Bone Grafting Options for Single-Level TLIF: So Many Options, What Is the Evidence?

Enoch Kim, Matthew Brennan, Pavithra Margabandu, Nicole Oska, Maria Cielito Robles, Anneliese Rademacher, Edvin Telemi, Tarek Mansour and Victor W. Chang

Int J Spine Surg published online 19 December 2023
https://www.ijssurgery.com/content/early/2023/12/15/8561

The International Journal of Spine Surgery
2397 Waterbury Circle, Suite 1,
Aurora, IL 60504, Phone: +1-630-375-1432

International Journal of Spine Surgery, Vol. 00, No. 0, 2023, pp. 1–8
https://doi.org/10.14444/8561

Bone Grafting Options for Single-Level TLIF: So Many Options, What Is the Evidence?

ENOCH KIM, BS[1*]; MATTHEW BRENNAN, BS[1*]; PAVITHRA MARGABANDU, BS[1]; NICOLE OSKA, BS[1]; MARIA CIELITO ROBLES, BS[2]; ANNELIESE RADEMACHER, BS[3]; EDVIN TELEMI, MD[3]; TAREK MANSOUR, MD[3]; AND VICTOR W. CHANG, MD[3]

[1]*School of Medicine, Wayne State University, Detroit, MI, USA;* [2]*College of Human Medicine, Michigan State University, East Lansing, MI, USA;* [3]*Department of Neurosurgery, Henry Ford Health Systems, Detroit, MI, USA*

[*]Enoch Kim and Matthew Brennan contributed equally to the work.

ABSTRACT

Background: This review seeks to investigate the clinically relevant bone graft materials in single-level transforaminal lumbar interbody fusion (TLIF) procedures as defined by (1) primary outcomes (ie, fusion rates and complication rates) and (2) patient-reported outcomes (ie, visual analog scale [VAS] and Oswestry disability index [ODI]). Because of the advantages in stimulating bone growth, autologous bone grafts such as the iliac crest bone graft (ICBG) have been the gold standard. Numerous alternatives to ICBG have been introduced. Understanding the risks and benefits of bone graft options is vital to optimizing patient care.

Methods: A PubMed search was performed for all clinical studies published between January 2008 and March 2023 that referenced the single-level TLIF procedure as well as one of the following grafts: autograft, allograft, bone morphogenetic protein (BMP), demineralized bone matrix, or mesenchymal stem cells (MSCs). Case studies and reports were excluded.

Results: Twenty-eight studies met the inclusion criteria. Studies from the PubMed search demonstrated similarly high fusion rates across nearly all graft materials, the lone exception being MSCs, which showed lower fusion rates. ICBG grafts experienced higher rates of postoperative graft site pain. The BMP graft material had high rates of radiculitis, heterogeneous ossification, and vertebral osteolysis. Patients saw an overall improvement in VAS and ODI scores with all graft materials.

Conclusion: Local autografts and ICBG have been the most studied. Fusion rates during single-level TLIF were similar across all graft materials except MSCs. Patient-reported pain levels improved after TLIF surgery regardless of the type of grafts used. While BMP implants have shown promising benefits, they have introduced a new array of complications not normally seen in ICBG implants. The study is limited by the lack of evidence of certain graft materials as well as nonuniformity in metrics evaluating the efficacy of graft materials.

Focus Issue Article

Keywords: bone graft, TLIF, single level, spinal fusion, autologous, ceramic, bone morphogenic protein, allograft, synthetics, mesenchymal stem cells

BACKGROUND

Transforaminal lumbar interbody fusion (TLIF) is an established approach to spinal fusion surgery that involves accessing the lower spine through the intervertebral foramina. The vertebral disc is subsequently removed, and a bone graft is placed to fuse the adjacent vertebral bodies. The current gold standard to achieve fusion is through iliac crest harvesting. However, studies have highlighted the postoperative complications and patient dissatisfaction due to discomfort from the harvest site.[1] Therefore, there has been a large push to discover alternative bone graft fusion materials. Several options have gained substantial attention and are being studied to determine their efficacy. These alternatives include autografts, allografts, demineralized bone matrices (DBMs), graft substitutes, mesenchymal stem cells (MSCs), autologous growth factors, and synthetic peptides.

To assess the efficacy of different bone graft materials, we must understand the biology of bone grafting. Autogenous bone grafts are used in TLIF procedures to initiate the formation of new bone. The 2 types of bone that can be harvested for bone grafts are cortical bone, which is dense, or cancellous bone, which is porous. Although cortical bone provides greater initial mechanical support, cancellous bone stimulates new bone growth more quickly and is therefore typically used in TLIF procedures.[2] Bone grafts achieve new bone formation through 3 biological processes: osteogenesis, osteoinduction, and osteoconduction.

Osteogenesis is the creation of new bone from either the graft or the host's cells. Cells from both cortical and

cancellous bone grafts can survive through surgery and begin to form new bone. Because of the large surface area and osteoblast-rich trabecular structure of cancellous grafts, they are excellent in areas requiring new bone formation.[2]

Osteoinduction involves the recruitment of MSCs to the implant site, which will then differentiate into chondroblasts and osteoblasts. This process is influenced by growth factors, which are stimulated by the removal of bone mineral. Examples of growth factors include bone morphogenetic proteins (BMPs), which belong to the regulatory protein superfamily, transforming growth factor-β. Angiogenesis occurs concurrently, aided by the release of vascular endothelial-derived growth factor.

Osteoconduction refers to bone growth along a surface such as a bone graft.[3] MSCs, capillaries, and tissues take up space along the scaffold created by the bone graft.

Autografts

Autogenous bone grafts, also known as autografts, are currently the most used material for single-level TLIF. During the TLIF procedure, laminectomy and facetectomy are performed, and when possible, local bone is collected. However, the amount of bone is not typically sufficient to supply the entirety of graft volume. Additionally, the bone collected may not have the osteogenic or osteoconductive potential seen in cancellous bone grafts.[4] Due to these limitations, additional grafts have been developed and used in conjunction with locally harvested bone grafts.

The gold standard of autogenous grafts used in TLIF procedures is the iliac crest bone graft (ICBG). Bone is harvested from the iliac crest and transplanted into the vertebral space. ICBGs confer an advantage due to complete histocompatibility as well as their osteogenic, osteoinductive, and osteoconductive properties.[5] Unlike allografts, there is no risk of diseases being spread. However, disadvantages of autografts stem from reliance on the health of the donor. Elderly and very young patients also may not have sufficient iliac bone to be used as graft material. Patients undergoing autograft harvesting can have an increase in operating time, blood loss, and postoperative pain at the harvest site.[6]

Allografts

Allografts function in the same manner as autografts, but the donor comes from another individual. The advantage of allografts is the decreased need for additional incisions and operating time during harvesting. Grafts are typically obtained from donors by harvesting cortical or cancellous bone, or both. To decrease the risk of transmitted diseases, allografts are sterilized via gamma radiation, which penetrates the tissue and eradicates any pathogens. However, gamma radiation can also alter the molecular structure of the tissue. This alteration retains the osteoconductive properties of the donor tissue, but the osteogenic and osteoinductive properties are diminished.[1] Although gamma radiation does eradicate most microorganisms in the donor tissue, there remains a lingering concern for transmission of viruses such as hepatitis B and C. In the context of TLIF procedures, allografts are used in conjunction with autografts to aid in fusion.[7]

Demineralized Bone Matrix

DBMs are allografts in which the inorganic, mineralized portion is removed. The organic portion of bone remains, containing growth factors and proteins that aid in bone growth. DBMs have the potential to assist in osteoinduction via growth factors like BMP, fibroblast growth factor, and transforming growth factor beta (TGF-β). DBMs can also contribute to osteoconduction through their collagenous and noncollagenous proteins.[8] DBMs may not provide as much structural support as autogenous grafts as they lack comparable structure. There is also some concern that contaminants such as ethylene glycol may permeate DBMs. Currently, DBMs are combined with autograft material to achieve their highest efficacy, though this is an area of growing innovation.[9] DBM products vary widely, ranging in form (putty, paste, and gel), type of carriers, and amount of actual DBM content.[10]

Bone Morphogenic Proteins

BMPs are composed of 20 different cytokines and growth factors in the TGF-β family. They have osteogenic capabilities and initiate downstream mediators related to osteoinduction and endochondral ossification.[11] BMPs are associated with some adverse effects in anterior cervical spine surgery, such as postoperative edema, osteolysis, dysphagia, and hematoma formation.[12] Although several studies found that BMPs, specifically recombinant human bone morphogenetic protein-2 (rhBMP-2), have similar or even higher rates of fusion than autologous grafts, some studies showed that BMPs also have higher risk of postoperative complications.[13]

Mesenchymal Stem Cells

MSCs are multipotent cells found in the bone marrow that aid in making and repairing skeletal tissues. They have been included in TLIF procedures because of their

ability to differentiate into osteoblasts and chondrocytes. Harvested stem cells from bone marrow aspirates are often combined with allografts to enhance osteogenic, osteoinductive, and osteoconductive properties. MSCs have been shown to exhibit similar rates of fusion as BMP in TLIF procedures. Unfortunately, MSCs have also been reported to cause harvesting site pain.[1]

Synthetic Peptides

Synthetic peptides, such as ceramics and calcium phosphates, are bone graft extenders that have been used in spinal fusion surgeries because of their biomechanical properties. They were designed to upregulate the activity of endogenous processes. P-15 is a 15-amino acid residue that binds to calcium phosphate substrates and enhances cell attachment and the production of extracellular matrix and factor production to produce new bone.[14] B2A is also a synthetic peptide that attaches to BMP receptors on BMP2, leading to the differentiation and proliferation of osteoblasts.

Ceramics

Ceramics are synthetic grafts that act as scaffolds when combined with hydroxyapatite (HA). The scaffolds provide osteoconductive support for various osteogenic cells and growth factors.[1] The synthetic origin means that there is zero risk of disease transfer and they can be shaped as needed. However, the material itself lacks osteogenic properties and must be supplemented with osteogenic cells and growth factors to promote proper fusion.[1]

METHODS

A PubMed database search of studies published from January 2008 to March 2023 was performed. We evaluated studies from the last 15 years to ensure that changes in surgical techniques, infection control, and pain management did not significantly influence the findings. Data from studies that focused on the comparison between grafts were used. Search criteria included studies that referenced (1) single-level TLIF and (2) one of the following: graft, autograft, allograft, biologics, BMP, ceramic, DBM, MSCs, or autologous growth factor. Retrospective studies, prospective studies, and systematic reviews were included. Additional inclusion criteria included studies that (1) examined the single-level TLIF procedure (ie, not multilevel or a different procedure); (2) reported at least one of the following outcomes: fusion rate, complication rate, or one of two patient-reported pain scale (visual analog scale [VAS] or Oswestry disability index [ODI]); and (3) evaluated fusion rates and patient-reported outcomes at least 1-year postoperation. Exclusion criteria included (1) case studies and case reports; (2) studies that mixed graft materials within study arms; and (3) studies that focused on graft delivery method or technique. Fusion rates, complication rates, and patient-reported outcomes were recorded for each study that met the inclusion criteria. The changes in VAS and ODI were reported as ΔVAS and ΔODI, respectively. ΔVAS was calculated as (pre-VAS score) – (post-VAS score). Although some studies reported VAS scores on a scale of 0 to 100, all scores were normalized to a 10-point scale. Similarly, ΔODI was calculated as (post-ODI score) – (pre-ODI score). The ΔSD for both outcomes was calculated as the square root of the sum of the squares of the pre- and post-SDs. The mean fusion rate per graft material was weighted by the number of patients in each study. The mean and SDs of each graft material's ΔVAS-back score were also weighted by the number of patients.

RESULTS

Twenty-eight publications satisfied the inclusion criteria. The study count by graft material was broken down as follows (some studies evaluated 2 different graft materials): allograft: 3, autograft: 11, BMP: 11, DBM: 2, HA paste: 2, ICBG: 6, MSC: 1, and synthetic proteins: 1. The Table shows the mean fusion rate and Δ VAS-back score for each bone graft material.

Autografts

A total of 364 patients across 6 studies using local autografts showed high rates of fusion ranging from 76% to 100%.[15–20] The complication rates of implants using solely local autografts were not well studied. However, 1 publication found that local autografts resulted in relatively low rates of radiculitis, seen in just 5.3% of the patients.[21] The rate of adjacent segment disease (ASD) in local autograft patients was also found

Table. Summary of mean fusion rate and ΔVAS-back score by graft material.

Graft Material	Mean Fusion Rate, %	ΔVAS-Back Score
Iliac crest bone graft	94.8	4.4 ± 4.1
Local autograft	92.5	3.26 ± 0.94
Allograft	96	2.86 ± 4.4
Demineralized bone matrix	92	4
Bone morphogenetic protein	92.1	-
Mesenchymal stem cell	59	-
Synthetic peptide	73.3	4.9
Ceramic	92.9	4.6 ± 2

Abbreviation: VAS, visual analog scale.

to be 5.3%.[21] Eight studies encompassing 613 patients saw a general decrease in VAS-leg and/or VAS-back scores when using local autografts.[16–23] The 3 studies that also reported ODI scores showed similar improvement in outcomes.[16,17,21] A study involving 87 patients utilized local autologous morselized bone. The study reported significant decreases in VAS-leg, VAS-back, and ODI ($P < 0.01$; Supplemental Table 1).[15] Seventy-nine patients across 2 studies using ICBG showed an average fusion rate of 95.3% and 94.5%.[16,24] Of the materials we studied, the highest complication rates were seen in those that used ICBG.[6] The overall complication rate with ICBG was found to be 45.5% with the most common complication of pain at the harvest site in 30.3% of patients.[6] The next most common complications in ICBG implants were lumbar wound infection and harvest site infection (6.1% and 3.1%–4.2%, respectively).[6,24] Lastly, radiculitis was seen in 3% of patients with ICBG implants.[6] A total of 218 patients across 4 studies reported improvements in both VAS and ODI scores with the use of ICBGs. The change in pre- and postoperative VAS scores ranged from 3.5 to 6.2, and the change in pre- and postoperative ODI scores ranged from 19.1 to 26 (Supplemental Table 1).[5,16,24,25]

Allografts

One study involving 75 patients who received autografts supplemented with allografts made from cortical and cancellous bones reported a fusion rate of 96%.[7] Data on the complication rates of patients receiving allografts were limited. One publication studied 142 patients with allograft implants.[26] It found the rate of pseudoarthrosis to be 4% and a relatively high rate of ASD of 10%. This led to a reoperation rate of 8% in patients receiving an allograft implant.[26] A total of 651 patients across 2 studies saw a general improvement in VAS-leg and VAS-back scores when using allografts, with the delta between pre- and postoperative scores ranging from 2.8 to 3.2 (Supplemental Table 1).[26,27] One study measuring pre- and postoperative ODIs found a significant improvement from 50.8 to 26 ($P < 0.001$) with the use of allografts (Supplemental Table 1).[27]

Bone Morphogenetic Protein

All studies discussed below employed rhBMP-2 unless otherwise specified. When paired with allografts, BMPs achieved a fusion rate of 78.1%.[28] However, when BMP was used with local autograft, fusion rates of 92.5% to 95.8% were reported.[13,29] Studies employing BMP in addition to local autograft found overall complication rates of 27.1% to 29.1%.[6,13] A retrospective review of 867 patients found the rate of heterotopic ossification (ie, the growth of bone in soft tissues and muscles) to be 13.5%.[29] Other common complications in patients receiving BMP implants included postoperative radiculitis (13.2%–16.7%) and vertebral osteolysis (5.8%–6.3%).[6,13,30] On the other hand, rates of pseudoarthrosis were relatively low in implants making use of BMP, ranging from 2.5% to 2.6%.[28,30] Rates of ASD and infection were not notably higher than other graft materials (5.9% and 1.9%, respectively).[30] In 201 patients across 3 studies, there was a general decrease in ODI scores. Two of those studies also showed improvement in VAS-leg and VAS-back scores with deltas ranging from 3.3 to 4.2 (Supplemental Table 1).[5,21,31]

Demineralized Bone Matrix

One study involving 25 patients who underwent placement of DBM reported an average fusion rate of 92%.[32] Due to the dearth of studies examining the outcomes of DBMs, data regarding complication rates of the material were not available. In 1 study involving 25 patients, the average VAS-leg score improved significantly, decreasing from 8 to 2 ($P < 0.05$), VAS-back score decreased from 6 to 2 ($P < 0.05$), and ODI decreased from 50 to 20 ($P < 0.05$; Supplemental Table 1).[32]

Ceramics

In a study involving 25 patients, the utilization of ceramic HA with an autograft resulted in a fusion rate of 91.7%.[24] Another study of 87 patients with HA graft implants reported a fusion rate of 93.2%.[33] A 2% infection rate was found among the 25 patients who underwent ceramic HA grafting.[24] The same publication found that the ODI score improved with an average delta of 30.2 (Supplemental Table 1).[33] ODI scores showed improvement with an average decrease of 26.1 (Supplemental Table 1).[33]

Mesenchymal Stem Cells

One study examined the rate of fusion in allografts with viable MSCs and found a fusion rate of 59% at 18 months.[28] MSCs exhibited a low overall complication rate of 23.1%. Allografts with viable MSCs and osteoprogenitor cells had relatively high rates of pseudoarthrosis at 7.7%.[28] The study involving MSCs did not report VAS or ODI.

Synthetic Peptides

A study of 15 patients compared 2 dosages of the synthetic peptide, B2A. Fusion rates at 12 months varied widely by dosage. Patients who received 750 μg/cm^3 achieved 100% fusion, whereas those who received 150 μg/cm^3 achieved 50% fusion.[10] This study found no difference in overall complication rates when comparing B2A to autograft using ICBG.[14] Both arms of this study employing B2A reported improvements in VAS-lower back and ODI scores.[14]

DISCUSSION

Fusion Rates

High fusion rates were reported across nearly all graft materials in 12 different studies. Local autograft, ICBG, and BMP paired with autograft experienced consistently high rates of fusion. One publication reported a similarly high rate of fusion in DBM.[32] The outlier graft material was implants using MSCs, which showed a fusion rate of just 59%.[28] This low fusion rate may be due to MSCs reliance on the osteoinductive properties of the scaffold and the sheer number of cells required for adequate tissue regeneration.[34]

In our review of allograft efficacy, we found a fusion rate of 96% by 12 months. There have been other studies that found similarly high fusion rates of 100% by 33 months.[35] However, these studies used allograft in conjunction with autografts. Reports of anterior lumbar interbody fusion procedures performed solely with allografts revealed an average fusion rate of 66%.[35,36] However, this cannot be extrapolated to TLIF procedures until direct studies are completed.

Fusion rates using the synthetic peptide B2A varied widely depending on the concentration of protein used. Higher concentration led to higher rates of fusion. B2A is unique such that it relies on endogenous levels of BMP-2 to activate tissue regeneration.[14]

Complications

While similarly high fusion rates may be seen across graft materials, the rates of complications can vary widely. The most studied graft materials were ICBG and BMP implants.

ICBG has been the gold standard for facilitating fusion in the single-level TLIF procedure. However, researchers have observed high rates of complications using ICBG, most often graft site pain (30.3%).[6] Infections at both the graft and implant sites were also not uncommon.[6] Surgeons have also found it difficult to procure sufficient graft materials in certain patient populations such as pediatric and elderly individuals, potentially increasing the risk of graft site pain.[1] The high overall complication rates in patients with ICBG implants have led to innovation in graft material alternatives.

The bulk of literature in this review examined complication rates related to the use of BMP. The overall complication rates in BMP were lower than those seen in ICBG (27.1%–29.1% in BMP and 45.5% in ICBG).[6] However, the most common types of complications differed depending on the material used. Complications in BMP grafts may stem from their strong osteoinductive properties, resulting in a propensity for invading surrounding tissues.[29] The most common complications in patients with BMP implants were radiculitis, heterotopic ossification, and vertebral osteolysis.[6,13,29] Researchers have explored ways to mitigate these complications. One study applied a hydrogel sealant (DuraSeal, Confluent Surgical Inc.,Waltham, MA, USA) to reduce BMP from seeping into the spinal canal, which significantly reduced the rate of radiculitis from 20.4% to 5.4%.[6] Other studies have found the dosage of BMP to be unrelated to the risk of radiculitis.[37,38]

Patient-Reported Outcomes: VAS and ODI

Across all types of bone graft materials and substitutes, there was a general decrease in VAS-leg, VAS-back, and ODI scores. The decrease in scores was representative of decreased pain. In the studies included in this review, the vast majority seemed to prefer using VAS as opposed to ODI. This may be due to VAS typically measuring the general subjective pain or discomfort a patient may be experiencing, whereas the ODI is specific for back pain. Although VAS and ODI scores are important indicators of patient outcomes, they should be paired with complication data to clearly indicate the effectiveness or adverse effects of using different grafts. It is also difficult to determine whether pain and discomfort originated from the graft material or type of cage used.

Emerging Materials

The field of bone grafts has continued to evolve as more advanced materials come to market. One such material is osteo allogenic morphogenic protein (OsteoAMP, Bioventus Surgical), a differentiated allograft that contains a wide spectrum of growth factors that support the regeneration and growth of bone at any stage. A study involving 226 patients who underwent OsteoAMP fusion experienced a 40% faster fusion at

6-, 12-, and 18-month follow-ups with 70% less complications when compared with recombinant BMP.[39] The study, however, did not control for surgical techniques and instrumentations, and clinical outcome was not observed.[39] Additionally, the anorganic bone material (ABM)/synthetic 15 amino acid polypeptide (P-15; i-FACTOR, Cerapedics Inc., Westminster, CO, USA) is a material originally approved by the US Food and Drug Administration for dental procedures.[40] A 40-patient study found a statistically significant superiority of ABM/P-15 to autologous graft in posterior lumbar interbody fusion procedures at 12 months (97.8% vs 82.2%; $P < 0.01$), though no significant difference persisted at 24 months.[40] Bioactive bone glass graft materials have also been used in spinal fusion procedures to chemically bind with surrounding bone, thereby improving bone growth and osteoconduction. One such bioactive glass bone graft (BioSphere Putty, Synergy Biomedical, Wayne, PA, USA) saw a 100% fusion rate in 103 TLIF patients and improvement in VAS scores in 82% of patients at 2 years postoperation.[41] Researchers have also studied platelet-rich plasma (PRP) as a useful adjunctive material in spinal fusion procedures. PRP may aid osteoinduction by providing useful growth factors to surrounding bone such as platelet-derived growth factor, transforming growth factor, epidermal growth factor, and epithelial cell growth factor. A meta-analysis found that implants using PRP saw significantly faster growth of bone mass than in those without PRP.[42] The industry of synthetic bone graft materials and adjuvants has sought to enhance bone growth through several different mechanisms, contributing to rapid innovation in the field.

Limitations

This study was limited by the lack of uniform metrics used by different studies. Many studies also failed to describe what demographic the data were derived from (ie, age and indication). Our review was also limited by the small number of studies that explored the efficacy and adverse effects of lesser-used graft materials, such as MSC, DBM, and synthetic peptides. Our review was limited to studies published within the past 15 years to mitigate the inclusion of data that may have been affected by changes in surgical technique, infection control, and pain management over the past few decades. This review did not include all emerging materials that are still being studied and developed. As new data involving novel graft materials emerge, comparisons can be made to the currently used materials.

CONCLUSION

While several alternatives have grown in popularity, ICBGs remain the gold standard when performing the single-level TLIF. No study comparing fusion rates to ICBG implants achieved statistically superior fusion rates. Similarly, studies evaluating patient-reported outcomes in other graft materials did not show a significant improvement over ICBG implants. Patients who received ICBG did experience higher complication rates, with the most common being pain at harvest site. BMP grafts may have come closest to the efficacy of ICBG implants. Although patients who received BMP grafts experienced lower complication rates overall, the breakdown of complications proved to be more complex. The most common adverse effect seen was radiculitis, followed by heterotopic ossification and vertebral osteolysis. The dosage of administered BMP had no effect on rates of radiculitis. One study did find, however, that the use of DuraSeal sealant reduced rates of postoperative radiculitis. Allografts showed promising fusion rates but did not sufficiently evaluate complications. The use of DBM did show similarly high fusion rates, though it was not well studied. Additionally, the lack of uniformity in the type and amount of DBM components prohibited any overall conclusions from being drawn. MSCs showed lower rates of overall complications, though the fusion rate did not reach the level seen in ICBG or other graft materials. Only 1 study that included 7 patients evaluated the B2A peptide. While this graft did show high fusion rates, complication rates were not clearly delineated. A larger sample size is needed to evaluate synthetic peptides. The goal of this systematic review was to analyze the variety of graft materials, their efficacy, and complication rates. We believe that focusing on fusion rates, complication rates, and patient outcomes, such as ODI and VAS, should be a uniform measure of determining the clinical efficacy of graft materials.

REFERENCES

1. D'Souza M, Macdonald NA, Gendreau JL, Duddleston PJ, Feng AY, Ho AL. Graft materials and biologics for spinal interbody fusion. *Biomedicines*. 2019;7(4):75. doi:10.3390/biomedicines7040075

2. Khan SN, Cammisa FP, Sandhu HS, Diwan AD, Girardi FP, Lane JM. The biology of bone grafting. *J Am Acad Orthop Surg*. 2005;13(1):77–86.

3. Albrektsson T, Johansson C. Osteoinduction, osteoconduction and osseointegration. *Eur Spine J*. 2001;10 Suppl2(Suppl2):S96–101. doi:10.1007/s005860100282

4. Vaccaro AR. The role of the osteoconductive scaffold in synthetic bone graft. *Orthopedics*. 2002;25(5 Suppl):s571–8. doi:10.3928/0147-7447-20020502-05

5. Haws BE, Khechen B, Narain AS, et al. Iliac crest bone graft for minimally invasive transforaminal lumbar interbody fusion: a prospective analysis of inpatient pain, narcotics consumption, and costs. *Spine (Phila Pa 1976)*. 2018;43(18):1307–1312. doi:10.1097/BRS.0000000000002599

6. Rihn JA, Patel R, Makda J, et al. Complications associated with single-level transforaminal lumbar interbody fusion. *Spine J*. 2009;9(8):623–629. doi:10.1016/j.spinee.2009.04.004

7. Tally WC, Temple HT, Subhawong TY, Ganey T. Transforaminal lumbar interbody fusion with viable allograft: 75 consecutive cases at 12-month follow-up. *Int J Spine Surg*. 2018;12(1):76–84. doi:10.14444/5013

8. Chang KY, Hsu WK. Spinal biologics in minimally invasive lumbar surgery. *Minim Invasive Surg*. 2018;2018:5230350. doi:10.1155/2018/5230350

9. Gruskin E, Doll BA, Futrell FW, Schmitz JP, Hollinger JO. Demineralized bone matrix in bone repair: history and use. *Adv Drug Deliv Rev*. 2012;64(12):1063–1077. doi:10.1016/j.addr.2012.06.008

10. Zhang H, Yang L, Yang X-G, et al. Demineralized bone matrix carriers and their clinical applications: an overview. *Orthop Surg*. 2019;11(5):725–737. doi:10.1111/os.12509

11. Gupta A, Kukkar N, Sharif K, Main BJ, Albers CE, El-Amin Iii SF. Bone graft substitutes for spine fusion: a brief review. *World J Orthop*. 2015;6(6):449–456. doi:10.5312/wjo.v6.i6.449

12. Hiremath GK, Steinmetz MP, Krishnaney AA. Is it safe to use recombinant human bone morphogenetic protein in posterior cervical fusion? *Spine (Phila Pa 1976)*. 2009;34(9):885–889. doi:10.1097/BRS.0b013e31819e334a

13. Rihn JA, Makda J, Hong J, et al. The use of Rhbmp-2 in single-level transforaminal lumbar interbody fusion: a clinical and radiographic analysis. *Eur Spine J*. 2009;18(11):1629–1636. doi:10.1007/s00586-009-1046-1

14. Sardar Z, Alexander D, Oxner W, et al. Twelve-month results of a multicenter, blinded, pilot study of a novel peptide (B2A) in promoting lumbar spine fusion. *J Neurosurg Spine*. 2015;22(4):358–366. doi:10.3171/2013.11.SPINE121106

15. Yang J, Yang Y, Wang G, et al. Is local autogenous morselized bone harvested from decompression through a posterior-transforaminal approach sufficient for single-level interbody fusion in the lower lumbar spine *BMC Musculoskelet Disord*. 2023;24(1):12. doi:10.1186/s12891-023-06131-4

16. Abou-Madawi AM, Ali SH, Abdelmonem AM. Local autograft versus iliac crest bone graft PSF-augmented TLIF in low-grade isthmic and degenerative lumbar spondylolisthesis. *Global Spine J*. 2022;12(1):70–78. doi:10.1177/2192568220946319

17. Kersten RFMR, Öner FC, Arts MP, et al. The SNAP trial: 2-year results of a double-blind multicenter randomized controlled trial of a silicon nitride versus a PEEK cage in patients after lumbar fusion surgery. *Global Spine J*. 2022;12(8):1687–1695. doi:10.1177/2192568220985472

18. Nemoto O, Asazuma T, Yato Y, Imabayashi H, Yasuoka H, Fujikawa A. Comparison of fusion rates following transforaminal lumbar interbody fusion using polyetheretherketone cages or titanium cages with transpedicular instrumentation. *Eur Spine J*. 2014;23(10):2150–2155. doi:10.1007/s00586-014-3466-9

19. Zhu C, He M, Mao L, et al. Titanium interlayer-mediated hydroxyapatite-coated polyetheretherketone cage in transforaminal lumbar interbody fusion surgery. *BMC Musculoskelet Disord*. 2021;22(1):918. doi:10.1186/s12891-021-04803-7

20. Sethi A, Lee S, Vaidya R. Transforaminal lumbar interbody fusion using unilateral pedicle screws and a translaminar screw. *Eur Spine J*. 2009;18(3):430–434. doi:10.1007/s00586-008-0825-4

21. Adams CL, Ogden K, Robertson IK, Broadhurst S, Edis D. Effectiveness and safety of recombinant human bone morphogenetic protein-2 versus local bone graft in primary lumbar interbody fusions. *Spine*. 2014;39(2):164–171. doi:10.1097/BRS.0000000000000089

22. Li Y, Liu S, He Z, Yu S, Tang M. Comparison of long-term efficacy of MIS-TLIF intraoperative implants in patients with osteoporosis. *Computational and Mathematical Methods in Medicine*. 2022;2022:1–8. doi:10.1155/2022/2565391

23. Sleem A, Marzouk A. Transforaminal lumbar interbody fusion with local bone graft alone for single-level isthmic spondylolisthesis. *Int J Spine Surg*. 2018;12(1):70–75. doi:10.14444/5012

24. NH, Voelker A, Heyde CE. Results of lumbar spondylodeses using different bone grafting materials after transforaminal lumbar interbody fusion (TLIF). *Eur Spine J*. 2017;26(11):2835–2842. doi:10.1007/s00586-017-5145-0

25. Xu Z, Zhang Z, Wu Y, Wang X. Posterior transforaminal debridement and interbody fusion with instrumentation for multisegment thoracic spinal tuberculosis: a midterm follow-up study. *Sci Rep*. 2022;12(1). doi:10.1038/s41598-022-23169-x

26. Kotani Y, Koike Y, Ikeura A, Tokunaga H, Saito T. Clinical and radiologic comparison of anterior-posterior single-position lateral surgery versus MIS-TLIF for degenerative lumbar spondylolisthesis. *J Orthop Sci*. 2021;26(6):992–998. doi:10.1016/j.jos.2020.10.013

27. Crandall DG, Revella J, Patterson J, Huish E, Chang M, McLemore R. Transforaminal lumbar interbody fusion with rhBMP-2 in spinal deformity, spondylolisthesis, and degenerative disease--part 2: BMP dosage-related complications and long-term outcomes in 509 patients. *Spine (Phila Pa 1976)*. 2013;38(13):1137–1145. doi:10.1097/BRS.0b013e3182880298

28. Overley SC, McAnany SJ, Anwar MA, et al. Predictive factors and rates of fusion in minimally invasive transforaminal lumbar interbody fusion utilizing rhBMP-2 or mesenchymal stem cells. *Int J Spine Surg*. 2019;13(1):46–52. doi:10.14444/6007

29. Niu S, Anastasio AT, Faraj RR, Rhee JM. Evaluation of heterotopic ossification after using recombinant human bone morphogenetic protein-2 in transforaminal lumbar interbody fusion: a computed tomography review of 996 disc levels. *Global Spine J*. 2020;10(3):280–285. doi:10.1177/2192568219846074

30. Wang E, Stickley C, Manning J, et al. Biologics and minimally invasive approach to tlifs: what is the risk of radiculitis *Int J Spine Surg*. 2020;14(5):804–810. doi:10.14444/7114

31. Haws BE, Khechen B, Patel DV, et al. Impact of iliac crest bone grafting on postoperative outcomes and complication rates following minimally invasive transforaminal lumbar interbody fusion. *Neurospine*. 2019;16(4):772–779. doi:10.14245/ns.1938006.003

32. Lin GX, Sharma S, Rui G, Song MS, Kim JS. Minimally invasive transforaminal lumbar interbody fusion with intraoperative fluoroscopy for disc space preparation: analysis of fusion rate and clinical results. *Oper Neurosurg (Hagerstown)*. 2020;19(5):557–566. doi:10.1093/ons/opaa178

33. Heinz von der Hoeh N, Villa T, Galbusera F, et al. Analysis of a unilateral bridging cage for lumbar interbody fusion: 2-year clinical results and fusion rate with a focus on subsidence. *World Neurosurg*. 2018;116:e308–e314. doi:10.1016/j.wneu.2018.04.195

34. Riester O, Borgolte M, Csuk R, Deigner HP. Challenges in bone tissue regeneration: stem cell therapy, biofunctionality and

antimicrobial properties of novel materials and its evolution. *Int J Mol Sci*. 2020;22(1):192. doi:10.3390/ijms22010192

35. Buser Z, Brodke DS, Youssef JA, et al. Allograft versus demineralized bone matrix in instrumented and noninstrumented lumbar fusion: a systematic review. *Global Spine J*. 2018;8(4):396–412. doi:10.1177/2192568217735342

36. Wetzel FT, Hoffman MA, Arcieri RR. Freeze-dried fibular allograft in anterior spinal surgery: cervical and lumbar applications. *Yale J Biol Med*. 1993;66(3):263–275.

37. Singh K, Nandyala SV, Marquez-Lara A, et al. Clinical sequelae after rhBMP-2 use in a minimally invasive transforaminal lumbar interbody fusion. *Spine J*. 2013;13(9):1118–1125. doi:10.1016/j.spinee.2013.07.028

38. Villavicencio AT, Burneikiene S. Rhbmp-2-induced radiculitis in patients undergoing transforaminal lumbar interbody fusion: relationship to dose. *Spine J*. 2016;16(10):1208–1213. doi:10.1016/j.spinee.2016.06.007

39. Roh JS, Yeung CA, Field JS, McClellan RT. Allogeneic morphogenetic protein vs. recombinant human bone morphogenetic protein-2 in lumbar interbody fusion procedures: a radiographic and economic analysis. *J Orthop Surg Res*. 2013;8:49. doi:10.1186/1749-799X-8-49

40. Lauweryns P, Raskin Y. Prospective analysis of a new bone graft in lumbar interbody fusion: results of a 2- year prospective clinical and radiological study. *Int J Spine Surg*. 2015;9:2. doi:10.14444/2002

41. Westerlund LE, Borden M. Clinical experience with the use of a spherical bioactive glass putty for cervical and lumbar interbody fusion. *J Spine Surg*. 2020;6(1):49–61. doi:10.21037/jss.2020.03.06

42. Manini DR, Shega FD, Guo C, Wang Y. Role of platelet-rich plasma in spinal fusion surgery: systematic review and meta-analysis. *Adv Orthop*. 2020;2020:8361798. doi:10.1155/2020/8361798

Funding: The authors received no financial support for the research, authorship, and/or publication of this article.

Declaration of Conflicting Interests: The authors report no conflicts of interest in this work.

Corresponding Author: Enoch Kim, School of Medicine, Wayne State University, 540 E Canfield St, Detroit, MI 48201, USA; enoch.kim@med.wayne.edu

Received 09 June 2023

Accepted 31 October 2023