The impact of demineralized bone matrix characteristics on pseudarthrosis and surgical outcomes after posterolateral lumbar decompression and fusion

ABSTRACT

Objectives: The objectives of our study were to compare the fusion rates and surgical outcomes of lumbar fusion surgery based on the (1) type of demineralized bone matrix (DBM) carrier allograft, (2) the presence/absence of a carrier, and (3) the presence of bone fibers in DBM.

Methods: Patients >18 years of age who underwent single-level posterolateral decompression and fusion (PLDF) between L3 and L5 between 2014 and 2021 were retrospectively identified. We assessed bone grafts based on carrier type (no carrier, sodium hyaluronate carrier, and glycerol carrier) and the presence of bone fibers. Fusion status was determined based on a radiographic assessment of bony bridging, screw loosening, or change in segmental lordosis >5°. Analyses were performed to assess fusion rates and surgical outcomes.

Results: Fifty-four patients were given DBM with a hyaluronate carrier, 75 had a glycerol carrier, and 94 patients were given DBM without a carrier. DBM carrier type, bone fibers, and carrier presence had no impact on 90-day readmission rates ($P = 0.195$, $P = 0.099$, and $P = 1.000$, respectively) or surgical readmissions ($P = 0.562$, $P = 0.248$, and $P = 0.640$, respectively). Multivariable logistic regression analysis found that type of carrier, presence of fibers (odds ratio [OR] = 1.106 [0.524–2.456], $P = 0.797$), and presence of a carrier (OR = 0.701 [0.370–1.327], $P = 0.274$) were also not significantly associated with successful fusion likelihood.

Conclusion: Our study found no significant differences between DBM containing glycerol, sodium hyaluronate, or no carrier regarding fusion rates or surgical outcomes after single-level PLDF. Bone particulates versus bone fibers also had no significant differences regarding the likelihood of bony fusion.

Keywords: Bone matrix, lumbar fusion, pseudarthrosis, surgical outcomes

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INTRODUCTION

Lumbar fusion often incorporates bone allograft to enhance fusion.[1] Bone grafting materials possess one or more aspects of three fundamental properties that enhance bone healing; osteoconductivity, osteoinductivity, and osteogenicity. Autograft possesses all three fundamental properties and is considered the gold standard of bone grafting.[2] However, there can be significant donor site morbidity and complications from autograft harvest.[3] Lumbar fusion surgeries have utilized fresh, fresh-frozen, and freeze-dried allograft bone from cadavers as an alternative to autograft. Despite the lack of morbidity associated with allograft implantation, several side effects, including graft-host interactions, union rates, structural integrity, and infections, have been associated

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with allograft use.[4,5] Demineralized bone matrix (DBM) was developed to avoid these complications by being processed to retain osteoconductivity and osteoinductivity with reduced immunogenicity when compared to unprocessed allograft.[2,6]

There are a variety of commercially available synthetic grafts, each with different properties. To improve the handling properties of DBM, some commercially available synthetic grafts use carriers such as sodium hyaluronate or glycerol. However, there is disagreement in the literature about the impact of carrier substances on bone formation, and there is a lack of literature directly comparing outcomes of spine surgery with hyaluronate-containing DBM, glycerol-containing DBM, and DBM absent of a carrier.[7-10] In addition, some authors have suggested the potential of fiber-containing allografts for generating osteoinduction.[11,12] Although a recent meta-analysis demonstrated that the use of DBM plus autograft in spinal fusion was associated with higher fusion rates than autograft alone, clinical studies comparing successful spinal fusion rates using grafts with sodium hyaluronate versus glycerol carriers have dissenting conclusions, necessitating further investigation to determine the efficacy of synthetic graft on successful fusion.[1,13-16]

Understanding the mechanism behind bone grafting materials, their role in spinal fusion, as well as their associated side effects, has grown in importance as the rate of spinal fusion procedures in the United States continues to increase.[17] Therefore, the objectives of our study were to compare the fusion rates and surgical outcomes of lumbar fusion surgery based on the (1) type of carrier material, (2) presence of carrier, and (3) presence of bone fibers in DBM.

METHODS

Upon obtaining Institutional Review Board approval, all patients ≥18 years of age with a complete set of preoperative and postoperative lumbar spine radiographs who underwent single-level posterolateral decompression and fusion (PLDF) at L3–L4 or L4–L5 by one of two fellowship-trained spine surgeons at our academic medical institution between 2014 and 2020 were retrospectively identified. Patients were excluded if the surgery was performed as a revision procedure or performed for infection, malignancy, or trauma. A similar surgical technique was utilized for all procedures. After exposure of the posterior elements, the transverse processes and lateral facets were decorticated. A combination of local autograft (harvested from the spinous processes and lamina) and DBM was placed in the lateral gutters for posterolateral fusion. The type of allograft chosen was based on attending preference. Three different types of allografts were used in our study that differed based on carrier type (glycerol, sodium hyaluronate, no carrier) and fiber content (fibers, no fibers). Both surgeons utilized all three products, with differences based upon the date of surgery.

Data extraction

Patient demographics, surgical characteristics, and clinical outcomes were collected through a Structured Query Language search and manual chart review of the electronic medical records. Demographic information collected included age, sex, body mass index (BMI), Charlson Comorbidity Index (CCI), and smoking status (nonsmoker, current smoker, and former smoker). Surgical characteristics collected included preoperative diagnosis (spondylolisthesis and nonspondylolisthesis), hospital length of stay (LOS), operative duration, and total levels decompressed. Clinical outcomes collected included 90-day readmissions, 90-day surgical readmissions, etiology for surgical readmission, 1-year revision procedures, and indication for revision surgery (nonunion and adjacent segment disease). The intraoperative use of bone grafts was determined by cross-referencing the recorded surgical implant list in the electronic medical record with the date of surgery and the operative note.

Radiographic evaluation

Postoperative anterior-posterior (AP), lateral, and flexion-extension radiographs from at least 6 months after the index procedure were reviewed via our institution's picture archiving and communication system (PACS; Sectra AB, Linköping, Sweden). Based on previous studies, radiographic evaluation was used to determined fusion status by assessing the presence of bony bridging, screw loosening, or segmental lordosis difference of $>5°$.[8,18] The AP radiograph was used to assess for bony bridging, which was defined by a radiopacity uniting the transverse processes either unilaterally or bilaterally at the surgical level.[18] The AP and flexion-extension radiographs were used to assess for screw loosening/hardware failure, defined as >2 mm of osteolysis surrounding at least two screws or visible instrumentation failure. Segmental lordosis was measured using the superior endplate of the superior vertebrae and inferior endplate of the inferior vertebrae on both flexion and extension radiographs.[19] The difference between the segmental lordosis on flexion and extension was calculated, and pseudarthrosis was defined as an angle $>5°$.[18,20] If any patient was found to have a lack of bone bridging fusion, evidence of screw loosening/hardware failure, or a $>5°$ difference in flexion and extension Cobb angles, then the patient was documented to have pseudarthrosis.[8] Two independent blinded research personnel trained by a spine fellow completed radiographic measures. Cohen's Kappa was determined to be 0.78 between these two observers indicating "substantial" agreement.[21]

Statistical analysis

Descriptive statistics, including means with standard deviation, were used to report patient demographics, surgical characteristics, clinical outcomes, and radiographic fusion parameters. All parameters were compared based on carrier material, presence of fibers, and presence of carrier material. The continuous variables were compared with Kruskal–Wallis *H*-tests or one-way analysis of variance test. Dichotomous variables were compared with Pearson's Chi-square or Fisher's exact tests. Bivariate analyses were conducted using bone bridging fusion, screw fusion, cobb fusion, and combined fusion. A multivariable logistic regression model was developed to measure the effect of the carrier material, the presence of fibers, and the presence of carrier material on the likelihood of achieving radiographic fusion following PLDF. Analysis of carrier material, presence of fibers, and presence of carrier material were performed independently, accounting for age, sex, BMI, CCI, smoking status, levels decompressed, and preoperative diagnosis. Statistical significance was set at $P < 0.05$. All statistical analyses were performed using R Studio version 4.0.2 (Boston, MA, USA).

RESULTS

Patient demographics and surgical characteristics

Two hundred and twenty-three single-level PLDFs were performed at our institution by the two surgeons who met the inclusion criteria between 2014 and 2020. Fifty-four patients were given DBM with sodium hyaluronate carrier, 75 patients were given DBM with glycerol carrier, and 94 patients were given DBM without a carrier. There were no significant differences in age ($P = 0.739$), sex ($P = 0.442$), BMI ($P = 0.470$), smoking status ($P = 0.801$), diabetes status ($P = 0.334$), or CCI ($P = 0.515$) between patients who received DBM with sodium hyaluronate, glycerol, or no carrier. Patients given sodium hyaluronate-containing carrier were less likely to have a spondylolisthesis diagnosis preoperatively (83.3% vs. 97.3% and 95.7%, $P = 0.007$). However, there were no differences between groups with regards to hospital LOS ($P = 0.189$), operative duration ($P = 0.933$), total levels decompressed ($P = 0.886$), and levels fused ($P = 0.314$) [Table 1].

Surgical outcomes

Between patients who received DBM with sodium hyaluronate carrier, glycerol carrier, or no carrier, there were no differences in 90-day readmission rates ($P = 0.195$), surgical readmissions ($P = 0.562$), or revision surgery rates ($P = 0.107$) [Table 2]. The presence of bone fibers in the DBM did not impact surgical outcomes, including 90-day readmission rates ($P = 0.099$), surgical readmissions ($P = 0.248$), or revision surgery rates ($P = 0.093$). Similarly, the presence of carrier in the DBM was not significantly associated with difference in 90-day readmission rates ($P = 1.000$), surgical readmission rates ($P = 0.640$), or revision surgery rates ($P = 1.000$) [Table 3].

Radiographic outcomes

Overall, radiographic fusion rates were similar (sodium hyaluronate carrier: 75.9% versus glycerol carrier: 78.7% versus no carrier: 71.3%, $P = 0.535$) [Table 4]. When grouping the bone matrix by those with fibers and those without, there was no difference in the fusion rate between groups (75.9% vs. 74.6%, $P = 0.983$). Similarly, there was no difference in fusion rates based on the presence of a carrier (71.3% vs. 77.5%, $P = 0.365$) [Table 5].

Multivariable logistic regression analysis

Multivariable logistic regression analysis found that glycerol carriers (odds ratio (OR) = 0.865 [0.355–2.141], $P = 0.750$) and no carrier (OR = 1.310 [0.587–3.044], $P = 0.517$), in reference to sodium hyaluronate, were not significant predictors of fusion. The presence of fibers (OR = 1.106 [0.524–2.456], $P = 0.797$) and the presence of a carrier (OR = 0.701 [0.370–1.327], $P = 0.274$) were also not significantly associated with fusion rates [Table 6].

DISCUSSION

Following the publication of the Kang *et al*., prospective study demonstrating that locally harvested bone and DBM is equivalent to locally harvested bone and iliac crest bone graft (ICBG), surgeons have increasingly moved away from harvesting iliac crest autograft in favor of a DBM product with locally harvested autograft.[22] However, subsequent studies have reached conflicting conclusions on the advantages of bone fibers and various carrier materials in DBM for promoting osteoinduction and bone fusion.[9-12,14,15] Our retrospective cohort study examined three different DBM formulations but found no differences in fusion rates when comparing carrier type, bone fibers, and carrier presence.

Although DBM with glycerol and hyaluronate carriers has been shown to provide clinically acceptable fusion rates, prior studies which have examined the difference between fusion rates with various DBM carriers have reached inconsistent results.[14,22-26] In the first side-by-side comparison of hyaluronate versus glycerol-containing bone DBM, Chang *et al*. analyzed 54 patients. They demonstrated that the fusion rates of posterolateral lumbar fusion surgery were not significantly different between hyaluronate (66.7%) and

Table 1: Demographics and surgical characteristics

	Sodium hyaluronate carrier (*n*=54), *n* (%)	Glycerol carrier (*n*=75), *n* (%)	No carrier (*n*=94), *n* (%)	*P*
Age (years)	65.8 (9.86)	66.7 (8.76)	66.6 (9.58)	0.739
Sex				
Female	30 (55.6)	37 (49.3)	42 (44.7)	0.442
Male	24 (44.4)	38 (50.7)	52 (55.3)	
BMI (kg/m^2)	29.9 (5.30)	28.9 (4.66)	28.8 (4.47)	0.470
Diabetes diagnosis	10 (18.5)	13 (17.3)	13 (13.8)	0.334
CCI	3.00 (1.90)	3.40 (1.87)	3.21 (2.03)	0.515
Smoking				
Nonsmoker	31 (57.4)	44 (58.7)	57 (60.6)	0.801
Current smoker	5 (9.26)	4 (5.33)	9 (9.57)	
Former smoker	18 (33.3)	27 (36.0)	28 (29.8)	
Hospital LOS (days)	188 (62.0)	181 (50.6)	180 (39.8)	0.189
Operative duration (min)	3.00 (1.45)	3.35 (1.61)	3.37 (4.06)	0.933
Total levels decompressed	1.56 (0.74)	1.62 (0.81)	1.57 (0.96)	0.886
Levels fused				
L3–L4	8 (14.8)	5 (6.67)	11 (11.7)	0.314
L4–L5	46 (85.2)	70 (93.3)	83 (88.3)	
Diagnosis				
Spondylolisthesis	45 (83.3)	73 (97.3)	90 (95.7)	0.007
Nonspondylolisthesis	9 (16.7)	2 (2.67)	4 (4.26)	

BMI - Body mass index; CCI - Charlson Comorbidity Index; LOS - Length of stay

Table 2: Readmissions and revisions based on carrier type

	Sodium hyaluronate carrier (*n*=54), *n* (%)	Glycerol carrier (*n*=75), *n* (%)	No carrier, *n* (%)	*P*
90-day readmissions	4 (7.41)	1 (1.33)	3 (3.19)	0.195
Surgical readmissions	2 (3.70)	1 (1.33)	1 (1.06)	0.562
Reason for surgical readmission				
Incision and drainage for infection	2 (3.70)	1 (1.33)	0	0.109
Nonspine orthopedics	0	0	1 (1.06)	1.000
Revision surgery	3 (5.56)	0	2 (2.13)	0.107
Reason for revision surgery				
Nonunion	1 (1.85)	0	1 (1.06)	0.715
ASD	2 (3.70)	0	1 (1.06)	0.257

ASD - Adjacent segment disease

glycerol (70.4%) DBM carriers ($P = 0.574$).[10] On the contrary, in an animal model of 18 rats per group, Peterson *et al*. demonstrated that the glycerol DBM carrier showed higher fusion rates than the hyaluronate-containing DBM carrier.[15] In a retrospective study comparing glycerol-containing versus freeze-dried DBM, Graham *et al*. performed a prospective analysis of 106 patients assessing radiographic fusion rates 6 months after anterior cervical discectomy and fusion. However, the authors did not identify any cases of pseudoarthrosis in their cohort.[9] Although the present study did find instances of pseudarthrosis, we also demonstrated that the presence and type of carrier material conferred no significant difference in fusion rate. Although some studies have suggested a difference between hyaluronate and glycerol carriers regarding fusion rates, clinically, there does not appear to be an appreciable difference that should guide surgeon decision-making.

DBM can be made of osseous particulates and bone fibers to augment autografts in spine surgery. However, due to the increased surface area and exposure to natural bone morphogenic proteins, some authors have suggested that cortical and cancellous fibers make patients more likely to achieve successful fusion.[27] A animal model by Abedi *et al*. demonstrated from PLDF in a rat model that particulate-based DBM leads to significantly less fusion than DBM comprised of bone fibers.[28] In a similar study, Martin *et al*. also demonstrated significantly higher rates of fusion after PLDF in a rabbit model when comparing fiber-based DBM to particulate-based DBM.[29] However, in the present study, the presence of bone fibers in the makeup of DBM did not significantly impact the rates of fusion. Although the preclinical literature has found that bone fibers generally lead to higher rates of successful fusion, the current investigation is the first to demonstrate that the effect of bone fibers within

Table 3: Readmissions and revisions based on bone fibers and carrier

	No fibers (*n*=54), *n* (%)	Fibers (*n*=169), *n* (%)	*P*[a]
90-day readmissions	4 (7.41)	4 (2.37)	0.099
Surgical readmissions	2 (3.70)	2 (1.18)	0.248
Reason for surgical readmission			
Incision and drainage for infection	2 (3.70)	1 (1.33)	0.109
Nonspine orthopedics	0	1 (0.59)	1.000
Revision surgery	3 (5.56)	2 (1.18)	0.093
Reason for revision surgery			
Nonunion	1 (1.85)	1 (0.59)	0.426
ASD	2 (3.70)	1 (0.59)	0.146
	No carrier (*n*=94), *n* (%)	**Carrier (*n*=129), *n* (%)**	***P*[a]**
90-day readmissions	3 (3.19)	5 (3.88)	1.000
Surgical readmissions	1 (1.06)	3 (2.33)	0.640
Reason for surgical readmission			
Incision and drainage for infection	0	3 (2.33)	0.265
Nonspine orthopedics	1 (1.06)	0	0.423
Revision surgery	2 (2.13)	3 (2.33)	1.000
Reason for revision surgery			
Nonunion	1 (1.06)	1 (0.78)	1.000
ASD	1 (1.06)	2 (1.55)	1.000

[a]$P<0.05$ is considered significant, ASD - Adjacent segment disease

Table 4: Fusion outcomes based on the type of carrier component

	Sodium hyaluronate carrier (*n*=54), *n* (%)	Glycerol carrier (*n*=75), *n* (%)	No carrier (*n*=94), *n* (%)	*P*
Bone bridging fusion				
Yes	45 (83.3)	67 (89.3)	85 (90.4)	0.410
No	9 (16.7)	8 (10.7)	9 (9.57)	
Screw fusion				
Yes	50 (92.6)	70 (93.3)	82 (87.2)	0.340
No	4 (7.41)	5 (6.67)	12 (12.8)	
Cobb fusion				
Yes	51 (94.4)	67 (89.3)	80 (85.1)	0.219
No	3 (5.56)	8 (10.7)	14 (14.9)	
Combined fusion[a]				
Yes	41 (75.9)	59 (78.7)	67 (71.3)	0.535
No	13 (24.1)	16 (21.3)	27 (28.7)	

[a]Bone fusion - radiopacity uniting the transverse processes on AP radiograph; screw fusion - lack of >2 mm of osteolysis surrounding at least two screws or visible instrumentation failure; cobb fusion - segmental lordosis difference of <5° between flexion and extension; combined fusion - if any of bone bridging, screw fusion, cobb fusion criteria were not met. AP - Anterior-posterior

DBM did not enhance fusion rates. Further study with large cohort sizes is required to confirm these findings.

In all aspects of spine surgery, it is important to examine not only fusion rates but also other surgical outcomes, including readmissions and complications. Some studies assess these outcomes with respect to the DBM used during surgery. Vaidya *et al*. studied 98 patients in a retrospective study demonstrating reduced surgical complication rates with DBM compared to rhBMP-2.[30] Similarly, Schizas *et al*. retrospectively studied the rates of surgical complications in patients receiving DBM with local autograft or ICBG, demonstrating no difference in complications between procedures.[31] To our knowledge, no study has assessed surgical outcomes between various types of DBM. Our results suggest no appreciable clinical difference in surgical outcomes, including rates of 90-day readmissions, surgical readmissions, and revision surgery, after PLDF between DBM-based carrier type, fiber presence, and carrier presence. Once again, based on these findings, we suggest that the choice of DBM should be determined by surgeon preference.

Our study is not without its limitations, including those inherent to retrospective review. To control for this, we only included single-level PLDFs performed by surgeons following the same surgical technique at the same hospital and ran multivariable regression analyses to account for the remaining differences in our cohort. Given that our

Table 5: Fusion outcomes based on the presence of bone fibers and carrier material

	No fibers (*n*=54), *n* (%)	Fibers present (*n*=169), *n* (%)	*P*[a]
Bone bridging fusion			
Yes	45 (83.3)	152 (89.9)	0.283
No	9 (16.7)	17 (10.1)	
Screw fusion			
Yes	50 (92.6)	152 (89.9)	0.754
No	4 (7.41)	17 (10.1)	
Cobb fusion			
Yes	51 (94.4)	147 (87.0)	0.206
No	3 (5.56)	22 (13.0)	
Combined fusion			
Yes	41 (75.9)	126 (74.6)	0.983
No	13 (24.1)	43 (25.4)	
	No carrier (*n*=94), *n* (%)	**Carrier present (*n*=129), *n* (%)**	***P*[a]**
Bone bridging fusion			
Yes	85 (90.4)	112 (86.8)	0.537
No	9 (9.57)	17 (13.2)	
Screw fusion			
Yes	82 (87.2)	120 (93.0)	0.219
No	12 (12.8)	9 (6.98)	
Cobb fusion			
Yes	80 (85.1)	118 (91.5)	0.203
No	14 (14.9)	11 (8.53)	
Combined fusion			
Yes	67 (71.3)	100 (77.5)	0.365
No	27 (28.7)	29 (22.5)	

[a]Bone fusion - radiopacity uniting the transverse processes on AP radiograph; screw fusion - lack of >2 mm of osteolysis surrounding at least two screws or visible instrumentation failure; cobb fusion - segmental lordosis difference of <5° between flexion and extension; combined fusion - if any of bone bridging, screw fusion, cobb fusion criteria were not met

Table 6: Multivariable logistic regression of combined fusion based on presence of bone fibers and carrier material

	OR	CI		*P*
		Lower 2.5%	Upper 97.5%	
Carrier type[a]				
Sodium hyaluronate: Reference				
Glycerol	0.865	0.355	2.141	0.750
No carrier	1.310	0.587	3.044	0.517
Presence of fibers[a]	1.106	0.524	2.456	0.797
Presence of carrier[a]	0.701	0.370	1.327	0.274

[a]Three separate multivariable analyses accounting for - age, sex, BMI, CCI, smoking status, levels decompressed and preoperative diagnosis were performed. CI - Confidence interval; BMI - Body mass index; OR - Odds ratio; CCI - Charlson Comorbidity Index

institution's standard of postoperative care includes plain radiographs to follow patients after single-level PLDFs, computed tomography scans are not routinely obtained to assess fusion status. Further, most studies cited in this manuscript rely on similar techniques to assess fusion.[26,31] Finally, this study may be limited by the sample size of the cohorts. Prior clinical studies assessing the fusion rates have not demonstrated a clinical difference between carrier components; thus, an effect size derived from these studies yielded unrealistic patient enrollment needed to determine a difference in fusion rates. We encourage additional literature with larger cohorts to assess fusion rates and surgical outcomes between DBM carriers and components.

CONCLUSION

DBM is commonly used in spine surgery to augment locally harvested autograft and promote fusion. However, differences between DBM products have raised questions about superiority based on carrier materials and the presence of bone fibers. Our study demonstrated no significant differences between fusion rates or surgical outcomes of single level PLDF between L3 and L5 with the use of DBM containing glycerol, hyaluronate, or no carrier. In addition, fusion and surgical outcomes were assessed based on the presence of bone particulates versus bone fibers in the DBM, and once again, there were no significant differences between the groups. Further, well-controlled, large cohort analyses may be needed to adequately interrogate the impact of various allograft options on outcomes after spine surgery.

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Conflicts of interest

There are no conflicts of interest.

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