Feature Article

Augmenting Local Bone With Grafton Demineralized Bone Matrix for Posterolateral Lumbar Spine Fusion: Avoiding Second Site Autologous Bone Harvest

Walter R. Sassard, MD* 
Dan K. Eidman, MD* 
Paul Milton Gray, Jr, MD† 
Jon E. Block, PhD‡ 
Richard Russo§ 
James L. Russell, PhD§ 
Elma M. Taboada§

ABSTRACT

Mineralization and integrity of the bone graft mass were evaluated among patients having posterolateral fusion. Grafting consisted of a composite of Grafton and "local" autologous bone (n=56) or iliac crest autograft alone (n=52). Mineralization was rated radiographically at baseline and at 3, 6, 12, and 24 months. Integrity was judged as fused or not fused. Mineralization ratings did not differ significantly between groups at any postoperative interval (P values of .25-1.00). The percentage of patients fused was similar in both groups (60% and 56% for Grafton and controls, respectively; P=.83). Fifteen control patients reported donor site pain. These findings warrant further evaluation of this composite.

Lumbar spine fusion is used to treat patients with intractable and often disabling low back or leg pain refractory to conservative management. This surgical technique is performed frequently in association with laminectomy or discectomy because these concomitant surgical interventions may compromise the stability of the spine, and fusing the affected vertebral segments may prevent subsequent back problems.

Fusion also is undertaken in patients with excessive vertebral slippage (ie, spondylolisthesis), degenerated disks, or chronic low back pain because fusion may reduce symptoms by diminishing instability associated with these disorders. Lastly, fusion often is proposed for patients in whom previous surgery, such as laminectomy, has failed (ie, failed back syndrome), with the reasoning that operative changes may have inadvertently produced instability, resulting in persistent pain.1

A current practice among surgeons performing lumbar fusion procedures is the use of internal fixation devices to provide rigid support for the bone graft mass and to allow early patient mobilization. The fusion mass itself is created initially by surgical placement of autologous bone usually harvested from a second operative site such as the iliac crest. In posterolateral procedures, bone graft is placed on either side of the vertebral column spanning the transverse processes of the affected vertebral segments.

Unfortunately, harvest of autologous bone from a second operative site has several shortcomings, the most important being the risk to the patient of residual donor site complications. A number of studies have documented both acute and chronic adverse events including infection, sensory loss, hematoma, scarring, fracture, herniation, and pelvic instability.2,4 A synthesis of the literature on outcomes of lumbar spine fusion found chronic donor site pain to be the most frequently reported complication.7

Consequently, there has been impetus to develop and investigate alternative grafting materials that obviate the need for secondary autologous bone harvesting. To date, alternative materials such as synthetic composites and poorly processed allografts have failed to perform as well as autologous bone in facilitating a solid arthrodesis.8
Allogeneic demineralized bone matrix (DBM) is a readily available graft material that can be processed to retain both osteoconductive and osteoinductive characteristics. Although results with this type of material for a variety of clinical applications have been encouraging, it has not been rigorously examined for use in lumbar spine fusion procedures. Moreover, the DBM used in many previous studies was not well characterized or processed with controlled, consistent methods. Grafton (Osteotech, Eatontown, NJ) is a specific allogeneic graft material that has been evaluated extensively in biocompatibility studies as well as in other laboratory investigations where it has been shown to induce new bone formation in a well-characterized athymic rat model. Nonetheless, the human clinical performance of Grafton has been studied only preliminarily in spine fusion.

This study compared the mineralization and integrity of posterolateral lumbar fusion in patients managed traditionally with autologous bone harvested from the iliac crest to a similar matched group of patients in whom the fusion mass consisted of a composite of Grafton DBM Gel and "local" bone obtained from laminectomy and decompaction.

### MATERIALS AND METHODS

The medical records of all patients who underwent lumbosacral spine fusion from November 1990 through November 1992 were examined to identify individuals whose surgical management included the use of Grafton DBM Gel. Fifty-six eligible patients were identified in whom bone grafting consisted of a composite of Grafton combined with local autologous bone obtained from a concomitant laminectomy or decompaction of the posterior vertebral elements.

Medical records from the same period also were examined to identify a comparison group in which spine fusion was performed in the traditional manner with autologous bone harvested from the iliac crest. Control autologous bone patients were selected only if they could be matched to a Grafton patient for gender, age (±5 years), and number of vertebral levels fused (±1 level).

Entrance eligibility for both groups also required that patients were 20 years, had undergone either a posterolateral or a combined posterolateral and posterior lumbar interbody fusion procedure with rigid pedicle screw fixation, and had received a minimum 9 months of postoperative care including an adequate number of follow-up radiographic studies to evaluate fusion status. Eligible patients were then prospectively monitored for at least 24 months following the index surgical procedure.

Patients were excluded if the operative indication included vertebral fracture, infectious disease, ankylosing spondylitis, neoplasm, congenital or adolescent idiopathic scoliosis, kyphosis, or achondroplasia. Patients also were excluded if electrical stimulation was used postoperatively.

Fifty-two autologous bone control patients were successfully identified as matches for 56 Grafton patients. Baseline information collected on each patient consisted of demographic characteristics, pertinent health history, and primary diagnosis and indication for spine fusion as well as surgical details of the fusion procedure.

Postoperative data pertaining to functional status, medical disposition, and clinical complications were collected for the following periods as available: 2 weeks and 3, 6, 12, and 24 months postoperatively. Anteroposterior plain radiographs taken at comparable postoperative intervals were evaluated to judge the integrity and mineralization of the developing fusion mass.

Radiographs for each patient were reviewed in toto by an independent radiologist blinded to the choice of graft material. The bone graft mass was judged to be fused if there was unanticipated bone bridging the transverse processes on at least one side of the fusion mass with no identifiable breaks, clefts, or areas of marked focal bone resorption. Definitive pseudoarthroses and fusion masses with marked bone resorption were judged as not fused.

The mineralization of the fusion mass was rated on a 4-point scale as detailed previously. Briefly, the status of each side of the fusion mass was judged separately as absent, mild, moderate, or extensive mineralization. These ratings were assigned numerical values ranging from 0-3, respectively. There was relatively close agreement between ratings for the two anatomical sides of the fusion; approximately 69%
of ratings from the two sides of the fusion mass were in complete agreement. Thus, numerical values from each side were summed and averaged producing a bone mineralization index ranging from 0-3 in 0.5-unit increments.

Baseline variables for the two study groups were characterized using descriptive statistics for continuous variables and frequency distributions for categorical variables. Differences in baseline characteristics between study groups were determined using the paired t test for continuous variables, the chi-square test for unordered categorical variables, and the Mann-Whitney test for ordered categorical variables. Radiographic ratings of fusion integrity (ie, fused/not fused) were compared between study groups using the chi-square test with Yate’s continuity correction. Bone mineralization indices were compared between study groups (and within selected subgroups) at each postoperative follow-up using the Mann-Whitney test.

Radiographic follow-up was fairly complete in the short-term postoperative period and less complete by 24 months postoperatively (2 weeks: n=90, 3 months: n=91, 6 months: n=92, 12 months: n=90, and 24 months: n=58). Therefore, the 24-month comparison was repeated after imputing any missing data with the most recently available radiographic rating; 28 values were imputed in the Grafton group and 22 values in the autologous bone group, primarily with ratings from 12 months postoperatively.

To evaluate potential predictors of graft maturity, a stepwise multiple regression procedure was undertaken with the 24-month bone mineralization index as the dependent variable and the following factors as potential predictors: age, study group, body mass index, number of levels fused, concomitant disectomy, smoking status, gender, and use of Steffee VSP instrumentation. This regression procedure was repeated, restricting the analysis to only patients in whom Steffee instru-

---

**TABLE 2**

Preoperative Diagnosis and Surgical Characteristics*  

<table>
<thead>
<tr>
<th></th>
<th>No. (%) Autologous Bone Group (n=52)</th>
<th>No. (%) Grafton Group (n=56)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical indication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disk herniation</td>
<td>27 (51.9)</td>
<td>39 (69.6)</td>
<td>.09</td>
</tr>
<tr>
<td>Deg disk disease</td>
<td>24 (46.2)</td>
<td>25 (44.6)</td>
<td>1.00</td>
</tr>
<tr>
<td>Segmental instability</td>
<td>37 (71.2)</td>
<td>39 (69.6)</td>
<td>1.00</td>
</tr>
<tr>
<td>Pseudoarthrosis</td>
<td>9 (17.3)</td>
<td>17 (30.4)</td>
<td>.17</td>
</tr>
<tr>
<td>Postlaminectomy pain</td>
<td>26 (50.0)</td>
<td>31 (55.4)</td>
<td>.72</td>
</tr>
<tr>
<td>Spondylolisthesis</td>
<td>15 (28.9)</td>
<td>6 (10.7)</td>
<td>.03</td>
</tr>
<tr>
<td>Spinal stenosis</td>
<td>11 (21.2)</td>
<td>6 (10.7)</td>
<td>.22</td>
</tr>
<tr>
<td>Other</td>
<td>3 (5.8)</td>
<td>4 (7.1)</td>
<td>1.00</td>
</tr>
<tr>
<td>Postolateral procedure</td>
<td>43 (82.7)</td>
<td>9 (16.1)</td>
<td>.001</td>
</tr>
<tr>
<td>Postolateral and postero-lumbar interbody procedure</td>
<td>9 (17.3)</td>
<td>47 (83.9)</td>
<td>.001</td>
</tr>
<tr>
<td>Instrumentation</td>
<td>Steffee VSP</td>
<td>19 (36.5)</td>
<td>54 (96.4)</td>
</tr>
<tr>
<td>Ragozinski</td>
<td>20 (38.5)</td>
<td>2 (3.6)</td>
<td>.001</td>
</tr>
<tr>
<td>Other</td>
<td>13 (25.0)</td>
<td>0 (0.0)</td>
<td>.001</td>
</tr>
<tr>
<td>Concomitant disectomy</td>
<td>29 (55.6)</td>
<td>47 (83.9)</td>
<td>.003</td>
</tr>
<tr>
<td>Concomitant laminectomy</td>
<td>48 (92.3)</td>
<td>54 (96.4)</td>
<td>.61</td>
</tr>
</tbody>
</table>

*Frequencies, % for all variables.  
†Represents multiple diagnoses per patient.

---

RESULTS

Table 1 compares baseline characteristics for both groups. While gender and extent of fusion were similar, the approximate 4-year difference in mean age (ie, 44 years for the control group versus 40 years for the Grafton group) between the two groups reached statistical significance (P<.05) regardless of the effort to match on this variable. In both groups, >60% of patients had undergone a previous surgery of the spine although most of these procedures did not involve a fusion procedure. For example, only 17% of autologous bone and 25% of Grafton patients’ current surgery involved a revision of a previously failed fusion procedure.

Indications for fusion surgery often involved multiple diagnoses (Table 2). For the most part, the distributions of surgical indication between study groups were similar. However, the proportion of patients presenting with spondylolisthesis was significantly greater among autologous bone patients than among Grafton patients. There was a higher proportion of disk herniation diagnoses among Grafton patients; this is reflected in a significantly greater frequency of concomitant disectomy procedures performed among patients managed with the Grafton composite.

Most postolateral fusion procedures in demineralized bone matrix patients involved a concomitant inter-body procedure, whereas fewer autologous bone patients underwent this combination fusion procedure. Most Grafton patients were surgically managed with one type of rigid metallic fixation device (ie, Steffee VSP). The type of rigid spinal fixation device was much more variable among autologous bone patients.

At each follow-up interval, there were no significant differences in bone mineralization index values for the two groups (P values of .25-1). At the near
term postoperative follow-up (ie, 2 weeks), 100% of Grafton patients and 98% of autologous bone patients had a bone mineralization index of 0.0 (P=1). By 12 months postoperatively, 64% of Grafton patients and 51% of autologous bone patients had a bone mineralization index ≥2 (ie, moderate mineralization) (P=.53).

At 24 months postoperatively, 61% of Grafton patients and 77% of autologous bone patients had mineralization index values ≥2 (P=.25). No significant difference in the distribution of mineralization index values was found between study groups when the 24-month comparison was repeated after imputing any missing mineralization values (P=.82). The groups were comparable with index values ≥2 among 66% (37/56) of Grafton patients and 65% (34/52) of autologous bone patients. The overall percentage of patients with values ≤1 also was similar between study groups at 24 months postoperatively (ie, 23% of Grafton versus 21% autologous bone patients).

The Figure illustrates the distribution of bone mineralization index values by study group at 12 months and for the imputed data set at 24 months, postoperatively. Similarly, 60% (33/55) of Grafton patients and 56% (28/50) of autologous bone patients were judged to be “fused” at study completion; these rates were not significantly different (P=.83).

Results reported in Table 2 indicate that certain potential prognostic factors were distributed differently between study groups. The proportion of patients presenting with spondylolisthesis (P=.03) and disk herniation (P=.09) differed between groups (Table 2). However, 24-month bone mineralization index values were not significantly different for patients with and without a herniated disk (P=.47) or with and without preoperative spondylolisthesis (P=.42).

The use of Steffee instrumentation was more prevalent among Grafton patients (Table 2); overall, patients managed with Steffee instrumentation had higher 24-month bone mineralization index values (P=.02). Alternatively, patients managed with Rogozinski instrumentation had lower bone mineralization scores than patients managed with all other instrumentation systems, both overall (P=.02) and among autologous bone patients exclusively (P=.03).

Similar findings were observed for the fusion integrity outcome as higher bone mineralization ratings and solid fusion were highly related (P=.0001). Indeed, a greater percentage of autologous bone patients managed with Steffee instrumentation had a solid fusion at study completion compared with autologous bone patients managed with other instrumentation systems (83% versus 41%; P=.009).

A higher proportion of surgeries among Grafton patients included a concomitant discectomy procedure (Table 2);
overall, patients with disectomy generally performed better with respect to bone mineralization ($P=0.09$). Disectomy was common among Grafton patients in whom Steffee instrumentation was used (44/54) and slightly less so among autologous bone patients (13/19). However, when only patients with disectomy were examined, no difference in 24-month bone mineralization was observed ($P=0.76$). Furthermore, autologous bone patients with and without disectomy performed similarly with respect to 24-month bone mineralization ratings ($P=0.73$).

In the initial stepwise regression procedure that included all study patients, four factors entered the model below the 0.05 significance threshold. The following factors are listed in the order of entry, with the $P$ value for entry and the portion of the variability in 24-month bone mineralization explained: Steffee instrumentation ($P=0.02$, $R^2=0.05$), smoking status ($P=0.02$, $R^2=0.046$), study group ($P=0.05$, $R^2=0.034$), and age ($P=0.04$, $R^2=0.037$). These four factors cumulatively explained approximately 17% ($R^2=0.167$) of the variability in the bone mineralization index.

In the second regression procedure, including only patients managed with Steffee instrumentation, only smoking status was significantly associated with the 24-month bone mineralization index, with smokers having generally worse ratings ($P=0.05$, $R^2=0.06$). Study group did not explain a significant portion of the variability in 24-month bone mineralization among the subgroup of patients managed with Steffee instrumentation.

The finding that smoking status was associated with bone mineralization index values among Steffee implant patients motivated additional exploratory comparisons. Study group differences were not found to be significant among Steffee patients who were smokers ($P=0.11$) or among Steffee patients who were not smokers ($P=0.18$).

There were few postoperative complications documented in patient medical records, and the frequency was generally similar between study groups. For example, operative site complications occurred among four Grafton patients and five autologous bone patients. The frequency of hardware problems was greater among autologous bone patients (i.e., 4 in Grafton and 8 in autologous patients), while miscellaneous complications occurred with a slightly greater frequency among Grafton patients (i.e., 12 [21.4%]) than autologous patients (7 [13.5%]).

Autograft donor site complications were avoided entirely among Grafton patients, whereas 3 autologous bone patients reported a complication at the donor site. Additionally, there were 21 episodes among 15 autologous bone patients of postoperative donor site pain. One Grafton patient reported donor site pain as a result of a previous surgery that involved autologous bone harvesting.

**DISCUSSION**

The overall findings of this retrospective study show that a composite graft of Grafton and local bone performs similarly to autologous bone harvested from the iliac crest with respect to mineralization and integrity of the fusion mass. By 12 months postoperatively, the majority of patients (64% of Grafton and 51% of autologous bone patients) were rated as having fusions of at least moderate mineralization. Little improvement in bone mineralization was realized by 24 months postoperatively, with 66% of Grafton and 65% of autologous bone patients having mineralization index values $\geq 2$ (i.e., moderate or better).

When the postoperative radiographs for each patient were evaluated in toto, approximately 60% of Grafton and 56% of autologous bone patients had achieved a solid arthrodesis; these fusion rates were not significantly different ($P=0.83$). The strikingly similar results in graft mineralization for both groups were corroborated in multivariate analyses, which found that study group accounted for only a small portion (3%) of the variability in 24-month bone mineralization ratings when other potential explanatory factors were considered concurrently. Importantly, study group did not emerge as a significant predictor of 24-month bone mineralization when the analysis was restricted to the subgroup of patients in which Steffee instrumentation was used.

The choice of instrumentation system may influence the degree and rate at which the fusion mass mineralizes and incorporates. Two rigid pedicle screw fixation systems were used predominantly in this study group. Overall, approximately 68% (73/108) of patients were managed with the Steffee VSP device, a pedicle screw/plate construct. In an additional 20% (22/108) of patients, the Rogozinski pedicle screw/rod system was used.

While rigid instrumentation systems generally have been shown to offer superior clinical performance characteristics compared with semirigid pedicle screw constructs or older nonpedicle screw systems, there is little evidence that use of any one rigid system results in better postoperative outcomes. Indeed, a historical cohort study of $>2000$ spondylolisthesis patients managed with various pedicle screw devices (63% screw/plate and 36% screw/rod) failed to observe any noteworthy differences in fusion rates or patient-related functional outcomes between different screw systems.

Nonetheless, the current study found that patients managed with Steffee instrumentation generally had superior mineralization ratings than patients managed with other rigid instrumentation systems. Multiple regression analysis found that use of Steffee instrumentation was the most important predictor of 24-month bone mineralization ($P=0.02$); however, it accounted for approximately 5% of the total variability.

The fusion rates for the two study groups (60% for Grafton and 56% for autologous bone patients) were lower than anticipated. However, estimates of solid fusion reported in the medical lit-
perature vary widely. In a review of 15 studies, Turner et al. found that 89±7.6% of posterolateral lumbar fusions formed a solid arthrodesis. A recent, large randomized study of posterolateral fusion reported a solid fusion rate of only 68% among patients with degenerative conditions of the lumbar spine managed with pedicle screw fixation and autologous bone grafting. The difference between these estimates may be due to the stringent and blinded evaluation of radiographs in the current study in which only unequivocal solid fusions were judged as fused and clinical symptoms were not considered.

Several previous studies suggest DBM, often in combination with autologous marrow or bone, can have similar performance characteristics to autograft, although the DBM graft in these studies was not specifically identified. The results of a prior spine fusion study suggest that Grafton DBM, in combination with some amount of autologous marrow or bone, performs similarly to autograft. The current evaluation of a Grafton composite graft provides encouraging evidence for this form of DBM for lumbar spine fusion. Indeed, the results with this Grafton composite were achieved without the need to harvest autologous material from a second operative site.

Randomized, controlled clinical investigations with concurrent autologous bone controls are in progress to confirm the preliminary finding that Grafton composites offer a viable alternative graft for spine fusion procedures.

REFERENCES


EDITORIAL DISCUSSION

ORTHOPEDICS: In that >95% of the Grafton patients were surgically managed with the Steffee VSP, does this bias the results of the study?

Sassard et al: All patients in this study were managed with rigid pedicle screw fixation. The predominant systems used were the screw/plate Steffee VSP device (68%, 73/108) and the screw/rod Rogozinski device (20%, 22/108). Although there was an imbalance in the use of these systems between the two study groups, we are unaware of any published experimental data that suggest either of these rigid systems is superior in respect to solid fusion rates or patient-related functional outcomes. In fact, the historical cohort data on pedicle screw usage submitted to the Food and Drug Administration to support reclassification of these devices for spondylolisthesis and vertebral fractures failed to observe any noteworthy differences between screw/plate and screw/rod pedicle screw systems.

The bone mineralization ratings were generally higher for patients managed with Steffee instrumentation compared with patients managed with other pedicle screw systems in this study, including the Rogozinski system. However, among the overall study population, use of Steffee instrumentation only accounted for approximately 5% of the variability in bone mineralization ratings when other potential predictor variables were considered concurrently in multiple regression analyses. Unfortunately, the available data and the retrospective design of this study did not allow further statistical examination of this question. Because a high percentage of the Grafton patients received the Steffee device, the analysis of bone mineralization ratings could
not be meaningfully stratified by instrumentation system to statistically adjust the analysis for this factor.

Although we noted the bone mineralization and fusion results in the autograft group were different depending on the instrumentation system, we did not explore whether other factors such as number of levels fused, preoperative diagnosis, or concomitant surgical procedures might have been attributable for this observed difference.

Further, because the autograft control group was not randomized to the different instrumentation systems, it is difficult to interpret the clinical significance of this finding. However, as these results suggest this factor may be important, we propose that future controlled clinical trials of grafting materials be standardized for instrumentation system or that intended instrumentation systems be an explicit stratification factor in the randomization of patients to study groups.

ORTHOPEDICS: What is the ratio of “local” bone to Grafton, and how important is local bone?

Sassard et al: An accurate estimate of the relative proportions of Grafton gel and local autologous bone was difficult to calculate from the patients’ medical records because these volumes are not routinely recorded. However, recently we examined our standard grafting practices more closely among a prospective series of cases. On average, we use one to two parts Grafton to one part local autograft, by volume.

The supplementation of Grafton gel with local autologous bone contributes additional form and structure to the composite, and facilitates easier operative site handling and implantation of the graft material. Additionally, the particulate autograft may provide a biologically active scaffold for vascular ingress and bone remodeling. Although it has been suggested cortical bone is generally more replete with osteoinductive growth factors than cancellous bone, we are unaware of any empirical evidence directly comparing the osteogenic potential of local and iliac crest autograft.

REFERENCES (EDITORIAL DISCUSSION)