



Clinical Study

Comparison of posterior cellular bonegraft options for single level lumbar spinal fusion: a randomized trial

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Abstract

BACKGROUND: Iliac bone autograft (IBG) is osteoinductive/osteogenic/osteoconductive but requires an additional harvesting procedure with known morbidities. Bone morphogenetic protein (BMP) is osteoinductive and effective in obtaining fusion but is used off label for posterior fusion, has multiple side effects, and is expensive. Stem cell bone products, both auto- and allograft are attractive osteoinductive alternatives that avoid morbidity related to the graft donor site and may have a better safety profile than BMP. Morcelized allograft bone is osteoconductive but not osteoinductive or osteogenic.

PURPOSE: Evaluate and compare the effectiveness of 6 types of viable or osteoinductive bone graft material in obtaining a solid posterior spinal fusion (PSF) for single level anterior/posterior lumbar spinal fusion. The bone grafts were IBG, BMP, autogenous stem cells (MSC) from concentrated bone marrow aspirate (BMA), allograft MSC from bone marrow, adipose tissue, or amniotic fluid, combined with inert cancellous allograft (Allo).

STUDY DESIGN/SETTING: Prospective, single-blinded randomized study of 6 cohorts and inert historical control.

PATIENT SAMPLE: Elective anterior-posterior lumbar spinal fusion of 175 patients.

OUTCOME MEASURES: Assessments included pre and postoperative back and leg pain (VAS) scores, Pain Drawing, disability (ODI) scores, pain medication usage, and 1-year postoperative thin-cut CT scans (read by blinded radiologists).

METHODS: Patients who were surgical candidates for a one-level anterior/posterior lumbar fusion were randomized to 1 of 6 types of posterior bone graft alternatives: IBG, BMP, BMA, allograft MSC derived from bone marrow combined with morcelized Allo (cAlloBone), adipose derived MSC combined with morcelized Allo (cAlloFat), or amnion derived MSC combined with morcelized Allo (cAlloAm). Historical Allo patients served as a negative control group. Each group (n = 27) had prospective outcomes and were followed for a minimum of 2 years. Fusion rate and outcomes were compared and referenced to Allo group.

RESULTS: All but 5 patients had a solid ASF. The posterior fusion rates were 98% for IBG, 94% for BMP, 85% for BMA, 67% for cAlloBone, 64% for cAlloFat, 62% for cAlloAm, and 50% for Allo. Outcomes were significantly improved for all measures for all groups and there was no difference between groups except cAlloFat had slightly greater improvement in back pain in the 7-12 month follow-up period. BMP was the most expensive graft material; cellular allografts had a high-cost relative to fusion rate.

CONCLUSIONS: For single level ASF/PSF, the PSF fusion rate was significantly greater for IBG and BMP followed by BMA. Various allograft MSC bone graft options resulted in lower fusion rates but may be greater than Allo. Outcomes were uniformly improved regardless of the type of graft used or the fusion status of the posterior fusion as long as the interbody fusion was solid. If bone graft cost savings is a consideration for PSF, then IBG has the greatest radiographic value, and Allo the greatest clinical value as long as the anterior interbody fusion is solid. © 2026 Elsevier Inc. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Key words:

Allograft; Bone graft; Bone marrow aspirate; Bone morphogenetic protein; Fusion; Iliac bone graft; MSC; Outcomes; Stem cells

Author disclosures: **GRB:** Patents (none).

FDA device/drug status: Not applicable (Allostem, AlloSource).

FDA device/drug status: approved (Trinity (Orthofix); NuCEL, Nutech).

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Introduction

Achieving successful spinal arthrodesis is related to fusion technique and type of bone graft material. A reliable technique is an anterior/posterior fusion procedure which includes a large bony endplate surface resulting in a reliable anterior spinal fusion, ASF, success rate [1,2]. Instrumentation helps stabilize the vertebra during the healing period which also increases the fusion rate [3]. The bone graft for the posterior spinal fusion, PSF, may come from a variety of sources. Historically, for PSF only fusions, iliac bone graft, IBG, was preferred as it has optimal healing due to its osteoinductive, osteoconductive and osteogenic properties and is also the standard material to which other bone graft substitutes are compared [4]. However, harvesting IBG has morbidities [5–12]. Alternatives to IBG generally include bone allograft (Allo), demineralized bone matrix (DBM), and ceramics which act primarily as a scaffold. Allo has no significant osteoinductivity or osteogenic ability and has been shown to have low fusion rates in adult lumbar spinal fusion patients [13,14]. Ceramics, even when combined with bone marrow aspirate, BMA, have a high rate of nonunion, and fusion assessment is also confounded by unreliable imaging, that is, the inability to identify true trabecular bone [15,16]. Another option to IBG is locally harvested autograft bone, but the quality and quantity is often limited [17–19]. Bone morphogenetic protein, BMP, has osteoinductive properties and a high success rate for spinal fusion [20–22].

An intriguing concept for a safe alternative to IBG and BMP is viable cellular products that include mesenchymal stem cells, MSCs, that may be induced to differentiate into osteoblasts or otherwise have osteogenic potential [23–25]. Bone derived stem cells may be autogenous or allograft. Autologous bone marrow aspirate, BMA, has viable host MSCs, is usually obtained from the iliac crest at the time of PSF [26]. Allo combined with BMA, can lead to fusion success [27–30]. Concentrating the cells and isolating them may further enhance fusion rates [31,32].

Three types of adult allograft derived MSC products have been commercialized and are appealing for ease of use and availability. They derive from different tissue sources; such as from human bone, adipose, and amniotic membrane/fluid (placental or “afterbirth”) tissues. However, published literature is limited to experimental and early clinical support, primarily for anterior cervical but also lumbar interbody fusions [33,34]. Bone derived MSC products have been studied the most. Overall, their efficacy is still unproven [25,35].

Human bone derived cellular allograft (cAlloBone) MSCs are processed in a certified bone bank from cadaveric bone to optimize cell count and often combined with morcelized bone allograft and/or DBM to enhance handling characteristics. The product is stored at deep freezing temperature. However, cryopreservation of cellular bone allografts may be potentially problematic [36]. Bone marrow allograft derived cells have highly variable fusion rates in

experimental animal studies, of which Trinity Elite (Orthofix, Lewisville, TX) may be the most promising [37]. This product has been shown to be effective in cervical fusions and foot/ankle fusions [38–40]. It has also demonstrated success in lumbar PSF and interbody fusion [41–43]. Another source of stem cells is derived from fatty tissue [44,45]. Preclinical studies have shown that allograft adipose (cAlloFat) as a source of stem cells results in bony fusion [46–51]. Amniotic membrane and fluid is also a cellular allograft product (cAlloAm) and has shown success in augmenting IBG in orthopedic foot and ankle surgery [52].

The purpose of the present study is to determine the ability to achieve a solid PSF using bone graft from 7 different sources. This included grafts with known high fusion rates, IBG and BMP, compared to the fusion rate for various MSC products with cellular auto- and allograft sources (BMA, cAlloBone, cAlloFat, cAlloAm) in a randomized fashion. These various bone grafts were also compared to an inert morcelized Allo historical control group. Secondly, clinical outcomes were assessed using various patient reported outcomes measurements (PROMS).

Methods

Consecutive patients who were surgical candidates for a one-level anterior/posterior lumbar fusion were eligible for inclusion into the study. Inclusion criteria included those with primary degenerative disc disease of 1 level with or without prior decompression, degenerative (but not lytic) spondylolisthesis grade 2 or less, and none or up to moderate stenosis that could be treated with a laminotomy but excluded those that needed extensive laminectomy (for more advanced stenosis) that would compromise the facet joint integrity required for trans-facet joint instrumentation. The study proposal underwent IRB review (HealthEast IRB #1510002). All the participants provided written informed consent. After completing IRB approved consent, patients were randomized, by computer generated program (<https://www.random.org/lists/>), to 5cc IBG or 1 of 5 other types of PSF osteoinductive bone graft alternatives: bone morphogenetic protein (BMP, small Infuse, Medtronic, Memphis, TN), autologous concentrated bone marrow aspirate (BMA) from the iliac crest (combined with 5cc Allo chips), allograft bone marrow derived stem cells (cAlloBone, 5.3cc Trinity Elite, Orthofix, Lewisville, TX), fat derived allograft stem cells (Allostem, AlloSource, Centennial, CO) combined with 5cc morcelized cancellous allograft (cAlloFat), or placental derived allograft stem cells (NuCel, Nutech, Birmingham, Alabama) combined with 5cc morcelized cancellous allograft (cAlloAm). There was no stratification prior to the randomization such as by smokers, preoperative opioid use. A historical control group of 5cc cancellous freeze-dried allograft (Allo) was used as an inert “negative” control group. There were 27 patients in each group. However, during the rolling enrollment period (8 years), AlloSource Allostem was withdrawn from the

market due to FDA requirements; thus, this group only had 14 patients (AlloSource untitled letter, FDA 2011). All anterior fusions used BMP (small Infuse). One BMP patient declined 1-year postoperative imaging and outcomes and was withdrawn from the study (thus $n = 26$). The decortication technique of the posterior fusion was identical for all patients and local bone shavings obtained during decortication was used to supplement all the various bone graft alternatives in a similar fashion [53]. All patients had identical fixation instrumentation implanted (anterior lumbar plate and posterior facet screws [2]. Posterior fusions had bone graft applied to the laminae and into the facet joints and were instrumented to eliminate posterior micromotion and subsequent pseudarthrosis as a confounding variable [54]. All the fusion procedures were performed by the lead author to ensure a uniform surgical technique across all bone graft type groups. Therefore, the surgical technique was as uniform as practically possible to minimize confounding variables related to the surgery with the only variable being the various posterior fusion bone graft materials. Patients were blinded to the posterior type of bone graft. The volume of bone graft was the same for each type, approximately 5cc, since this volume of IBG is unlikely to cause donor site pain which could be a confounding factor in pain outcomes assessment [55].

The costs for each bone graft product were obtained directly from the surgical facility based on their contracts (Table 1). IBG cost was from time-driven activity-based costing at \$37 per minute $\times$ 20 minutes and an additional \$600 for bone graft harvest instruments packaging/sterilization, for a total of \$1340 [56].

Postoperatively, all patients were followed for a minimum of 2 years. During this time radiographs were obtained and lumbar CT. Thin-cut CT scans of the fused level were obtained at approximately 1 year postoperatively to assess fusion success of both anterior and posterior spinal columns. Specifically for the posterior fusion, if only a unilateral fusion was identified, the fusion was tallied as half-

fused. A *composite* pseudarthrosis rate was determined by adding bilateral (counted as 1) and unilateral nonunions (counted as 1/2) and then divided by the number of patients in the group. All CT scans were read by 1 of 2 radiologists, each with over 20 years' experience and who restrict their practice to spinal imaging. Both radiologists were blinded to the type of bone graft used in the fusion. The limited (to the levels fused) CT scan had 2.88 mSv radiation exposure, or similar to 1 year's worth of background radiation.

Secondary endpoints of clinical outcomes were assessed pre and postoperatively with multiple outcome instruments: visual analog scales (VAS) for back and leg pain; pain drawing; Oswestry disability index (ODI); pain medication usage (nonopioid and opioids); and patient self-assessment of procedure success over a minimum 2-year follow-up period. Outcome results were entered by office personnel (blinded to the type of bone graft) into computer spreadsheets, with the treating surgeon blinded to these results. The historical control group consisted of a retrospective cohort of consecutive patients which fit the inclusion/exclusion criteria, had the same surgical procedure, and had their PSF with freeze-dried allograft morcelized bone. Additional surgeries were tracked for all groups, including pseudarthrosis repair, adjacent level decompression, adjacent-level fusion extension, spinal cord stimulator implantation, and posterior instrumentation removal.

Statistical comparisons were made for differences in fusion rates, outcomes, self-assessment of success, and pain medication use between the 7 bone graft groups. Fusion rates between bone graft groups utilized ordinal logistic regression analysis. This was also applied for analysis of fusion rate difference between male versus female, age, and smoker versus nonsmokers. Outcomes within each group comparing pre versus each postoperative follow-up period was determined using a 2-sample paired *t*-test of the means for all the outcomes scales. Anova testing was used to compare the mean outcome change between groups at each follow-up visit relative to preoperative values. Differences

Table 1
Demographics

Demographics	IBG	BMP	BMA	cAlloBone	cAlloAm	cAlloFat	Allo
# Patients	27	26	27	27	27	14	27
Age (mean years)	48.6	51.2	51.5	52.7	55.0	51.8	57.6
Female (%)	59%	46%	52%	59%	44%	71%	41%
Smokers (%)	44%	54%	19%	33%	52%	36%	22%
Prior decompression (%)	15%	35%	26%	26%	22%	21%	37%
Concurrent decompression (%)	37%	38%	33%	48%	37%	50%	37%
Level Fused, L5–S1	67%	31%	44%	48%	52%	64%	37%
L4–5	30%	65%	44%	44%	33%	36%	41%
L3–4 or proximal	4%	4%	11%	7%	15%	0%	22%
Bone Graft cost (\$)	1340	3451	1660 [†]	2727	2216 [‡]	2768	160

*IBG, iliac bone graft; BMP, bone morphogenetic protein; BMA, concentrated bone marrow aspirate; cAlloBone, cellular bone allograft; cAlloAM, cellular amniotic tissue; cAlloFat, cellular fat allograft; Allo, freeze-dried bone allograft chips.

[†] \$1500 (centrifuge disposables) + \$160 (5cc cancellous allograft chips) = \$1660.

[‡] \$2056 (medium, 1ml) + \$160 (5cc cancellous allograft chips) = \$2216.

between groups at each postoperative period for self-assessment rate of success, repeating surgery under similar conditions, recommending treatment to others were analyzed with Fisher's Exact test. The difference between groups as to the change in use of nonopioid and opioid pain medications were analyzed using the Generalized Estimating Equations (GEE) model and Fisher's Exact test. Differences in VAS back pain and VAS ODI in fusions versus pseudarthrosis were analyzed using a 2-sample t-test. Examining if fusion outcomes were better for 1 treatment group over another were analyzed with ordinal logistic regression. Probability values of less than 0.05 were considered statistically significant.

Results

The patient demographics found minimal differences between the various bone graft groups (Table 1). Age, percentage of patients who had prior decompression surgery at the same level and those that had concurrent laminotomy at the time of their PSF were similar. L4–5 and L5–S1 were the most common levels treated. Although cAlloFat had a higher proportion of female to male patients, this was statistically not different. The BMA group had less smokers, but this too was not statistically different ($p=.083$). Of the 176 patients enrolled, the number of patients that had incomplete data was minimal (5%). One BMP patient withdrew. One BMA and 1 cAlloAm patients were deceased due to nonspinal conditions. Another BMA patient had a new injury with a fracture to another region of the spine. There were 3 patients in the cAlloBone group that were lost or declined to participate at the 2 to 4-year follow-up period. Two patients in the Allo group were lost to follow-up, one at 1 to 2-year period and the other at 2 to 4-year period.

The primary outcome of PSF success as determined by fine-cut CT scans was for bridging bone (Fig. 1). Within groups, there was no statistical evidence that smoking status, age, level of fusion, or sex (male vs female at the time of birth) was related to PSF rate. However, for all groups

combined, age was associated with a lower fusion rate (Table 2). IBG and BMP had the highest PSF rates (Table 3). The cellular allograft products had composite PSF rates of approximately 66% which was less than for autologous cellular graft (BMA). Allo had the lowest PSF rate. One patient in each cAlloBone and cAlloAm and another 3 in the Allo group had anterior interbody nonunion. All patients who had an anterior nonunion had a posterior nonunion as well, and all occurred at L4–5 or L5–S1. Statistically between the posterior bone graft types, there were significant PSF rate differences; Table 4 presents PSF rates relative to Allo. Allo had significantly lower fusion rates at approximately 43 times lower odds of fusion compared with IBG, ≈ 20 times lower odds of fusion compared to BMP, and ≈ 5 times lower odds of fusion compared to BMA. All 3 cellular allograft groups, cAlloBone, cAlloFat and cAlloAm had significantly lower fusion rates than IBG; specifically ≈ 20 times lower odds of fusion (OR=0.05, 95% CI: 0.01–0.43), ≈ 24 times lower odds of fusion (OR=0.04, 95% CI: 0.004–0.39), and ≈ 26 times lower odds of fusion (OR=0.04, 95% CI: 0.005–0.33), respectively. Similarly, all 3 cellular allograft groups, cAlloBone, cAlloFat and cAlloAm had significantly lower fusion rates than BMP; specifically ≈ 9 times lower odds of fusion (OR=0.11, 95% CI: 0.02–0.56), ≈ 11 times lower odds of fusion (OR=0.09, 95% CI: 0.02–0.53), and ≈ 11 times lower odds of fusion (OR=0.09, 95% CI: 0.02–0.44), respectively.

Outcome instruments found significant improvement within all groups in VAS back pain and leg pain scores at all follow-up periods (Figs. 2, 3 and Tables 5, 6). For pain drawing, all patient groups had significant improvement at all follow-up periods (Fig. 4 and Table 7). For ODI, all patient groups had significant improvement at all follow-up periods (Fig. 5 and Table 8). There was no correlation between outcomes and PSF status. Between groups, the only difference between the groups was that cAlloFat had a greater improvement in back pain at the first follow-up period compared to Allo and BMP ($p<.05$). Between groups, there was no



Fig. 1. A,B,C. High resolution CT scan of solid facet joint fusion for a cellular bone allograft patient; Axial (A), sagittal reconstruction (B), and coronal images. Asterisks indicated location of fused facet joint.

Table 2

Ordinal logistic regression analysis of fusion outcomes by age, smoking status, and sex

Predictor	Comparison	Odds ratio	95% CI	p-value
Age	Per year increase	1.07	(1.01, 1.13)	.021
Smoking Status	Yes vs. No	1.11	(0.21, 6.00)	.899
Sex	Male vs. Female	0.71	(0.17, 2.96)	.442

Odds ratios are adjusted for the type of posterior bone graft, which was significantly associated with the outcome.

Table 3

Postoperative CT imaging and Additional Procedures

Postoperative CT imaging	IBG	BMP	BMA	cAlloBone	cAlloAm	cAlloFat	Allo
Posterior solid fusion (%)	96%	88%	78%	60%	56%	50%	37%
Posterior unilateral pseudarthrosis (%)	4%	8%	22%	15%	15%	29%	26%
Posterior bilateral pseudarthrosis (%)	0%	4%	0%	26%	30%	21%	37%
Posterior composite pseudarthrosis (%)	2%	8%	15%	33%	38%	36%	50%
Anterior Interbody pseudarthrosis (%)	0%	0%	0%	4%	4%	0%	11%
Additional procedures (%)							
Postoperative adjacent segment decompression	4%	0%	7%	4%	4%	14%	7%
Postoperative adjacent segment fusion	11%	8%	7%	4%	4%	7%	11%
Pseudarthrosis repair	0%	0%	0%	4%	4%	0%	7%
Posterior Instrumentation removal [†]	0%	0%	0%	0%	0%	0%	0%
Spinal cord stimulator placement	0%	0%	4%	4%	4%	0%	4%

*IBG = iliac bone graft; BMP, bone morphogenetic protein; BMA, concentrated bone marrow aspirate; cAlloBone, cellular bone allograft; cAlloAM, cellular amniotic tissue; cAlloFat, cellular fat allograft; Allo, freeze-dried bone allograft chips.

[†] Not related to pseudarthrosis repair.

Table 4

Ordinal logistic regression analysis of fusion radiographic outcome by group

Bone graft group (vs. Allo)	Odds ratio	95% CI	p-value
cAlloFat	0.55	(0.16, 1.86)	.228
BMA	0.2	(0.07, 0.62)	.005
IBG	0.02	(0.003, 0.19)	<.0001
BMP	0.05	(0.01, 0.25)	<.0001
cAlloAm	0.59	(0.21, 1.61)	.299
cAlloBone	0.46	(0.17, 1.26)	.131

Odds ratios (OR) are from ordinal logistic regression with cumulative logit link.

difference in the amount of improvement of leg pain, pain drawing and ODI at any follow-up period relative to preoperative status. There were 5 patients with an anterior interbody pseudarthrosis; none had significant improvement in outcomes at any follow-up period except for VAS Back pain at the first follow-up period.

All groups had substantial reductions in overall pain medication use which improved over time (Tables 9 and 10). With regard to opioids, there was at least a 50% reduction for all groups. Some variability was related to some patients having multiple prescribers. There was no significant difference in the use of opioid pain medication at any follow-up period between all 7 groups, and no difference in the change in opioid use between groups. Nonopioid pain medication was significantly reduced in all groups except

the nonrandomized control Allo group, at the initial follow-up period ($p < .025$). During the initial follow-up period, BMP had significantly greater use of nonopioid medication compared to cAlloAm. At final follow-up, the rate of nonopioid use was similar in all groups. The rate of patients not using any pain medication varied from 27% to 50%.

Self-assessment of overall success was statistically similar for all groups at all follow-up periods, except at the 1 to 2 year follow-up period, cAlloBone had a significantly lower success rate than IBG and cAlloAm (Table 11). When queried as to “Would you repeat the surgery under similar conditions?” and “Would you recommend the treatment to others?” similarly high rates were found for all groups, and there no difference between groups at any follow-up period and (Table 11).

Costs of various bone graft products varied, with BMP as the most expensive and Allo the least expense (Table 1). IBG and BMA had moderate costs but less than the cellular allograft products.

Additional surgeries were generally <15% among all the groups (Table 3). Allo had the greatest rate of pseudarthrosis repair and correlated to those patients who had anterior interbody nonunion in addition to their posterior nonunion.

Discussion

This study compared, in a randomized fashion, 6 types of grafts with various osteoinductive properties to a historical inert “negative” control group (Allo) for single level fusion.

Low Back Pain VAS

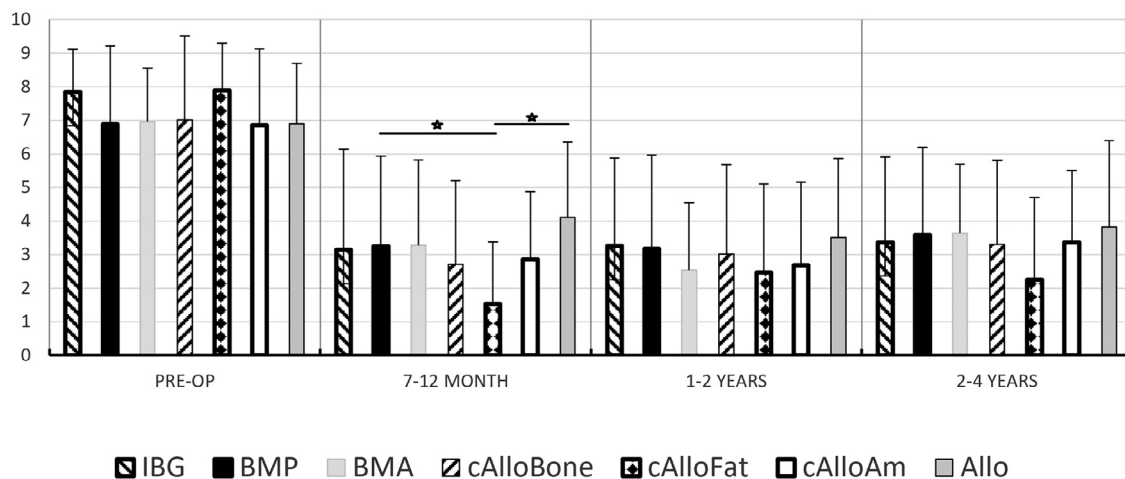


Fig. 2. Back pain VAS scores (mean $\pm$ SD) over time for 6 randomized posterior bone graft groups and allograft control. Between groups, cAlloFat had significantly greater back pain improvement at the 7–12 month follow-up period relative to BMP and Allo.

Leg Pain VAS

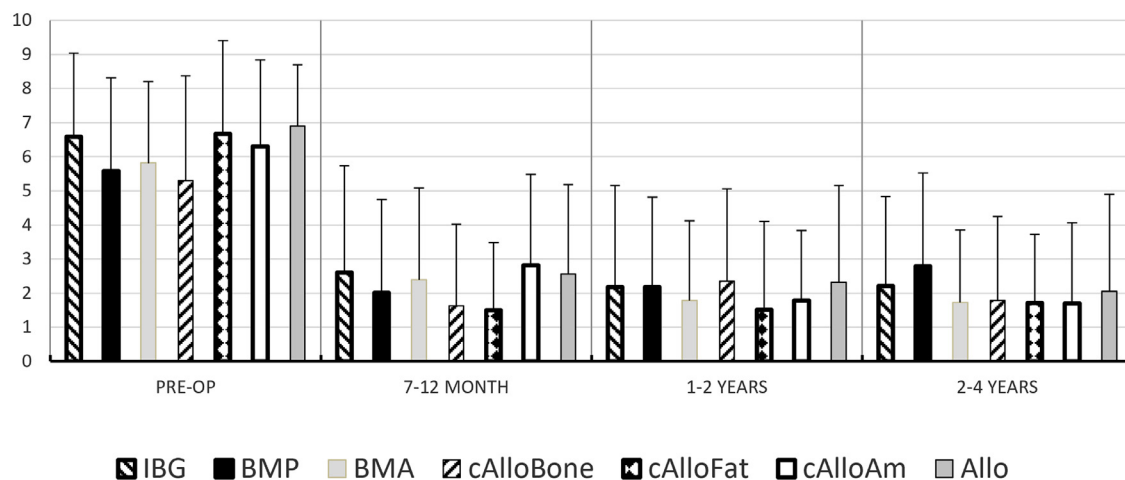


Fig. 3. Leg pain VAS scores (mean $\pm$ SD) over time for 6 randomized posterior bone graft groups and allograft control.

All patients had a similar fusion technique used to minimize confounding factors that may influence fusion rates. BMP and autografts with known osteoinductive and osteogenic potential had high rates of fusion. Cellular allografts had modest fusion success rates, but greater than Allo (although not significantly given the sample sizes of this study). If the interbody fusion was solid, then there was no relationship between clinical success and posterior fusion status.

Specifically, the high rate of posterior fusion for IBG and BMP of the current study agrees with prior investigations [20,58,59]. The present study found an 85% fusion rate for the BMA group which is consistent with prior studies evaluating BMA combined with allograft bone with reported fusion rates of 79% to 85% [27,60–62]. Unlike bone grafts with osteogenic potential, the Allo negative control group

had the lowest PSF rate of only 50% which is agreement with prior studies that have a range of 0% to 70% fusion [13,63–65].

The 3 different allografts with MSCs, bone, fat, and amniotic/placentally derived products had similar PSF fusion rates of 63% to 67%. Bone marrow allograft derived cells, cAlloBone, has the most clinical investigations. The present study was not able to achieve the high PSF fusion rates (>85% using plain radiograph criteria) previously reported [42,43,66]. Although the PSF fusion rates in the present study are low compared to IBG or BMP, cAlloBone may have higher fusion rates in interbody applications [41,67–70]. Other types of allograft derived MSC bone graft have limited clinical studies. Adipose derived cells, cAlloFat, have support for bone formation in experimental studies

Table 5

Change in VAS back pain within bone graft treatment groups

Type of posterior bone graft—5cc*	Mean	Std Dev	95% CI	p-value
IBG				
VAS back pain 7–12 month follow-up period	4.60	2.97	(3.40, 5.80)	<.0001
VAS back pain 1–2 year follow-up period	4.48	2.67	(3.41, 5.57)	<.0001
VAS back pain 2–4 year follow-up period	4.48	2.80	(3.37, 5.59)	<.0001
BMP				
VAS back pain 7–12 month follow-up period	4.30	2.79	(3.20, 5.41)	<.0001
VAS back pain 1–2 year follow-up period	3.93	2.82	(2.79, 5.07)	<.0001
VAS back pain 2–4 year follow-up period	3.66	2.92	(2.43, 4.89)	<.0001
BMA				
VAS back pain 7–12 month follow-up period	3.99	2.52	(2.99, 4.98)	<.0001
VAS back pain 1–2 year follow-up period	4.16	2.68	(3.10, 5.22)	<.0001
VAS back pain 2–4 year follow-up period	3.39	3.00	(2.18, 4.61)	<.0001
cAlloBone				
VAS back pain 7–12 month follow-up period	3.64	2.49	(2.63, 4.64)	<.0001
VAS back pain 1–2 year follow-up period	3.71	2.72	(2.61, 4.81)	<.0001
VAS back pain 2–4 year follow-up period	3.28	2.73	(2.16, 4.41)	<.0001
cAlloAm				
VAS back pain 7–12 month follow-up period	6.36	2.02	(5.19, 7.53)	<.0001
VAS back pain 1–2 year follow-up period	5.41	2.65	(3.88, 6.94)	<.0001
VAS back pain 2–4 year follow-up period	5.64	2.60	(4.14, 7.14)	<.0001
cAlloFat				
VAS back pain 7–12 month follow-up period	3.82	2.42	(2.82, 4.82)	<.0001
VAS back pain 1–2 year follow-up period	4.46	2.45	(3.45, 5.47)	<.0001
VAS back pain 2–4 year follow-up period	3.28	2.54	(2.23, 4.33)	<.0001
Allo				
VAS back pain 7–12 month follow-up period	2.90	2.67	(1.80, 4.00)	<.0001
VAS back pain 1–2 year follow-up period	3.43	2.14	(2.40, 4.36)	<.0001
VAS back pain 2–4 year follow-up period	3.21	2.21	(2.30, 4.12)	<.0001

* IBG, iliac bone graft; BMP, bone morphogenetic protein; BMA, concentrated bone marrow aspirate; cAlloBone, cellular bone allograft; cAlloAM, cellular Amniotic tissue; cAlloFat, cellular fat allograft; Allo, freeze-dried bone allograft chips.

such as in rat calvariae [71]. However, other studies have found limitations of adipose derived stem cells. This has been seen in experimental studies, including athymic rats suggesting the local cellular environment may detrimentally affect ability to produce fusion [47,72]. Amniotic membrane and fluid is a cellular allograft product (cAlloAm), which has been used clinically in interbody fusion with a small study finding ASF fusion rate of 76% [73].

Given the relatively low fusion rate identified in this study for allograft stem cells, further basic science research is needed to help effect bony differentiation of this type of MSC to be useful for arthrodesis [74,75]. Greater understanding is needed in the molecular signaling pathways to transform the presumed progenitor allograft cells into functional osteoblasts. Factors affecting successful arthrodesis include unknown viable MSC counts, the variable local environmental effects such as host fusion bed and effects of preservatives/cryoprotective agents on MSC viability [36,76,77]. Advances in cryopreservation may enhance allograft cell viability and maximize viable cell count.

Statistical analysis found no relationship between clinical success and posterior fusion rate consistent with a prior study that found success is related to the status of anterior fusion [54]. The Allo group had the lowest PSF rate and lowest interbody fusion rate. A solid interbody fusion may

enhance the PSF rate but not be clinically meaningful. However, if a solid PSF enhances interbody fusion then a surgeon may strive to use a bone graft that optimizes PSF healing, which secondarily promotes interbody fusion and improved outcomes. Keeping this in mind, if one assesses cost, Allo, is by far the least expensive but possibly risking a higher rate of interbody nonunion and recurrent symptoms. One can also view this from a *value* perspective; that is *cost per fusion rate*. From most expensive to lowest value (for the authors' hospital system), this calculates to cAlloFat at \$4306, cAlloBone at \$4091, BMP at \$3662, cAlloAm at \$3520, BMA at \$1948, IBG at \$1162, and Allo at \$320. If 1 desires low cost and a high fusion rate, then IBG may be favored. One must keep in mind that the total cost of spinal fusion surgery is far greater than any of the bone graft options of this study.

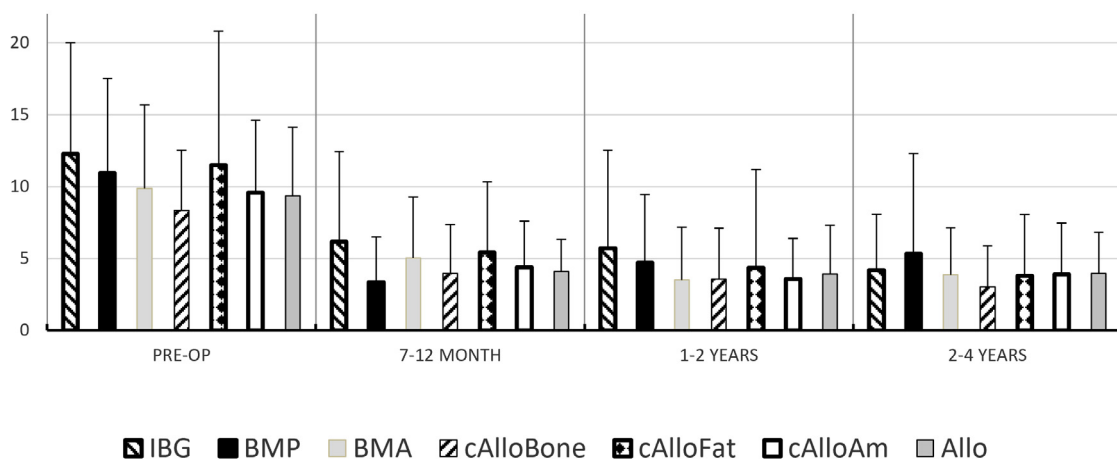
Limitations include relatively small sample size per bone graft group and the cAlloFat group was quite small, and unknown viable MSC counts for the cellular allograft groups. The small sample size per bone graft group makes the results fragile. A post hoc power analysis was performed based on the observed distribution of fusion outcomes across graft groups. At 80% power and a two-sided alpha of 0.05, the estimated sample sizes required to detect differences between groups exceeded the current study size

Table 6

Change in VAS leg pain within bone graft treatment groups

Type of posterior bone graft—5cc*	Mean	Std Dev	95% CI	p-value
IBG				
VAS leg pain 7–12 month follow-up period	3.88	3.43	(2.50, 5.27)	<.0001
VAS leg pain 1–2 year follow-up period	4.32	3.06	(3.08, 5.56)	<.0001
VAS leg pain 2–4 year follow-up period	4.38	3.36	(3.05, 5.71)	<.0001
BMP				
VAS leg pain 7–12 month follow-up period	3.67	3.45	(2.30, 5.04)	<.0001
VAS leg pain 1–2 year follow-up period	2.98	4.04	(1.35, 4.62)	<.0001
VAS leg pain 2–4 year follow-up period	3.92	4.14	(2.17, 5.67)	<.0001
BMA				
VAS leg pain 7–12 month follow-up period	3.48	3.10	(2.25, 4.70)	<.0001
VAS leg pain 1–2 year follow-up period	4.52	2.83	(3.40, 5.64)	<.0001
VAS leg pain 2–4 year follow-up period	4.67	3.68	(3.18, 6.16)	<.0001
cAlloBone				
VAS leg pain 7–12 month follow-up period	3.57	2.83	(2.43, 4.71)	<.0001
VAS leg pain 1–2 year follow-up period	3.40	2.88	(2.23, 4.56)	<.0001
VAS leg pain 2–4 year follow-up period	2.68	3.24	(1.34, 4.02)	<.0001
cAlloAm				
VAS leg pain 7–12 month follow-up period	5.18	3.02	(3.44, 6.92)	<.0001
VAS leg pain 1–2 year follow-up period	5.16	3.07	(3.39, 6.94)	<.0001
VAS leg pain 2–4 year follow-up period	4.96	3.18	(3.13, 6.80)	<.0001
cAlloFat				
VAS leg pain 7–12 month follow-up period	3.62	3.14	(2.32, 4.92)	<.0001
VAS leg pain 1–2 year follow-up period	4.28	2.74	(3.15, 5.41)	<.0001
VAS leg pain 2–4 year follow-up period	4.14	2.90	(2.95, 5.34)	<.0001
Allo				
VAS leg pain 7–12 month follow-up period	3.76	3.50	(2.32, 5.20)	<.0001
VAS leg pain 1–2 year follow-up period	3.76	3.74	(2.15, 5.38)	<.0001
VAS leg pain 2–4 year follow-up period	4.16	3.49	(2.72, 5.60)	<.0001

* IBG, iliac bone graft; BMP, bone morphogenetic protein; BMA, concentrated bone marrow aspirate; cAlloBone, cellular bone allograft; cAlloAM, cellular Amniotic tissue; cAlloFat, cellular fat allograft; Allo, freeze-dried bone allograft chips.

Pain Drawing ⁵⁷Fig. 4. Pain Drawing scores (mean $\pm$ SD) over time for 6 randomized posterior bone graft groups and allograft control.

for several key comparisons. Specifically, comparisons between IBG/BMP and BMA, BMA and cellular allografts, and cellular allografts versus Allo would require approximately 110, 142, and 355 total subjects, respectively, when

maintaining the observed group allocation ratios. Given the current sample size, the study is underpowered for several comparisons, particularly those involving cellular allografts versus Allo. As a result, nonsignificant findings should be

Table 7

Change in pain drawing[†] within bone graft treatment groups

Type of posterior bone graft—5cc*	Mean	Std Dev	95% CI	p-value
IBG				
Pain drawing 7–12 month follow-up period	6.15	8.32	(2.79, 9.52)	.0009
Pain drawing 1–2 year follow-up period	6.62	7.64	(3.53, 9.70)	.0002
Pain drawing 2–4 year follow-up period	8.07	9.43	(4.34, 11.8)	.0001
BMP				
Pain Drawing 7–12 month Follow-up Period	4.37	4.81	(2.47, 6.27)	<.0001
Pain Drawing 1–2 year Follow-up Period	4.96	4.86	(3.00, 6.93)	<.0001
Pain Drawing 2–4 year Follow-up Period	5.79	4.94	(3.70, 7.88)	<.0001
BMA				
Pain drawing 7–12 month follow-up period	5.19	4.31	(3.48, 6.89)	<.0001
Pain drawing 1–2 year follow-up period	6.00	5.15	(3.96, 8.04)	<.0001
Pain drawing 2–4 year follow-up period	5.88	4.97	(3.88, 7.89)	<.0001
cAlloBone				
Pain drawing 7–12 month follow-up period	7.58	6.52	(4.94, 10.2)	<.0001
Pain drawing 1–2 year follow-up period	6.23	5.69	(3.93, 8.53)	<.0001
Pain drawing 2–4 year follow-up period	5.48	6.07	(2.97, 7.99)	.0001
cAlloAm				
Pain drawing 7–12 month follow-up period	6.07	8.66	(1.07, 11.1)	.021
Pain drawing 1–2 year follow-up period	7.14	10.0	(1.35, 12.9)	.020
Pain drawing 2–4 year follow-up period	7.71	8.57	(2.77, 12.7)	.0050
cAlloFat				
Pain drawing 7–12 month follow-up period	4.71	5.92	(2.21, 7.21)	.0007
Pain drawing 1–2 year follow-up period	6.56	5.92	(4.12, 9.00)	<.0001
Pain drawing 2–4 year follow-up period	6.00	5.33	(3.80, 8.20)	<.0001
Allo				
Pain drawing 7–12 month follow-up period	5.50	5.00	(3.39, 7.61)	<.0001
Pain drawing 1–2 year follow-up period	4.41	4.75	(2.30, 6.51)	.0003
Pain drawing 2–4 year follow-up period	5.04	5.35	(2.83, 7.25)	<.0001

* IBG, iliac bone graft; BMP, bone morphogenetic protein; BMA, concentrated bone marrow aspirate; cAlloBone, cellular Bone allograft; cAlloAM, cellular amniotic tissue; cAlloFat, cellular fat allograft; Allo, freeze-dried bone allograft chips.

[†] Pain Drawing scoring as in reference [57].

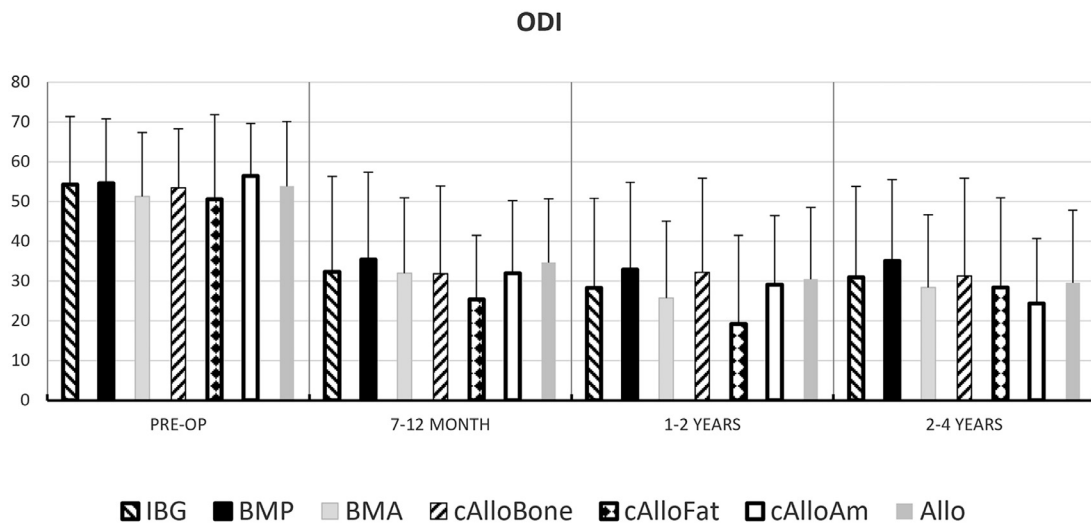


Fig. 5. ODI scores (mean $\pm$ SD) over time for 6 randomized posterior bone graft groups and allograft control.

interpreted with caution, as they may reflect limited statistical power rather than true absence of effect. Conversely, statistically significant findings, particularly those with large effect sizes, are likely to represent robust associations,

although the relatively small sample size may contribute to wider confidence intervals and reduced precision of effect estimates. Additionally, a control group of local only bone autograft was not assessed, which leads one to wonder if

Table 8

Change in ODI within bone graft treatment groups

Type of posterior bone graft—5cc*	Mean	Std Dev	95% CI	p-value
IBG				
ODI 7–12 month follow-up period	20.65	20.35	(12.43, 28.87)	<.0001
ODI 1–2 year follow-up period	24.85	20.77	(16.47, 33.24)	<.0001
ODI 2–4 year follow-up period	23.34	22.90	(14.28, 32.40)	<.0001
BMP				
ODI 7–12 month follow-up period	21.66	17.72	(14.65, 28.67)	<.0001
ODI 1–2 year follow-up period	21.97	19.89	(13.93, 30.00)	<.0001
ODI 2–4 year follow-up period	24.44	22.46	(14.96, 33.93)	<.0001
BMA				
ODI 7–12 month follow-up period	24.44	17.64	(17.47, 31.42)	<.0001
ODI 1–2 year follow-up period	27.32	17.69	(20.32, 34.31)	<.0001
ODI 2–4 year follow-up period	31.57	18.68	(24.03, 39.12)	<.0001
cAlloBone				
ODI 7–12 month follow-up period	19.23	16.78	(12.45, 26.01)	<.0001
ODI 1–2 year follow-up period	21.72	16.35	(15.11, 28.32)	<.0001
ODI 2–4 year follow-up period	19.02	18.81	(11.26, 26.79)	<.0001
cAlloAm				
ODI 7–12 month follow-up period	25.18	25.38	(10.53, 39.84)	.0026
ODI 1–2 year follow-up period	31.42	21.58	(18.96, 43.88)	.0001
ODI 2–4 year follow-up period	22.22	21.98	(9.53, 34.91)	.0023
cAlloFat				
ODI 7–12 month follow-up period	19.26	15.57	(12.83, 25.69)	<.0001
ODI 1–2 year follow-up period	25.47	14.76	(19.37, 31.56)	<.0001
ODI 2–4 year follow-up period	23.00	16.46	(16.21, 29.80)	<.0001
Allo				
ODI 7–12 month follow-up period	18.17	19.36	(10.00, 26.35)	.0001
ODI 1–2 year follow-up period	20.79	17.51	(12.83, 28.76)	<.0001
ODI 2–4 year follow-up period	24.94	20.00	(16.50, 33.39)	<.0001

* IBG, Iliac Bone Graft, BMP, Bone Morphogenetic Protein, BMA, concentrated Bone Marrow Aspirate, cAlloBone, cellular Bone Allograft, cAlloAM, cellular Amniotic tissue, cAlloFat, cellular Fat Allograft, Allo, freeze-dried bone Allograft chips.

Table 9

Opioid pain medication use is distinct entity from Non-opioid pain medication use, which is a distinct entity from No pain medication

Opioid pain medication use (%)	IBG	BMP	BMA	cAlloBone	cAlloAm	cAlloFat	Allo
Preoperative	78	65	48	59	59	57	63
7–12 month follow-up period	37	31	26	41	19	36	35
1–2 year follow-up period	37	27	15	27	26	14	23
2–4 year follow-up period	37	28	12	19	15	14	15
Nonopioid pain medication use (%)							
Preoperative	48	42	78	52	48	50	67
7–12 month follow-up period	19	31	30	15	11	7	62
1–2 year follow-up period	41	35	40	31	37	14	50
2–4 year follow-up period	52	52	46	46	38	43	58
No pain medication at final follow-up (%)	27	37	42	37	37	50	37

*IBG, Iliac Bone Graft, BMP, Bone Morphogenetic Protein, BMA, concentrated Bone Marrow Aspirate, cAlloBone, cellular Bone Allograft, cAlloAM, cellular Amniotic tissue, cAlloFat, cellular Fat Allograft, Allo, freeze-dried bone Allograft chips.

Table 10

NSAID use effect is separate from Narcotic use effect

NSAID use effect	DF	Chi-Square	p-value
Bone graft group	6	9.93	.128
Time	3	9.3	.026
Group x Time	18	24.4	.142
Narcotic use effect			
Bone graft group	6	5.62	.467
Time	3	12.3	.006
Group x Time	18	17.2	.512

Generalized estimating equation (GEE) model with binomial distribution, logit link, and exchangeable working correlation structure. NSAID use = 1 and Narcotic use = 1 were modeled as the event. Joint tests are reported.

Table 11
Self-assessment of global success

	Type of posterior bone graft†—5cc								Significant pairwise comparison(s)*
	IBG	BMP	BMA	cAlloBone	cAlloAm	cAlloFat	Allo	Fisher's Exact p-value	
Self-assessment of surgical success (%)									
7–12 month follow-up period	96	92	93	70	89	86	77	.092	—
1–2 year follow-up period	93	88	92	69	96	100	77	.036	cAlloAm vs. cAlloBone: 96% vs. 69% (p=.011)
2–4 year follow-up period	85	76	96	73	85	86	81	.328	—
Would you repeat the surgery for similar condition (%)									
7–12 month follow-up period	78	92	81	70	85	71	69	.307	—
1–2 year follow-up period	85	81	92	73	89	100	69	.131	—
2–4 year follow-up period	85	80	88	77	96	86	65	.097	—
Recommend the surgery to others for similar condition (%)									
7–12 month follow-up period	93	96	93	85	93	86	85	.733	—
1–2 year follow-up period	85	92	92	81	93	100	85	.257	—
2–4 year follow-up period	85	76	88	81	92	100	85	.309	—

*Overall p-values were calculated using Fisher's exact test. Follow-up pairwise Fisher's exact tests were examined only for outcomes with a statistically significant overall test; only statistically significant pairwise comparisons are shown.

† IBG = Iliac Bone Graft, BMP, Bone Morphogenetic Protein, BMA, concentrated Bone Marrow Aspirate, cAlloBone, cellular Bone Allograft, cAlloAM, cellular Amniotic tissue, cAlloFat, cellular Fat Allograft, Allo, freeze-dried bone Allograft chips.

the Allo PSF rate was due to the type of bone graft or due to the local bone graft. Clinical outcome limitations include variable opioid tolerance which could not be controlled. The study is from a single center (and all procedures by the lead author), which ensures uniform surgical technique, however, may not be generalizable.

In summary, using a consistent surgical technique, various stem cell related bone graft options, particularly allograft types, result in lower PSF rates than IBG or BMP for posterior lumbar fusion. These stem cell products show promise but will depend on additional research to optimize viable cell count and transformation into functional osteoblasts [78]. Outcomes are uniformly improved for single level ASF/PSF regardless of the status of the posterior fusion so long as the interbody fusion is solid. If bone graft cost savings is a consideration for PSF, then IBG is most radiographically effective (highest fusion rate for the cost), and Allo is most clinically cost effective in the presence of a solid interbody fusion. Given the relationship between solid ASF and outcomes, further optimization of ASF techniques are warranted. That is, successful fusion depends on numerous factors in addition to type of bone graft material; these include the biomechanical environment which affect's Wolff's law (such as surgical construct rigidity, implant stiffness, obesity, patient activity, etc.), fusion bed preparation, implant surface properties, and patient factors such as bone density, bony endplate blood supply, nutrition, etc.

Level of Evidence

2, Randomized single center therapeutic trial.

Ethical approval

Ethical review was by Institutional Review Board (HealthEast IRB #1510002).

Source of funding

No external funds were received.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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