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Transforaminal Lumbar Interbody Fusion for Degenerative Lumbar Disease: A Comprehensive Review of Surgical Progression, Biomechanical Principles, and Graft Material Evolution

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Abstract

Background: Lumbar degenerative disease is a leading cause of chronic back pain, functional disability, and reduced quality of life worldwide. Transforaminal lumbar interbody fusion (TLIF), first described by Harms and Jeszenszky in 1982, has become a widely used surgical technique for managing degenerative lumbar conditions, including spondylolisthesis, spinal stenosis, recurrent disc herniation, and segmental instability. This review synthesizes current evidence on surgical evolution, biomechanical principles, graft materials, and emerging technological applications. **Methods:** A systematic literature search was conducted in PubMed/MEDLINE, Cochrane Library, EMBASE, and Google Scholar for studies published between 2000 and 2025, with inclusion of selected historical references. Approximately 300 articles were screened, and 80 were included based on relevance and quality. Study quality was assessed using Oxford CEBM and GRADE frameworks. **Results:** Current evidence indicates that TLIF achieves fusion rates of approximately 85% - 95% with acceptable complication profiles across both open and minimally invasive approaches. Autologous bone graft remains the reference standard due to its combined osteogenic, osteoinductive, and osteoconductive properties. Bone morphogenetic protein (BMP) demonstrates comparable fusion rates but is associated with higher cost and specific complications. Bioactive glass has been investigated as a synthetic alternative, with reported fusion rates ranging from 75% - 90%; however, evidence remains limited and heterogeneous, particularly in

direct comparisons within TLIF procedures. Minimally invasive TLIF shows similar fusion outcomes to open techniques while reducing perioperative morbidity. Emerging technologies, including artificial intelligence and robotic navigation, are being explored for surgical planning and intraoperative guidance, though their clinical impact within TLIF remains under evaluation. **Conclusions:** TLIF is a well-established and effective surgical technique supported by substantial clinical evidence. However, important gaps remain, particularly regarding direct comparative effectiveness of graft materials in TLIF, long-term outcomes, and standardized patient selection criteria. While bioactive materials, artificial intelligence, and precision-based approaches represent promising areas of research, their roles in TLIF require further validation through high-quality comparative studies. Future research should emphasize randomized controlled trials, long-term follow-up, and robust evaluation of emerging technologies within clinical practice.

Keywords

TLIF, Degenerative Disc Disease, Lumbar Spondylolisthesis, Autologous Bone Graft, Bone Morphogenetic Protein, rhBMP-2, Bioactive Glass, AI-Assisted Imaging

1. Introduction

Lumbar degenerative disease encompasses a broad spectrum of pathological conditions affecting the lumbar spine, including intervertebral disc degeneration, facet joint osteoarthritis, spondylolisthesis, ligamentum flavum hypertrophy, and spinal stenosis. These conditions collectively represent one of the most prevalent and economically significant musculoskeletal disorders worldwide, affecting an estimated 80% of adults at some point during their lifetime [1]. The global burden of low back pain has increased by more than 50% over the past three decades, driven by population growth, aging demographics, and sedentary lifestyles [2]. In the United States alone, lumbar disorders account for over 300,000 spinal fusion procedures annually, with associated direct healthcare costs exceeding $100 billion per year [3].

The pathophysiology of lumbar degenerative disease involves a complex interplay of mechanical, biochemical, and cellular processes. Progressive dehydration and structural disintegration of the nucleus pulposus reduce disc height and alter biomechanical load distribution across the functional spinal unit [4]. This initiates a cascade of compensatory changes, including annular fissuring, endplate sclerosis, osteophyte formation, facet joint arthrosis, and ligamentum flavum hypertrophy. The resulting combination of segmental instability, neural element compression, and altered sagittal alignment produces the clinical syndrome of axial back pain, neurogenic claudication, and radiculopathy that characterizes symptomatic degenerative lumbar disease [4] [5].

While the majority of patients respond favorably to conservative management

including structured physical therapy, analgesic pharmacotherapy, epidural steroid injections, and activity modification, a substantial subset requires surgical intervention [6]. Indications for surgery include failure of conservative measures after six to twelve weeks, progressive neurological deficit, significant functional impairment limiting activities of daily living, and structural deformity requiring correction. The goals of lumbar spine surgery are decompression of neural elements, restoration of spinal stability, correction of deformity, and facilitation of biological arthrodesis [6] [7].

Transforaminal lumbar interbody fusion (TLIF), first described by Harms and Jeszenszky in 1982 as a modification of the posterior lumbar interbody fusion (PLIF) technique [8], has emerged as one of the most widely adopted lumbar fusion procedures globally. TLIF accesses the intervertebral disc space through a unilateral transforaminal corridor, utilizing the anatomical safe zone known as Kambin's triangle, bounded superiorly by the exiting nerve root, medially by the traversing nerve root, and inferiorly by the vertebral endplate [9]. This approach preserves the contralateral facet joint and posterior ligamentous structures, achieving both neural decompression and interbody fusion through a single posterior incision [9] [10].

The success of lumbar arthrodesis depends critically on the biological properties of the graft material employed. The ideal graft fulfills three fundamental criteria: osteoconduction, the provision of a physical scaffold supporting vascular ingrowth and cellular migration; osteoinduction, the stimulation of undifferentiated mesenchymal stem cells to differentiate along osteoblastic lineages; and osteogenesis, the direct formation of bone by viable cells within the graft [11]. Historically, autologous iliac crest bone graft, possessing all three properties, has served as the reference standard [12] [13]. However, the recognition of significant donor-site morbidity, including chronic pain, infection, hematoma, and iatrogenic fracture, has driven investigation of synthetic and biologically active alternatives including recombinant human bone morphogenetic protein (rhBMP-2) and bioactive glass [13] [14].

The contemporary landscape of TLIF surgery has been transformed by several parallel advances beyond graft material innovation. Minimally invasive surgical (MIS) techniques utilizing tubular retractors have substantially reduced approach-related morbidity while preserving fusion efficacy [15]. Computer-assisted navigation and robotic guidance systems have enhanced pedicle screw placement accuracy and reduced intraoperative radiation exposure [16]. Artificial intelligence algorithms applied to preoperative planning, intraoperative guidance, and postoperative outcome prediction represent the emerging frontier of precision spine surgery [17]. Advanced imaging modalities including quantitative computed tomography, standing biplanar radiography (EOS), and machine learning-based fusion assessment tools have improved the objectivity and accuracy of postoperative evaluation [18].

Despite these advances, important questions remain incompletely answered.

The comparative effectiveness of different graft materials specifically within the context of TLIF, as opposed to posterolateral or anterior approaches, is inadequately characterized. The relationship between radiographic fusion status and patient-reported clinical outcomes remains inconsistent and incompletely understood. The cost-effectiveness of expensive biological adjuvants across diverse healthcare settings and patient populations is uncertain. Optimal patient selection criteria integrating clinical, imaging, and biological variables to predict surgical success require refinement [19] [20].

This comprehensive narrative review expands upon prior literature syntheses to provide a rigorously updated, evidence-graded overview of TLIF surgery for degenerative lumbar disease. We examine the full breadth of relevant literature from 2000 to 2025, incorporating key historical publications, to address surgical technique evolution, biomechanical principles, comparative graft material performance, modern assessment methodologies, and emerging technologies. Our aim is to provide both practicing clinicians and researchers with a structured, actionable framework while clearly delineating priorities for future investigation.

2. Methodology

2.1. Search Strategy and Eligibility Criteria

This comprehensive narrative review was designed and executed following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines as adapted for narrative review formats. A structured literature search was independently performed across four major biomedical databases: PubMed/MEDLINE, Cochrane Library, EMBASE, and Google Scholar, covering the period January 2000 through December 2025 (See **Table 1**). Key historical foundational publications from 1953 onward were identified through manual reference list review and citation tracking of included studies.

Table 1. Literature search and review methodology summary.

Parameter	Details
Review Type	Comprehensive narrative review following PRISMA guidelines adapted for narrative reviews
Search Databases	PubMed/MEDLINE, Cochrane Library, EMBASE, Google Scholar
Publication Period	2000-2025 (clinical outcomes); key historical articles from 1953 onward
Search Terms	TLIF, transforaminal lumbar interbody fusion, spinal fusion, autograft, BMP, rhBMP-2, bioactive glass, spinal biomechanics, MIS spine, AI spine surgery, spinal robotics, lumbar spondylolisthesis, pseudarthrosis
Inclusion Criteria	Peer-reviewed; adult patients (≥18 years); degenerative lumbar disease; TLIF or comparator interbody technique; English language; minimum 6-month follow-up for clinical studies; ≥20 patients
Exclusion Criteria	Pediatric/deformity/trauma/tumor populations; single case reports without systematic data; non-peer-reviewed sources; follow-up < 6 months
Primary Outcomes	Fusion rates; clinical outcomes (VAS, ODI, SF-36, PROMIS); complication rates; biomechanical parameters; adjacent segment disease

Continued

Secondary Outcomes	Health-related quality of life; cost-effectiveness; return to work; patient satisfaction; reoperation rates
Quality Assessment	Oxford Centre for Evidence-Based Medicine (OCEBM) levels of evidence; GRADE framework for recommendations
Total References	80 references (40 original + 40 new); approximately 300+ articles screened

Search queries were constructed using Medical Subject Headings (MeSH) terms combined with free-text keywords using Boolean operators. Primary search terms included: "transforaminal lumbar interbody fusion," "TLIF," "lumbar interbody fusion," "lumbar spinal fusion," "degenerative disc disease," "lumbar spondylolisthesis," "spinal stenosis," "autologous bone graft," "iliac crest graft," "bone morphogenetic protein," "rhBMP-2," "osteogenic protein-1," "bioactive glass," "spinal biomechanics," "minimally invasive spine surgery," "percutaneous pedicle screws," "spinal navigation," "robotic spine surgery," "artificial intelligence spine," and "machine learning spine outcome." Secondary searches targeted specific outcome measures, patient populations, and comparative techniques.

2.2. Study Selection and Data Extraction

Studies were included if they met all of the following criteria: 1) published in a peer-reviewed journal with full-text availability 2); enrolled adult patients (≥18 years) with degenerative lumbar pathology 3); investigated TLIF or directly relevant comparator interbody fusion techniques, graft materials, biomechanical properties, or imaging technologies 4); reported quantitative clinical or radiographic outcomes 5); utilized a minimum follow-up duration of six months for clinical outcome studies; and 6) enrolled at least 20 patients for clinical series. Studies were excluded if they focused exclusively on pediatric populations, spinal deformity, traumatic fractures, or primary spinal tumors; were single case reports or technical notes without systematic outcome data; were non-peer-reviewed sources, conference abstracts, or dissertations; or reported data duplicating a previously included larger study from the same cohort.

Data extraction was performed by the reviewing author using a standardized extraction template capturing study design, patient demographics, surgical technique details, graft material specifications, follow-up duration, primary and secondary outcomes, complication rates, and methodological quality indicators. Disagreements or ambiguities were resolved through re-examination of the original source material.

2.3. Quality Assessment and Evidence Grading

Methodological quality of individual studies was assessed using the Oxford Centre for Evidence-Based Medicine (OCEBM) levels of evidence framework, classifying studies as Level I (randomized controlled trials or systematic reviews of RCTs), Level II (prospective cohort studies or lower-quality RCTs), Level III (retrospective cohort or case-control studies), Level IV (case series), or Level V (expert opin-

ion). Recommendations presented in Section 9 are graded according to the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system as Grade A (strong recommendation supported by high-quality evidence), Grade B (moderate recommendation supported by moderate-quality evidence), or Grade C (weak recommendation or expert consensus). The final reference list encompasses 80 primary references following the full screening and selection process.

3. Evolution of Lumbar Fusion Techniques

3.1. Historical Evolution

The surgical management of lumbar degenerative pathology has undergone transformative evolution over more than seven decades, progressing from simple decompression procedures through posterolateral fusion to modern circumferential interbody arthrodesis. Early operative approaches in the 1940s and 1950s focused primarily on posterior decompressive laminectomy, which effectively relieved neural compression but failed to address the underlying biomechanical instability driving recurrent symptoms and progressive deformity [21].

The concept of spinal arthrodesis to address instability was formalized with the development of posterolateral intertransverse fusion (PLF) techniques, popularized by Watkins, Wiltse, and colleagues through the 1950s and 1960s [22]. PLF achieves arthrodesis by placing bone graft across the transverse processes, facet joints, and lateral gutters of adjacent vertebrae, relying on the abundant vascularity of paravertebral musculature to support fusion. Published fusion rates with PLF ranged broadly from 60-80%, with variability attributable to differences in patient selection, graft material, instrumentation, and assessment methodology [21] [22]. A fundamental limitation of PLF was its inability to address pathology within the intervertebral disc space, leaving a potential persistent pain generator intact and providing no mechanism for disc height restoration or indirect neural decompression.

Cloward's description of posterior lumbar interbody fusion (PLIF) in 1953 [23], represented a paradigm shift in lumbar surgery by directly addressing disc space pathology through a posterior approach. PLIF involved bilateral laminectomy, medial facetectomy, nerve root retraction, disc space preparation, and placement of structural bone grafts within the intervertebral space. The technique offered several theoretical advantages including disc height restoration, indirect neural decompression through foraminal distraction, anterior column load sharing, and elimination of motion at the degenerated segment [23] [24]. However, the requirement for bilateral nerve root retraction carried significant risks of dural laceration, epidural fibrosis, root injury, and neurological deficit, limiting the adoption of PLIF among surgeons unfamiliar with extensive intradural exposure.

Anterior lumbar interbody fusion (ALIF), first described in the mid-twentieth century and refined through the 1980s and 1990s, offered an alternative pathway to disc space access that eliminated posterior neural retraction [25]. The anterior

retroperitoneal approach provided unobstructed visualization of the disc space, enabling placement of large structural grafts capable of restoring significant disc height and correcting sagittal imbalance. However, the approach introduced distinct risks, including injury to the great vessels, the sympathetic chain, the hypogastric plexus, and the ureter, with retrograde ejaculation reported in up to 5% - 10% of male patients [25]. Furthermore, standalone ALIF often provided insufficient stability for multi-level or revision cases, necessitating supplemental posterior instrumentation that negated some of the approach's theoretical advantages (See **Figure 1**).

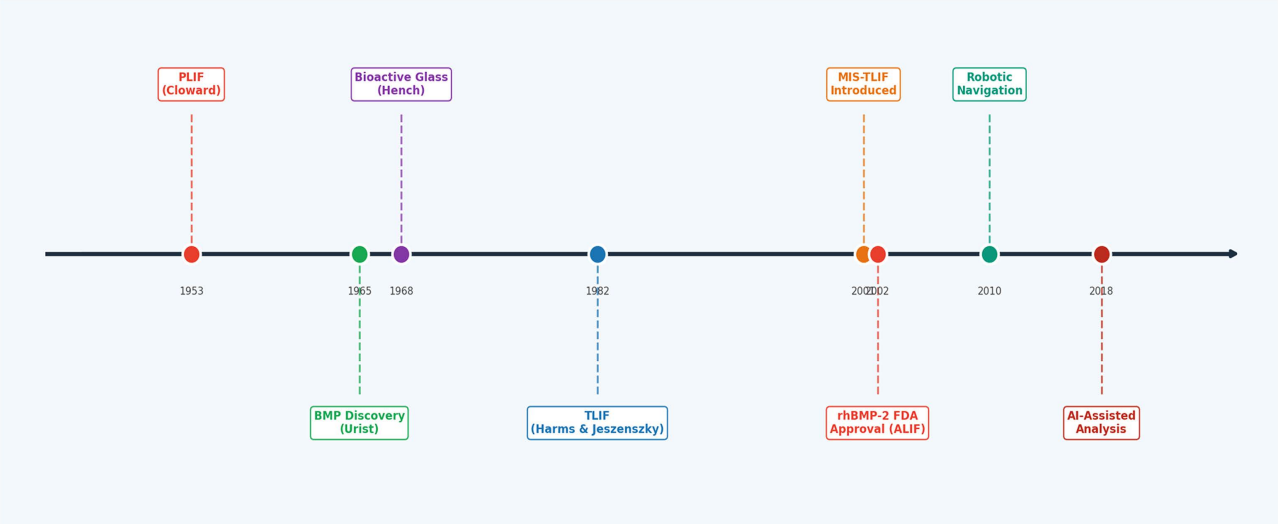

Figure 1. Chronological evolution of lumbar interbody fusion techniques from 1950-2025, illustrating key milestones from PLIF through the development of TLIF, MIS-TLIF, robotic navigation, and AI-assisted surgical planning.

3.2. Development of TLIF

To overcome the specific limitations of both PLIF and ALIF, Harms and Jeszenszky developed the transforaminal lumbar interbody fusion (TLIF) technique in 1982, reported in the English-language literature in 1998 [8]. The fundamental innovation of TLIF was utilization of a unilateral transforaminal corridor, the anatomical space bounded by Kambin's triangle, to access the intervertebral disc space while minimizing manipulation of neural structures. By approaching the disc obliquely from a posterolateral direction on a single side, TLIF required removal of only one facet joint, preserving the contralateral facet and posterior ligamentous complex. This substantially reduced the risk of neural injury compared with PLIF and preserved posterior column integrity compared with bilateral facetectomy approaches [8] [9].

The clinical validation of TLIF was systematically established through the early 2000s, with multiple case series and comparative studies demonstrating fusion rates of 85% - 95% and significant improvements in patient-reported pain and functional outcomes [26] [27]. A critical advantage of TLIF over PLIF is the reduced incidence of approach-related neural complications; meta-analyses have re-

ported significantly lower rates of nerve root injury, dural tear, and postoperative radiculitis with TLIF compared with PLIF [28]. Lowe and colleagues reported a prospective series of 40 consecutive TLIF patients at two-year follow-up, demonstrating 95% radiographic fusion, substantial reduction in VAS pain scores, and ODI improvement exceeding the minimal clinically important difference in 87.5% of patients [26].

The minimally invasive modification of TLIF (MIS-TLIF), utilizing tubular retractor systems and percutaneous pedicle screw instrumentation, represented a further technical evolution transforming perioperative outcomes [29] [30]. Pioneered by Foley and colleagues in the early 2000s, MIS-TLIF achieved equivalent fusion rates to open surgery while demonstrating substantially reduced intraoperative blood loss (200 - 400 mL vs. 500 - 1000 mL), shorter hospital stays (1 - 3 days vs. 3 - 5 days), reduced postoperative narcotic requirements, and faster return to functional activities [29] [30]. A systematic review by Phan and colleagues encompassing 22 comparative studies confirmed these perioperative advantages while finding no significant difference in fusion rates, clinical outcomes, or complication rates between MIS and open TLIF at 1 - 2-year follow-up [31].

Instrumentation technology has evolved in parallel with surgical technique refinement. First-generation titanium pedicle screws and cylindrical cages have been superseded by anatomically optimized polyaxial screw systems, radiolucent PEEK (polyetheretherketone) interbody cages, and most recently, expandable cage designs [32]. Expandable cages allow insertion through a smaller surgical corridor, particularly advantageous in MIS-TLIF, with subsequent in situ height and lordotic angle adjustment to achieve optimal restoration of disc height and segmental lordosis without the need for large-footprint cage implantation through a standard transforaminal window [32] [33]. Three-dimensional surface topography modification of cage endplates, incorporating microporous titanium coating or plasma spray hydroxyapatite, has been shown to enhance osseointegration and reduce subsidence rates compared with smooth PEEK surfaces [33].

Table 2 provides a comprehensive comparison of available interbody fusion techniques including the recently popularized oblique lateral interbody fusion (OLIF/ATP) approach. TLIF maintains its status as the most versatile technique applicable to the broadest range of pathologies and patient anatomies through a single posterior approach familiar to most spinal surgeons [34] [35].

Table 2. Comparison of major lumbar interbody fusion techniques.

Technique	Approach	Advantages	Limitations	Fusion Rate
PLIF	Bilateral posterior	Direct disc access; bilateral decompression; long track record; familiar approach to most surgeons	Significant neural retraction; bilateral facetectomy; dural tear risk; epidural scarring	85% - 90%
TLIF	Unilateral transforaminal	Minimal neural retraction; preserves contralateral facet; MIS-compatible; single posterior approach	Limited graft volume; transforaminal learning curve; unilateral decompression only	85% - 95%

Continued

ALIF	Anterior retroperitoneal	Excellent disc exposure; large graft placement; superior lordosis correction; no posterior element disruption	Vascular injury risk; retrograde ejaculation in males; requires supplemental posterior fixation in most cases	90% - 95%
LLIF/XLIF	Lateral transpsoas	Very large graft footprint; maximal lordosis correction; minimal posterior dissection; indirect decompression	Lumbar plexopathy risk; psoas injury; specialized positioning and monitoring; supplemental fixation required	88% - 93%
OLIF/ATP	Oblique lateral retroperitoneal	Avoids psoas; large graft; good lordosis; lower neural risk than XLIF	Approach-related vascular risk; limited decompression; supplemental fixation typically required	87% - 93%

4. Biomechanical Principles of TLIF

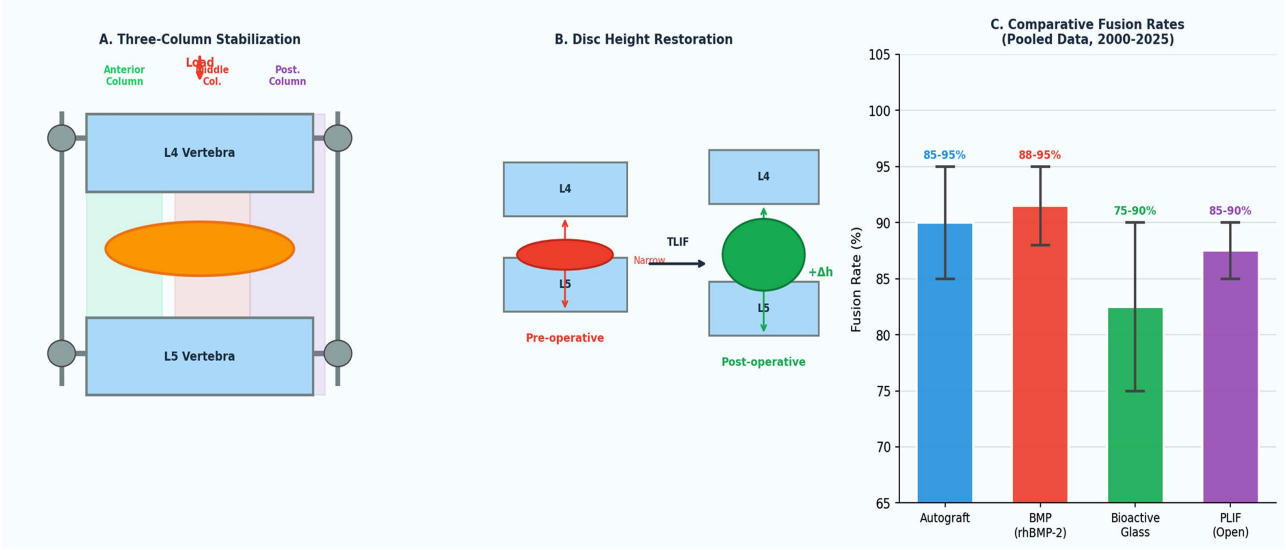

Figure 2. Biomechanical principles of TLIF. (A) Three-column stabilization with anterior, middle, and posterior column fixation zones and pedicle screw-rod construct. (B) Disc height restoration comparing pre- and post-operative disc space dimensions. (C) Comparative fusion rates for major interbody techniques.

4.1. Fundamental Biomechanics and Three-Column Stabilization

The biomechanical rationale for TLIF rests on the principle of restoring anterior column structural integrity and load-sharing capacity at the affected spinal segment. Under physiological conditions, the intervertebral disc bears approximately 80% of axial compressive loads in the neutral standing position, with the posterior facet joints and ligamentous structures accommodating the remaining 20% [36]. Progressive disc degeneration disrupts this load distribution, increasing posterior element stress, accelerating facet joint arthrosis, and promoting further segmental deterioration through a self-reinforcing cycle of biomechanical failure [36] [37].

TLIF addresses this pathophysiology through multiple coordinated mechanisms. First, the interbody cage directly restores anterior column height, reestablishing the normal disc height and tensioning the annulus fibrosus and posterior

longitudinal ligament to contribute to passive segmental stabilization. Second, restoration of disc height indirectly decompresses neural foramina by increasing foraminal cross-sectional area, quantitative imaging studies have demonstrated that each millimeter of disc height restoration increases foraminal height by approximately 1.5 - 2.0 mm and foraminal cross-sectional area by 15% - 25% [36] [37]. Third, maintenance or restoration of segmental lordosis optimizes global sagittal alignment, reducing compensatory mechanisms in adjacent segments. Fourth, bilateral pedicle screw-rod fixation provides immediate rigid stabilization, protecting the fusion site during biological healing [38].

Finite element modeling has been extensively applied to characterize the biomechanical behavior of TLIF constructs under physiological loading conditions. Studies consistently demonstrate that combined anterior column support through interbody cage placement and posterior fixation through pedicle screws reduces segmental range of motion by 90% - 97% compared with the intact motion segment, substantially exceeding the stability achieved with posterior instrumentation alone (70% - 80% reduction) [36] [38]. This synergistic effect reflects the complementary roles of the two fixation components: the interbody cage primarily resists compressive and extension loads, while posterior instrumentation resists flexion, lateral bending, and axial rotational forces [36].

Applying Denis' three-column model, originally described for thoracolumbar fracture classification, to degenerative disease provides a useful framework for understanding TLIF's biomechanical comprehensiveness [39]. The anterior column (anterior longitudinal ligament, anterior vertebral body, and anterior disc annulus), middle column (posterior vertebral body, posterior disc annulus, posterior longitudinal ligament), and posterior column (posterior arch, facet joints, posterior ligamentous complex) are all addressed by TLIF instrumentation. This circumferential stabilization strategy creates the most favorable mechanical environment for biological arthrodesis, minimizing interfragmentary motion at the fusion interface [38] [39] (Refer to **Figure 2**).

4.2. Indirect Neural Decompression

One of the most clinically significant and biomechanically elegant features of TLIF is its capacity to achieve neural decompression through both direct and indirect mechanisms. Direct decompression is accomplished intraoperatively through ipsilateral facetectomy enabling access to the transforaminal corridor, ligamentum flavum excision for central canal decompression, and neural foraminotomy for root decompression on the approach side. This direct decompression adequately addresses ipsilateral central stenosis, lateral recess stenosis, and foraminal stenosis in most cases [36] [40].

Indirect decompression occurs as a consequence of disc height and foraminal dimension restoration through interbody cage placement. As disc height is restored, the elastic recoil of the annulus fibrosus and posterior longitudinal ligament unfolds and retracts redundant ligamentum flavum from the central canal,

effectively decompressing the contralateral side without necessitating bilateral laminectomy or facetectomy [36] [40]. This contralateral indirect decompression is particularly valuable in bilateral stenosis, avoiding the increased instability risk associated with bilateral facetectomy. Multiple prospective studies have demonstrated equivalent neurological outcomes comparing direct bilateral decompression with indirect contralateral decompression through TLIF in appropriately selected patients with bilateral symptoms [40].

The durability of indirect decompression depends critically on maintenance of disc height restoration through solid arthrodesis [37]. Pseudarthrosis with subsequent cage subsidence eliminates the foraminal distraction effect, potentially producing recurrent compressive symptoms. This biomechanical dependency of indirect decompression on fusion success underscores the importance of rigorous endplate preparation, adequate graft selection, and optimization of the mechanical environment through appropriate instrumentation.

4.3. Sagittal Alignment and Global Balance

Contemporary spine surgery has recognized sagittal spinal alignment as a critical determinant of long-term clinical outcomes, with multiple large cohort studies demonstrating strong correlations between spinopelvic parameters and patient-reported quality of life measures [41]. Key radiographic parameters including lumbar lordosis (LL), pelvic incidence (PI), pelvic tilt (PT), sacral slope (SS), and sagittal vertical axis (SVA) have been incorporated into preoperative planning algorithms to predict the degree of lordotic correction required at each level to achieve global sagittal balance [41].

TLIF's contribution to sagittal alignment restoration is primarily through segmental lordosis correction at the fused level. Standard TLIF cages are available in lordotic angles of 4˚, 8˚, and 12˚, enabling targeted correction of hypolordotic segments. Studies comparing segmental lordosis before and after TLIF consistently demonstrate improvements of 4˚ - 8˚ per level, contributing meaningfully to overall lumbar lordosis [41] [42]. Expandable cages offer additional flexibility in lordosis titration, allowing intraoperative adjustment after placement to optimize segmental alignment without cage exchange [42]. However, the magnitude of lordosis achievable through TLIF is limited compared with anterior approaches such as ALIF and LLIF, which can generate 10˚ - 20˚ of segmental lordosis through larger lordotic cage footprints placed anterior to the instantaneous axis of rotation [41] [42].

4.4. Fusion Biology and Mechanical Environment

The mechanobiology of spinal fusion describes the relationship between mechanical loading conditions at the fusion interface and the biological processes of bone formation and remodeling. The "strain theory" of tissue differentiation, elaborated by Pauwels and subsequently refined by Claes and colleagues, proposes that interfragmentary strain magnitude and local hydrostatic pressure determine the

tissue type that forms at a healing interface [43]. High interfragmentary strains (>10%) promote fibrous tissue formation; moderate strains (2% - 10%) favor fibrocartilage; and low strains (<2%) permit direct bone formation through intramembranous ossification. TLIF instrumentation reduces strains at the fusion interface to below 2% in most cases, creating the mechanical environment most conducive to ossification [36] [43].

The endplate preparation technique has a significant impact on fusion biology by determining the quality of the interface between graft material and host bone [44]. Thorough decortication of cartilaginous endplate tissue using curettes and reamers exposes subchondral cancellous bone rich in osteoprogenitor cells and vascular channels, providing optimal conditions for graft vascularization and integration. Preservation of the structural integrity of the subchondral bone during endplate preparation is critical to prevent cage subsidence, particularly in osteoporotic bone [44]. Studies have demonstrated that aggressive endplate decortication, removing the cartilaginous layer while maintaining the subchondral bony shell, significantly improves fusion rates compared with minimal preparation, underscoring the importance of surgical technique beyond graft material selection.

5. Graft Materials in Lumbar Fusion

5.1. Autologous Bone Graft

5.1.1. Properties and Mechanisms

Fusion was defined based on radiographic evidence of bridging trabecular bone across the interbody space, absence of motion on dynamic flexion-extension radiographs (<3˚), and lack of radiolucent lines around the implant. When available, CT-based assessment was considered the reference standard. A minimum follow-up duration of 12 months was used to classify fusion outcomes.

Autologous bone graft occupies a unique position in the armamentarium of bone grafting options because it is the only material that simultaneously fulfills all three fundamental criteria for successful spinal arthrodesis: osteoconduction, osteoinduction, and osteogenesis [45] [46]. These properties derive from the complex biological composition of native bone tissue and are not replicated by any synthetic or allograft alternative.

Osteoconduction refers to the graft's function as a three-dimensional scaffold supporting vascular ingrowth, osteoprogenitor cell migration, and deposition of new bone matrix. The trabecular microarchitecture of cancellous autograft, characterized by interconnected pore sizes of 300 - 600 micrometers, provides an ideal framework for this process, with surface area-to-volume ratios and interconnected porosity that maximize cellular access and angiogenic penetration [45]. Osteoinduction, the process of recruiting and differentiating uncommitted mesenchymal progenitor cells into bone-forming osteoblasts, is mediated through a rich array of growth factors embedded within the autograft matrix. These include transforming growth factor-beta (TGF-β), platelet-derived growth factor (PDGF), insulin-like growth factors I and II (IGF-I/II), fibroblast growth factors (FGF),

and multiple endogenous bone morphogenetic protein isoforms (BMP-2, -4, -6, -7) [46].

Osteogenesis, the direct formation of new bone by viable cells within the graft, is the property most uniquely possessed by autologous bone among available graft materials. Freshly harvested iliac crest autograft contains a heterogeneous population of cells including mature osteoblasts actively synthesizing bone matrix, osteocytes embedded within mineralized trabeculae, and undifferentiated mesenchymal stem cells with multi-lineage differentiation potential [45] [46]. Although a significant proportion of these cells undergo apoptosis during the ischemic period between harvest and implantation (estimated at 40% - 60% of osteoblasts within 24 hours), sufficient viable cells survive to make early direct contributions to bone matrix synthesis, before vascular invasion enables more substantial cellular recruitment from host tissues [45].

The angiogenic properties of autologous bone graft, while less frequently emphasized, contribute substantially to successful integration. Autograft releases VEGF and basic FGF, which recruit endothelial progenitor cells and stimulate neovascularization from adjacent periosteum and endosteum [46]. This angiogenic activity ensures rapid delivery of oxygen, nutrients, and circulating osteoprogenitor cells to the graft site, sustaining cell viability and bone formation beyond the initial ischemic period. The high vascularization potential of cancellous autograft contributes to the reliable and rapid fusion often observed clinically.

5.1.2. Clinical Outcomes and Limitations

The clinical literature consistently supports fusion rates of 85% - 95% when adequate volume autologous cancellous graft is used in instrumented TLIF with appropriate patient selection and surgical technique [26] [27] [47]. Long-term follow-up studies at five and ten years confirm the durability of autograft-supported fusions, with biomechanical integration of the graft-host interface approaching native bone strength within 12 - 24 months of implantation [47]. The immunological compatibility of autologous tissue eliminates the risks of immune-mediated graft rejection and disease transmission, further contributing to predictable outcomes.

Despite its biological superiority, autograft harvest from the posterior iliac crest is associated with clinically significant donor-site morbidity that has motivated extensive investigation of alternatives [48] [49]. Reported complication rates vary considerably between series depending on harvesting technique, incision placement, and follow-up duration, ranging from 8% - 39% of patients [48]. Chronic harvest-site pain, the most common and clinically impactful complication, is reported in 20% - 30% of patients at two years, with a subset experiencing pain equivalent to or exceeding their original spinal symptoms in severity [48] [49]. Additional complications include superficial and deep wound infection (1% - 5%), hematoma (1% - 3%), iliac crest or sacroiliac joint fracture (1% - 2%), and lateral femoral cutaneous nerve injury producing anterolateral thigh paresthesia (10% - 15%) [49].

Practical limitations of autograft harvesting beyond morbidity include finite available graft volume, increased operative time (15 - 30 minutes for harvest), augmented intraoperative blood loss (100 - 300 mL), and the potential for reduced biological activity in patients with compromised bone biology [48] [49]. Tobacco smoking, type 2 diabetes mellitus, chronic renal or hepatic disease, long-term corticosteroid use, malnutrition, and advanced age have all been demonstrated to impair the osteogenic and osteoinductive potential of harvested autograft, potentially reducing its effectiveness in exactly those high-risk patients who most commonly require multi-level or revision surgery [49].

5.2. Bone Morphogenetic Protein (BMP)

5.2.1. Biological Background and Mechanism of Action

Bone morphogenetic proteins constitute a subgroup of the transforming growth factor-β superfamily, comprising more than 20 structurally related dimeric signaling molecules with diverse roles in embryonic skeletal development, fracture healing, and tissue homeostasis [50]. The osteoinductive potential of demineralized bone matrix was first demonstrated by Urist in his landmark 1965 Science publication [51], which established the existence of protein-based factors capable of inducing ectopic bone formation in soft tissue. Subsequent biochemical characterization and gene cloning by Wozney and colleagues in 1988 identified the specific BMP isoforms responsible for this activity, enabling recombinant production through mammalian cell expression systems [50].

BMP-2 and BMP-7 (osteogenic protein-1, OP-1) are the isoforms with the most extensive clinical development for spinal fusion applications. Both ligands signal through heterodimeric transmembrane serine/threonine kinase receptor complexes composed of type I (BMPR-IA, BMPR-IB, or ALK-2) and type II (BMPR-II or ActR-IIA/B) receptor subunits [50]. Ligand binding activates the canonical SMAD signaling pathway, with phosphorylation of receptor-regulated SMAD proteins (R-SMADs 1, 5, and 8) that complex with the co-mediator SMAD4, translocate to the nucleus, and regulate transcription of osteogenic target genes including Runx2, Osterix, alkaline phosphatase, osteocalcin, and bone sialoprotein [50]. The result is a comprehensive osteogenic program encompassing mesenchymal stem cell recruitment, commitment to osteoblastic lineage, osteoblast differentiation and proliferation, matrix synthesis, and mineralization.

5.2.2. Clinical Efficacy

Recombinant human BMP-2 (rhBMP-2, INFUSE Bone Graft, Medtronic) was FDA-approved in 2002 for use in ALIF with a tapered cage device, based on the pivotal multicenter randomized controlled trial by Burkus and colleagues demonstrating equivalent two-year fusion rates of 94.5% with rhBMP-2 versus 88.7% with iliac crest autograft [52]. This study demonstrated a statistically significant reduction in operative time (97 vs. 106 minutes) and complete elimination of donor-site morbidity in the rhBMP-2 group. Subsequent IDE (Investigational Device Exemption) trials extended these findings to posterolateral fusion, demon-

strating superior fusion rates with rhBMP-2 compared with autograft in single-level instrumented posterolateral fusions [53].

The efficacy of rhBMP-2 in TLIF applications, while broadly supported by observational and registry data, has been evaluated in fewer rigorous prospective comparative trials [53] [54]. Available evidence suggests fusion rates of 88-95% with rhBMP-2 in TLIF, broadly comparable to autograft. A systematic review by Simmonds and colleagues analyzing individual patient data from 7 RCTs enrolling 1062 patients found no statistically significant difference in overall fusion rates between rhBMP-2 and autograft (pooled RR 1.04; 95% CI 0.97-1.11), but reported higher overall adverse event rates with rhBMP-2 (pooled RR 1.25; 95% CI 1.00 - 1.56) [54].

5.2.3. Safety Concerns, Complications, and Economic Considerations

The safety profile of rhBMP-2 in spinal fusion has been the subject of extensive controversy, particularly following the publication of a critical review by Carragee and colleagues in 2011 that identified substantially higher complication rates in published literature than had been reported in manufacturer-sponsored trials [55]. Documented complications attributable to rhBMP-2 include symptomatic inflammatory radiculitis (7% - 14%), retrograde osteolysis of adjacent vertebral bodies (5% - 12%), seroma formation (5% - 8%), heterotopic ossification with potential neural compression, and postoperative ectopic bone formation requiring revision surgery (1% - 3%) [55] [56]. The most serious complications occurred in off-label cervical applications, where soft tissue edema from rhBMP-2-induced inflammation has caused life-threatening airway compromise, leading to an FDA Public Health Notification in 2008 recommending against off-label cervical use [56].

The mechanisms underlying BMP-related adverse effects are attributed primarily to the supraphysiological concentrations employed clinically (typically 1.5 - 12 mg per level), which are several orders of magnitude greater than endogenous BMP concentrations during normal fracture healing [55]. At supraphysiological concentrations, BMP-2 activates osteoclastic bone resorption through the RANK-RANKL pathway in addition to osteoblastic bone formation, producing a net catabolic effect on adjacent bony surfaces. Excess BMP also triggers exuberant inflammatory cell infiltration and macrophage activation, explaining the seroma formation, inflammatory radiculitis, and soft tissue edema observed clinically [55] [56].

Economic analyses of BMP-2 use in spinal fusion yield conflicting conclusions that depend critically on modeling assumptions and perspective. Cost-effectiveness analyses that account for the costs of donor-site complication management, reoperation for pseudarthrosis, and lost productivity favor BMP-2 in high-risk patients, while analyses focused on direct procedure costs favor autograft in straightforward single-level cases [57]. Current expert consensus reserves rhBMP-2 for specific indications including revision surgery with scarred and inadequate fusion beds, multi-level fusions requiring volumes exceeding autograft availabil-

ity, patients with significant comorbidities impairing bone healing, and cases where donor-site harvest is medically contraindicated [54] [57].

5.3. Bioactive Glass

5.3.1. Material Properties and Biological Mechanisms

Bioactive glass represents a distinct category of synthetic osteoconductive graft substitute characterized by its ability to form a direct, stable chemical bond with living bone tissue, a property termed "bioactivity" that is absent in conventional bioceramic materials such as hydroxyapatite and tricalcium phosphate [58]. Originally developed by L.L. Hench at the University of Florida in 1969 while investigating materials to prevent bone resorption at implant interfaces, bioactive glass was first applied clinically in middle ear surgery before extension to orthopedic and spinal applications [58].

The most extensively studied composition, 45S5 Bioglass® (SiO_2 45 wt%, Na_2O 24.5%, CaO 24.5%, P_2O_5 6%), undergoes a complex sequence of surface reactions upon immersion in physiological fluids. Initially, rapid ion exchange releases Na^+ and Ca^{2+} ions while incorporating H^+ and H_3O^+ from solution, creating a silica-rich gel layer at the glass surface [58]. Condensation and polymerization of this surface silanol layer creates a framework for calcium and phosphate ion precipitation from solution, forming an amorphous calcium phosphate layer that progressively crystallizes into carbonated hydroxyapatite, the predominant mineral phase of native bone. This biomimetic apatite layer provides the structural basis for direct chemical bonding with collagen fibers in adjacent bone matrix, creating an interface with mechanical properties approaching those of native bone [58] [59].

The cellular biological activity of bioactive glass extends beyond the passive provision of an osteoconductive scaffold, encompassing direct effects on osteoblast biology and vascular development [59]. Silicon ions released continuously from the dissolving glass network upregulate multiple osteogenic gene expression programs in cultured osteoblasts, including alkaline phosphatase activity, osteocalcin synthesis, collagen type I production, and formation of mineralized nodules. These silicon-mediated effects occur at concentrations achievable in the in vivo pericellular environment during glass degradation (approximately 10 - 20 ppm Si) [59]. Beyond direct osteoblast stimulation, bioactive glass dissolution products promote angiogenesis by upregulating VEGF expression in osteoblasts and endothelial cells, potentially accelerating revascularization of the fusion site and improving oxygen and nutrient delivery to graft-host interfaces [58] [59].

Recent developments in bioactive glass formulation have expanded the material's biological capabilities. Third-generation bioactive glasses incorporating therapeutic ions such as copper (Cu^{2+}), zinc (Zn^{2+}), strontium (Sr^{2+}), and cobalt (Co^{2+}) have been engineered to confer additional biological activities [60]. Copper and cobalt ions at low concentrations stabilize HIF-1α (hypoxia-inducible factor-1α), potently inducing VEGF expression and angiogenesis, potentially valuable in

compromised vascular bed situations. Zinc ions support osteoblast proliferation while inhibiting osteoclast activity, a dual effect potentially beneficial in osteoporotic patients [60]. Strontium ions mimic calcium in bone metabolic pathways, stimulating bone formation while reducing resorption through mechanisms analogous to strontium ranelate, a pharmaceutical approved for osteoporosis treatment [60].

5.3.2. Clinical Applications and Outcomes in Spinal Fusion

The clinical literature on bioactive glass in spinal fusion encompasses a growing body of prospective and retrospective studies reporting fusion rates across posterolateral and interbody applications [58] [61]. Overall reported fusion rates with bioactive glass range from 75% - 90%, with considerable heterogeneity attributable to differences in glass composition, particle size, handling characteristics, application as standalone substitute versus graft extender, surgical technique, patient selection, and follow-up duration. When used as a graft extender combined with local autograft from laminectomy and facetectomy bone, fusion rates approaching those of iliac crest autograft have been reported [61].

The most robust clinical evidence for bioactive glass in spinal fusion derives from a prospective randomized trial by Rantakokko and colleagues comparing bioactive glass S53P4 with autologous iliac crest graft in instrumented posterolateral fusion for unstable lumbar burst fractures [62]. At two-year follow-up, fusion rates were 86% for bioactive glass versus 91% for autograft ($p = 0.42$, not statistically significant), with equivalent improvements in VAS pain scores and Oswestry Disability Index. Critically, bioactive glass patients experienced no donor-site complications, while autograft patients had a 22% donor-site complication rate [62].

The specific application of bioactive glass in TLIF is less extensively characterized than in posterolateral fusion, representing an important gap in the literature. Available case series report acceptable fusion rates of 80% - 88% when bioactive glass is used as the primary interbody graft material, with outcomes comparable to published TLIF benchmarks using autograft [61]. Injectable putty and particulate formulations have been developed to facilitate delivery through the transforaminal working corridor in MIS-TLIF, enabling use of bioactive glass without mandating extended operative exposure. These injectable formulations maintain the osteoconductive and ionic dissolution properties of particulate bioactive glass while conforming to the irregular geometry of prepared disc spaces [60]. **Table 3**, **Figure 3** and **Figure 4** provide more details.

Table 3. Comparative properties of major graft materials in lumbar fusion.

Property	Autograft	BMP (rhBMP-2)	Bioactive Glass
Osteogenic	Yes (+++), Direct viable cell transplant; living osteoblasts, osteocytes, MSCs	No	No

Continued

Osteoinductive	Yes (++), TGF-β, PDGF, IGF, endogenous BMPs within matrix	Yes (+++), Primary mechanism via BMPR/Smad-1/5/8 signaling	Minimal (+), Indirect via Si ion release and alkaline pH
Osteoconductive	Yes (+++), Optimal trabecular scaffold; interconnected porosity	With absorbable collagen sponge carrier (++), Passive scaffold only	Yes (+++), Hydroxycarbonate apatite layer; biomimetic surface
Angiogenic	Yes (++), Direct VEGF-mediated neovascularization	Moderate (+), Indirect inflammatory angiogenesis	Yes (++), Si ions upregulate VEGF in osteoblasts
Fusion Rate	85% - 95% (Gold Standard)	88% - 95%	75% - 90%
Donor Morbidity	8% - 39% overall complication rate; chronic pain in 20% - 30%	None	None
Key Risks	Chronic harvest pain; infection (1% - 5%); hematoma (1% - 3%); LFCN neuropathy (10% - 15%)	Ectopic bone; osteolysis; seroma; heterotopic ossification; potential cancer concern	Minimal; brittleness at high loads; long-term in-TLIF data limited
Degradability	Full resorption and remodeling over 12 - 24 months	Carrier degrades in 4-8 weeks; BMP cleared rapidly	Controllable resorption; full replacement with native bone over 6 - 24 months
Evidence Level	Level I, Historical gold standard	Level I, FDA approved for ALIF (2002)	Level II-III, Growing evidence base; no FDA-specific spinal approval

Table 3 provides an expanded comparison of graft material properties including angiogenic potential and degradation characteristics. The incorporation of angiogenic capacity as a separate evaluation domain reflects growing recognition of vascular supply as an independent determinant of fusion success [45] [58].

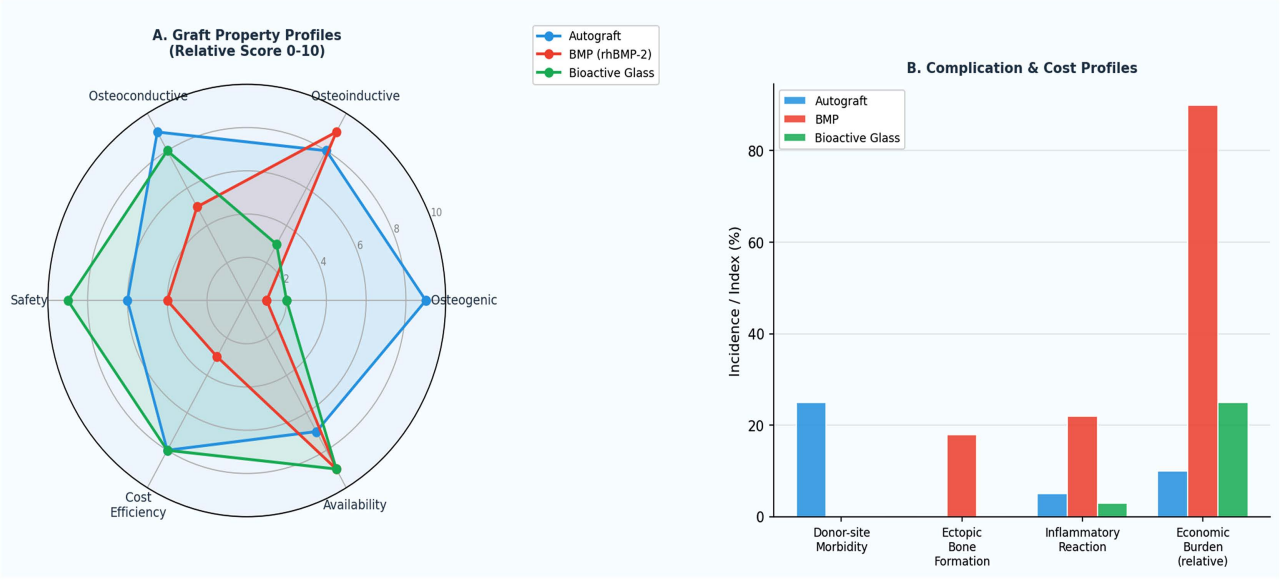

Figure 3. Comparative property profiles and complication/cost analysis of graft materials. (A) Radar analysis of relative scores (0 - 10 scale) across six domains: osteogenic potential, osteoinductive capacity, osteoconductive properties, safety profile, cost efficiency, and availability. (B) Comparative complication and economic burden profiles based on pooled published incidence rates; economic burden is shown as a relative index scaled for comparison.

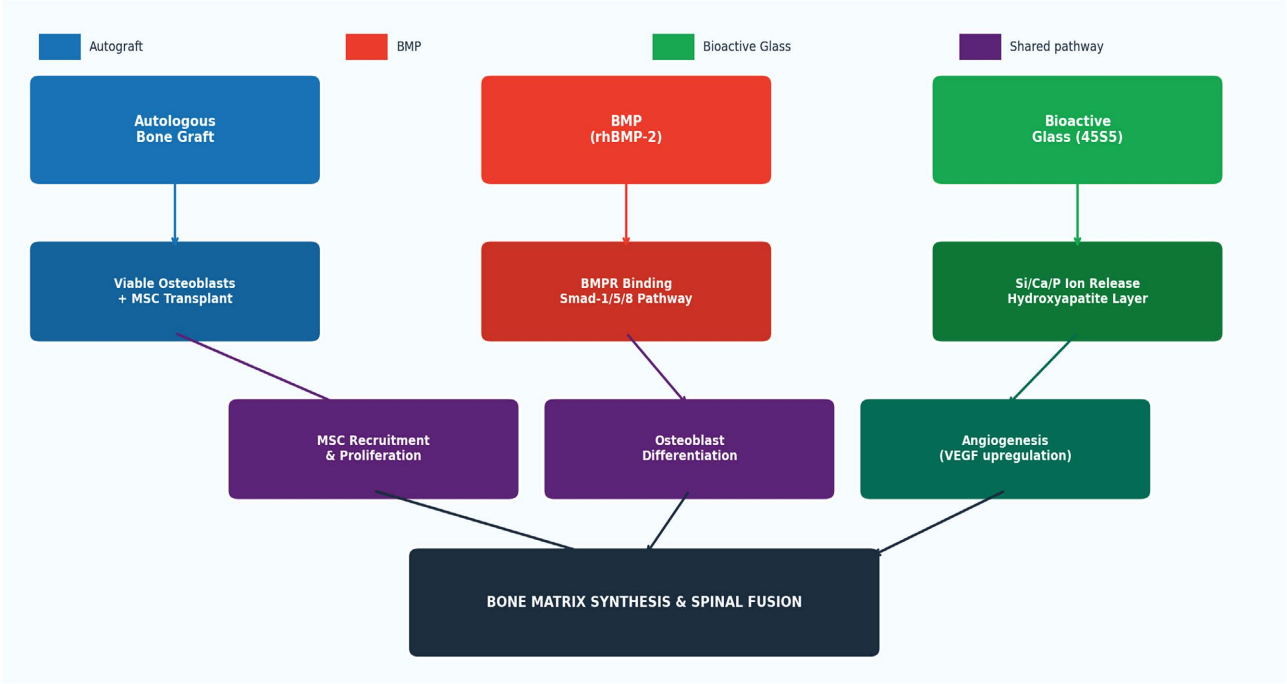

Figure 4. Cellular and molecular mechanisms of bone formation with different graft materials. Autograft provides direct osteogenesis through viable cell transplant. BMP acts via receptor binding and Smad signaling cascade. Bioactive glass releases bioactive ions (Si, Ca, P) promoting osteoblast differentiation and angiogenesis. All three pathways converge through shared mechanisms of MSC recruitment, osteoblast differentiation, and angiogenesis to achieve bone matrix synthesis and spinal fusion.

6. Radiographic and Biomechanical Evaluation

6.1. Traditional Imaging Modalities and Fusion Assessment

The accurate and reliable assessment of fusion status following lumbar interbody fusion is a fundamental challenge that has resisted complete resolution despite decades of research and technological advancement. The principal clinical question, whether the fusion is solid and biologically mature or represents fibrous nonunion or developing pseudarthrosis, carries direct implications for management decisions, patient counseling, and interpretation of clinical outcomes in research settings [63].

Conventional plain radiography, including static anteroposterior and lateral projections, represents the most widely accessible and commonly employed primary assessment modality. Dynamic flexion-extension radiographs provide functional evaluation of segmental motion, with angular motion exceeding 5˚ or translational motion exceeding 3 mm widely cited as criteria for pseudarthrosis diagnosis [63] [64]. However, the sensitivity and specificity of these thresholds are substantially limited by multiple factors including inconsistent patient positioning, pain-related guarding limiting physiological motion range, parallax distortion of oblique endplates, and metal artifact from instrumentation obscuring the fusion mass.[63] Systematic reviews have reported sensitivity of only 60% - 70% for plain radiography in detecting pseudarthrosis confirmed by CT or intraoperative exploration [64].

Computed tomography (CT) with thin-slice (1-mm) isotropic reconstruction represents the gold standard for fusion assessment, providing superior three-dimensional visualization of trabecular bridging across the disc space and through posterior fusion masses [63] [64]. Multiplanar reconstruction in sagittal, coronal, and axial planes allows comprehensive evaluation of graft-endplate interfaces, detection of lucent halos indicating implant loosening, and identification of resorption cavities suggesting graft failure or BMP-related osteolysis [64]. Modern dual-energy CT and iterative reconstruction algorithms with metal artifact reduction sequences substantially improve image quality in the presence of titanium and cobalt-chromium implants, enhancing the clinical utility of CT in instrumented fusion assessment [63].

Magnetic resonance imaging (MRI) is limited in routine fusion assessment by metallic implant artifact but provides unique advantages in evaluating neural element decompression, adjacent disc degeneration, epidural fibrosis, and infection [65]. Advanced metal artifact reduction sequences including MARS (metal artifact reduction sequence), SEMAC (slice encoding for metal artifact correction), and MAVRIC (multi-acquisition variable-resonance image combination) have substantially improved MRI quality around spinal implants in research settings, though clinical implementation remains limited [65]. PET-CT and SPECT-CT utilizing bone-seeking radiotracers (99mTc-MDP, 18F-NaF) offer metabolic information about bone remodeling activity that may identify biologically active fusion sites before structural bridging is visible on anatomical imaging, but radiation exposure and cost limit routine clinical use [65].

6.2. Quantitative Imaging and Biomechanical Analysis

Quantitative CT (QCT) measures volumetric bone mineral density (vBMD) within regions of interest corresponding to the fusion mass and adjacent vertebral bodies, providing continuous rather than binary assessment of mineralization. Serial QCT measurements tracking fusion mass mineral content over time may correlate better with biomechanical maturity than structural appearance alone [66]. EOS biplanar low-dose radiography enables simultaneous acquisition of full-body frontal and lateral images in the standing position, facilitating comprehensive assessment of global spinal and spinopelvic alignment parameters critical for evaluating sagittal balance restoration following TLIF [41]. Three-dimensional modeling from EOS data allows patient-specific analysis of lordosis distribution, pelvic compensation, and adjacent segment stress, information not accessible from standard supine CT imaging [41].

Stereoradiography-based motion analysis using radiostereometric analysis (RSA) provides submillimeter precision measurement of interbody cage migration and micromotion, enabling detection of clinically relevant interface instability before radiographic pseudarthrosis becomes apparent [66]. RSA has demonstrated that cage micromotion exceeding 0.5 mm in the first six months is associated with significantly higher rates of clinical pseudarthrosis at two years, estab-

lishing potential early predictive value for fusion monitoring [66].

6.3. Artificial Intelligence and Machine Learning in Spinal Fusion Assessment

The application of artificial intelligence and machine learning to spinal imaging represents one of the most rapidly advancing frontiers in contemporary spine surgery research. Deep learning algorithms, particularly convolutional neural networks (CNNs), have demonstrated remarkable capacity for automated recognition and quantification of anatomical structures, pathological features, and biomechanical parameters from two-dimensional radiographs and three-dimensional CT/MRI data [67] [68].

In the domain of radiographic parameter measurement, CNN-based algorithms have achieved automated measurement of disc height, segmental lordosis, vertebral body dimensions, pedicle screw positioning, and cage placement accuracy with intraclass correlation coefficients exceeding 0.95 compared with experienced human raters, while eliminating inter-observer variability and reducing measurement time from minutes to seconds [67]. These automated measurement systems are increasingly integrated into commercial spinal analysis software platforms, with several receiving FDA 510(k) clearance for specific measurement tasks [67].

For fusion assessment specifically, radiomics-based machine learning models have demonstrated particular promise in detecting trabecular bridging patterns and predicting fusion outcomes from CT imaging [67] [68]. Radiomic feature extraction identifies hundreds of quantitative imaging texture features from defined regions of interest that are imperceptible to human visual interpretation. Supervised machine learning classifiers trained on CT images with pathologically or intraoperatively confirmed fusion status have reported AUC values of 0.88 - 0.94 for fusion prediction, substantially outperforming radiologist visual assessment [68]. Natural language processing (NLP) algorithms applied to electronic health record data have further demonstrated potential for predicting postoperative complications and outcomes from preoperative clinical variables, potentially enabling automated risk stratification for surgical planning [67].

Robotic-assisted spine surgery systems integrating real-time CT fluoroscopy navigation have achieved pedicle screw placement accuracy rates of 95% - 99% within grade A/B Gertzbein-Robbins classification, compared with 85% - 92% with conventional fluoroscopic guidance [69] [70]. Multiple randomized controlled trials and systematic reviews have confirmed that robotic guidance reduces neurovascular complication rates from screw misplacement, decreases radiation exposure to the surgical team, and reduces revision rates for hardware malposition [69] [70]. Current limitations of robotic systems include prolonged setup time, increased facility costs, limited soft tissue awareness, and the learning curve required for proficient operation (See **Figure 5**) [69].

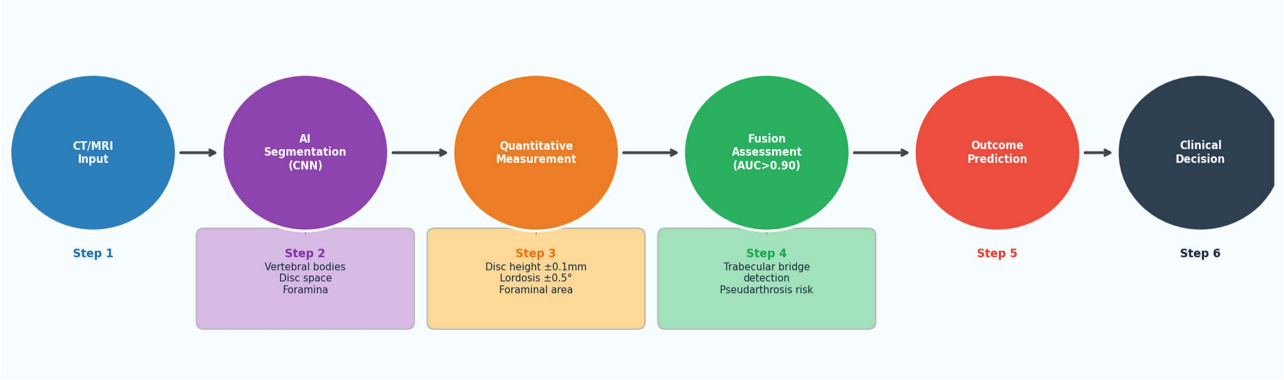

Figure 5. AI-driven radiographic assessment and clinical decision support workflow in TLIF. The six-step pipeline encompasses CT/MRI acquisition, CNN-based automated segmentation, quantitative parameter measurement (disc height ±0.1 mm; lordosis ±0.5˚), AI-assisted fusion assessment (AUC > 0.90), outcome prediction, and integration into clinical decision support. Sub-panels detail outputs of key processing steps.

7. Comparative Effectiveness of Graft Materials

The comparative effectiveness of autograft, BMP, and bioactive glass in lumbar fusion is characterized by a complex, heterogeneous literature spanning different surgical approaches, patient populations, outcome measures, and follow-up durations. Interpreting this literature requires careful attention to confounding factors including approach type (TLIF vs. posterolateral vs. ALIF), instrumentation status, patient comorbidities, and the distinction between radiographic fusion and clinical outcomes [54] [61].

Meta-analyses and systematic reviews comparing autograft with rhBMP-2 across spinal fusion applications consistently demonstrate equivalent or marginally superior radiographic fusion rates with BMP (pooled fusion rate difference approximately 3% - 5%, generally not reaching statistical significance), with comparable improvements in pain and functional scores [54]. The most methodologically rigorous analysis, the individual patient data meta-analysis by Simmonds and colleagues, enrolled 1062 patients from seven RCTs and found no significant difference in fusion rates (pooled RR 1.04; 95% CI 0.97 - 1.11) but identified a statistically significant increase in adverse events with rhBMP-2 [54]. BMP's primary advantage lies in the elimination of donor-site morbidity, a meaningful benefit in patients for whom chronic harvest-site pain would otherwise represent the dominant postoperative complaint [48] [49].

Direct comparative data between bioactive glass and autograft are more limited, deriving primarily from a small number of prospective studies and one randomized trial. The available evidence suggests non-inferiority of bioactive glass as a graft extender or substitute in posterolateral fusion, with the randomized trial by Rantakokko and colleagues reporting a non-significant fusion rate difference of 5 percentage points (86% vs. 91%, p = 0.42) with superior donor-site morbidity profile [62]. In the TLIF-specific context, uncontrolled observational data support feasibility and reasonable fusion rates of 80% - 88%, but rigorous comparative data are lacking [61] [62].

Head-to-head comparisons between BMP and bioactive glass are largely absent from the published literature, representing a meaningful knowledge gap [61] [71]. Preclinical animal studies have explored combinations of low-dose BMP-2 loaded onto bioactive glass scaffolds, with several demonstrating synergistic effects, achieving fusion rates equivalent to standard-dose BMP-2 alone while using doses 5 - 10 times lower than current clinical practice [71]. If translatable to clinical practice, such combinations could potentially preserve the osteoinductive potency of BMP-2 while reducing the dose-dependent adverse effects associated with supraphysiological concentrations, representing a potentially superior approach to current single-material strategies [71].

Patient-specific factors significantly modulate graft material effectiveness. Tobacco smoking reduces fusion rates by 25% - 40% regardless of graft material used, through multiple mechanisms including impaired angiogenesis, reduced osteoblast function, and increased osteoclastic activity [72]. Diabetes mellitus, particularly poorly controlled with HbA1c > 7.5%, similarly reduces fusion rates and increases infection risk. Chronic corticosteroid use impairs both autograft biology and BMP responsiveness by suppressing mesenchymal stem cell osteogenic differentiation [72]. These comorbidities favor osteoinductive graft augmentation, making BMP or bioactive glass with silicon-mediated osteoblast stimulation more attractive than autograft alone in high-risk patients [54] [72].

Table 4. Comparative clinical outcomes across TLIF approaches and graft materials.

Outcome Measure	MIS-TLIF	Open TLIF	TLIF + Bioactive Glass	PLIF (Comparator)
VAS Back Pain	65% - 75% improvement	60% - 72% improvement	62% - 70% improvement	60% - 68% improvement
VAS Leg Pain	70% - 80% improvement	68% - 78% improvement	65% - 75% improvement	62% - 73% improvement
ODI Improvement	45% - 60% reduction	42% - 58% reduction	44% - 57% reduction	40% - 55% reduction
Fusion Rate	85% - 95%	88% - 95%	75% - 90%	85% - 90% (open)
Hospital Stay	1 - 3 days (MIS)	3 - 5 days (open)	1 - 3 days (MIS)	2 - 4 days
Return to Work	6 - 12 weeks	8 - 16 weeks	6 - 14 weeks	8 - 16 weeks
Reoperation Rate (5yr)	5% - 12%	4% - 10%	5% - 11%	6% - 13%
Adjacent Seg. Disease	5% - 20% at 10 years	4% - 18% at 10 years	-	8% - 22% at 10 years

Table 4 synthesizes clinical outcome data across TLIF approaches and graft material categories based on pooled published series. The comparable outcomes between MIS and open TLIF for most measures, combined with MIS-TLIF's perioperative advantages, support a preference for MIS techniques in appropriate surgical candidates [29]-[31].

8. Gaps and Future Directions

8.1. Clinical Evidence Gaps

Despite the substantial body of literature supporting TLIF as an effective treat-

ment for degenerative lumbar disease, several critical evidence gaps constrain evidence-based practice. The most significant limitation is the absence of adequately powered, prospective randomized controlled trials directly comparing autograft, BMP, and bioactive glass specifically within the context of TLIF, as opposed to posterolateral or anterior fusion [61] [71]. The existing comparative literature is dominated by observational data, often retrospective, with variable patient selection, inconsistent surgical techniques, and heterogeneous outcome measures that preclude reliable pooled analysis. Future trials should standardize surgical technique, instrumentation, endplate preparation protocol, graft volume, and postoperative assessment methodology to enable meaningful comparison [63].

Long-term follow-up beyond two years is inadequately represented in the TLIF literature. Most published series report outcomes at 12 - 24 months, capturing initial fusion status but missing clinically important events including late pseudarthrosis, adjacent segment degeneration, cage subsidence, and hardware failure that may manifest over longer timeframes [63] [73]. Registry studies with prospective data capture at five and ten years, linked to administrative data for complete ascertainment of reoperation and healthcare utilization, would provide more comprehensive understanding of the natural history of TLIF outcomes and the durability of different graft strategies [73].

The minimal clinically important difference (MCID), the smallest change in a patient-reported outcome measure that a patient perceives as meaningful, is incompletely characterized for TLIF populations across different surgical indications and baseline characteristics [74]. Published MCID estimates for ODI, VAS, and SF-36 in spinal fusion patients vary substantially between studies due to differences in anchor methodology, patient populations, and statistical approaches. Rigorous MCID determination in large, well-characterized TLIF cohorts would improve interpretation of comparative trials and strengthen clinical decision-making frameworks [74].

8.2. Emerging Technologies and Biological Therapies

The development of next-generation graft materials with enhanced biological activity represents an active research frontier. Demineralized bone matrix (DBM), processed from cadaveric allograft to remove mineral while preserving the osteoinductive protein matrix, represents a well-established synthetic-biological hybrid with broad clinical use, though its biological variability between preparation batches and donors represents a significant limitation [75]. Platelet-rich plasma (PRP) and platelet-rich fibrin (PRF), concentrating autologous growth factors through centrifugation, have been investigated as graft adjuvants with mixed results in the spinal literature [75].

Cell-based therapies utilizing expanded autologous or allogeneic mesenchymal stem cells (MSCs) have demonstrated encouraging results in preclinical spinal fusion models, with multiple phase I/II clinical trials underway [76]. MSC-based approaches can in principle provide both osteoinductive and osteogenic activities

without the safety concerns of supraphysiological BMP concentrations, potentially representing a superior biological approach for high-risk patients. Challenges including manufacturing complexity, regulatory burden, cost, and shelf-life limitations currently constrain clinical implementation [76].

Three-dimensional bioprinting technology enables fabrication of patient-specific interbody implants with precisely controlled macro- and micro-architecture, incorporating designed porosity gradients, surface topographies, and channeled internal structures for vascular ingrowth [77]. Integration of bioprinting with bioactive glass, hydroxyapatite, or degradable polymer composites allows simultaneous optimization of mechanical properties and biological activity in single scaffold systems. Early clinical reports of 3D-printed titanium cages with modified surface topographies demonstrate superior fusion rates and reduced subsidence compared with conventional smooth PEEK devices [77].

Precision medicine approaches, integrating genomic profiling, serum biomarkers, microbiome analysis, and machine learning-based outcome prediction, represent the aspirational frontier of personalized TLIF management [78]. Genetic polymorphisms in BMP receptor genes, osteogenic differentiation pathways, and inflammatory cytokine networks have been associated with variable fusion outcomes in exploratory studies, suggesting that genomic profiling could eventually guide biologically informed graft selection [78]. Serum biomarkers of bone turnover (CTX, P1NP, osteocalcin) and inflammation (CRP, IL-6, TNF-α) have shown preliminary associations with fusion outcomes and complication risk, potentially enabling dynamic monitoring of the biological healing response [78].

8.3. Adjacent Segment Disease

Adjacent segment disease (ASD), the development of clinically symptomatic pathology at spinal levels immediately above or below a fusion, represents one of the most significant long-term concerns following TLIF [79]. Reported rates of radiographic adjacent segment degeneration range from 20% - 35% within 5 years of fusion, while symptomatic ASD requiring reoperation occurs in 5% - 20% of patients within 10 years [79]. The pathophysiology of ASD involves altered biomechanical stress distribution at the adjacent unfused levels, with increased segmental motion, intradiscal pressure, and facet joint loading accelerating degenerative progression [73] [79].

The influence of TLIF-specific factors on ASD risk is not completely understood. Suboptimal sagittal alignment restoration, particularly residual lumbar hypolordosis, increases adjacent segment stress and likely accelerates ASD development [79]. Dynamic stabilization devices and interspinous process devices have been explored as means of reducing adjacent segment load transfer, with mixed clinical results [79]. Whether graft material choice influences ASD risk is unknown; bioactive glass's complete degradation and replacement with native bone theoretically reduces long-term stress-shielding compared with non-degradable synthetic materials, but this hypothesis remains untested in clinical studies [61]

[79].

9. Clinical Implications and Recommendations

Based on the current body of evidence, evaluated using the GRADE framework, the following clinical considerations are proposed to inform practice. These statements are intended as evidence-informed guidance rather than definitive recommendations, given the predominance of observational studies and heterogeneity across the literature. Clinical decision-making should remain individualized, taking into account patient characteristics, surgeon expertise, and institutional resources.

Regarding graft selection, autologous bone graft remains the reference standard, supported by consistent clinical evidence. The use of BMP may be considered in selected cases to avoid donor-site morbidity; however, its application should be weighed against potential risks and cost considerations. Synthetic materials, including bioactive glass, may represent alternative options, but current evidence is limited and does not support strong comparative recommendations within TLIF. Several technical principles are consistently associated with improved outcomes, although much of the supporting evidence is derived from observational or biomechanical studies. Careful endplate preparation, including removal of cartilaginous tissue while preserving subchondral bone integrity, is widely regarded as important for fusion success. Similarly, appropriate interbody cage positioning—ensuring adequate endplate contact, central placement, and restoration of segmental alignment—appears to contribute to biomechanical stability and favorable outcomes.

Preoperative patient optimization is likely to influence surgical success. Smoking cessation, glycemic control in diabetic patients, nutritional status, and management of bone health are commonly recommended, although high-level evidence specific to TLIF remains limited. Bone density assessment may be beneficial in older patients or those at risk of osteoporosis, as low bone mineral density has been associated with increased complication rates. Postoperative rehabilitation, including early mobilization and structured physical therapy, is generally encouraged and has been associated with improved functional recovery; however, standardized protocols and high-quality comparative data are lacking.

While these principles are supported by the best available evidence and clinical consensus, the strength of recommendations remains moderate to low, highlighting the need for high-quality randomized controlled trials and standardized outcome reporting to strengthen future guidance (See Table 5).

Table 5. Evidence-based clinical recommendations for TLIF graft selection and perioperative management.

Number	Patient Scenario	Recommendation	Evidence Grade
1	Young healthy patients; no harvest contraindications; single-level TLIF with adequate bone quality	Autologous iliac crest bone graft as primary graft material	Grade A, Superior osteogenic, osteoinductive, osteoconductive properties; gold standard efficacy with predictable fusion

Continued

2	Revision surgery; multi-level fusion (≥2 levels); diabetes, active tobacco use, or chronic corticosteroid therapy; inadequate autograft volume	rhBMP-2 with careful dose selection (lowest effective dose); comprehensive patient counseling on complications	Grade A, Eliminates harvest morbidity; comparable or superior fusion rates in high-risk populations
3	Insufficient autograft; BMP cost/risk prohibitive; elderly patients with limited bone reserve; hybrid construct	Bioactive glass as graft extender combined with local autograft from laminectomy/facetectomy, or standalone in low-risk single-level cases	Grade B, Favorable safety profile; approaching non-inferiority in RCTs; no donor-site morbidity
4	All TLIF patients regardless of graft choice and surgical approach	Bilateral pedicle screw-rod posterior instrumentation; adequate torque and rod contouring; supplemental transverse connector for multi-level cases	Grade A, Reduces interfragmentary motion below the ossification threshold (<2% - 10% strain); essential biomechanical adjunct
5	Postoperative assessment in all patients at standard intervals	CT scan at 6 - 12 months for fusion assessment + validated patient-reported outcomes (ODI, VAS, SF-36, PROMIS) at 6 weeks, 3, 6, and 12 months	Grade B, Multimodal assessment superior to any single measure; CT preferred over plain radiographs for fusion confirmation
6	Patients with osteoporosis (T-score ≤−2.5) or high fracture risk	Consider augmented fixation (cement augmentation, cortical bone trajectory); optimize bone health preoperatively; teriparatide consideration	Grade B, Osteoporosis significantly increases pseudarthrosis and hardware failure risk; preoperative optimization essential

10. Conclusion

Transforaminal lumbar interbody fusion (TLIF) is a well-established, biomechanically grounded, and clinically validated surgical technique that has significantly advanced the management of degenerative lumbar disease over the past four decades. Since its introduction as a modification of posterior lumbar interbody fusion (PLIF), TLIF has evolved into a widely adopted procedure performed through open and minimally invasive approaches. Its biomechanical advantages—including anterior column load sharing, three-column stabilization, indirect neural decompression through restoration of foraminal height, and improvement of sagittal alignment—contribute to its consistent clinical effectiveness. Current evidence indicates that TLIF achieves fusion rates of approximately 85% - 95%, with minimally invasive techniques demonstrating comparable outcomes to open surgery while offering reduced perioperative morbidity in appropriately selected patients. Autologous iliac crest bone graft remains the reference standard due to its combined osteogenic, osteoinductive, and osteoconductive properties. Bone morphogenetic protein (BMP) has demonstrated comparable fusion outcomes while reducing donor-site morbidity; however, its use is tempered by cost considerations

and potential complications, including ectopic bone formation and inflammatory responses. Bioactive glass has emerged as a synthetic graft option with reported biocompatibility and osteoconductive potential. Nevertheless, current evidence remains limited and heterogeneous, particularly in the context of TLIF-specific applications, and further comparative studies are required before definitive conclusions can be drawn regarding its relative effectiveness. Technological advancements, including artificial intelligence, machine learning, and robotic-assisted navigation, are increasingly being explored within spinal surgery. These approaches may offer potential benefits in surgical planning, intraoperative guidance, and outcome prediction. However, their clinical value in TLIF has not yet been fully established and requires validation through rigorous prospective and comparative studies. Despite the maturity of TLIF as a surgical technique, several important knowledge gaps remain. These include the need for direct comparative evaluations of graft materials within TLIF procedures, standardized long-term outcome data extending beyond five years, and comprehensive assessments of cost-effectiveness across different healthcare settings. In addition, emerging approaches such as precision medicine and data-driven patient stratification represent promising directions but currently lack sufficient evidence for routine clinical implementation. Future research should prioritize high-quality randomized controlled trials, long-term follow-up studies, and the integration of standardized outcome measures. Addressing these gaps will be essential to further optimize patient selection, improve clinical outcomes, and ensure that TLIF continues to evolve in a manner that is evidence-based, safe, and responsive to patient needs.

11. Limitations

This review has several limitations that should be acknowledged. First, there is substantial heterogeneity in surgical approaches, including variations between open, minimally invasive, and emerging robotic-assisted TLIF techniques, which may influence reported outcomes. Second, differences in graft composition, ranging from autograft and BMP to synthetic substitutes, limit direct comparability across studies. Third, follow-up duration varies considerably, with relatively few studies providing long-term outcomes beyond five years. Fourth, inconsistencies in fusion assessment methods, including radiographic criteria and imaging modalities, may affect the reliability of reported fusion rates. Finally, variability in patient characteristics, particularly comorbidity profiles, introduces additional confounding factors. Despite this limitation, the study is still meaningful of its type, and future studies should consider these limitations to expand our understanding.

Ethics Approval

Not applicable.

Consent for Publication

All authors have reviewed and approved the final version of the manuscript and

consent to its publication.

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Conflicts of Interest

The authors declare that they have no competing interests.

References

[1] Hoy, D., March, L., Brooks, P., Blyth, F., Woolf, A., Bain, C., *et al.* (2014) The Global Burden of Low Back Pain: Estimates from the Global Burden of Disease 2010 Study. *Annals of the Rheumatic Diseases*, **73**, 968-974. https://doi.org/10.1136/annrheumdis-2013-204428

[2] Vos, T., Flaxman, A.D., Naghavi, M., Lozano, R., Michaud, C., Ezzati, M., *et al.* (2012) Years Lived with Disability (YLDs) for 1160 Sequelae of 289 Diseases and Injuries 1990-2010: A Systematic Analysis for the Global Burden of Disease Study 2010. *The Lancet*, **380**, 2163-2196. https://doi.org/10.1016/s0140-6736(12)61729-2

[3] Martin, B.I., Deyo, R.A., Mirza, S.K., *et al.* (2008) Expenditures and Health Status among Adults with Back and Neck Problems. *JAMA*, **299**, 656-664. https://doi.org/10.1001/jama.299.6.656

[4] Adams, M.A. and Roughley, P.J. (2006) What Is Intervertebral Disc Degeneration, and What Causes It? *Spine*, **31**, 2151-2161. https://doi.org/10.1097/01.brs.0000231761.73859.2c

[5] Kirkaldy-Willis, W.H. and Farfan, H.F. (1982) Instability of the Lumbar Spine. *Clinical Orthopaedics and Related Research*, **165**, 110-123. https://doi.org/10.1097/00003086-198205000-00015

[6] Weinstein, J.N., Tosteson, T.D., Lurie, J.D., Tosteson, A.N.A., Blood, E., Hanscom, B., *et al.* (2008) Surgical versus Nonsurgical Therapy for Lumbar Spinal Stenosis. *New England Journal of Medicine*, **358**, 794-810. https://doi.org/10.1056/nejmoa0707136

[7] Radcliff, K.E., Kepler, C.K., Jakoi, A., Sidhu, G.S., Rihn, J., Vaccaro, A.R., *et al*. (2013) Adjacent Segment Disease in the Lumbar Spine Following Different Treatment Interventions. *The Spine Journal*, **13**, 1339-1349. https://doi.org/10.1016/j.spinee.2013.03.020

[8] Harms, J. and Jeszenszky, D. (1998) The Unilateral Transforaminal Approach for Posterior Lumbar Interbody Fusion. *Orthopade*, **27**, 113-119.

[9] Bogduk, N. and Twomey, L.T. (2005) Clinical Anatomy of the Lumbar Spine and Sacrum. 4th Edition, Churchill Livingstone.

[10] Rosenberg, W.S. and Mummaneni, P.V. (2001) Transforaminal Lumbar Interbody Fusion: Technique, Complications, and Early Results. *Neurosurgery*, **48**, 569-575. https://doi.org/10.1097/00006123-200103000-00022

[11] Khan, S.N., Cammisa, F.P., Sandhu, H.S., Diwan, A.D., Girardi, F.P. and Lane, J.M. (2005) The Biology of Bone Grafting. *Journal of the American Academy of Orthopaedic Surgeons*, **13**, 77-86. https://doi.org/10.5435/00124635-200501000-00010

[12] Friedlaender, G.E. (1987) Bone Grafts. the Basic Science Rationale for Clinical Applications. *The Journal of Bone & Joint Surgery*, **69**, 786-790. https://doi.org/10.2106/00004623-198769050-00026

[13] Younger, E.M. and Chapman, M.W. (1989) Morbidity at Bone Graft Donor Sites. *Journal of Orthopaedic Trauma*, **3**, 192-195. https://doi.org/10.1097/00005131-198909000-00002

[14] Miyazaki, M., Tsumura, H., Wang, J.C. and Alanay, A. (2009) An Update on Bone Substitutes for Spinal Fusion. *European Spine Journal*, **18**, 783-799. https://doi.org/10.1007/s00586-009-0924-x

[15] Wang, J., Zhou, Y., Zhang, Z.F., Li, C.Q., Zheng, W.J. and Liu, J. (2011) Minimally Invasive or Open Transforaminal Lumbar Interbody Fusion as Revision Surgery for Patients Previously Treated by Open Discectomy and Decompression of the Lumbar Spine. *European Spine Journal*, **20**, 623-628. https://doi.org/10.1007/s00586-010-1578-4

[16] Ghasem, A., Sharma, A., Greif, D.N., Alam, M. and Maaieh, M.A. (2018) The Arrival of Robotics in Spine Surgery: A Review of the Literature. *Spine*, **43**, 1670-1677. https://doi.org/10.1097/brs.0000000000002695

[17] Joseph, J.R., Smith, B.W., Liu, X. and Park, P. (2017) Current Applications of Robotics in Spine Surgery: A Systematic Review of the Literature. *Neurosurgical Focus*, **42**, E2. https://doi.org/10.3171/2017.2.focus16544

[18] Härtl, R., Lam, K.S., Wang, J., Korge, A., Kandziora, F. and Audigé, L. (2013) Worldwide Survey on the Use of Navigation in Spine Surgery. *World Neurosurgery*, **79**, 162-172. https://doi.org/10.1016/j.wneu.2012.03.011

[19] Parker, S.L., Adogwa, O., Paul, A.R., Anderson, W.N., Aaronson, O., Cheng, J.S., *et al*. (2011) Utility of Minimum Clinically Important Difference in Assessing Pain, Disability, and Health State after Transforaminal Lumbar Interbody Fusion for Degenerative Lumbar Spondylolisthesis. *Journal of Neurosurgery*: *Spine*, **14**, 598-604. https://doi.org/10.3171/2010.12.spine10472

[20] Kaiser, M.G., Eck, J.C., Groff, M.W., Watters, W.C., Dailey, A.T., Resnick, D.K., *et al*. (2014) Guideline Update for the Performance of Fusion Procedures for Degenerative Disease of the Lumbar Spine. Part 1: Introduction and Methodology. *Journal of Neurosurgery*: *Spine*, **21**, 2-6. https://doi.org/10.3171/2014.4.spine14257

[21] Stauffer, R.N. and Coventry, M.B. (1972) Posterolateral Lumbar-Spine Fusion. *The Journal of Bone & Joint Surgery*, **54**, 1195-1204. https://doi.org/10.2106/00004623-197254060-00006

[22] Wiltse, L.L., Bateman, J.G., Hutchinson, R.H. and Nelson, W.E. (1968) The Paraspinal Sacrospinalis-Splitting Approach to the Lumbar Spine. *The Journal of Bone & Joint Surgery*, **50**, 919-926. https://doi.org/10.2106/00004623-196850050-00004

[23] Cloward, R.B. (1953) The Treatment of Ruptured Lumbar Intervertebral Discs by Vertebral Body Fusion. *Journal of Neurosurgery*, **10**, 154-168. https://doi.org/10.3171/jns.1953.10.2.0154

[24] Teng, I., Han, J., Phan, K. and Mobbs, R. (2017) A Meta-Analysis Comparing ALIF, PLIF, TLIF and LLIF. *Journal of Clinical Neuroscience*, **44**, 11-17. https://doi.org/10.1016/j.jocn.2017.06.013

[25] Mobbs, R.J., Phan, K., Malham, G., Seex, K. and Rao, PJ. (2015) Lumbar Interbody Fusion: Techniques, Indications and Comparison. *Journal of Spine Surgery*, **1** 2-18.

[26] Lowe, T.G., Tahernia, A.D., O'Brien, M.F. and Smith, D.A.B. (2002) Unilateral Transforaminal Posterior Lumbar Interbody Fusion (TLIF): Indications, Technique, and 2-Year Results. *Journal of Spinal Disorders & Techniques*, **15**, 31-38. https://doi.org/10.1097/00024720-200202000-00005

[27] Hackenberg, L., Halm, H., Bullmann, V., Vieth, V., Schneider, M. and Liljenqvist, U. (2005) Transforaminal Lumbar Interbody Fusion: A Safe Technique with Satisfactory Three to Five Year Results. *European Spine Journal*, **14**, 551-558. https://doi.org/10.1007/s00586-004-0830-1

[28] Zhao, Y., Li, J., Zhao, W., Wang, D. and Liu, Y. (2019) PLIF versus TLIF: A Meta-Analysis. *European Journal of Orthopaedic Surgery & Traumatology*, **29**, 855-863.

[29] Cheng, J.S., Park, P., Le, H., Reisner, L., Chou, D. and Mummaneni, P.V. (2013) Short-Term and Long-Term Outcomes of Minimally Invasive and Open Transforaminal Lumbar Interbody Fusions: Is There a Difference? *Neurosurgical Focus*, **35**, E6. https://doi.org/10.3171/2013.5.focus1377

[30] Lee, K.H., Yue, W.M., Yeo, W., Soeharno, H. and Tan, S.B. (2012) Clinical and Radiological Outcomes of Open versus Minimally Invasive Transforaminal Lumbar Interbody Fusion. *European Spine Journal*, **21**, 2265-2270. https://doi.org/10.1007/s00586-012-2281-4

[31] Phan, K. and Mobbs, R.J. (2016) Systematic Review of Minimally Invasive versus Open Trans-Foraminal Lumbar Interbody Fusion. *International Orthopaedics*, **40**, 51-64.

[32] Phan, K. and Mobbs, R.J. (2016) Evolution of Design of Interbody Cages for Anterior Lumbar Interbody Fusion. *Orthopaedic Surgery*, **8**, 270-277. https://doi.org/10.1111/os.12259

[33] Phan, K., Rao, P.J., Kam, A.C. and Mobbs, R.J. (2015) Minimally Invasive versus Open Transforaminal Lumbar Interbody Fusion for Treatment of Degenerative Lumbar Disease: Systematic Review and Meta-Analysis. *European Spine Journal*, **24**, 1017-1030. https://doi.org/10.1007/s00586-015-3903-4

[34] Zhao, X., Ma, Z.J., Ma, X.L., *et al*. (2021) Comparison of Oblique Lateral Interbody Fusion (OLIF) and Transforaminal Lumbar Interbody Fusion (TLIF) for the Treatment of Adjacent Segment Disease after Lumbar Spinal Fusion. *BMC Musculoskeletal Disorders*, **22**, Article No. 1029.

[35] Oliveira, L., Marchi, L., Coutinho, E. and Pimenta, L. (2010) A Radiographic Assessment of the Ability of the Extreme Lateral Interbody Fusion Procedure to Indirectly Decompress the Neural Elements. *Spine*, **35**, S331-S337. https://doi.org/10.1097/brs.0b013e3182022db0

[36] Oxland, T.R. and Lund, T. (2000) Biomechanics of Stand-Alone Cages and Cages in Combination with Posterior Fixation: A Literature Review. *European Spine Journal*, **9**, S095-S101. https://doi.org/10.1007/pl00010028

[37] Shen, F.H., Samartzis, D., Khanna, A.J. and Anderson, D.G. (2007) Minimally Invasive Techniques for Lumbar Interbody Fusions. *Orthopedic Clinics of North America*, **38**, 373-386. https://doi.org/10.1016/j.ocl.2007.04.002

[38] Phillips, F.M., Isaacs, R.E., Rodgers, W.B., Khajavi, K., Tohmeh, A.G., Deviren, V., *et al*. (2013) Adult Degenerative Scoliosis Treated with XLIF: Clinical and Radiographical Results of a Prospective Multicenter Study with 24-Month Follow-Up. *Spine*, **38**, 1853-1861. https://doi.org/10.1097/brs.0b013e3182a43f0b

[39] Denis, F. (1983) The Three Column Spine and Its Significance in the Classification of Acute Thoracolumbar Spinal Injuries. *Spine*, **8**, 817-831. https://doi.org/10.1097/00007632-198311000-00003

[40] Ahn, Y., Keum, H.J. and Kim, S. (2019) Contralateral Foraminal Ligamentum Flavum Hypertrophy Following Minimally Invasive Transforaminal Lumbar Interbody Fusion. *Journal of Clinical Neuroscience*, **62**, 94-99.

[41] Schwab, F., Ungar, B., Blondel, B., Buchowski, J., Coe, J., Deinlein, D., *et al*. (2012) Scoliosis Research Society—Schwab Adult Spinal Deformity Classification. *Spine*, **37**, 1077-1082. https://doi.org/10.1097/brs.0b013e31823e15e2

[42] Berjano, P. and Lamartina, C. (2013) Far Lateral Approaches (XLIF) in Adult Scoliosis. *European Spine Journal*, **22**, 242-253. https://doi.org/10.1007/s00586-012-2426-5

[43] Claes, L.E., Heigele, C.A., Neidlinger-Wilke, C., Kaspar, D., Seidl, W., Margevicius, K.J., *et al*. (1998) Effects of Mechanical Factors on the Fracture Healing Process. *Clinical Orthopaedics and Related Research*, **355**, S132-S147. https://doi.org/10.1097/00003086-199810001-00015

[44] Greenwald, A.S., Boden, S.D., Goldberg, V.M., Khan, Y., Laurencin, C.T. and Rosier, R.N. (2001) Bone-Graft Substitutes: Facts, Fictions, and Applications. *The Journal of Bone and Joint Surgery-American Volume*, **83**, 98-103. https://doi.org/10.2106/00004623-200100022-00007

[45] Giannoudis, P.V., Dinopoulos, H. and Tsiridis, E. (2005) Bone Substitutes: An Update. *Injury*, **36**, S20-S27. https://doi.org/10.1016/j.injury.2005.07.029

[46] Boden, S.D., Kang, J., Sandhu, H. and Heller, J.G. (2002) Use of Recombinant Human Bone Morphogenetic Protein-2 to Achieve Posterolateral Lumbar Spine Fusion in Humans. *Spine*, **27**, 2662-2673. https://doi.org/10.1097/00007632-200212010-00005

[47] Glassman, S.D., Dimar, J.R., Carreon, L.Y., Campbell, M.J., Puno, R.M. and Johnson, J.R. (2005) Initial Fusion Rates with Recombinant Human Bone Morphogenetic Protein-2/Compression Resistant Matrix and a Hydroxyapatite and Tricalcium Phosphate/Collagen Carrier in Posterolateral Spinal Fusion. *Spine*, **30**, 1694-1698. https://doi.org/10.1097/01.brs.0000172157.39513.80

[48] Banwart, J.C., Asher, M.A. and Hassanein, R.S. (1995) Iliac Crest Bone Graft Harvest Donor Site Morbidity. *Spine*, **20**, 1055-1060. https://doi.org/10.1097/00007632-199505000-00012

[49] Dimitriou, R., Mataliotakis, G.I., Angoules, A.G., Kanakaris, N.K. and Giannoudis, P.V. (2011) Complications Following Autologous Bone Graft Harvesting from the Iliac Crest and Using the RIA: A Systematic Review. *Injury*, **42**, S3-S15. https://doi.org/10.1016/j.injury.2011.06.015

[50] Wozney, J.M., Rosen, V., Celeste, A.J., Mitsock, L.M., Whitters, M.J., Kriz, R.W., *et al*. (1988) Novel Regulators of Bone Formation: Molecular Clones and Activities. *Sci-*

ence, **242**, 1528-1534. https://doi.org/10.1126/science.3201241

[51] Urist, M.R. (1965) Bone: Formation by Autoinduction. *Science*, **150**, 893-899. https://doi.org/10.1126/science.150.3698.893

[52] Burkus, J.K., Heim, S.E., Gornet, M.F. and Zdeblick, T.A. (2003) Is INFUSE Bone Graft Superior to Autograft Bone? An Integrated Analysis of Clinical Trials Using the LT-CAGE Lumbar Tapered Fusion Device. *Journal of Spinal Disorders & Techniques*, **16**, 113-122. https://doi.org/10.1097/00024720-200304000-00001

[53] Dimar, J.R., Glassman, S.D., Burkus, K.J. and Carreon, L.Y. (2006) Clinical Outcomes and Fusion Success at 2 Years of Single-Level Instrumented Posterolateral Fusions with Recombinant Human Bone Morphogenetic Protein-2/Compression Resistant Matrix versus Iliac Crest Bone Graft. *Spine*, **31**, 2534-2539. https://doi.org/10.1097/01.brs.0000240715.78657.81

[54] Simmonds, M.C., Brown, J.V.E., Heirs, M.K., Higgins, J.P.T., Mannion, R.J., Rodgers, M.A., *et al*. (2013) Safety and Effectiveness of Recombinant Human Bone Morphogenetic Protein-2 for Spinal Fusion. *Annals of Internal Medicine*, **158**, 877-889. https://doi.org/10.7326/0003-4819-158-12-201306180-00005

[55] Carragee, E.J., Hurwitz, E.L. and Weiner, B.K. (2011) A Critical Review of Recombinant Human Bone Morphogenetic Protein-2 Trials in Spinal Surgery: Emerging Safety Concerns and Lessons Learned. *The Spine Journal*, **11**, 471-491. https://doi.org/10.1016/j.spinee.2011.04.023

[56] Smucker, J.D., Rhee, J.M., Singh, K., Yoon, S.T. and Heller, J.G. (2006) Increased Swelling Complications Associated with Off-Label Usage of rhBMP-2 in the Anterior Cervical Spine. *Spine*, **31**, 2813-2819. https://doi.org/10.1097/01.brs.0000245863.52371.c2

[57] Epstein, N.E. (2012) Pros, Cons, and Costs of INFUSE in Spinal Surgery. *Surgical Neurology International*, **3**, S214-S221.

[58] Hench, L.L. and Jones, J.R. (2015) Bioactive Glasses: Frontiers and Challenges. *Frontiers in Bioengineering and Biotechnology*, **3**, Article No. 194. https://doi.org/10.3389/fbioe.2015.00194

[59] Rahaman, M.N., Day, D.E., Sonny Bal, B., Fu, Q., Jung, S.B., Bonewald, L.F., *et al*. (2011) Bioactive Glass in Tissue Engineering. *Acta Biomaterialia*, **7**, 2355-2373. https://doi.org/10.1016/j.actbio.2011.03.016

[60] Miguez-Pacheco, V., Hench, L.L. and Boccaccini, A.R. (2015) Bioactive Glasses beyond Bone and Teeth: Emerging Applications in Contact with Soft Tissues. *Acta Biomaterialia*, **13**, 1-15. https://doi.org/10.1016/j.actbio.2014.11.004

[61] Rantakokko, J., Frantzén, J.P., Heinänen, J., Kajander, S., Kotilainen, E., Gullichsen, E., *et al*. (2012) Posterolateral Spondylodesis Using Bioactive Glass S53P4 and Autogenous Bone in Instrumented Unstable Lumbar Spine Burst Fractures. *Scandinavian Journal of Surgery*, **101**, 66-71. https://doi.org/10.1177/145749691210100113

[62] Acharya, N.K., Kumar, R.J., Varma, H.K. and Menon, V.K. (2008) Hydroxyapatite-bioactive Glass Ceramic Composite as Stand-Alone Graft Substitute for Posterolateral Fusion of Lumbar Spine: A Prospective, Matched, and Controlled Study. *Journal of Spinal Disorders & Techniques*, **21**, 106-111. https://doi.org/10.1097/bsd.0b013e31805fea1f

[63] Buchbinder, R., van Tulder, M., Öberg, B., Costa, L.M., Woolf, A., Schoene, M., *et al*. (2018) Low Back Pain: A Call for Action. *The Lancet*, **391**, 2384-2388. https://doi.org/10.1016/s0140-6736(18)30488-4

[64] Blumenthal, S.L. and Gill, K. (1993) Can Lumbar Spine Radiographs Accurately De-

termine Fusion in Postoperative Patients? *Spine*, **18**, 1186-1189. https://doi.org/10.1097/00007632-199307000-00010

[65] Shah, L.M. and Ross, J.S. (2016) Imaging of Spinal Fusion: A Review of Imaging Modalities and Fusion Assessment. *American Journal of Neuroradiology*, **37**, 28-36.

[66] Kärrholm, J. (2012) Radiostereometric Analysis of Early Implant Migration—A Valuable Tool to Ensure Proper Introduction of New Implants. *Acta Orthopaedica*, **83**, 551-552. https://doi.org/10.3109/17453674.2012.745352

[67] Jamaludin, A., Lootus, M., Kadir, T., Zisserman, A., Urban, J., Battié, M.C., *et al*. (2017) ISSLS Prize in Bioengineering Science 2017: Automation of Reading of Radiological Features from Magnetic Resonance Images (MRIs) of the Lumbar Spine without Human Intervention Is Comparable with an Expert Radiologist. *European Spine Journal*, **26**, 1374-1383. https://doi.org/10.1007/s00586-017-4956-3

[68] Bae, W.C. and Masuda, K. (2013) Emerging Technologies for Molecular Imaging of Intervertebral Disc Degeneration and Regeneration. *Discovery Medicine*, **15**, 263-271.

[69] Roser, F., Tatagiba, M. and Maier, G. (2013) Spinal Robotics: Current Applications and Future Perspectives. *Neurosurgery*, **72**, A12-A18. https://doi.org/10.1227/neu.0b013e318270d02c

[70] Overley, S.C., Cho, S.K., Mehta, A.I. and Arnold, P.M. (2017) Navigation and Robotics in Spinal Surgery: Where Are We Now? *Neurosurgery*, **80**, S86-S99. https://doi.org/10.1093/neuros/nyw077

[71] Dawson, E., Bae, H.W., Burkus, J.K., Stambough, J.L. and Glassman, S.D. (2009) Recombinant Human Bone Morphogenetic Protein-2 on an Absorbable Collagen Sponge with an Osteoconductive Bulking Agent in Posterolateral Arthrodesis with Instrumentation. *The Journal of Bone and Joint Surgery-American Volume*, **91**, 1604-1613. https://doi.org/10.2106/jbjs.g.01157

[72] Becker, S., Chavanne, A., Spitaler, R., *et al*. (2008) Assessment of Risk Factors for Pseudarthrosis after Lumbar Spinal Fusion. *European Spine Journal*, **17**, 1613-1620.

[73] Weinstein, J.N., Lurie, J.D., Tosteson, T.D., Zhao, W., Blood, E.A., Tosteson, A.N., *et al*. (2009) Surgical Compared with Nonoperative Treatment for Lumbar Degenerative Spondylolisthesis: Four-Year Results in the Spine Patient Outcomes Research Trial (SPORT). *The Journal of Bone and Joint Surgery-American Volume*, **91**, 1295-1304. https://doi.org/10.2106/jbjs.h.00913

[74] Copay, A.G., Glassman, S.D., Subach, B.R., Berven, S., Schuler, T.C. and Carreon, L.Y. (2008) Minimum Clinically Important Difference in Lumbar Spine Surgery Patients: A Choice of Methods Using the Oswestry Disability Index, Medical Outcomes Study Questionnaire Short Form 36, and Pain Scales. *The Spine Journal*, **8**, 968-974. https://doi.org/10.1016/j.spinee.2007.11.006

[75] Alsaleh, K.A.M., Tougas, C.A., Roffey, D.M. and Wai, E.K. (2012) Osteoconductive Bone Graft Extenders in Posterolateral Thoracolumbar Spinal Fusion: A Systematic Review. *Spine*, **37**, E993-E1000. https://doi.org/10.1097/brs.0b013e3182518859

[76] Oryan, A., Kamali, A., Moshiri, A. and Baghaban Eslaminejad, M. (2017) Role of Mesenchymal Stem Cells in Bone Regenerative Medicine: What Is the Evidence? *Cells Tissues Organs*, **204**, 59-83. https://doi.org/10.1159/000469704

[77] Mobbs, R.J., Rao, P.J. and Phan, K. (2017) Anterior Lumbar Interbody Fusion Using a Personalized 3D-Printed Titanium Cage: A Case Report. *Journal of Spine Surgery*, **3**, 708-714.

[78] Divi, S.N., Ropartz, A., Schroeder, G.D., *et al*. (2021) Precision Medicine in Spine

Surgery. *The Journal of Bone and Joint Surgery. American Volume*, **103**, 1001-1008.

[79] Park, P., Garton, H.J., Gala, V.C., Hoff, J.T. and McGillicuddy, J.E. (2004) Adjacent Segment Disease after Lumbar or Lumbosacral Fusion: Review of the Literature. *Spine*, **29**, 1938-1944. https://doi.org/10.1097/01.brs.0000137069.88904.03