Osseous Healing With a Composite of Allograft and Demineralized Bone Matrix: Adverse Effects of Smoking

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Abstract

We report on our use of a composite graft of lyophilized cancellous allogenic chips and demineralized bone matrix (DBM; Grafton®; Osteotech, Eatontown, NJ) to manage traumatic osseous defects and nonunions.

Data were prospectively collected from all patients who received this composite bone graft between 1996 and 2000. Only acute fractures with bone loss resulting in a uncontained defect and atrophic non-unions were included in the present study. Demographic data and complications related to composite use, tobacco use, and other comorbidities that could affect healing were evaluated.

One hundred seven patients (112 bone graft sites) were followed up for a mean of 32 months (range, 12–60 months). Graft sites included the forearm, femur and tibia. Of the 112 patients, there were 56 smokers (25 non-unions and 31 fractures) and 56 non-smokers (28 fractures and 28 non-unions). Healing occured in 38/56 smokers compared with 49/56 non-smokers. In failed cases, smoking was characteristic in 7/9 non-unions and 11/16 fractures. There were 26 acute uncontained injuries, 29 acute contained defects, and 67 nonunions. Grafting sites were radius/ulna (13 cases), humerus (17), femur (31), and tibia/fibula (51). Significant comorbidities were diabetes mellitus (4 cases), fungal osteomyelitis (1), and pulmonary alveolar proteinosis (1). Eight (73%) of the 11 patients with graft failure had a significant smoking history.

This composite graft is an option for managing osseous defects and nonunions traditionally treated with autologous bone grafting but should be used with caution when treating patients who are smokers.

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Smoking, which continues to be a leading cause of preventable death in the United States, led to 440,000 premature deaths between 1995 and 1999.[1] In the United States, 52.4 million people smoke almost 800 billion cigarettes annually, according to estimates.[2] The reported adverse effects of smoking on bone healing have received attention in orthopedics.

Chronic nicotine consumption has been implicated in a multitude of systemic processes that ultimately affect bone structure and metabolism.[3] Some of the reported harmful effects associated with nicotine consumption are infection, nonunion, and malunion[4-6]; delays in wound and bone healing, decreased blood flow, and revascularization of defects[6-8]; and reduced bone density leading to lower biomechanical strength.[7,9] Further, the antiestrogenic effects of smoking contribute to advancing osteoporosis in postmenopausal women and aging men.[10] Similarly, rate of bone loss is higher for smokers than for a matched population of nonsmokers.[11,12] Although the effects of nicotine on bone healing have been through indirect associations in human studies, most of the inhibitory effects of nicotine on bone metabolism have been found only in animal models.[6-9,13-15] In some studies, the effects of nicotine consumption on radiographic and clinical healing of osseous fractures of appendicular structures were clinically evaluated in humans. Previous results at our institution showed, for smokers, decreased healing rates with a composite of allograft and demineralized bone matrix.[16]

For the present study, we hypothesized that smoking would adversely affect the performance of such non-autogenous composites in fracture reconstruction. We evaluated the effects of smoking on inpatients who had either a nonunion or a fracture with bone loss treated with a composite graft of cancellous allograft and commercially available DBM.

Materials and Methods

Out of a group of 223 patients, we retrospectively reviewed a subgroup of 107 patients with 112 graft sites of either a nonunion (NU) or a severe fracture (FX) with enough bone loss to require acute bone grafting. Fractures needing bone graft were characterized by bone loss, severe devascularization, or another condition that would most likely result in nonunion in the absence of early grafting. Non-unions were characterized by failure to heal within 6 months, or lack of radiographic progression of healing between two 6-week office visits. Smoking was identified from medical records and patient interviews and defined as more than 10

cigarettes per day within 3 months of the indexed procedure. Patients who were using smokeless tobacco, cigars, nicotine patches, or nicotine gum were excluded, as we could not establish a quantitative measure of consumption for comparison with cigarette use.

The graft material used in all cases was a composite of cancellous allograft chips and DBM in a 4:1 ratio by volume. Patients were excluded if they received iliac crest bone graft or a bone stimulator or had a closed head injury. Patients were followed up at routine intervals, and minimal follow-up was 18 months. A success outcome was defined as clinical and radiographic healing at 2 successive follow-ups, and a failure outcome was defined as any clinical or radiographic evidence of nonunion (eg, painful ambulation, hardware failure, persistent lucency, graft material resorption).

Routine medical and demographic data were collected, and patients were stratified into NU and FX groups.

Results

There were 107 (60 male, 47 female) patients with a mean age of 42 years (range, 16–90 years). Mean follow-up was 47 weeks (range, 18–60 weeks). There were 112 bone graft sites: 13 radius/ulna (5 diaphyseal, 8 metaphyseal), 17 humerus (13 diaphyseal, 4 metaphyseal), 31 femur (12 diaphyseal, 19 metaphyseal), and 51 tibia/fibula (37 diaphyseal, 14 metaphyseal). There were 53 patients (53 sites) with NU and 54 patients (59 sites) with FX. Of these 54 fractures, 44 were open fractures (7 radius/ulna, 10 humerus, 7 femur, 20 tibia/fibula).

There were 56 patients who were smokers and 56 patients who were non-smokers. The S and NS groups did not differ in number of comorbidities, and their mean ages were similar (S, 41 years; NS, 43 years). There were no other demographic or comorbid differences between these groups.

Overall, 87 (77%) of the 112 graft sites healed. Eight of these sites united after a second composite bone grafting—resulting in a cumulative success rate of 85% (95/112). A significant smoking history was found for 18 (72%) of the 25 failed cases. Healing was uncomplicated in 65% (34/52) of the patients in the S group versus 87% (48/55) patients in the NS group.

Of the 53 NU bone graft sites, 25 were in the S group and 28 were in the NS group. Of these 53 sites, 44 (83%) healed, and 9 failed. Of the 9 failures, 7 (78%) were in the S group. Healing occurred for 72% (18/25) of the sites in the S group versus 93% (26/28) of the sites in the NS group. The NU odds ratio was 5.0, but these S–NS differences were not statistically significant ($P = .1$).

Of the 59 FX bone graft sites, 31 were in the S group and 28 were in the NS group. Of these 59 sites, 43 (73%) healed, and 16 failed. Of the 16 failures, 11 (69%) were in the S group. Healing occurred for 65% (20/31) of the sites in the S group versus 82% (23/28) of the sites in the NS group. The FX odds ratio was 2.5, but these S–NS differences were not statistically significant ($P = .2$).

Discussion

Our results suggest that nicotine consumption may be a significant comorbidity that negatively influences the performance of a composite of allograft and DBM for the treatment of bony defects. Although the scarcity of data implicating a direct relationship between smoking and nonunion or failure of bone healing in humans prevents us from making generalizations, results from this study provide further clinical evidence of a correlation between smoking and osseous healing. We found that, in the absence of other demographic differences and comorbidities, allograft–DBM composite performed reasonably well in the absence of chronic smoking—suggesting the potential utility of this composite as an alternative to iliac crest autograft. However, in the presence of systemic nicotine the success rate of the allograft–DBM composite seemed to diminish in non-unions (the success rate for the smoking group was only 65%). Of particular interest were the variable results found when we evaluated the data as an aggregate group and when stratified.

Allograft and DBM may lack the specific healing factors or neoangiogenic activity required in smokers to counter the relative antiangiogenic and metabolic effects induced by nicotine and smoke by-products. Notably, the composite seemed more efficacious in treating nonunions than in treating acute fractures. It may be that there is more devascularization from trauma in the acute scenario, whereas there is a healing response with better tissue revascularization in the nonunion scenario. Although our findings are not statistically significant, the odds ratios and trends are strong and imply that, with a larger sample size, such differences may become significant. We did not perform a power analysis.

Although investigators in various fields of medicine have found that the effects of smoking are a significant comorbidity affecting patient treatment, investigators in orthopedics have generated minimal data. With smoking still a strong influence in society, orthopedic physicians should consider the harmful effects of smoking on bone healing and should provide better management strategies when treating smokers. Our study results suggest that smoking is a significant enough factor in the inhibition of bone healing to warrant further investigation in this field.

We have found that bone graft substitutes are viable, less expensive, easily tolerated substitutes for autogenous bone grafting. When we conducted this study, the mean cost of 15 cm^3 cancellous allograft was $200, and 10 cm^3 DBM was $450. The amount of bone typically available from the posterior crest is approximately 40 cm^3, so the equivalent amount of cancellous allograft (3×15 cm^3) and DBM (1×10 cm^3) would have to be approximately 55 cm^3 to get a 3:1 mix. Current costs of the allograft are $350 per 15 cm^3 allograft and $1500 for 15 cm^3 DBM—giving a total cost of approximately $2250 ($1050 for allograft and $1500 for DBM). The cost to harvest autograft was estimated to be approximately $4000.[17] Even with such a cost savings, we could not justify the use of allograft and Grafton

DBM, especially in the presence of chronic smoking. We acknowledge that it is unlikely that other DBM composites will fare much better, considering the implication that a primary reason for lack of success is vascularity.

We did not find any statistically significant differences in this study despite a clear trend disfavoring smoking. There may be many reasons for such a limitation, including the study design, homogeneity of the cases, and, of course, sample size. The study design was a retrospective review with its inherent flaws, but we were comfortable with the consistency of treatment by the same trauma surgeons. Patient variety remains a problem with all studies, and especially so with less common and complex conditions such as non-union. In fact, it may be nearly impossible to exclude all confounders in such patients, since the nature of the initial injury and all subsequent treatments are hard to characterize. Thus we are relegated to studying lower-quality data sets in such conditions. We did not do a formal power analysis to determine the number of cases needed to ensure a type II error. As is the case with all such studies, we felt that the most suitable method would have been to limit study to only one bone, such as the tibia. A power analysis of this particular bone would have required too many patients for the time span of the study. Therefore, this study acknowledges that it demonstrates some descriptive findings and trends associated with smoking and must be limited in its conclusiveness.

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The authors report no actual or potential conflicts of interest in relation to this article.

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