Failure in Lumbar Spinal Fusion and Current Management Modalities

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Abstract

Lumbar spinal fusion is a commonly performed procedure to stabilize the spine, and the frequency with which this operation is performed is increasing. Multiple factors are involved in achieving successful arthrodesis. Systemic factors include patient medical comorbidities—such as rheumatoid arthritis and osteoporosis—and smoking status. Surgical site factors include choice of bone graft material, number of fusion levels, location of fusion bed, adequate preparation of fusion site, and biomechanical properties of the fusion construct. Rates of successful fusion can vary from 65 to 100%, depending on the aforementioned factors. Diagnosis of pseudoarthrosis is confirmed by imaging studies, often a combination of static and dynamic radiographs and computed tomography. Once pseudoarthrosis is identified, patient factors should be optimized whenever possible and a surgical plan implemented to provide the best chance of successful revision arthrodesis with the least amount of surgical risk.

Keywords
- lumbar spinal fusion
- neurosurgery
- spine surgery
- pseudoarthrosis

Spinal fusion surgery is a commonly performed procedure, both in the United States and around the world. First reported in 1911, it was initially performed to inhibit the progress of deformity in patients with Pott's disease.[1] Now, ~500,000 arthrodeses are performed in the United States every year, and the rate has been increasing.[2] Spinal fusion is the bony union of two or more vertebral bodies. The goal is to join together consecutive motion segments for the purpose of stabilizing an unstable spine. Common causes of instability include degenerative, traumatic, metastatic, or infectious. Solid arthrodesis is also desired for long-term stability after surgery to correct a spinal deformity, such as sagittal imbalance or scoliosis.

Biology of Bone Healing

Bone healing and spinal arthrodesis occur similarly. There are three phases: inflammatory, repair, and remodeling.[3] During the inflammatory phase, a hematoma is formed around the fusion bed, with resulting infiltration of macrophages, polymorphonuclear cells, and fibroblasts. These cells release metabolic factors promoting the formation of granulation tissue and the migration of mesenchymal cells, and factors necessary for vascular proliferation, such as vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and epidermal growth factor (EGF).[4] Following the infiltration of inflammatory factors, the repair phase

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involves repopulation of progenitor cells at the host–graft interface, with subsequent chondrogenic and osteogenic development, maturation of a collagen matrix, and ossification to form woven bone. Finally, woven bone undergoes remodeling through an interplay between osteoblasts and osteoclasts, yielding the final mature fusion.

Local and Systemic Factors Affecting Spinal Fusion

Numerous systemic factors may influence the ability to achieve a successful arthrodesis. Medical comorbidities such as rheumatoid arthritis and osteoporosis may negatively affect fusion rates. Additional systemic factors include nutritional status and medications. Systemic steroids inhibit the inflammatory phase of bone healing and the differentiation of progenitor cells, and decrease synthesis of extracellular matrix. Other common inhibitory medications include nicotine and nonsteroidal anti-inflammatory drugs (NSAIDs). Systemic factors may also promote bone healing, such as growth hormone, thyroid hormone, parathyroid hormone, and estrogens.[5] Local nonsurgical factors may influence fusion rate, such as prior radiation treatment, but may not be optimizable.

Smoking

Smoking is perhaps the single most controllable risk factor for pseudoarthrosis after spinal fusion. Nicotine has deleterious effects on the vertebral bone biology, fusion healing, and overall gene expression,[6] primarily affecting the repair phase of bone healing.[7] Theiss et al reported the downregulation of gene expression of bone morphogenetic proteins (BMP)-2, -4, and -6; basic fibroblast growth factor (bFGF); and VEGF in a rabbit model with exposure to nicotine.[8] The existing vascular network undergoes vasoconstriction and endothelial damage, preventing onset of angiogenesis. Additional effects include inhibition of periosteal cell proliferation, increased cortisol production, decreased estrogen and calcitonin production, and a decrease in calcium absorption. The final result is a decrease in both bone mineral density and bone formation.

Factors inducing angiogenesis are most critically involved in the third to fourth week after spinal fusion, and new bone formation within the first 6 months. Glassman et al reported on the rates of pseudoarthrosis in smokers and nonsmokers.[9] They found a nonunion rate of 26.5 and 14.2%, respectively. For smokers who quit for more than 6 months postoperatively, nonunion rate was 17.1%. The authors concluded that smoking cessation reverses the negative impact of smoking on spinal fusion. Smoking cessation is recommended for at least 4 weeks prior to spinal fusion surgery, and up to 6 months after surgery.[6] Unfortunately, 60% of patients are found to relapse at 3 months postoperatively, and 61% of patients at 6 months.[10]

Nonsteroidal Anti-inflammatory Drugs

Adequate pain control following lumbar spinal fusion may be challenging. Multimodal pain regimens following orthopaedic surgery of the lower extremities have become routine, but their use after spine surgery has been more limited.[11] One particular class of agent, NSAIDs, act through the inhibition of cyclooxygenase (COX), with resulting inhibition of prostaglandin formation. However, prostaglandin E2 is an important positive factor in early inflammatory phase of bone healing, and NSAIDs have been associated with an inhibitory effect on spinal fusion. Ketorolac in particular has proven effective in postoperative pain management after orthopaedic procedures, leading to a decrease in morphine requirement and hospital stay,[12] but its use after spine surgery has been associated with pseudoarthrosis in a dose-dependent manner. Administration of ketorolac for more than 2 days and/or at a dose of greater than 120 mg/day has been implicated in pseudarthrosis after lumbar spinal fusion surgery.[13] Conversely, Pradhan et al reported that administration of ketorolac for less than 48 hours postoperatively has no significant effect on spinal fusion.[14] Perioperative NSAID use following spine surgery has remained controversial, with some support that selective COX-2 inhibitors or short-term, low-dose nonselective COX inhibitors do not increase the rate of nonunion.

Surgical Factors Affecting Fusion

Numerous factors affecting fusion are directly controllable by the spine surgeon. These include choice of bone graft, location of fusion site, graft site preparation, number of fusion levels, construct design, and biological modifiers. All of these factors should be taken into account in the formation and implementation of a surgical plan. The goal is to optimize patient outcomes by providing the highest chance of successful arthrodesis with the least surgical risk.

Properties of Bone Graft and Graft Selection

Multiple biological properties of bone graft will influence fusion rate: osteoconductivity, osteoinductivity, osteogenicity, mechanical strength, and vascularity.[5,15] Osteoconductivity refers to the ability of the graft to serve as a scaffold for bone healing, allowing for the attachment, proliferation, and differentiation of osteogenic precursor cells. Osteoinductivity refers to the ability of a graft to induce stem cell differentiation into osteoblasts. Multiple soluble factors have been associated with graft osteoinductivity. Many are part of the transforming growth factor–β (TGF-β) superfamily of growth factors, including BMP-2. Osteogenicity is the ability of the bone graft to provide osteoprogenitor cells, which eventually differentiate into osteoblasts and osteocytes. Mechanical strength of graft material may be important for load sharing when placed in the anterior column. Finally, successful fusion requires adequate blood supply for the recruitment of osteoinductive and osteogenic agents, and this may be directly achieved with the use of vascularized autograft.

Bone graft from an autologous source is the only graft material with osteogenic potential (►**Table 1**). Iliac crest

Table 1 Relative bone graft activity

Graft	Osteogenesis	Osteoconduction	Osteoinduction	Mechanical properties	Vascularity
Autograft					
Bone marrow	++	+/−	+	−	−
Cancellous	++	++	+	+	−
Cortical	+	+	+/−	++	−
Vascularized	++	+	+	++	++
Allograft					
Cancellous	−	+	+	+	−
Cortical	−	+/−	+/−	++	−
Demineralized	−	++	+++	−	−

Note: − = no activity; + = maximal activity.
Source: Adapted from Khan et al, Table 1.[5]

autograft is considered the gold standard for spinal fusion, but is limited by donor-site morbidities such as pain, hematoma, infection, and nerve injury, as well as added operative time and blood loss. Other common sources of autograft include local bone (for example, laminectomy bone), rib, or fibula. Regardless of the source, supply of autograft may be limited and bone graft extenders may be required.

Allograft bone does not contain live cells and provides only osteoconductive and osteoinductive potential. It is generally stored in fresh frozen or freeze-dried forms. Supply of allograft is theoretically abundant, but there is a small risk of disease transmission that is dependent on its processing. Demineralized bone matrix (DBM) is a form of allograft produced by acid extraction of bone, removing the mineral phase and leaving a matrix of collagenous and noncollagenous proteins. DBM has varying degrees of osteoconductive and osteoinductive potential without significant mechanical support. An additional option of bone graft extender is synthetic. Grafts such as β-tricalcium phosphate provide only a mechanical scaffold and are solely osteoconductive. Furthermore, the rate of resorption of synthetic grafts is an important consideration in their use, but they are readily available and carry no risk of disease transmission.[16] The selection of bone graft material for a given procedure must balance the innate graft properties that promote fusion, the quantity of graft material required, and the risks associated with their use and harvest.

Bone Morphogenetic Protein

Recombinant human bone morphogenetic protein–2 (rhBMP-2) is a synthetic protein with strong osteoinductive properties that has been used as an alternative to autologous bone graft in spinal fusion. The popularity of BMP has grown over the past two decades, with a variety of on- and off-label indications. On-label indication is single-level degenerative disc disease or spondylolisthesis in the lumbar spine, implanted via anterior or lateral interbody fusion accompanied by specific interbody devices. However, up to 85% of cases using BMP-2 has been performed in an off-label manner,[17] with the majority being posterior or transforaminal lumbar interbody fusions, or posterolateral lumbar fusions.

Multiple studies have demonstrated the efficacy on BMP-2 in lumbar spinal fusion. Arthrodesis rates have been comparable, if not superior, to iliac crest autograft for a variety of primary indications and fusion techniques.[18,19] In the setting of revision surgery for pseudoarthrosis, BMP-2 is at least as effective as bone graft. In a systematic review, Bodalia et al reported a 92.3% fusion rate with BMP-2, with a faster time to union when compared with bone graft alone.[20] More recently, the safety profile for use of BMP-2 has come under closer investigation.[21] Complications in the lumbar spine include retrograde ejaculation, subsidence, postoperative radiculitis, ectopic bone formation, osteolysis, and a concern for carcinogenesis.[22,23] Nevertheless, BMP-2 continues to be a strong option when tackling cases with a high risk of nonunion, such as in smokers or long fusions, when there is proven pseudoarthrosis or when other graft options are lacking or contraindicated.

Graft Location

Location of the fusion surface greatly influences the ability to achieve solid arthrodesis. Site of arthrodesis may be the anterior column, performed by interbody technique. This is a favorable fusion environment where the graft is placed under compression. With resulting load sharing and a vascularized recipient surface, fusion can be reliably achieved. Alternatively, fusion may be performed via a posterior approach. Posterior fusion surfaces include the paired facet joints and the intertransverse gutter. Posterior approach is familiar to all spine surgeons and allows ready access over multiple levels, but the graft surface is not load sharing and the graft is placed under tension. Lastly, combined anterior and posterior fusion (360° fusion) may be performed, but the complication rates are higher than either approach alone.[24]

Surgical Site Preparation

Adequate preparation of the fusion bed is vital to achieving solid arthrodesis. This includes the proper removal of all soft tissue, adequate hemostasis, decortication of non–load-bearing surfaces, and proper placement of bone graft. For interbody technique, this involves meticulous removal of disc material and cartilaginous endplates without damaging the bony endplates required for mechanical stability. For a posterolateral fusion, bony surfaces and paired facet joints are decorticated and interposing soft tissue such as muscle or cartilage carefully removed. Decortication allows for local marrow stimulation and release of osteoinductive proteins and an adjunct blood supply; this must be counterbalanced against overzealous technique leading to thermal necrosis at the graft site.

Fusion Construct

Performing a spinal fusion with instrumentation allows creation of a rigid construct that eliminates motion between segments and increases the fusion rate.[25,26] In the lumbar spine, the most common technique for spinal instrumentation is posterior pedicle screw fixation. Posterior screw fixation via cortical bone trajectory has been recently described in the lumbar spine[27] and is commonly indicated for fixation in osteopenic or osteoporotic bone.[28] Additional instrumentation techniques include anterior or lateral fixation into the vertebral bodies, frequently performed to supplement interbody fusion performed through the same surgical approach. Rigid fixation is particularly important at junctional levels which experience greater biomechanical stress. Additional levels of fixation may be required for example, iliac instrumentation in long fusions extending to the lumbosacral junction. In a cadaveric study, Cunningham et al reported long fusions above L3 significantly increased the strain on S1 screws and recommended supplemental fixation with iliac screws.[29]

Global and regional spinal alignment can also affect fusion rates. Positive sagittal balance places greater strain on the fusion construct. The resulting cantilever moment may result in early failure. Thoracolumbar junction is particularly vulnerable to failure given the biomechanical transition from rigid, kyphotic thoracic spine to mobile, lordotic lumbar spine. Thoracolumbar kyphosis greater than 20° has been associated with pseudoarthrosis.[30] In the setting of significant deformity, correction may require a combination of interbody fusions, spinal osteotomies, and long-segment instrumentation.

Electric Bone Growth Stimulation

Electric stimulation in the postoperative period has been used to augment fusion. Passage of an electric current results in increased collagen synthesis and fibrocyte recruitment to the fusion site. Direct current stimulation (DCS) requires intraoperative placement of electrodes in contact with the fusion mass. Pulsed electromagnetic field stimulation (PEMFS) and capacitively coupled electrical stimulation (CCES) may be applied externally. In an updated clinical guideline for use of bone growth stimulators as an adjunct for lumbar fusion, Kaiser et al found limited evidence for the use of DCS in patients younger than 60 years, but insufficient evidence to recommend for or against the use of PEMFS or CCES.[31]

Surgical Fusion of the Lumbar Spine

The lumbar spine is the most common site for spinal arthrodesis. It is typically performed for degenerative conditions with evidence of mechanical instability, such as spondylolisthesis or adult scoliosis. Multiple surgical approaches are available to achieve fusion in the lumbar spine.[32] When selecting surgical approach, consideration should be paid to the level of spinal fusion, number of fusion levels required, spinal alignment, and the possibility of concurrent autograft harvest.

Posterior approach for lumbar spinal fusion is the most commonly performed technique. The fusion bed is typically through the facet joints and intertransverse gutters, often supplemented with posterior pedicle screw instrumentation.[19,33] The intervertebral disc space may also be accessed from a posterior approach and an interbody fusion performed via posterior lumbar interbody fusion (PLIF) or transforaminal lumbar interbody fusion (TLIF) techniques (►**Fig. 1**). Posterior fusions may be performed via open or minimally invasive techniques (MI-TLIF). Posterior approach is the workhorse for lumbar spinal fusion and allows ready access and rigid fixation over multiple spinal levels. Disadvantages include pain from dissection and retraction of the paraspinal muscles, potential for nerve root injury, limited surface area for fusion, and a limited ability to correct sagittal alignment without additional osteotomy.

Access to the lumbar spine may also be obtained from an anterior or lateral approach. Anterior approach to the lumbar spine is performed in the supine position with retroperitoneal dissection (anterior lumbar interbody fusion [ALIF]), and allows access to the intervertebral discs of the mid to lower lumbar spine. The greatest surgical risk is vascular. Ligation of the iliolumbar vein is necessary for safe retraction of the aorta and inferior vena cava at or above the level of the bifurcation, generally at L4–5, and surgical exposure by an experienced vascular surgeon is recommended. The cephalad limit to anterior access is frequently the L3–4 disc space.

Lateral approach to the lumbar spine has been gaining in popularity. The patient is positioned in the lateral decubitus position, and the anterior column of the lumbar spine is accessed by splitting the oblique muscles, followed by retroperitoneal dissection to the intervertebral disc space. Lateral access is a favored by many surgeons for its relative technical ease and the ability to address multiple levels; it is also well

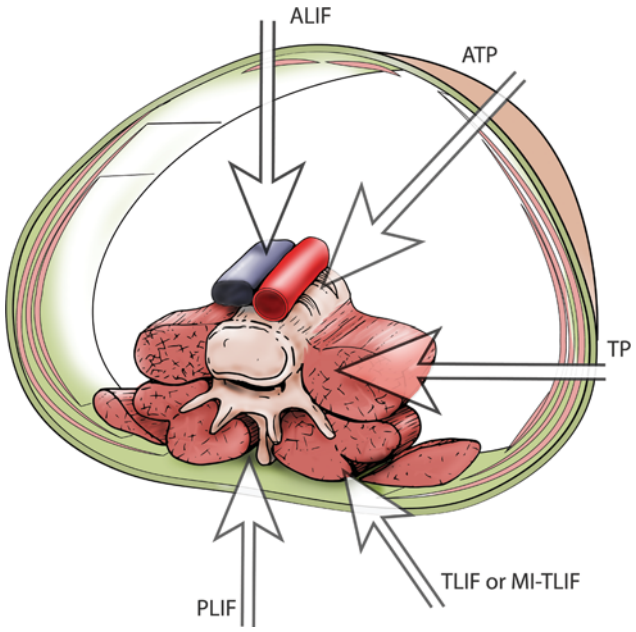

Fig. 1 Surgical approaches to the lumbar spine for interbody fusion techniques. The five primary interbody fusion approaches are shown here schematically: anterior (ALIF), lateral or extreme lateral interbody fusion (LLIF or XLIF), oblique lumbar interbody fusion/anterior to psoas (OLIF/ATP), transforaminal lumbar interbody fusion (TLIF) or minimally invasive transforaminal lumbar interbody fusion (MI-TLF), and posterior lumbar interbody fusion (PLIF). Reproduced with permission from Baylor College of Medicine.

tolerated by most patients. An additional benefit is the ability to provide correction in the coronal plane for scoliotic deformities. Variation in surgical approach is dependent on its relation to the psoas muscle. Transpsoas approach (TP) (lateral lumbar interbody fusion [LLIF], extreme lateral interbody fusion [XLIF])[34] may have a higher rate of nerve injury, particularly at more caudal levels. Symptoms include thigh pain, numbness, and quadriceps weakness. Incidence of neurologic complications has been reported at upwards of 30% in the immediate postoperative period, with the vast majority of cases being transient in nature.[35] Furthermore, access to the caudal levels (L5–S1, occasionally L4–5) may be restricted by the pelvic brim. Anterior to psoas approach (ATP) (oblique lateral interbody fusion [OLIF]) allows oblique access to the disc space with posterior retraction of the psoas muscle.[36] Rate of neurologic injury is lower with ATP approach, and more caudal levels of the lumbar spine can be accessed, but there is a greater potential for vascular injury.[37] Disc space access via anterior or lateral approaches (ALIF, TP, ATP) is more extensive than through posterior techniques (PLIF, TLIF) and allows for placement of graft material spanning a wider surface area. In addition, there is greater ability to correct sagittal plane malalignment via anterior or lateral interbody fusion. Supplemental fixation may be performed through the same surgical approach, or via separate posterior approach.

Varying fusion rates of the lumbar spine have been reported and are dependent on the presence of instrumentation and surgical approach. Zdeblick reported 65% successful arthrodesis without instrumentation, increasing to 77% with semirigid instrumentation, and 95% with rigid instrumentation.[38] Christensen et al demonstrated 80% fusion rate with posterolateral arthrodesis with instrumentation for degenerative lumbar disease, but a 92% fusion rate with the addition of ALIF.[39] More recent studies have shown similar results in fusions performed for degenerative lumbar disease, with successful arthrodesis in 84 to 92% in posterior lumbar fusion with rigid instrumentation.[40] Addition of anterior, transforaminal, or posterior interbody technique to rigid fixation increases the fusion rate to 88 to 100%. Similar fusions rates have been reported for lateral interbody fusions.[41]

Assessing Fusion Status

The increase in the number of lumbar spinal fusions performed has seen a concomitant rise in the number of pseudoarthroses. Detection of pseudarthrosis can be challenging, and the presence or absence of solid arthrodesis has not always been correlated with clinical outcomes.

Kornblum et al reported 56% "good" or "excellent" outcomes despite pseudoarthrosis in patients undergoing posterolateral lumbar spinal fusion for degenerative spondylolisthesis.[42]

Conversely, as low those 26% of patients with pseudoarthrosis undergoing revision fusion will improve to "good" or "excellent" despite a 94% fusion rate.[43]

Diagnosis of pseudoarthrosis begins with clinical suspicion. When symptomatic, pain is the most common complaint. Pain is predominantly axial lower back in location, often with a mechanical component, but may additionally involve neurologic symptoms such as neurogenic claudication or radiculopathy. Diagnosis should be confirmed radiographically. The most common imaging modality is plain radiography in orthogonal planes. Arthrodesis is confirmed by observing solid bone bridging across the site of attempted fusion. If a posterolateral fusion was performed, solid bridging of the transverse processes may be observed on an anteroposterior view (►**Fig. 2A–E**). If an interbody fusion was performed, then bony bridging may be seen across the disc space. Pseudoarthrosis is indicated by the absence of bridging ossification or by the presence of a radiolucent line across the fusion mass. If instrumentation is present, pseudoarthrosis may be indicated by hardware fracture (►**Fig. 2A,B**) or loosening (►**Fig. 3A–E**). Multiple studies have reported on the sensitivity (85–89%) and specificity (60–62%) of static radiographs in the assessment of a solid fusion.[44] Dynamic radiographs in flexion and extension may increase sensitivity, but not specificity.[45] In the absence of instrumentation, motion through the prior fusion is indicative pseudoarthrosis, although

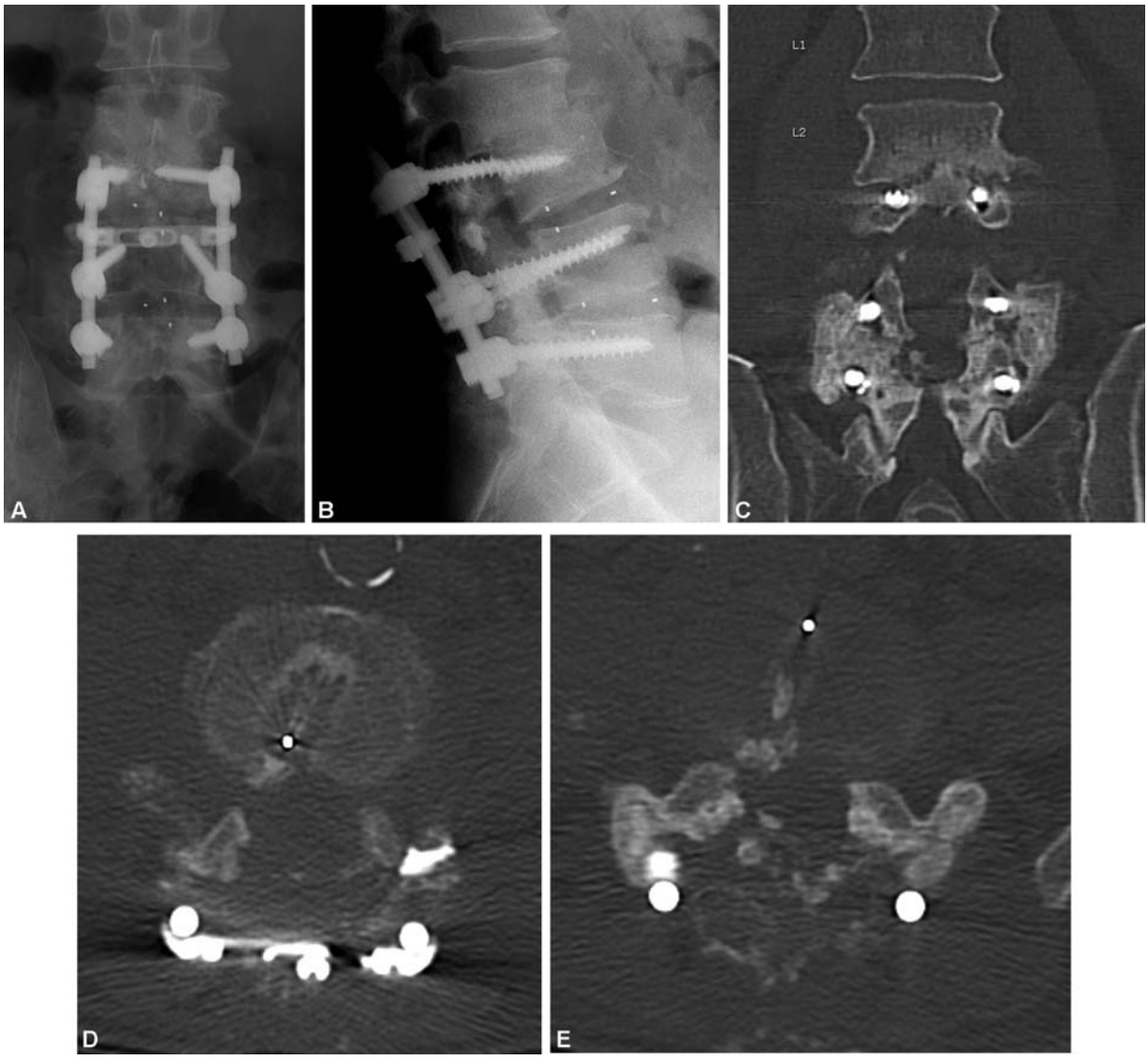

Fig. 2 A 67-year-old man, smoker, 4 years s/p multiple posterior lumbar spinal surgeries, complicated by postoperative surgical site infection treated with multiple debridements and antibiotics. Static AP and lateral radiographs demonstrate posterior instrumentation and interbody devices spanning L3–5 and adjacent-level kyphotic collapse (**A**,**B**). Fractured L3 pedicle screw is indicative of pseudoarthrosis at L3–4, although intertransverse fusion mass is seen spanning L4–5. Fine cut axial CT scan with coronal reconstruction confirms failure of fusion at L3–4 (**C**,**D**), but solid arthrodesis at L4–5 (**C**,**E**). s/p, status-post.

there is no universal agreement to the degree of motion required.

Computed tomography (CT) scans with thin cut axial images and three-dimensional (3D) reconstructions afford the greatest accuracy in diagnosis of a solid arthrodesis. Presence of bilateral intertransverse bridging bone is indicative of a solid posterior arthrodesis (►**Fig. 2C**). Conversely, absence of facet fusion is more indicative of pseudarthrosis (►**Fig. 2D**). CT is recommended as the imaging study of choice to assess fusion status.[34] Other imaging modalities have also been described, such as magnetic resonance imaging (MRI), ultrasonography, and technetium-99m bone scan, but these modalities are not recommended for the assessment of fusion status following spine surgery. The gold standard for assessment of fusion is intraoperative exploration, but the invasive nature of this modality precludes its routine use for diagnostic purposes.

Management of Pseudoarthrosis in the Lumbar Spine

Once symptomatic pseudarthrosis of the lumbar spine has been confirmed, management will consist of identifying its contributing factors and their optimization. A common systemic contributor is nicotine intake; when possible, cessation of smoking should precede revision surgery and extend for a period of time after surgery. Osteoporosis may contribute to insufficient rigidity of fixation and an

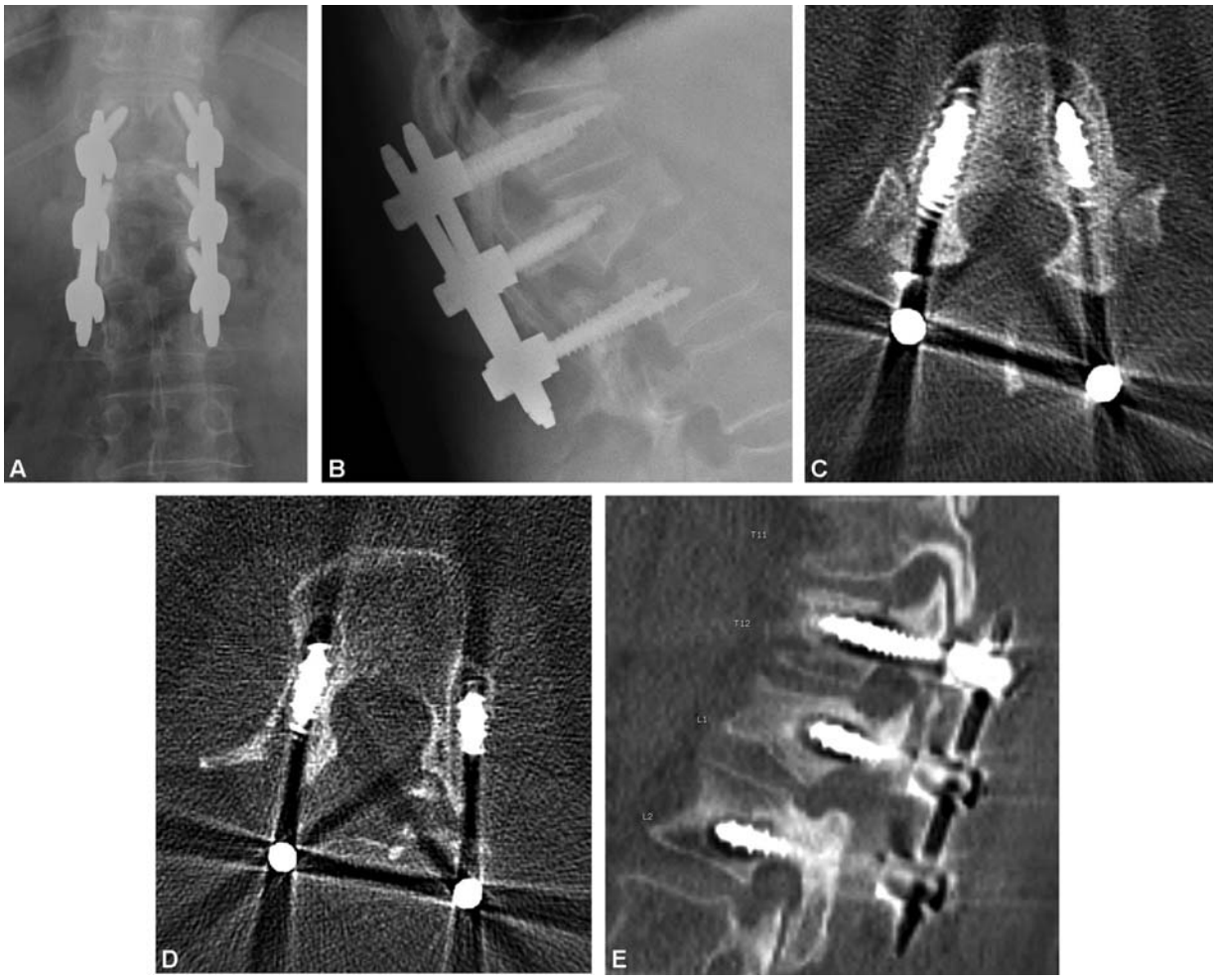

Fig. 3 A 57-year-old woman with diffuse large B-cell lymphoma and pathologic fracture of L1, 2 years postoperatively from posterior laminectomy and instrumented fusion T12–L2 and postoperative radiation therapy to the surgical site. Static AP and lateral radiographs (**A**,**B**) demonstrate loosening of pedicle screw instrumentation, as indicated by haloing around the screws. Haloing is confirmed by axial fine-cut CT scan at T12 and L2 (**C**,**D**) with sagittal reconstruction (**E**).

increase in bone mineral density prior to revision may be indicated.

Contributing surgical factors should be addressed and a surgical plan implemented to optimize fusion. These include access for surgical approach, techniques for rigid fixation, availability of bone graft material, supplemental biologics such BMP-2, and the use of vascularized bone graft. A change in surgical approach may involve the use of interbody technique to repair a failed posterolateral fusion, or performing a posterior fusion with rigid fixation for a failed anterior or lateral interbody fusion. Commonly, revision circumferential fusion may be required (►**Fig. 4A, B**). Technique of fixation may need to be altered. If prior posterior fixation is present, instrumentation fracture or loosening may preclude rigid fixation using similar technique. Other than an increase in screw diameter or length, fixation from an alternative approach (anterior or lateral), or using an alternative technique (such as cortical bone trajectory) should be considered. Choice of bone graft may also be altered, with greater consideration for use of iliac crest autograft if available. Additional consideration should be given to use of osteobiologics such as rhBMP-2, or electric bone growth stimulator. Finally, if other options to optimize the fusion milieu are unavailable or contraindicated, vascularized bone grafting may be indicated.

Conclusion

An increase in the rate of lumbar spinal fusion surgery has resulted in a concomitant rise in the number of pseudoarthroses. Imaging studies should include a combination of radiographs and CT scan to confirm diagnosis. Once identified, any modifiable systemic risk factors should be addressed. Surgical treatment should be individualized to improve the chance of successful revision fusion—such as optimizing the choice of graft material, surgical approach,

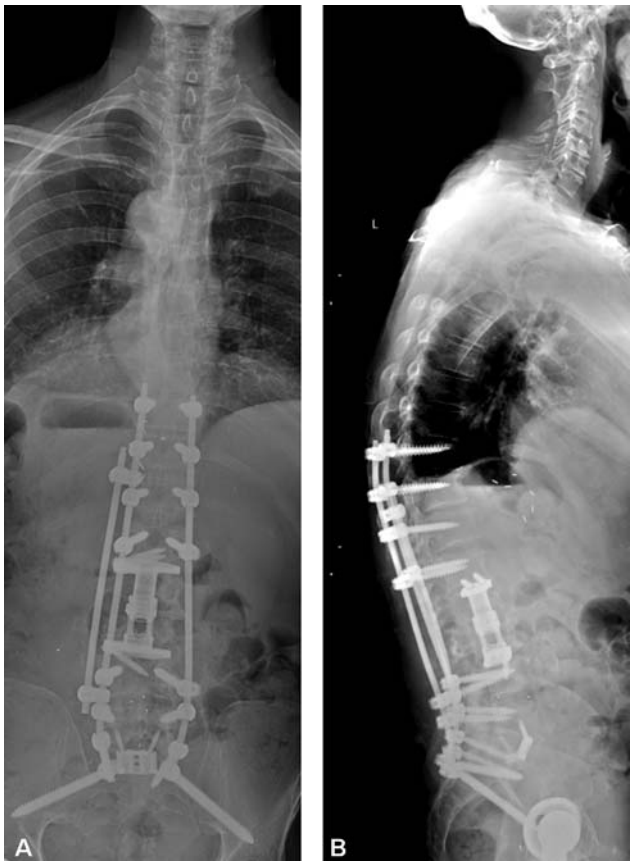

Fig. 4 Full length anteroposterior and lateral static radiographs after revision surgery for patient shown in ►**Fig. 2**. Preoperative bone mineral density, nutrition, and smoking status were optimized, and clearance of prior surgical-site infection confirmed prior to surgery. (**A**,**B**) Staged revision was performed, with posterior instrumentation removal and osteotomies, anterior corpectomies of L2 and L3 with reconstruction, anterior lumbar interbody fusion at L5–S1, and posterior instrumented fusion T10–pelvis with use of rhBMP-2.

and biomechanical fixation—within the limits of surgical risks and surgeon comfort.

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Conflict of Interest
None declared.

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References

1 Albee FH. Transplantation of a portion of the tibia into the spine for Pott's disease. J Am Med Assoc 2007;460:14–6
2 Rajaee SS, Bae HW, Kanim LE, Delamarter RB. Spinal fusion in the United States: analysis of trends from 1998 to 2008. Spine 2012; 37(01):67–76
3 Burchardt H, Enneking WF. Transplantation of bone. Surg Clin North Am 1978;58(02):403–427
4 Kalfas IH. Principles of bone healing. Neurosurg Focus 2001;10 (04):E1
5 Khan SN, Cammisa FP Jr, Sandhu HS, Diwan AD, Girardi FP, Lane JM. The biology of bone grafting. J Am Acad Orthop Surg 2005;13 (01):77–86
6 Berman D, Oren JH, Bendo J, Spivak J. The effect of smoking on spinal fusion. Int J Spine Surg 2017;11(04):29
7 Daftari TK, Whitesides TE Jr, Heller JG, Goodrich AC, McCarey BE, Hutton WC. Nicotine on the revascularization of bone graft. An experimental study in rabbits. Spine 1994;19(08):904–911
8 Theiss SM, Boden SD, Hair G, Titus L, Morone MA, Ugbo J. The effect of nicotine on gene expression during spine fusion. Spine 2000;25(20):2588–2594
9 Glassman SD, Anagnost SC, Parker A, Burke D, Johnson JR, Dimar JR. The effect of cigarette smoking and smoking cessation on spinal fusion. Spine 2000;25(20):2608–2615
10 Carlson BB, Burton DC, Jackson RS, Robinson S. Recidivism rates after smoking cessation before spinal fusion. Orthopedics 2016; 39(02):e318–e322
11 Kurd MF, Kreitz T, Schroeder G, Vaccaro AR. The role of multimodal analgesia in spine surgery. J Am Acad Orthop Surg 2017;25 (04):260–268
12 Kinsella J, Moffat AC, Patrick JA, Prentice JW, McArdle CS, Kenny GN. Ketorolac trometamol for postoperative analgesia after orthopaedic surgery. Br J Anaesth 1992;69(01):19–22
13 Li J, Ajiboye RM, Orden MH, Sharma A, Drysch A, Pourtaheri S. The effect of ketorolac on thoracolumbar posterolateral fusion: a systematic review and meta-analysis. Clin Spine Surg 2018;31 (02):65–72
14 Pradhan BB, Tatsumi RL, Gallina J, Kuhns CA, Wang JC, Dawson EG. Ketorolac and spinal fusion: does the perioperative use of ketorolac really inhibit spinal fusion? Spine 2008;33(19):2079–2082
15 Prolo DJ. Biology of bone fusion. Clin Neurosurg 1990;36:135–146
16 Grabowski G, Cornett CA. Bone graft and bone graft substitutes in spine surgery: current concepts and controversies. J Am Acad Orthop Surg 2013;21(01):51–60
17 Ong KL, Villarraga ML, Lau E, Carreon LY, Kurtz SM, Glassman SD. Off-label use of bone morphogenetic proteins in the United States using administrative data. Spine 2010;35(19):1794–1800
18 Simmonds MC, Brown JV, Heirs MK, et al. Safety and effectiveness of recombinant human bone morphogenetic protein-2 for spinal fusion: a meta-analysis of individual-participant data. Ann Intern Med 2013;158(12):877–889
19 Fu R, Selph S, McDonagh M, et al. Effectiveness and harms of recombinant human bone morphogenetic protein-2 in spine fusion: a systematic review and meta-analysis. Ann Intern Med 2013;158(12):890–902
20 Bodalia PN, Balaji V, Kaila R, Wilson L. Effectiveness and safety of recombinant human bone morphogenetic protein-2 for adults with lumbar spine pseudarthrosis following spinal fusion surgery: a systematic review. Bone Joint Res 2016;5(04):145–152
21 Carragee EJ, Hurwitz EL, Weiner BK. A critical review of recombinant human bone morphogenetic protein-2 trials in spinal surgery: emerging safety concerns and lessons learned. Spine J 2011; 11(06):471–491
22 Carragee EJ, Chu G, Rohatgi R, et al. Cancer risk after use of recombinant bone morphogenetic protein-2 for spinal arthrodesis. J Bone Joint Surg Am 2013;95(17):1537–1545
23 Cahill KS, McCormick PC, Levi AD. A comprehensive assessment of the risk of bone morphogenetic protein use in spinal fusion surgery and postoperative cancer diagnosis. J Neurosurg Spine 2015;23(01):86–93

24 Fritzell P, Hägg O, Wessberg P, Nordwall ASwedish Lumbar Spine Study Group. Chronic low back pain and fusion: a comparison of three surgical techniques: a prospective multicenter randomized study from the Swedish lumbar spine study group. Spine 2002;27 (11):1131–1141
25 Fischgrund JS, Mackay M, Herkowitz HN, Brower R, Montgomery DM, Kurz LT. 1997 Volvo Award winner in clinical studies. Degenerative lumbar spondylolisthesis with spinal stenosis: a prospective, randomized study comparing decompressive laminectomy and arthrodesis with and without spinal instrumentation. Spine 1997;22(24):2807–2812
26 Matz PG, Meagher RJ, Lamer T, et al. Guideline summary review: an evidence-based clinical guideline for the diagnosis and treatment of degenerative lumbar spondylolisthesis. Spine J 2016;16 (03):439–448
27 Santoni BG, Hynes RA, McGilvray KC, et al. Cortical bone trajectory for lumbar pedicle screws. Spine J 2009;9(05):366–373
28 Tortolani PJ, Stroh DA. Cortical bone trajectory technique for posterior spinal instrumentation. J Am Acad Orthop Surg 2016; 24(11):755–761
29 Cunningham BW, Sefter JC, Hu N, Kim SW, Bridwell KH, McAfee PC. Biomechanical comparison of iliac screws versus interbody femoral ring allograft on lumbosacral kinematics and sacral screw strain. Spine 2010;35(06):E198–E205
30 How NE, Street JT, Dvorak MF, et al. Pseudarthrosis in adult and pediatric spinal deformity surgery: a systematic review of the literature and meta-analysis of incidence, characteristics, and risk factors. Neurosurg Rev 2019;42(02):319–336
31 Kaiser MG, Eck JC, Groff MW, et al. Guideline update for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 17: bone growth stimulators as an adjunct for lumbar fusion. J Neurosurg Spine 2014;21(01):133–139
32 Mobbs RJ, Phan K, Malham G, Seex K, Rao PJ. Lumbar interbody fusion: techniques, indications and comparison of interbody fusion options including PLIF, TLIF, MI-TLIF, OLIF/ATP, LLIF and ALIF. J Spine Surg 2015;1(01):2–18
33 Ghogawala Z, Dziura J, Butler WE, et al. Laminectomy plus fusion versus laminectomy alone for lumbar spondylolisthesis. N Engl J Med 2016;374(15):1424–1434
34 Ozgur BM, Aryan HE, Pimenta L, Taylor WR. Extreme lateral interbody fusion (XLIF): a novel surgical technique for anterior lumbar interbody fusion. Spine J 2006;6(04):435–443
35 Kwon B, Kim DH. Lateral lumbar interbody fusion: Indications, outcomes and complications. J Am Acad Orthop Surg 2016;24 (02):96–105
36 Silvestre C, Mac-Thiong JM, Hilmi R, Roussouly P. Complications and morbidities of mini-open anterior retroperitoneal lumbar interbody fusion: oblique lumbar interbody fusion in 179 patients. Asian Spine J 2012;6(02):89–97
37 Quillo-Olvera J, Lin GX, Jo HJ, Kim JS. Complications on minimally invasive oblique lumbar interbody fusion at L2-L5 levels: a review of the literature and surgical strategies. Ann Transl Med 2018;6(06):101
38 Zdeblick TA. A prospective, randomized study of lumbar fusion. Preliminary results. Spine 1993;18(08):983–991
39 Christensen FB, Hansen ES, Eiskjaer SP, et al. Circumferential lumbar spinal fusion with Brantigan cage versus posterolateral fusion with titanium Cotrel–Dubousset instrumentation: a prospective, randomized clinical study of 146 patients. Spine 2002; 27(23):2674–2683
40 Chun DS, Baker KC, Hsu WK. Lumbar pseudarthrosis: a review of current diagnosis and treatment. Neurosurg Focus 2015;39(04): E10
41 Teng I, Han J, Phan K, Mobbs R. A meta-analysis comparing ALIF, PLIF, TLIF and LLIF. J Clin Neurosci 2017;44:11–17
42 Kornblum MB, Fischgrund JS, Herkowitz HN, Abraham DA, Berkower DL, Ditkoff JS. Degenerative lumbar spondylolisthesis with spinal stenosis: a prospective long-term study comparing fusion and pseudarthrosis. Spine 2004;29(07):726–733, discussion 733–734
43 Carpenter CT, Dietz JW, Leung KY, Hanscom DA, Wagner TA. Repair of a pseudarthrosis of the lumbar spine. A functional outcome study. J Bone Joint Surg Am 1996;78(05):712–720
44 Choudhri TF, Mummaneni PV, Dhall SS, et al. Guideline update for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 4: radiographic assessment of fusion status. J Neurosurg Spine 2014;21(01):23–30
45 Brodsky AE, Kovalsky ES, Khalil MA. Correlation of radiologic assessment of lumbar spine fusions with surgical exploration. Spine 1991;16(6, Suppl):S261–S265