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# Allograft Versus Demineralized Bone Matrix in Instrumented and Noninstrumented Lumbar Fusion: A Systematic Review

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## Abstract

**Study Design:** Systematic review.

**Objectives:** The aim was to determine the fusion efficacy of allograft and demineralized bone matrix (DBM) in lumbar instrumented and noninstrumented fusion procedures for degenerative lumbar disorders.

**Methods:** A literature search was conducted using the PubMed and Cochrane databases. To be considered, publications had to meet 4 criteria: patients were treated for a degenerative lumbar disorder, a minimum group size of 10 patients, use of allograft or DBM, and at least a 2-year follow-up. Data on the study population, follow-up time, surgery type, grafting material, fusion rates, and its definition were collected.

**Results:** The search yielded 692 citations with 17 studies meeting the criteria including 4 retrospective and 13 prospective studies. Six studies used DBM and 11 employed allograft alone or in the combination with autograft. For the allograft, fusion rates ranged from 58% to 68% for noninstrumented and from 68% to 98% for instrumented procedures. For DBM, fusion rates were 83% for noninstrumented and between 60% and 100% for instrumented lumbar fusion procedures.

**Conclusions:** Both allograft and DBM appeared to provide similar fusion rates in instrumented fusions. On the other hand, in noninstrumented procedures DBM was superior. However, a large variation in the type of surgery, outcomes collection, lack of control groups, and follow-up time prevented any significant conclusions. Thus, studies comparing the performance of allograft and DBM to adequate controls in large, well-defined patient populations and with a sufficient follow-up time are needed to establish the efficacy of these materials as adjuncts to fusion.

## Keywords

systematic review, lumbar spine, spinal fusion, allograft, demineralized bone matrix, autograft

## Introduction

Lumbar spine fusion with and without instrumentation is frequently a treatment of choice for various spinal pathologies. Several studies have demonstrated an increase in the number of cases and associated costs in the past few decades.[1-3]

Various factors including surgical technique, primary or revision surgery, use of instrumentation, grafting materials, and patient comorbidities have an impact on fusion success. For instance, deleterious effects of cigarette smoking on spinal fusion have been highlighted in several studies.[4-6] Graft materials play a crucial role in bone remodeling, and the adequate choice is dependent on patient's condition as well as the surgical approach. Ideally, the graft material should be osteoconductive,

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osteoinductive, and osteogenic. Autologous iliac crest bone graft (ICBG) represents the only stand-alone graft with all 3 components needed for fusion. Studies have shown that ICBG performed better in single- and 2-level fusions than in 3 or more level procedures.[7-18] Additionally, studies have shown that the fusion rates with ICBG are often lower in noninstrumented than in instrumented lumbar procedures.[8,11-13] While ICBG has all 3 desired graft properties, several drawbacks including donor comorbidities, limited supply, and various complications have been noted.[19-21]

As a result, the use of alternative materials such as allograft, demineralized bone matrix (DBM), synthetic materials (calcium sulfates, calcium phosphates, or hydroxyapatite), growth factors, and cell- or platelet-based therapies has greatly increased. Each of these graft materials has certain pros and cons that will guide patient selection. Allograft is readily available in large amounts and does not carry ICBG-related complications, in particular the harvest morbidity. During preparation, allografts are depleted of cells and growth factors and primarily provide osteoconduction with minor osteoinductivity. Its main disadvantages are immunogenicity and disease transmission.[22] Based on the preparation procedure, allografts can be divided into 3 groups: fresh-frozen, freeze-dried, and DBM. Fresh-frozen allografts provide the highest mechanical stability, but at the same time they carry the highest risk of disease transmission. On the other hand, DBM has certain osteoinductive capabilities in addition to osteoconduction.[23] However, studies have shown a large lot-to-lot variability.[24] Various studies have looked at the use of allograft in lumbar spine in combination with ICBG or as a stand-alone graft. In posterolateral instrumented fusion, An et al reported no fusion with freeze-dried allograft, while Gibson et al found similar outcomes and revision rates at 6-year follow-up.[25,26] Freeze-dried allografts in combination with autograft bone have been also used in deformity corrections, achieving over 90% fusion rates.[27,28] At the same time several studies have looked at the DBM fusion potential in lumbar spine. Both Vaccaro et al and Cammisa et al reported similar fusion rates between DBM mixed with bone marrow aspirate or ICBG and ICBG alone.[17,29] Despite the large number of clinical studies utilizing those graft materials, the existing reviews are often narrative rather than systematic,[30-36] or the level of evidence is limited due to a small sample size, short follow-up times, lack of appropriate controls, or incomplete outcome information.[19,21,30,36-41]

The purpose of this systematic review was to determine the fusion efficacy of allograft and DBM in lumbar instrumented and noninstrumented fusion procedures for degenerative lumbar disorders.

## Materials and Methods

### Search Strategy

A clinical epidemiologist performed a literature search using PubMed and 5 databases of the Cochrane Library in November 2013 and January 2014, respectively (Figure 1). Since the employed terminology is extremely diverse, the search strings were kept general to avert the risk of missing eligible publications. In order to be included in the review, allograft bone and DBM had to be used in fusion procedures for degenerative conditions of the lumbar spine. Any type of allograft bone or DBM was eligible for inclusion in the review as long as it was not used in combination with freshly harvested ICBG. The reason for this exclusion was that (1) if ICBG autograft was part of the graft, it would remain unclear whether the effect on fusion stemmed from the autograft or the alternative material, and (2) the goal of the review was to evaluate the potential of allograft and DBM as substitutes for ICBG.

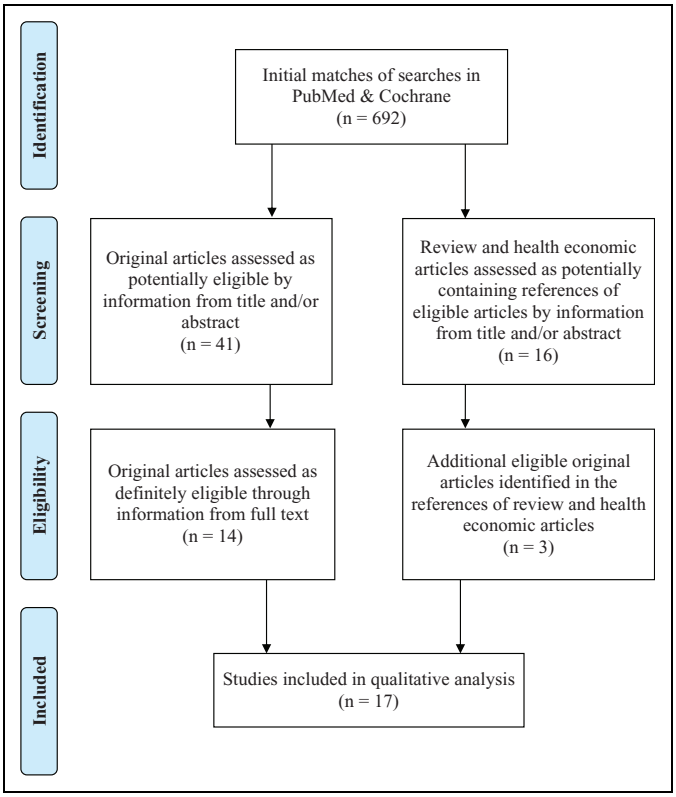


**Figure 1.** PRISMA 2009 flow diagram. From Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the PRISMA statement. *PLoS Med.* 2009;6(6):e1000097. doi:10.1371/journal.pmed1000097.

### Study Selection

Titles and abstracts of the initial matches were independently screened by 2 reviewers to identify eligible original publications. The initial search included original articles and articles with a focus on health economic aspects. When the title or the abstract were not sufficient to determine the eligibility, the full text was used. Whenever the 2 reviewers had a disagreement concerning the eligibility, a third reviewer decided.

### Inclusion and Exclusion Criteria

Original publications were included if the following inclusion criteria were met:

1. *Population:* Adult patients being diagnosed with one of the following degenerative lumbar spine conditions: stenosis, radiculopathy, back pain, neurogenic claudication, degenerative spondylolisthesis, or lumbar adult degenerative deformity. The minimum group size was set at 10 patients. In studies where only one of the included groups met our eligibility criteria, only that group was analyzed.
2. *Intervention:* Patients had to undergo posterolateral or anterior fusion regardless of employment of cages and/or instrumentation.
3. *Comparison group:* Studies comparing allograft or DBM to autograft were included and results are presented for both intervention and control groups. Noncomparative studies were also included. When a comparison group was another graft material, the results of these studies were analyzed as if they were stand-alone results of a noncomparative study.
4. *Outcomes/time frame:* To be included studies had to have a minimum follow-up time of 2 years (mean) and had to contain radiological assessment of fusion.

Original publications were excluded if any of the following criteria applied:

1. *Population:* The majority of study patients suffered from nondegenerative diseases, for example, isthmic spondylolisthesis or idiopathic scoliosis.
2. *Intervention:* Revision surgery or the allograft or DBM was used to supplement ICBG.
3. *Time frame:* The publication date was before 1993.

### Data Extraction

Information on study population, follow-up time, intervention (type of surgery and allograft used), fusion success, and its definition were collected. A standardized data extraction form was used. Any study characteristics that could have led to bias, for example, details about lost to follow-up or potential conflict of interest, were also captured.

### Data Analysis

Due to the high variability among studies with regard to study focus, procedural type, definition of fusion, as well as the indication for surgery, all analysis were done on an individual level.

## Results

A total of 692 potentially eligible original articles were identified (Figure 1). From those, 41 articles were retrieved for full-text evaluation and 14 were deemed appropriate for inclusion. Additionally, the full text of 16 review and health economic articles was screened for further eligible references and another 3 articles were included in the review. Subsequently, all eligible articles were screened for overlapping patient populations. Since there was no population overlap, all 17 articles were included in this review. No randomized controlled trial (RCT) comparing allograft or DBM to autograft met the eligibility criteria (Table 1).

### Allograft

Eight prospective and 3 retrospective studies comparing allograft to autograft in posterior and anterior fusion with and without instrumentation were included. Only 5 out of 11 studies had groups with allograft alone. In the prospective study done by Andersen et al, 94 patients underwent instrumented (54.3%) or noninstrumented (45.7%) posterior lumbar fusion (PLF) procedures with fresh frozen femoral head allograft.[42] At 12 and 24 months, a fusion rate of 68% for noninstrumented and 81% for instrumented fusion was reported (Tables 2 and 3). Additional 3 prospective studies on PLF[43] and posterior lumbar interbody fusion (PLIF)[44,45] enrolled 16 to 89 patients and graft material included autograft mixed with various forms of allograft (freeze-dried,[43] machined,[44] or cortical[45]). In all 3 studies patients underwent instrumented procedures, resulting in fusion rates between 91.6% and 98% at 24 months. For anterior fusion procedures 2 retrospective[46,47] and 3 prospective studies[48-50] looked at the use of allograft in instrumented[46,48] and noninstrumented[47,49,50] fusion. Four out of 5 studies used structural allograft alone,[47-50] with 2 studies using fibular[49,50] and 2 femoral bone graft.[47,48] In a case-control study done by Faundez et al, the type of structural allograft used for anterior interbody fusion included tricortical iliac crest allograft in 41 patients (59.7%), milled femoral ring in 12 (17.9%), patella allograft alone in 11 (16.4%), and a combination of patella allograft and iliac crest allograft in 4 patients (6%).[46] Two instrumented studies reported 82% fusion rates at 24 and 33 months, similar pseudarthrosis rates (13%), and significant improvements in the clinical outcomes.[46,48] On the other hand, in the 3 noninstrumented anterior lumbar interbody fusion (ALIF) studies fusion rates were lower 58% to 66% and one study reported that 85% of the cases had graft subsidence.[47,49,50] Although the fusion rates were lower than in instrumented studies, all 3 studies reported improvement in the clinical outcomes and return to work.

Three studies reported on the use of allograft in transforaminal lumbar interbody fusion (TLIF) procedures. Faundez et al used a boomerang-shaped allograft spacer in 2 slightly different designs with 61.5% of the patients receiving a semilunar femoral ring graft and the other 38.5% having a split femoral ring allograft.[46] At 33 months, the authors reported 77% fusion rates and improvement in the Short Form-36 (SF-36) score (Tables 2 and 3).[46] Two additional nonrandomized studies utilizing TLIF with combination of local autograft and structural allograft were included in this review.[51,52] The studies enrolled

**Table 1.** Overview of Results.

| Author, Year | Sample Size | Follow-up (FU) Time | Indication | Levels (Number, Location) | Intervention | Fusion Rate | Reoperations |
|---|---|---|---|---|---|---|---|
| *PLF, structural allograft, instrumented and noninstrumented* | | | | | | | |
| Andersen, 2009 (prospective) | 51 noninstrumented; 43 instrumented | 4.3 years | "Spinal stenosis surgery where fusion was deemed necessary due to instability or the need for extensive decompression, or a high degree of back pain."<br>*Instrumented:*<br>Degenerative 1 (2.3%)<br>Stenosis 18 (41.9%)<br>Stenosis + deg. olisthesis 12 (27.9%)<br>Stenosis + deg. scoliosis 12 (27.9%)<br>*Noninstrumented:*<br>Degenerative 3 (5.9%)<br>Stenosis 30 (58.8%)<br>Stenosis + deg. olisthesis 12 (23.5%)<br>Stenosis + deg. scoliosis 6 (11.8%)<br>*Previous spine surgery:*<br>Instrumented 14 (32.6%)<br>Uninstrumented 8 (15.7%) | 1 level 18 (35.3%)<br>2 levels 19 (37.3%)<br>3 levels 12 (23.5%)<br>4 and 5 levels 2 (3.9%)<br>No information on location | PLF with fresh-frozen allograft (femoral head) | 68% at 12 and 24 months | *Instrumented:*<br>9/43 (20.9%), of these 4 were hardware removals due to loosening<br>*Noninstrumented:*<br>6/51 (11.8%) |
| *PLF, allograft chips, instrumented* | | | | | | | |
| Ploumis, 2010 (prospective) | 16 (only allograft group considered) | 2 years | Degenerative lumbar scoliosis and spinal stenosis | "Up to 3 levels from L1-S1" | Instrumented PLF with allograft (freeze-dried cancellous chips) with local autograft | 93.7% at 24 months | No reoperations |
| *PLIF, structural allograft, instrumented* | | | | | | | |
| Arnold, 2009 (prospective) | 89 | Up to 24 months | Disc failure or prolapse 53 (73.6%)<br>Osteophytic spondylosis 21 (29.2%)<br>Facet hypertrophy osteoarthritis 24 (33.3%)<br>Congenital spinal stenosis 2 (2.8%)<br>Spondylolysis 10 (13.9%)<br>Spondylolisthesis, pars defect 16 (22.2%)<br>Spondylolisthesis, degenerative 8 (11.1%)<br>Degenerative scoliosis 3 (4.2%)<br>Trauma-induced instability 3 (4.2%)<br>[figures refer to 72 patients w/ 12-month FU; *patients may have multiple indications*] | 1 level: 52 patients (72.2%)<br>2 levels: 20 patients (27.8%)<br>Location: L2-S1 | Instrumented PLIF (without cage), machined allograft PLIF spacers.<br>Autograft with or without allograft extender was placed around and between PLIF spacers (surgeon's discretion) | 98% at12 and 24 months | 3 Reoperations:<br>1 Repositioning of bone grafts because of posterior migration at 2 months<br>1 Cephalad extension of fusion plus decompression caused by stenosis above index level at 42 months<br>1 Repair of pseudomeningocele |
| Kakiuchi, 1998 (prospective) | 71 patients presented as 2 groups:<br>≤50 years: 33 patients<br>≥60 years: 38 patients | 41 months | ≤*50 years group:* Disc herniation or post-discectomy failed back: 38 (53.5%)<br>≥*60 years group:* Degenerative spondylolisthesis: 33 (46.5%) | L3-4: 6 (8.5%)<br>L4-5: 46 (64.8%)<br>L5-S1: 19 (26.8%) | 1-level PLIF with pedicle screws and hooks and rods, with or without any internal fixation<br>Structural cortical bone allograft with cancellous bone autograft | 91.6% at 24 months | No reoperations |
| *ALIF ± posterior instrumentation, structural allograft, instrumented* | | | | | | | |
| Faundez, 2009 (retrospective) | 65 ALIF with posterior fusion (presented here)<br>68 TLIF, transforaminal lumbar interbody fusion (presented below) | *Radiological:* 33 months | Primary diagnosis of symptomatic disc degeneration (SDD) at 1 or 2 levels | 1 level: 21%<br>2 levels: 79%<br>No location information | ALIF combined with rods or translaminar facet screws (no cage). Posteriorly mix of morcellized allograft and local autograft | 82% at 33 months | Revision surgery for pseudarthrosis<br>9 (13.2%) patients<br>Pseudarthrosis documented and patients considered for possible future revision because of symptoms: 3 (4.4%) patients |

*(continued)*

**Table 1.** (continued)

| Author, Year | Sample Size | Follow-up (FU) Time | Indication | Levels (Number, Location) | Intervention | Fusion Rate | Reoperations |
|---|---|---|---|---|---|---|---|
| Slosar, 2007 (prospective) | 30 (only allograft group considered) | 24 months | Predominant low back pain refractory to nonsurgical treatment, painful DDD (L3-S1), grade I-II spondylolisthesis, degenerative scoliosis | 1 level: 30%<br>2 levels: 50%<br>3 levels: 20% | Instrumented ALIF with structural allograft (femoral ring) with additional chips in its middle | Grade 1 (solid fusion): 82%<br>Grade 2 (bridging bone): 7%<br>Grade 3 (not fused): 11%<br>at 24 months | 4 patients (13%) reoperated for pseudarthrosis and 1 pending |
| *TLIF, structural allograft, instrumented* | | | | | | | |
| Faundez, 2009 (retrospective) | 68 TLIF (presented here)<br>65 ALIF with posterior fusion (presented above) | *Radiological:* 33 months | Primary diagnosis of symptomatic disc degeneration (SDD) at 1 or 2 levels | TLIF:<br>1 level: 51%<br>2 levels: 49%<br>No location information | Instrumented TLIF with allograft spacer and local autograft behind the allograft spacer | 77% at 33 months | Revision surgery for pseudarthrosis: 12 (18.5%) patients<br>Pseudarthrosis documented and patients considered for possible future revision because of symptoms: 3 (4.6%) patients |
| Kim, 2011 (retrospective) | 56 | 32.4 months | Recurred disc herniation: 5 (8.9%)<br>Degenerative spondylolisthesis: 22 (39.3%)<br>Isthmic spondylolisthesis: 18 (32.1%)<br>Foraminal stenosis: 11 (19.6%) | Not documented | TLIF with Capston cage and instrumentation. Local autograft and allobone | Grade I: 73.2%<br>Grade II: 23.2%<br>at 32.4 months | None mentioned |
| Houten, 2006 (prospective) | 33 (independent radiological review in 23) | *Clinical:* 37 months<br>*Radiological:* 11 months | Isthmic spondylolisthesis: 8 (24%)<br>Recurrent disc herniation: 14 (42%)<br>DDD: 11 (33%) | L3-L4: 2 (6.1%)<br>L4-L5: 16 (48.5%)<br>L5-S1: 14 (42.4%)<br>L4-S1: 1 (3.0%) | Instrumented TLIF with structural allograft and local autograft | 100% at 11 months | 3 patients with hardware removals after fusion mass had consolidated |
| *ALIF, structural allograft, noninstrumented* | | | | | | | |
| Wetzel 1993 (prospective) | (Only lumbar group considered): 24 | 24 months | Degenerative disease: 22 (91.6%)<br>Lumbar fracture: 1 (4.2%)<br>Thoracolumbar kyphosis: 1 (4.2%) | 1 level: 9 (37.5%)<br>2 levels: 12 (50%)<br>3 levels: 2 (8.35%)<br>4 levels: 1 (4.15%)<br>Majority: L4-5 and L5-S1 | ALIF with fibular allograft | 58% at 27 months (plain X-ray) | No reoperations |
| Vamvanij, 1998 (prospective) | Allograft group: 11<br>Control groups (all ICBG)<br>PLF + pedicle screw: 13<br>PLF + facet screw: 16<br>ALIF w BAK cage: 16 | 4.2 years | Internal disc disruption | *ALIF+ allograft (N = 11):*<br>1-level: 11 (100%)<br>*ICBG PLF + pedicle screw (N = 13):*<br>1 level: 4 (30.8%)<br>2 levels: 7 (53.8%)<br>3 levels 2 (15.4%)<br>*ICBG PLF + facet screw (N = 16)*<br>1 level: 9 (56.25%)<br>2 levels: 7 (43.75%)<br>*ICBG ALIF w BAK (N = 16)*<br>1 level: 7 (43.75%)<br>2 levels: 9 (56.25%) | Allograft group: ALIF with fibula allograft<br>Various ICBG control groups (none of them stand-alone ICBG ALIF):<br>ICBG PLF + pedicle screw<br>ICBG PLF + facet screw<br>ICBG ALIF w BAK | *ALIF w allograft:* 60%<br>*ICBG PLF + pedicle screw:* 69%<br>*ICBG PLF + facet screw:* 50%<br>*ICBG ALIF w BAK+ facet fusion:* 88% at 4.2 years | No reoperations |
| Kumar, 1993 (retrospective) | 32 | 24-48 month | "Patients who underwent single-level anterior lumbar fusions" | Only 1 level fusions<br>L3-4: 2 (6.25%)<br>L4-5: 14 (43.75%)<br>L5-S1: 16 (50.00%) | ALIF with femoral strut allograft | Arthrodesis: 66%<br>Functional arthrodesis: 22%<br>Nonunion: 12% at 24 months | None reported |
| *PLF DBM, noninstrumented* | | | | | | | |
| Epstein NE, 2008 (prospective) | 75 | *Clinical:* 3.3 years<br>*Radiological:* 1 year | Patients undergoing multilevel lumbar laminectomies and noninstrumented fusions using lamina autograft and DBM.<br>5 patients w/ previous lumbar surgeries, of these 3 with multiple previous lumbar surgeries | Patients underwent average 4.9 level lumbar laminectomies and 2.0 level noninstrumented posterolateral lumbar fusions | PLF with DBM osteofil without cage or instrumentation | 82.7% at 12 months | *2 secondary interventions:* 1 postoperative seroma; 1 secondary instrumented 1-year postoperatively |

*(continued)*

**Table 1.** (continued)

| Author, Year | Sample Size | Follow-up (FU) Time | Indication | Levels (Number, Location) | Intervention | Fusion Rate | Reoperations |
|---|---|---|---|---|---|---|---|
| *PLF DBM, instrumented* | | | | | | | |
| Epstein NA and JA, 2007 (prospective) | 140 patients (95 one level, 45 two levels) | *Clinical:* 3.4 years<br>*Radiological:* up to 12 months until fusion was documented | Patients undergoing multilevel lumbar laminectomies and instrumented fusions using lamina autograft and DBM.<br>*One-level fusion patients:*<br>Degenerative spondylolisthesis: 62 (65.3%)<br>Spondylolisthesis with lysis: 20 (21.1%)<br>Lateral disc/stenosis requiring full facetectomy: 13 (13.7%) (including 10 patients w/ previous lumbar surgeries)<br>*Two-level fusion patients:*<br>Degenerative spondylolisthesis: 39 (86.7%)<br>Spondylolisthesis with lysis: 6 (13.3%) (including 10 patients w/ previous lumbar surgeries) | *1-level fusions:* average 3.7 level lumbar laminectomies/patient with fusion in:<br>L2-L4 0<br>L3-L4 8 (5.7%)<br>L4-L5 57 (40.7%)<br>L3-L5 0<br>L5-S1 30 (12.4%)<br>L4-S1 0<br>*2-level fusions:* average 4.2 level lumbar laminectomies/patient with fusion in:<br>L2-L4 3 (2.1%)<br>L3-L4 0<br>L4-L5 0<br>L3-L5 20 (14.3%)<br>L5-S1 0<br>L4-S1 22 (15.7%) | PLF with DBM Osteofil without cage but with instrumentation, with lamina autograft | *1-level fusions:*<br>On 2D-CT 92.6%<br>On dynamic X-ray: 97.9%<br>*2-level fusions:*<br>On 2D-CT 91.1%<br>On dynamic X-ray: 95.6%<br>at up to 12 months until fusion was documented | *Second surgery for symptomatic pseudarthrosis:* (patients assessed as unstable on F/E X-ray)<br>*1-level fusion:* 2 (2.1%)<br>*2-level fusion:* 2 (4.4%) |
| Kang, 2012 (prospective) | 46 randomized 2:1<br>DBM: 30<br>ICBG: 16 | 2 years | Spinal stenosis with degenerative spondylolisthesis | All 1-level | DBM Grafton combined w/ local autograft vs ICBG | DBM group: 86% (28 patients)<br>ICBG group: 92% (13 patients)<br>at 2 years | No reoperations |
| *PLF/PLIF DBM, instrumented* | | | | | | | |
| Sassard, 2000 (prospective) | DBM group: 56<br>Autologous bone (control) group: 52 | 2 years | *DBM:*<br>Disk herniation 39 (69.6%)<br>Deg disk disease 25 (44.6%)<br>Segmental instability 39 (69.6%)<br>Pseudoarthrosis 17 (30.4%)<br>Postlaminectomy pain 31 (55.4%)<br>Spondylolisthesis 6 (10.7%)<br>Spinal stenosis 6 (10.7%)<br>Other 4 (7.1%)<br>*Control:*<br>Disk herniation 27 (51.9%)<br>Deg disk disease 24 (46.2%)<br>Segmental instability 37 (71.2%)<br>Pseudoarthrosis 9 (17.3%)<br>Postlaminectomy pain 26 (50.0%)<br>Spondylolisthesis 15 (28.9%)<br>Spinal stenosis 11 (21.2%)<br>Other 3 (5.8%) | *Levels fused:*<br>*DBM:*<br>1 level 19 (33.9%)<br>2 levels 33 (58.9%)<br>3 levels 4 (7.1%)<br>*Control:*<br>1 level 21 (40.4%)<br>2 levels 20 (38.5%)<br>3 levels 11 (21.2%)<br>(location not documented) | PLF or PLIF with DBM Grafton without cage but with instrumentation<br>*DBM:*<br>PLF: 16%<br>PLIF: 84%<br>*Control (ICBG):*<br>PLF: 83%<br>PLIF: 17% | *DBM:* 60%<br>*Control:* 56%<br>at final FU (24-month radiographs used for final analysis, earlier radiographs used for imputation in case of missing value) | None reported |

*(continued)*

**Table 1.** (continued)

| Author, Year | Sample Size | Follow-up (FU) Time | Indication | Levels (Number, Location) | Intervention | Fusion Rate | Reoperations |
|---|---|---|---|---|---|---|---|
| *TLIF DBM, instrumented* | | | | | | | |
| Park, 2011 (retrospective) | 66 | 2 years | Spondylolytic spondylolisthesis: 23 (34.85%)<br>(Meyerding Grade 1, Grade 2): (12, 11) (18.2%; 16.65%)<br>Degenerative spondylolisthesis: 24 (36.35%)<br>(Meyerding Grade 1, Grade 2): (22, 2) (33.35%; 3%)<br>Degenerative lumbar instability*: 19 (28.8%)<br>*Segmental instability defined as $\geq$4 mm of translation or $\geq 10^{\circ}$ of angular motion on preoperative flexion and extension radiographs. | L3-4: 5 (7.6%)<br>L4-5: 40 (60.6%)<br>L5-S1: 21 (31.8%) | Instrumented TLIF with DBM (OsteofilRT) + local autograft | Grade 1 (definitely solid): 50%<br>Grade 2 (possibly solid): 27.3%<br>Grade 3 (probably not solid): 3%<br>Grade 4 (definitely not solid): 19.7%<br>at 2 years | No reoperations |
| *ALIF and TLIF with structural allograft and DBM, instrumented* | | | | | | | |
| Vaidya, 2007 (prospective) | (Only lumbar allograft + DBM group considered since control group included rhBMP)<br>11 ALIF in 16 levels<br>18 TLIF in 25 levels | 24 months | Revision surgery 13<br>Discogenic pain 7<br>Adult scoliosis 5<br>Spondylolisthesis 4 | ND | Instrumented ALIF and TLIF with structural allograft and DBM (no DBM brand information available) | 100% at 24 months | Reoperations in 4 patients (all scoliosis): 1 postoperative infection; 3 iliac screw removals for buttock pin |

Abbreviations: PLF, posterior lumbar fusion; PLIF, posterior lumbar interbody fusion; ALIF, anterior lumbar interbody fusion; DDD, degenerative disc disease; CT, computed tomography; ICBG, iliac crest bone graft; TLIF, transforaminal lumbar interbody fusion.

**Table 2.** Definition of Fusion and Fusion Success.

| Author, Year | Fusion Rate | Definition of Fusion |
|---|---|---|
| *PLF, structural allograft, instrumented and noninstrumented* | | |
| Andersen, 2009 | Instrumented: 81% at 12 and 24 months<br>Noninstrumented: 68% at 12 and 24 months | According to Christensen FB, Laursen M, Gelineck J, Eiskjaer SP, Thomsen K, Bunger CE. Interobserver and intraobserver agreement of radiograph interpretation with and without pedicle screw implants: the need for a detailed classification system in posterolateral spinal fusion. *Spine.* 2001;26:538-544.<br>Continuous intertransverse bony bridge had a minimum of one of the two sides indicating a fusion at that level. "Fusion" indicated this quality of fusion at all intended levels, "doubtful fusion" indicated suboptimal quality at one or more levels including fusion mass hidden behind the instrumentation, and "nonunion" indicated definite lack of fusion at one or more of the intended levels. If the fusion was doubtful in any way, the case was excluded from classification as "fused." |
| *PLF, allograft chips, instrumented* | | |
| Ploumis, 2010 | 93.7% at 24 months | Presence of bridging bone between the transverse processes and measured translation and angulation on dynamic radiographs using digital calipers. In addition to bridging bone $\leq 5^{\circ}$ of angular motion and $\leq 2$ mm of translation were required to classify the cases as successfully fused, as per the definition of successful fusion provided by the FDA for use in clinical trials involving investigational devices to attain spinal fusion. |
| *PLIF, structural allograft, instrumented* | | |
| Arnold, 2009 | 98% at 12 and 24 months | Fusion parameters included but were not limited to the following: less than 12% anterior/posterior translation on F-E radiographs, less than 5° rotation (Cobb angle) between FE radiographs, and maintenance of disc height from 6 to 12 and 24 months, plus radiographic evidence of bridging trabecular bone.<br>For two-level fusion to be deemed successful, both levels had to meet the fusion criteria. |
| Kakiuchi, 1998 | 91.6% at 24 months | Fusion was defined as evidence of bilateral continuous bridging of trabecular bone as well as less than 3 mm of translation and less than 5° of angular motion on lateral flexion-extension radiographs. CT scans were assessed for continuous bone formation throughout the length of the fusion bed.<br>Fusion was finally rated as: 1. Fused; 2. Indeterminate; 3. not fused<br>For the final 24-month fusion status analysis, the subjects' radiological results were assessed as follows. Included in the final analysis were all subjects who reached the 12-month FU time point. If a subject had a radiograph and/or a CT scan that was assessed by the independent radiologist as "fused" at month 12 or at month 24 (when applicable), then the subject was classified as "fused" in the final analysis. If all the radiographs or CT scans obtained at months 12 and 24 were assessed as "not fused" and/or "indeterminate," then the subject was classified as "not fused" in the final analysis.<br>Radiographical: preoperatively and immediately after surgery and at 6 weeks, 3, 6, 12, and 24 months postoperatively.<br>Flexionextension radiographs and computed tomographic (CT) scans (high-resolution axial, sagittal, and coronal reformatting) were obtained at 12-month FU.<br>If not fused at 12 months, additional CT scans obtained at 24-month FU<br>If fused no additional CT scan at 24-month FU. |
| *ALIF ± posterior instrumentation, structural allograft, instrumented* | | |
| Faundez, 2009 | 82% at mean 33 months | Based on CT scans:<br>• Solid radiological fusion*: bridging bone in both anterior (at least 30% endplate surface) and posterior columns or anterior column alone<br>• Partial radiological fusion*: anterior column "probably fused" with any fusion status of posterior column<br>• Inadequate radiological fusion: at least anterior column "not fused" or "probably not fused," with any fusion status posteriorly<br>• Indeterminate radiological fusion: indeterminate anterior fusion status with any fusion status posteriorly<br>*Considered as adequate. |
| Slosar, 2007 | Grade 1: 82%<br>Grade 2: 7%<br>Grade 3/4: 11%<br>at 24 months | Based on X-ray<br>Grade I: Fused with remodeling and trabeculae present (considered as fused)<br>Grade II: Graft intact, not fully remodeled and incorporated, no lucency (considered as fused)<br>Grade III: Graft intact, potential lucency present at the top or bottom graft (not considered as fused)<br>Grade IV: Fusion absent with collapse/resorption of graft (not considered as fused) |
| *TLIF, structural allograft, instrumented* | | |
| Faundez, 2009 | 77% at mean 33 months | • Based on CT scans:<br>• Solid radiological fusion was defined as bridging bone in both anterior (at least 30% endplate surface) and posterior columns or anterior column alone (considered adequate)<br>• Partial radiological fusion: anterior column "probably fused" with any fusion status of posterior column (considered adequate)<br>• Inadequate radiological fusion: at least anterior column "not fused" or "probably not fused," with any fusion status posteriorly<br>• Indeterminate radiological fusion: indeterminate anterior fusion status with any fusion status posteriorly |
| Kim, 2011 | Bridwell grade I 73.2%<br>Bridwell grade II 23.2%<br>at a mean of 32.4 months | Grades according to Bridwell's anterior fusion grades<br>Grade I: Fusion with remodeling and trabeculae<br>Grade II: Graft intact, not fully remodeled, no radiolucencies<br>Grade III" Graft intact, but a definite lucency<br>Grade IV" Definitely not fused, collapse<br>Bridwell KH, Lenke LG, McEnery KW, Baldus C, Blanke K. Anterior fresh frozen structural allografts in the thoracic and lumbar spine. Do they work if combined with posterior fusion and instrumentation in adult patients with kyphosis or anterior column defects? *Spine (Phila Pa 1976).* 1995;20:1410-1418. |

*(continued)*

**Table 2.** (continued)

| Author, Year | Fusion Rate | Definition of Fusion |
|---|---|---|
| Houten, 2006 | 100% at 11 months | 1.The absence of movement on flexion-extension X-ray films<br>2.Presence of bone bridging between the graft and adjacent vertebral end-plates<br>3.Lack of lucency around spinal instrumentation |
| *ALIF, structural allograft, noninstrumented* | | |
| Wetzel, 1993 | 58% at 27 months (plain X-ray) | Fusion was graded as solid according to visual inspection, if mature trabecular lines crossed all levels fused on plain X-rays.<br>Additionally, X-rays were digitized and the amount of angular change (Cobb angle) and translational change between the cranial and caudal bodies included in the fusion were quantified. Fusion was felt to have occurred if, on serially digitized films, the Cobb angle changed less than 4°, and translation was less than 3 mm.<br>Fusion was assessed by assessing sagittal change by digital roentgenopgraphs. If less than 3 mm of change had occurred, this was taken to represent fusion. |
| Vamvanij, 1998 | 60% at a mean of 4.2 years | Fusion was determined when bone formation was visualized by radiographic evaluation, connecting all attempted transverse processes bilaterally, or bridging the adjacent vertebral endplates. |
| Kumar, 1993 | On plain X-rays: 66%<br>On dynamic X-ray: 22%<br>Nonunion: 12%<br>at 24 months | Presence of fusion was based on plain radiographs appearance; categorized into three groups<br>1. Arthrodesis: absence of translucent line at the graft- vertebral end-plate interface, the presence of trabeculation crossing the interspace and less than 2° of motion on flexion-extension radiography.<br>2. Functional arthrodesis: evidence of stability as there was less than 2° of motion on flexion-extension radiography and the presence of bridging bone anterior or posterior to the femoral graft. A translucent line was observed separating the vertebral end-plate from the bone graft on one or both sides however.<br>3. Nonunion: Motion greater than 2° on flexion-extension analysis and the presence of a translucent line on plain x-rays at the vertebra-femoral graft interface. |
| *PLF DBM, noninstrumented* | | |
| Epstein NE, 2008 | 82.7% at 12 months | Fusion assessment on 2D-CT scans and dynamic X-rays.<br>*2D-CT criteria* for fusion included the demonstration of bony trabeculation/continuity of bone fragments between transverse processes, and/or facet fusion.<br>*Dynamic X-ray criteria* for stability included <3 mm of translation, and <5 degrees of angulation. Patients were considered as demonstrating pseudarthrosis if they were "not fused" using either dynamic X-ray or 2D-CT examinations by either observer. |
| *PLF DBM, instrumented* | | |
| Epstein NE and JA, 2007 | *1-level fusions:*<br>On 2D-CT 92.6%<br>On dynamic X-ray: 97.9%<br>*2-level fusions:*<br>On 2D-CT 91.1%<br>On dynamic X-ray: 95.6%<br>at up to 12 months until fusion was documented | *Fusion criteria on dynamic X-rays:* <3 mm of translation and <5 degrees of angulation.<br>*2D-CT criteria of fusion:* bony trabeculation and continuous fusion mass extending between adjacent transverse processes with a lack of screw loosening (absence of lucency surrounding the screws). |
| Kang, 2012 | DBM group: 86%<br>ICBG group: 92%<br>at 2 years | Fusion was defined as evidence of bilateral continuous bridging of trabecular bone as well as less than 3 mm of translation and less than 5° of angular motion on lateral flexion-extension radiographs. CT scans were assessed for continuous bone formation throughout the length of the fusion bed.<br>Fusion was finally rated as: 1. fused, 2. indeterminate, 3. not fused<br>For the final 24-month fusion status analysis, the subjects' radiological results were assessed as follows. Included in the final analysis were all subjects who reached the 12-month FU time point. If a subject had a radiograph and/or a CT scan that was assessed by the independent radiologist as "fused" at month 12 or at month 24 (when applicable), then the subject was classified as "fused" in the final analysis. If all the radiographs or CT scans obtained at months 12 and 24 were assessed as "not fused" and/or "indeterminate," then the subject was classified as "not fused" in the final analysis.<br>Radiographical: preoperatively and immediately after surgery and at 6 weeks, 3, 6, 12, and 24 months postoperatively.<br>Flexion extension radiographs and computed tomographic (CT) scans (high-resolution axial, sagittal, and coronal reformatting) were obtained at 12-month FU.<br>If not fused at 12 months, additional CT scans obtained at 24-month FU<br>If fused no additional CT scan at 24-month FU |

*(continued)*

**Table 2.** (continued)

| Author, Year | Fusion Rate | Definition of Fusion |
|---|---|---|
| *PLF/PLIF DBM, instrumented* | | |
| Sassard, 2000 | 60% at final FU (24-month radiographs used for final analysis, earlier radiographs used for imputation in case of missing value) | The bone graft mass was judged to be fused if there was uninterrupted bone bridging the transverse processes on at least one side of the fusion mass with no identifiable breaks, clefts, or areas of marked focal bone resorption. Definitive pseudoarthroses and fusion masses with marked bone resorption were judged as not fused. |
| *TLIF DBM, instrumented* | | |
| Park, 2011 | Grade 1: 50%<br>Grade 2: 27.3%<br>Grade 3: 3%<br>Grade 4 19.7%<br>at 2 years | According to Burkus JK, Foley KT, Haid R, LeHuec JC. Surgical interbody research group—radiographic assessment of interbody fusion devices: fusion criteria for anterior lumbar interbody surgery. *Neurosurg Focus*. 2001;10:E1.<br>On flexion/extension lateral radiographs: No motion (acceptable intraobserver measurement error was 3° angular rnotion or 3 mm of translation)<br>On CT scan: continuous bony bridge within/around the cage (incorporation of the grafted bone into the vertebral end plates)<br>New bone formation adjacent to or within the cage and/or fused posterior facet joint (the opposite side of TLIF approach)<br>On dynamic radiographs and/or CT scan: Lack of radiolucent lines around the graft and cage as well as absence of a lucent hollow around the pedicle screws<br>Subdivision of fusion into four grades:<br>Grade 1 (definitely solid): no motion on flexion-extension radiographs, continuous bony bridge within/around the cage, new bone formation adjacent to or within the cage, and/or fused posterior facet joint on CT scan<br>Grade 2 (possibly solid): no motion on dynamic radiographs-and continuous bony incorporation within/around the cage, without evidence of new bone formation adjacent to or within the cage or facet joint fusion<br>Grade 3 (probably not solid): no motion excluding evidence of bony incorporation within/around the cage<br>Grade 4 (definitely not solid): motion on dynamic radiographs with no evidence of bony bridge within/around the cage<br>Standing anteroposterior, lateral, flexion, and extension radiographs of the lumbosacral spine were collected from preoperative and final postoperative visit for the fusion assessment. Postoperative CT scan was also obtained at the final visit.<br>They considered the Grades 1 and 2 as a radiographic solid fusion and the Grades 3 and 4 as a nonunion. |
| *ALIF and PLIF with structural allograft and DBM, instrumented* | | |
| Vaidya, 2007 | 100% at 24 months | Radiological loss of the allograft end-plates, the end of progression of subsidence, and the stabilization of clinical symptoms as measured by the Oswestry Disability Index and VAS. |

Abbreviations: PLF, posterior lumbar fusion; PLIF, posterior lumbar interbody fusion; ALIF, anterior lumbar interbody fusion; CT, computed tomography; TLIF, transforaminal lumbar interbody fusion.

**Table 3.** Availability of Power Calculation.

| Author, Year | Intervention | Fusion rate | Power Calculation or Sample Size Justification |
|---|---|---|---|
| *PLF, structural allograft, instrumented and noninstrumented* | | | |
| Andersen, 2009 | PLF with fresh frozen allograft<br>Instrumented and noninstrumented | Instrumented: 81%<br>Noninstrumented: 68%<br>at 12 and 24 months | No information provided on sample size determination/ power |
| *PLF, allograft chips, instrumented* | | | |
| Ploumis, 2010 | Instrumented PLF with allograft (freeze-dried cancellous chips) with local autograft | 93.7% at 24 months | No information provided on sample size determination/ power |
| *PLIF, structural allograft, instrumented* | | | |
| Arnold, 2009 | PLIF without cage but with instrumentation | 98% at 12 and 24 months | No information provided on sample size determination/ power |
| Kakiuchi, 1998 | 1-level PLIF with pedicle screws, and hooks and rods, with or without any internal fixation | 91.6% at 24 months | No information provided on sample size determination/ power |
| *ALIF ± posterior instrumentation, structural allograft, instrumented* | | | |
| Faundez, 2009 | ALIF combined with rods or translaminar facet screws (no cage) | 82% at 33 months | No information provided on sample size determination/ power |
| Slosar, 2007 | Instrumented ALIF with structural allograft (femoral ring) with additional chips in its middle | Grade 1: 82%<br>Grade 2: 7%<br>Grade 3/4: 11%<br>at 24 months | No information provided on sample size determination/ power |
| *TLIF, structural allograft, instrumented* | | | |
| Faundez, 2009 | TLIF without cage but with instrumentation | 77% at 33 months | No information provided on sample size determination/ power |
| Kim, 2011 | TLIF with Capston cage and instrumentation | Bridwell grade I: 73.2%<br>Bridwell grade II: 23.2%<br>at 32.4 months | No information provided on sample size determination/ power |
| Houten, 2006 | Instrumented TLIF with structural allograft and local autograft | 100% at 11 months | No information provided on sample size determination/ power |
| *ALIF, structural allograft, noninstrumented* | | | |
| Wetzel, 1993 | ALIF with fibular allograft | 58% at 27 months (plain X-ray) | No information provided on sample size determination/ power |
| Vamvanij, 1998 | Allograft group:<br>ALIF with fibula allograft<br>Various ICBG control groups, (none standalone ICBG ALIF):<br>ICBG PLF + pedicle screw<br>ICBG PLF + facet screw<br>ICBG ALIF w BAK | 60% at 4.2 years | No information provided on sample size determination/ power |
| Kumar, 1993 | ALIF with femoral strut allograft | On plain X-rays: 66%<br>On dynamic X-ray: 22%<br>Nonunion: 12%<br>at 24 months | No information provided on sample size determination/ power |
| *PLF DBM, noninstrumented* | | | |
| Epstein NE, 2008 | PLF with DBM Osteofil without cage or instrumentation | 82.7% at 12 months | No information provided on sample size determination/ power |
| *PLF DBM, instrumented* | | | |
| Epstein NE and JA, 2007 | PLF with DBM Osteofil without cage but with instrumentation | *One-level fusions:*<br>On 2D-CT 92.6%<br>On dynamic X-ray: 97.9%<br>*Two-level fusions:*<br>On 2D-CT: 91.1%<br>On dynamic X-ray: 95.6%<br>at up to 12 months until fusion was documented | No information provided on sample size determination/ power |

*(continued)*

**Table 3.** (continued)

| Author, Year | Intervention | Fusion rate | Power Calculation or Sample Size Justification |
|---|---|---|---|
| Kang, 2012 | instrumented PLF: DBM Grafton combined w/ local autograft vs ICBG | DBM group: 24 (86%)<br>ICBG group: 12 (92%)<br>at 2 years | No information provided on sample size determination/ power |
| *PLF/PLIF DBM, instrumented* | | | |
| Sassard, 2000 | PLIF with DBM Grafton without cage but with instrumentation<br>*DBM:*<br>PLF: 16%<br>PLIF: 84%<br>*Control:*<br>PLF: 83%<br>PLIF: 17% | DBM: 60%<br>Control: 56%<br>at final FU<br>(24-month radiographs used for final analysis, earlier radiographs used for imputation in case of missing value) | No information provided on sample size determination/ power |
| *TLIF DBM, instrumented* | | | |
| Park, 2011 | Instrumented TLIF with DBM (OsteofilRT) + local autograft | Grade 1: 50%<br>Grade 2: 27.3%<br>Grade 3: 3%<br>Grade 4: 19.7%<br>at 2 years | No information provided on sample size determination/ power |
| *ALIF and PLIF, structural allograft and DBM, instrumented* | | | |
| Vaidya, 2007 | Instrumented ALIF and TLIF with structural allograft and DBM (no DBM brand information available) | 100% at 24 months | No information provided on sample size determination/ power |

Abbreviations: PLF, posterior lumbar fusion; PLIF, posterior lumbar interbody fusion; ALIF, anterior lumbar interbody fusion; CT, computed tomography; TLIF, transforaminal lumbar interbody fusion.

33 to 68 patients and there was no control group. Fusion rates were 73.2% at 32.4 months[51] and 100% at 11 months.[52] Both studies reported improvements in the clinical outcomes assessed by Oswestry Disability Index (ODI), Visual Analogue Scale, or Prolo Scale.[51,52]

### Demineralized Bone Matrix

Six studies on DBM, 1 noninstrumented[53] and 5 instrumented,[9,54-57] were included in this review. Five (4 prospective and 1 retrospective) studies looked at DBM in posterior fusion,[9,53-56] and one prospective study utilized DBM for both anterior and posterior procedures.[57]

In the noninstrumented PLF study, 75 patients received lamina autograft and DBM paste at a 1:1 ratio (Osteofil, Medtronics Sofamor Danek, Memphis, TN).[53] At 12 months, 82.7% of the patients were deemed to be fused and the authors reported an improvement in the SF-36 score at the 1- and 2-year follow-up.[53] In 2 prospective studies patients underwent PLF with DBM and local graft.[9,54] In the study done by Epstein et al, 95 patients underwent single- and 45 two-level PLF with lamina autograft and DBM paste in a 50:50 ratio (Osteofil, Medtronics Sofamor Danek).[54] Fusion rates assessed on 2D computed tomography were 92.6% for 1-level and 91.1% for 2-level procedures up to 12 months postoperatively (Tables 2 and 3). When the fusion was assessed on dynamic X-rays, the rates were 97.9% for 1-level and 95.6% for 2-level procedures. Kang and coworkers enrolled 46 patients randomly assigned to Grafton DBM Matrix (Medtronics, Memphis, TN) with local bone (30 patients) or ICBG (16 patients).[9] At the 2-year follow-up, fusion rates of the DBM and ICBG groups were similar (86% vs 92%) along with the ODI and SF-36 score.[9]

Three studies, 2 prospective and 1 retrospective, utilized a combination of DBM and autograft in PLF/PLIF, TLIF, or ALIF procedures.[55-57] In a prospective case-control study, 56 patients underwent PLF or PLF/PLIF with Grafton DBM and local autograft, and 52 patients received ICBG.[55] At 24 months, the results showed a 60% fusion rate in the DBM and a 56% fusion rate in the control group (Tables 2 and 3). However, this difference was not statistically significant.[55] On the other hand, 100% fusion rates and minimal graft subsidence were reported by Vaidya et al, where patients underwent either ALIF (11) or TLIF (18) procedures with DBM and allograft.[57] In a retrospective study, 66 patients underwent TLIF with a combination of DBM paste (OsteofilRT DBM paste; Regeneration Technologies Inc, Alachua, FL) and local autograft.[56] At the 2-year follow-up, solid fusion was achieved in 77% of the patients; however, there were no significant differences in the clinical outcomes between patients with solid fusion and nonunion (Tables 2 and 3).[56]

### Study Demographics and Surgery

A sufficient description of patient baseline characteristics (age, gender distribution, and diagnoses) was given in 11 out of 17 citations.[9,42-44,46,48,50,52,54,55] Yet only 7 articles explicitly described the inclusion and exclusion criteria for study participation.[9,44,46,48,50,51,55] None of the publications provided a power calculation or justified their sample size.

The number of fused levels was provided by 15 out of 17 studies,[9,42-50,52-55,57] but only one third of the studies specified the exact locations.[45,47,52-54]

### Outcome Assessment

In the majority of studies, the fusion assessment was performed by an independent or blinded observer.[9,43,44,46-48,50,52-55,57] The definition of fusion varied between the studies, with no studies having the same fusion assessment protocol (Table 2). When analyzing the individual fusion definitions in relation to the achieved fusion rates, there were no discrepancies between the fusion percentage and the assessment stringency (Table 2).

### Lost to Follow-up

In general, the rates of lost to follow-up were quite variable. Eight studies that documented radiological and clinical outcomes at various time points did not make any statements with regards to "lost to follow- up."[43,45,47,49,50,53,54,57] On the other hand, in the studies done by Kim et al[51] and Houten et al,[52] all of the patients had complete follow-ups for both radiological and clinical outcomes. Andersen et al reported clinical outcomes after a mean of 4.3 years and radiological outcomes up to 24 months. The follow-up rate in this study was 79%.[42] This was the sole study that provided information on why patients were lost to follow-up and also analyzed the characteristics of patients included in the follow-up versus those lost to follow-up. In the studies conducted by Arnold et al[44] and Sassard et al,[55] the number of patients available for follow-up decreased from 12 to 24 months, from 83% to 54%[44] and from 81% to 76%,[55] respectively. Similar results for the clinical outcomes were observed in a study conducting by Kang et al.[9] In the study done by Faundez and coworkers, radiological data was available for 59% of the ALIF and 54% of TLIF patients at 33 months, and the clinical follow-up rate was 64%.[46] Slosar and coworkers followed-up patients up to 24 months for both radiological and clinical outcomes, and only 3 patients dropped over the 24-month time period.[48]

### Conflict of Interest Declaration

In 7 of the 17 articles, no conflict of interest statements was provided.[42,45-47,50-52] Six studies were funded by the industry,[9,48,49,53-55] and in 2 publications, some authors declared a consultancy role for the manufacturer of the used allograft.[44,48]

## Discussion

The purpose of this review was to determine the fusion efficacy of allograft and DBM in lumbar instrumented and noninstrumented fusion procedures for degenerative lumbar disorders. Seventeen studies met the inclusion criteria. However, a large variation in fusion rates, a lack of control group, and follow-up

time prevented any significant conclusions. There were no obvious differences between allograft and DBM with regard to instrumented fusion procedures. For the allograft, the fusion rates were between 58% and 68% for noninstrumented lumbar fusions[42,47,49,50] and between 73% and 100% for instrumented fusions with and without additional local autograft.[42-46,48,51,52] Regarding DBM, one study reported fusion rates of 82.7% for noninstrumented fusion,[53] with the remaining studies reporting between 60% and 100% for instrumented procedures with or without autograft.[9,54-57]

Autograft is the only graft material that has all 3 characteristics of the ideal graft: osteoconductivity, osteogenecity, and osteoinduction. Despite being considered the gold standard, a wide range of fusion rates has been reported in the literature. The use of autograft in instrumented lumbar fusion procedures has led to fusion rates between 54% and 99%,[7-18,29] and for noninstrumented fusion between 30% and 100%.[10,11,58-64]

Based on those findings, allograft and DBM use had fusion ranges that overlap with autograft fusion rate ranges. Those results are in line with the recommendations created by Fischer and coworkers using Guyatt criteria and focusing on non–bone morphogenetic protein graft materials.[39] In their review, a 1B grade was given to allograft use in PLF and ALIF approaches, reflecting a strong recommendation with a clear benefit to most of the patients. For DBM, the grading was dependent on whether DBM was used as a substitute or extender. The authors gave a 1C grade for PLF and ALIF surgeries due to the lack of RCTs.

Although the allograft and DBM can provide comparable fusion rates, our review found a large variability between the studies. There are several reasons that may have contributed to the heterogeneity, including the variability in the surgical approaches used to achieve fusion. Surgical techniques have been a subject of previous research and some of the approaches have demonstrated a clear advantage over others. Future prospective longitudinal studies are needed to establish what approach and material are best for a patient.

The diversity in diagnosis as well as the number of surgical levels was high, leading to too many confounding variables. Studies on allograft included spinal stenosis, degenerative lumbar scoliosis, spondylolisthesis, disc herniation or prolapse, trauma, and several others.[42-52] The number of fused levels varied between single- to 5-level fusion, sometimes within the same study. Similar to the allograft studies, diagnosis heterogeneity was seen in the studies focusing on DBM.[9,53-57] Furthermore, most of the studies with DBM included patients with failed surgery or pseudarthrosis as part of their cohorts. If recorded, the number of fused levels ranged between 1 and 5 vertebra. Another limitation in all of the studies was the methodological weakness. Most of the studies were purely observational without a control group and included poorly defined and/or mixed indications, procedures, and implants. None of the publications provided a power analysis or sample size justification.

Although most of the studies described the protocol for fusion assessment, there was no consistency in the definition of fusion. The differences in the individual fusion definitions revealed that patients deemed as fused in one study would be assessed as partially or inadequately fused in another study (Table 2). Only in 4 studies fusion rates were assessed by multiple observers, surgeons, and/or radiologists[43,53,56,57]; however, blinded assessment was done in only 2 studies.[43,53] None of the 17 studies included in this review reported intra- or interobserver kappa values on fusion assessment reliability.

Aside from the surgical and clinical inconsistencies, the DBM preparation techniques are likely a strong contributor to the differences in fusion rates. Different methods of processing and sterilization influence DBM osteoinductivity, which together with the type of carrier and donor's variability contribute to the wide range in fusion rates.

## Conclusion

Based on an analysis of 17 studies, this review found a large variation in the fusion rates, surgical approaches, lack of control groups, and follow-up time preventing any significant conclusions. No RCT comparing allograft or DBM to autograft as an adjunct to fusion met the eligibility criteria for this review. Well-designed RCTs employing standardized surgical techniques, addressing the clinical safety and efficacy of allograft and DBM compared to autograft in large, homogeneous patient populations, and a sufficient follow-up time are needed to unequivocally establish the usefulness and efficacy of these materials as an adjunct to fusion.

### Declaration of Conflicting Interests

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Surgitech, Expanding Orthopaedics, Osprey, Bone Biologics, Curative Biosciences, Pearldiver; Board of directors: North American Spine Society (Second Vice President), North American Spine Foundation (nonfinancial), Cervical Spine Research Society (travel expenses), AO Spine/AO Foundation (honorariums for board position); Fellowship support: AO Foundation (spine fellowship funding paid to institution).

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