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Demineralized Bone Matrix Fibers plus Allograft Bone for Multilevel Posterolateral Spine Fusion: A Game Changer?

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Abstract

Introduction: While autograft bone is the gold standard for multilevel posterolateral lumbar fusion, bone substitutes and graft extenders such as allograft bone, ceramics and demineralized bone matrix (DBM) have been used to avoid the morbidity and insufficient quantity associated with harvesting autologous bone. The primary objective of this retrospective study was to determine whether, in patients with increased risk of operative nonunion related to multilevel fusion, adding DBM fibers to mineralized bone allograft resulted in better fusion than using allograft alone. The secondary objectives were to evaluate how adding DBM fibers affects functional disability, low back pain, intraoperative blood loss and the nonunion rate. **Methods:** This retrospective study involved a chart review of consecutive patients who underwent multilevel lumbar spinal fusion and were operated on by a single surgeon. The patients were divided into two groups: 14 patients received mineralized bone allograft (control group) and 14 patients received a combination of mineralized bone allograft and DBM (experimental group). Patients were reviewed at a mean of 16.4 ± 2.2 months after surgery at which point CT scans were analyzed to determine whether fusion had occurred; Oswestry disability index (ODI) and pain were also evaluated. **Results:** A mean of 5 levels [min 2, max 13] were fused in these patients. Posterolateral fusion as defined by the Lenke classification was not significantly different between groups. The experimental DBM group had a significantly better composite fusion score than the control group ($P < 0.0001$). No differences were found in ODI, pain and nonunion rate between groups. Intraoperative blood loss was lower in the DBM group compared to the control group but not significantly. There were no complications during or after the surgery. **Discussion:** Adding DBM fibers to allograft bone during multilevel posterolateral spinal fusion was safe and produced better composite fusion than using allograft only as an autograft extender.

Keywords

Spine Surgery, Demineralized Bone Fibers, Bone Substitutes, Retrospective Study

1. Introduction

When performing posterolateral fusion, one of the options to supplement local autograft (LA) material (*i.e.*, laminectomy bone shavings) is to add mineralized bone allograft instead of harvesting bone from the iliac crest. In their study evaluating the rate of posterolateral lumbar fusion with various biologics, Hsu *et al.* [1] reported that allograft alone had the lowest fusion rate (52%) followed by autologous bone marrow (74%), iliac crest bone graft (79%), ceramics (87%), LA alone (89%), demineralized bone matrix (DBM) (89%) and bone morphogenetic protein-2 (94%).

According to a meta-analysis done in 2020 by Han *et al.* [2], there is no significant difference in the rate of posterolateral fusion or interbody fusion between DBM and autograft. One advantage of using DBM is that it reduces the amount of autograft that needs to be harvested from the iliac crest and thus the risk of donor site complications, including hematoma and blood loss. This becomes even more crucial when multiple levels are being fused and more bone grafting material is needed. Furthermore, DBM is both osteoconductive and osteoinductive. In a 2014 study conducted in dental implantology, Borg and Mealey provided histologic evidence of increased new bone formation with a 70:30 mineralized: demineralized bone allografts compared to mineralized bone allograft alone [3]. Based on these results, we would also expect that DBM would perform better than mineralized bone allograft—which is osteoconductive only—when used as an LA extender.

The main purpose of this retrospective study was thus to determine whether, in patients with increased risk of operative nonunion related to multilevel fusion, adding a fixed ratio of DBM fibers to mineralized bone allograft resulted in better fusion than mineralized bone allograft alone in multilevel posterolateral lumbar fusion. The secondary objectives were to evaluate how adding DBM fibers affects functional disability, low back pain, intraoperative blood loss and nonunion rate.

2. Materials and Methods

This study involved a chart review of consecutive patients who underwent multilevel lumbar spinal fusion and were operated on by a single surgeon between January 7, 2018 and November 19, 2020. The date of last follow-up was February 08, 2022. This single center, retrospective review of nonrandomized, prospectively collected data was conducted in accordance with STROBE guidelines [4]. No IRB approval was required in our country since this was a retrospective chart review of registry data; the principles outlined in the Declaration of Helsinki were followed. Patient consent was obtained during their 12-month postoperative follow-up visit to allow their data to be analyzed.

Patients between 18 and 65 years of age who had pain and/or neurological impairment for more than 6 months without improvement despite pharmacological treatment were candidates for lumbar fusion surgery. Patients were excluded from the analysis if they underwent revision surgery, pedicle subtraction osteotomy, were operated for kyphosis or bone fracture, or if they had less than 12 months of follow-up.

For this analysis, we selected the patients who underwent multilevel instrumented transforaminal lumbar interbody fusion (TLIF) with posterior lumbar fusion (PLF) and divided them in two groups:

- Mineralized bone allograft only (PHOENIX, TBF, France).
- Mineralized bone allograft + DBM fibers (F-PHOENIXDBM, TBF, France).

Initially, this surgeon used mineralized allograft for PLF (control group). When 100% cortical fiber DBM with verified osteoinductive properties became commercially available, the surgeon started using a mixture of 30% DBM (1 vial of 4 cm^3) with 70% mineralized bone allograft (12 - 15 cm^3) for the PLF (experimental group). Otherwise, the surgical technique did not differ between patients.

The surgical technique started by making lateral skin incisions, gradually separating the muscles and fascia, and then performing laminectomy (LA). After a complete facetectomy (sometimes bilateral), diskectomy was done to decompress the spinal cord and any slipped vertebrae were reduced. The vertebral bodies were then decorticated and distracted. The empty disc space was filled with LA bone shavings and a titanium cage (Shark for L5-S1 and Banana for other lumbar levels, NEURO FRANCE Implants). Posterior instrumentation consisting of pedicle screws and rods (S.E.S. system, NEURO FRANCE Implants) was added after posterolateral decortication. To supplement this instrumentation, LA bone shavings plus mineralized allograft (control group) or LA bone shavings plus mineralized allograft 70% and DBM 30% (experimental group) were added.

The primary endpoint was radiological fusion assessed on CT scans of the lumbar spine at 12 to 15 months after surgery. Radiological fusion was chosen as the primary endpoint to assess osseointegration. PLF was evaluated by a radiologist based on the 4-grade system defined by the Lenke classification [5]. Interbody fusion was evaluated by a radiologist based on the Brantigan, Steffee, Fraser (BSF) score [6]. Radiographic fusion was also evaluated by the surgeon using a composite score corresponding to the sum of the modified Lenke and BSF classifications (Table 1 and Table 2).

The secondary endpoints were functional disability according to the Oswestry Disability Index (ODI) version 2 [7], low back pain evaluated on a visual analog scale (VAS), number of levels fused, intraoperative blood loss (volume in suction canisters) and the nonunion rate. Any post-surgical complications were documented to assess the safety of adding DBM fibers.

Table 1. Modified Lenke classification.

Grade	Description
0	Definitely solid with bilateral trabeculated stout fusion masses present
1	Possibly solid with a unilateral large fusion mass and a contralateral fusion mass
2	Possibly solid with a unilateral large fusion mass and a contralateral small fusion mass
3	Probably not solid with a small fusion mass bilaterally
4	Probably not solid with a small fusion mass not bilaterally
5	Definitely not solid with bone graft resorption
6	Obvious nonunion bilaterally

Table 2. Modified Brantigan, Steffee, Fraser (BSF) classification.

Grade	Description
0	Radiographic fusion: bone bridges at the fusion area with the density originally achieved at surgery. Radiographic fusion through one cage.
1	Radiographic fusion: bone bridges at less than half the fusion area close to the density originally achieved at surgery. Radiographic fusion through one cage (half of the fusion area with lucency < 1 mm on the opposite side).
2	Radiographic fusion: bone bridges at least half of the fusion area close to the density originally achieved at surgery. Radiographical fusion through one cage (half of the fusion area with lucency > 1 mm on the opposite side).
3	Radiographical locked nonunion indicated by lucency < 1 mm visible in the middle of the cages with solid bone growing into the cage from each vertebral endplate.
4	Radiographical locked nonunion indicated by lucency > 1 mm visible in the middle of the cages with solid bone growing into the cage from each vertebral endplate.
5	Significant resorption of the bone graft, or lucency visible around the periphery of the graft or cage.
6	Radiographical pseudarthrosis is indicated by collapse of the construct, loss of disc height, vertebral slip, broken screws, displacement of the carbon cage.

Demographic data collected were age, sex, smoking habits and alcohol consumption at the time of surgery.

The data were analyzed retrospectively by comparing two groups: the final 14 consecutive patients treated with mineralized allograft bone before DBM fibers with the defined criteria were available at our facility (up to January 2020) and the first 14 consecutive patients treated with mineralized allograft bone and DBM fibers after January 2020.

Continuous variables were compared using an independent two-sample t-test or the Wilcoxon rank-sum test to determine any significant difference between the groups. Fischer's exact test or the Chi-squared test was used for categorical variables. The null hypothesis was rejected when $\alpha < 0.05$ (two-tailed). Statistical analyses were performed using R 4.0.2 software.

Table 3. Demographic, fusion score, pain and ODI outcomes.

Demographic	Control group	Experimental group	*P* value[#]
Number of patients	14	14	
Age in years	38 ± 9 [18 - 49]	49 ± 16 [16 - 69]	0.0072*
Sex (men/women)	6/8 (43%/57%)	6/8 (43%/57%)	1.0000
Smoker (%)	50%	0%	0.0058*
Alcohol consumption (%)	21%	7%	0.5956
Number of spinal levels fused	5.1 ± 3.4 [3 - 13]	5.1 ± 3.5 [2 - 13]	0.7762
Follow-up time in months	16.4 ± 1.9 [14 - 20]	16.3 ± 2.6 [13 - 22]	0.8673
Posterolateral fusion: Lenke classification			
Lenke A	13 (93%)	13 (93%)	1.0000
Lenke B	1 (7%)	0 (0%)	
Lenke C	0 (0%)	0 (0%)	
Lenke D	0 (0%)	1 (7%)	
Radiographic posterolateral and interbody fusion: composite score			
Composite fusion score	2.14 ± 0.53 [2 - 4]	0.71 ± 2.67 [0 - 10]	<0.0001*
ODI			
Preoperative	52.43 ± 16.51 [20 - 76]	55.71 ± 13.29 [24 - 72]	
Postoperative	21.00 ± 6.69 [12 - 36]	25.00 ± 8.62 [0 - 38]	
Delta (post – preoperative)	−31.43 ± 14.09 [−52 - −4]	−30.71 ± 14.90 [−56 - −4]	0.8973
Pain			
Preoperative	6.07 ± 1.82 [2 - 9]	5.86 ± 2.54 [0 - 9]	
Postoperative	1.71 ± 0.99 [0 - 3]	1.64 ± 1.28 [0 - 3]	
Delta (post – preoperative)	−4.36 ± 1.65 [−7 - −2]	-4.21 ± 2.49 [−7 - +1]	0.8593

Results expressed as mean ± SD [min. – max.] or number of patients (% of patients in the group). [#]Independent t-test; Wilcoxon rank sum test; Fisher's exact test; Pearson's Chi-squared test.

3. Results

Based on the above inclusion and exclusion criteria, the data from 28 patients were analyzed: 14 patients had received mineralized bone allograft (control group) and 14 patients had received a combination of mineralized bone allograft and DBM fibers (DBM group).

Sex distribution, alcohol consumption and number of fused spinal levels were similar for both groups. Patients in the experimental DBM group were significantly older than those in the control group (49 vs 38 years old, P = 0.0072). The share of smokers at the time that surgery was proposed was significantly higher in the control group (50% vs 0%, P = 0.0058). Patients were followed for a mean of 16.4 ± 2.2 months after surgery (**Table 3**). The indications for surgery were either decompensated scoliosis (or deformity) or spondylolisthesis. No decompression procedures were done on these patients.

The posterolateral fusion rate was equal in the experimental DBM group and in the control group (93%). The difference in Lenke fusion grade between groups was not statistically significant. The composite radiographic fusion was significantly better in the experimental DBM group than the control group (P < 0.0001) (**Figure 1**).

ODI scores improved in both groups from baseline to the follow-up visit but there was no statistically significant difference between groups. Lumbar pain decreased in both groups after surgery relative to baseline. There was no statistically significant difference between groups in the patients' pain levels.

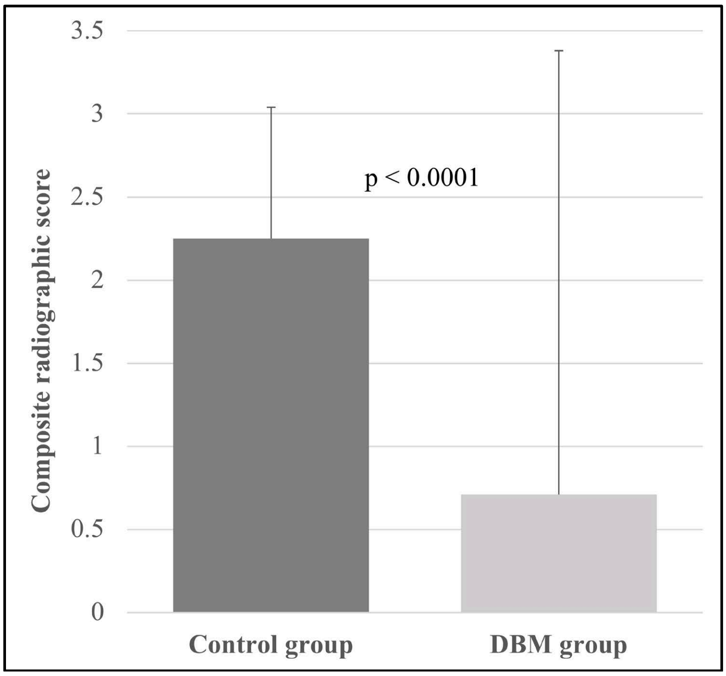

Figure 1. Composite radiographic posterolateral and interbody fusion score. A lower score indicates better fusion. Results expressed as mean ± SD. The difference between groups was statistically significant based on the Wilcoxon rank sum test (p < 0.0001).

There was less intraoperative blood loss in the DBM group (332 ± 125 mL [150 - 600]) than in the control group (454 ± 227 mL [200 - 1000]); however, this difference was not statistically significant (P = 0.0951). The nonunion rate did not differ between groups: 7% (1/14 patients) in both groups. The nonunions were triggered by the patient falling or the fixation screws breaking. There were no intraoperative or postoperative complications in either group.

4. Discussion

The main finding of this study was that adding DBM fibers to mineralized bone allograft did not improve multilevel PLF relative to using mineralized bone allograft only. However, adding DBM fibers led to significantly better combined fusion score (posterolateral fusion + interbody fusion) versus using mineralized bone allograft only (P < 0.0001). No differences were found in the function, pain level and nonunion rate between groups. There was less intraoperative blood loss when DBM was used, but not to a significant extent.

Limitations of this study are related to its retrospective design. The two groups were not exactly comparable as the patients were older in the experimental DBM group and there were more smokers in the control group. The fact that 50% of patients in the control group were initially smokers is for example a confounding variable, given that smoking is associated with higher rates of nonunion [8]. Despite the large number of smokers in this group, the fusion rate with allograft bone was 90% at a mean follow-up of 16 months. We have no other data on potential confounding factors, such as the patients' hormonal balance and activity levels.

Nonunion rates have been shown to be significantly higher when the fusion spans three or more levels [9] [10]. In our study, a mean of five levels were fused successfully in 93% of patients when using allograft bone and 93% when using allograft bone plus DBM fibers. Since the fusion rate is high in the control group, it is no surprise that adding DBM fibers did not further improve the PLF rate. To our knowledge, ours is the only study comparing DBM fibers to allograft as LA graft extenders in complex multilevel PLF, while using LA only at the TLIF site. It is also unique in that it evaluated a set ratio of DBM plus allograft (30%/70%) in instrumented fusions. Furthermore, this DBM product is a 100% cortical fiber formulation, which has better handling properties than DBM particulate and better osteoconductive performance [11] [12].

The complication rate is higher following multilevel fusion due to longer operative time, more intraoperative blood loss and requirement for additional bone graft, especially in older patients [13]. There were no intraoperative or postoperative complications in our study where the patients ranged in age from 16 to 69 years. Adding DBM as a graft extender curtailed some of the intraoperative blood loss in these patients.

Multilevel PLF requires a tremendous volume of bone graft material. While the required bone can be harvested from the iliac crest, this procedure has considerable morbidity and may not yield sufficient bone. The volume of autologous laminectomy bone harvested locally is also not sufficient when more than two levels are being fused. In this context, DBM is an effective LA extender and may reduce intraoperative blood loss and operative time versus autologous iliac bone graft for long (≥3 levels) instrumented PLF [14].

The results of this study are not generalizable to the broader population given that all patients were operated on by a single surgeon at a single healthcare facility. Nevertheless, the fusion rates found in this study are consistent with the range of fusion rates reported in a 2017 systematic review [15]. The fusion rate when using allograft ranged from 68% to 98%, while the fusion rate when using DBM was between 60% and 100% for instrumented lumbar fusion procedures. Our findings could apply to patients who have similar characteristics as the study sample and are undergoing multilevel lumbar PLF.

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Informed Consent

Written informed consent was obtained from all patients and/or families.

Conflicts of Interest

Laurence Barnouin is an employee of Tissue Bank of France, which provided the DBM and allograft products used in this study. Arnaud Bodin received payment from TBF for the data collection. Remy Coulomb, Vincent Haignere, Pascal Kouyoumdjian declare that they have no relevant financial or non-financial interests to report.

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