chips in all cases, as they were not intended for structural support.

If there were no secondary procedures performed from which bone could be obtained or the bone obtained from these areas was not of adequate quality then allogenic impregnated MSC graft material was used. The graft was only used as a bone void filler or adjunct for soft bone, but was not used as a strut or meant for mechanical support of the fusion or fixation. Multiple screw fixation, 2-5 crossed screws, was used for all cases. The appropriate number of screws used was determined by the surgeon until it was felt the first MPJ arthrodesis site was adequately fixated (Figure 2).

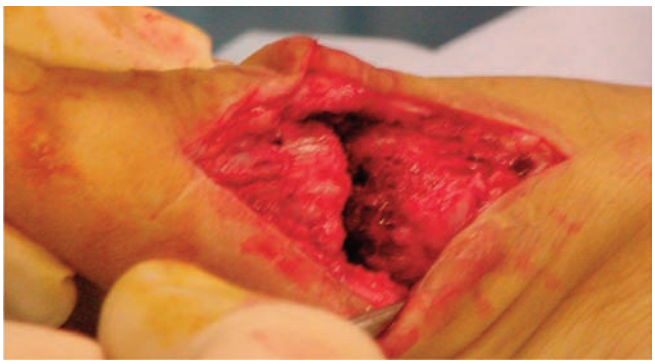

Figure 1. Prepared joint surfaces with cystic and osteopenic changes to the first metatarsal head.

## RESULTS

Tables 1 to 5 depict the statistical results of the study. The patients in this study were well distributed between the treatment groups with regard to sex and age as depicted in Tables 2 and 3.

The average radiographic time for fusion in the end-to-end arthrodesis was 6.76 weeks (range 4-12). The time for radiographic fusion in the autograft group was 6.69 weeks (range 4-11). The average radiographic time for fusion in the allograft MSC group was 7.0 weeks (range 4-12). An ANOVA test was used and revealed a *P* value of 0.676, which showed no clinical statistical significance between the treatment groups that did achieve fusion. However this data does not take into consideration the nonunions as a time period for union could not be calculated for these patients (Table 3).

The average time to clinical and functional fusion in the end-to-end arthrodesis was 6.46 weeks (range 4-10). The time for time to clinical and functional fusion in the autograft group was 6.52 weeks (range 4-11). The average time to clinical and functional fusion in the allograft MSC group was 6.53 weeks (range 4-12). A Scheffe test of homogenous subsets was used and revealed a *P* value of 0.966, which showed no clinical statistical significance between the treatment groups. All patients in this study achieved clinical or functional union regardless of radiographic presence of nonunion (Table 3).

There were a total of 6 nonunions in the MSC allograft group, 3 nonunions in the autograft group, and 2 nonunions in the control group. Pearson chi-square test was used to determine that the *P* value between all 3 treatment groups was 0.209. A 2-sample test of proportions was used to more precisely calculate the *P* value of the nonunion rates between only the autograft group and the MSC allograft group, which was 0.177 (Table 3). The percentage of procedures achieving fusion in the control group was 96.0%. in the autograft group was 95.2%, and in the MSC allograft group was 88.2% (Table 3).

The percentages of patients that would have the procedure again and were satisfied with the procedure were 96% in the end-to-end fusion group, 98% in the autograft group, and 92% in the allograft/MSC group. There was no statistical significance between the 3 treatments groups (Table 4).

There were no nonunions in the 12 diabetic patients in the study. There were 2 nonunions in 5 obese patients, which was statistically significant with a *P* value of 0.036. There were 5 nonunions in the RA group of 15 patients, which was statistically significant with a *P* value of 0.001. There were 5 nonunions in the group of 32 patients that smoked, which was statistically significant with a *P* value of 0.024. There was an overlap between the patients with obesity, RA, and those that were smokers (Table 5).

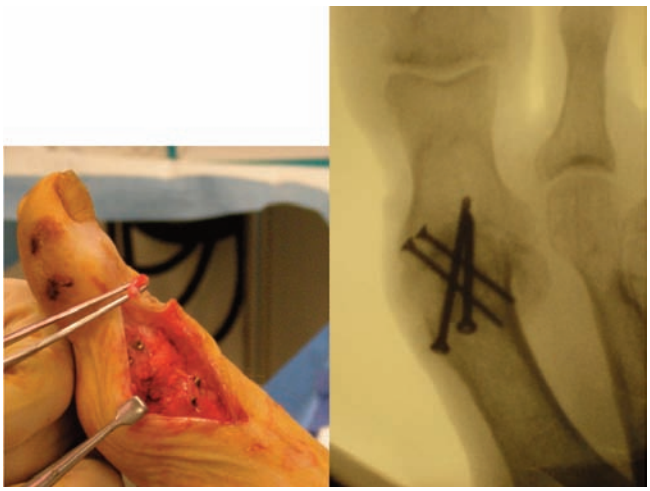

Figure 2. Intraoperative and fluoroscopic view of the first metatarsophalangeal joint fusion fixation technique used. Two to 5 crossed screws were used until the first metatarsophalangeal joint was felt to be adequately fixated.

## DISCUSSION

The control group that was used in this study did have a slightly different patient population than those in the autograft group and the MSC allograft group. The patients in the end-to-end arthrodesis groups all had sufficient bone quality with no evidence of soft bone, bony voids, or large bony cysts. As such these patients we expect to have a higher reported fusion rate as evidenced in the literature (8, 9). The patients in the control vary from the other two groups studied in that these two graft groups did have different and less than desirable bone quality. However, the autograft group and the allograft group had the same indications for the need of grafting material, and they can be compared together and appropriate results deduced. Thus, the control group is used as a guide to compare to other published data

**Table 2**

### SEX DISTRIBUTION BETWEEN GROUPS

| | Treatment Group | | Total |
|---|---|---|---|
| | Allograft | Autograft | End-to-End |
| Male | 20 | 31 | 21 | 72 |
| Female | 31 | 31 | 31 | 93 |
| **Total** | **51** | **62** | **52** | **165** |

Pearson Chi-square = 1.650. *P* = 0.438

**Table 3**

## COMPARISON BETWEEN THE 3 TREATMENT GROUPS

| | N | Mean Age | Time to Clinical Union (weeks) | Time to Radiographic Union (Weeks) | Total Radiographic Nonunions | % of Radiographic Fusion |
|---|---|---|---|---|---|---|
| Allograft MSC | 51 | 62.2 ± 1.98 (range 33 -89) | 6.53 ±1.39 (range 4-12) | 7 ± 1.98 (range 4-12) | 6 | 88.20% |
| Autograft | 62 | 62.16 ± 1.7 (range 40-88) | 6.52 ±1.46 (range 4-12) | 6.69 ± 1.70 (range 4-11) | 3 | 95.20% |
| End to End arthodesis | 52 | 61.71 ± 1.72 (range 39-80) | 6.46 ±1.31 (range 4-10) | 6.76 ± 1.72 (range 4-12) | 2 | 96.00% |
| *P* | | 0.967* | 0.966† | 0.676* | 0.209‡ 0.177§ 0.296¶ | n/a |

* ANOVA test
†Scheffe test of homogenous subsets
‡Pearson Chi-Square
§ 2 sample test of proportions between only Allograft MSC and Autograft groups
e¶Fischer's exact test between only Allograft MSC and Autograft groups

**Table 4**

## PATIENT SATISFACTION RESULTS

| | Treatment Group | | Total |
|---|---|---|---|
| | Allograft | Autograft | End-to-End |
| Have procedure again? | | | |
| Yes | 47 | 61 | 50 | 158 |
| No | 4 | 1 | 2 | 7 |
| Patient Satisfaction % | 92% | 98% | 96% | |
| **Total** | **51** | **62** | **52** | **165** |

Pearson Chi-square = 2.703. *P* = 0.259

**Table 5**

## CO-MORBID CONDITIONS AND NONUNION RATE

| Co-morbidity | N | Non-union | *P* |
|---|---|---|---|
| Diabetes | 12 | 0 | 1.00* |
| Obesity | 5 | 2 | 0.036* |
| Rheumatoid Arthritis | 15 | 5 | 0.001† |
| Smoker | 32 | 5 | 0.024† |

*Fisher's Exact test.
† Pearson Chi-square.

and to then serve as a control for comparing the other 2 studied groups presented here.

This study confirms our original hypothesis that autograft from surrounding areas and allogenic bone graft impregnated with MSC are both viable options for the foot and ankle surgeon to use when a bone void deficit or surgical anatomy require use of bone adjunct to help facilitate union. This being evidenced from our results that the time to radiographic and clinical fusion rate and patient satisfaction are similar for each group. The nonunion rate showed a trend that that the autograft group was more effective than the MSC allograft group but all parameters showed no statistically significant difference in outcome. This was most likely due to the lower total number of nonunions present among all treatment groups.

Once again it must be reiterated that these grafts were not used as structural support to obtain length in a revisional surgery. All cases were primary first MPJ fusions. The data presented here cannot be directly extrapolated and applied to revisional or primary cases where bone graft is used as a structural graft. Additional studies that specifically studied that premise would be necessary to make certain conclusions.

If indeed localized bone autograft can be used, then this study would support the use of that surrounding bone. However it is realized that often time the quality and amount

of bone are not readily available intraoperatively. Many times there are unforeseen cystic changes, deficits, and bone voids that are realized upon denuding the cartilage down to the subchondral bone upon preparation of the first MPJ. We do recognize that having to harvest local graft elsewhere would increase the amount of operative time (10) and potentially risk donor site morbidity (10, 11) such as prolonged pain and infection. Our results demonstrate that the potential to eliminate these complications with the use of the MSC allograft is now a viable option for the surgeon. We feel that further study regarding cost and benefit versus morbidity of bone graft harvesting is warranted as this was not one of the aims of this study. However, this is an appropriate question amid the era of cost containment within the current healthcare setting.

Our results also confirm previously held knowledge about the increase rate of nonunion in smoking patients. As always proper patient education and encouraging the patient to refrain from smoking until union is achieved is advised. Proper patient education is also encouraged in RA and obese patients as there was shown to be an increased chance of nonunion rate in these groups. These patients need to be aware of the higher risk of nonunion to prepare them for realistic expectations. It has been suggested in the literature that there is an increased rate of nonunions in diabetic patients (12) but this was not evident in our patient population, contrary to our original hypothesis. However, our population of diabetics in this study was small, and we cannot truly make the conclusion that they are not at increased risk for non-unions. Larger populations would need to be studied in all of the co-morbid condition groups for the most accurate verification of our results.

The results of this study once again confirm that if one is faced with the need to use bone grafting for any situation discussed previously, MSC impregnated allograft is a viable alternative. If one has a choice between readily available autograft from the residual first metatarsal head or secondary procedures then this should be used. However, if this autograft is of poor quality or unavailable, the surgeon should feel comfortable using of the MSC impregnated allograft when the need of a graft exists.

## ACKNOWLEDGMENTS

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