

Research Progress in Lumbar Interbody Fusion (LIF) Techniques and Bone Biomaterials

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Abstract: This paper aims to review recent research progress in lumbar interbody fusion (LIF) techniques and bone biomaterials for treating low back pain resulting from lumbar instability and/or deformity. A comprehensive search was conducted in PubMed, Science Citation Index-Expanded (SCI-E), and SpringerLink databases from their inception until April 2023. The search focused on relevant articles published within the past five years, using keywords such as lumbar fusion approach, lumbar interbody fusion cage, lumbar fusion stem cells, lumbar fusion biomaterials, and bone biology of lumbar fusion. Currently, lumbar interbody fusion techniques encompass posterior, anterior, lateral, oblique, and minimally invasive approaches. The transforaminal oblique lumbar fusion approach is gaining popularity due to its ability to minimize paraspinous muscle dissection and nerve traction. Despite advancements in surgical techniques, the incidence of fusion failure after LIF remains high, ranging from 7% to 20%, and is even higher in patients with osteoporosis. This review also discusses the improvement of fusion materials properties and the development of new bone biological products incorporating nanomaterials to enhance the release of effective osteogenic proteins and mesenchymal stem cells for promoting lumbar interbody fusion. Significant advancements have been made in surgical techniques for LIF over the past few decades. However, postoperative nonfusion continues to be a major challenge. Future solutions are expected to arise through the development of more efficient surgical techniques, fusion cages, and bone biomaterials.

Keywords: Lumbar interbody fusion, Interbody fusion, Surgical techniques, Bone biomaterials, Bone biologics

1. Introduction

The annual incidence of lumbar spine disease accompanied by low back pain (LBP) as the primary symptom is estimated to range from 6.3% to 15.4%. Low back pain (LBP) is one of the most prevalent musculoskeletal disorders. Approximately 75% to 80% of adults experience low back pain at least once in their lifetime [1]. Low back pain can be categorized into two types: primary (nonspecific/idiopathic) and secondary. Conservative measures are often used to treat primary low back pain, while surgical intervention may be considered for secondary low back pain, or when conservative treatment fails to achieve desired results [2]. Primary low back pain is primarily targeted through conservative treatment, while surgical treatment aims to address secondary low back pain, or primary cases that do not respond to conservative measures [3]. Traditional lumbar interbody fusion/arthrodesis (LIF) is a treatment option that utilizes posterior or anterior internal fixation to stabilize painful motion segments, restore lumbar physiological lordosis, correct deformities, and provide indirect decompression [4]. Currently, various surgical approaches have been developed for lumbar interbody fusion, including anterior LIF (ALIF), posterior LIF (PLIF), transforaminal LIF (TLIF), extreme or lateral LIF (XLIF/LLIF), oblique LIF (OLIF), and minimally invasive TLIF (MIS-TLIF) [5].

The fusion rate of lumbar fusion has increased in recent decades due to advancements in surgical

techniques and interbody fusion cage design for treating low back pain [6]. However, studies indicate that the incidence of bone fusion failure after lumbar interbody fusion (LIF) still ranges between 7% and 20%, with a significantly higher rate observed for cases involving three or more intervertebral space levels [7]. In patients with osteoporosis, the failure rate of LIF bone fusion at a single-gap level can be as high as 29% [8]. Autologous iliac crest grafting (ICBG) has traditionally been regarded as the standard approach for promoting lumbar interbody bony fusion [9]. Nonetheless, the collection of autologous bone is associated with complications, such as intraoperative complications and donor site pain [10]. Therefore, preventing bone fusion failure or pseudarthrosis formation following lumbar interbody fusion has become a focal point for spinal surgeons. This article aims to review the existing literature on bone fusion after LIF, with a focus on surgical techniques and bone biomaterials.

2. Surgical techniques and clinical outcomes of LIF

2.1 Posterior LIF (PLIF)

Cloward introduced the technique of posterior lumbar interbody fusion (PLIF) in the 1950s, enabling access to the intervertebral disc [11]. PLIF has gained widespread recognition as an established technique. PLIF surgery can potentially provide benefits for patients exhibiting segmental instability, recurrent disc protrusion, symptomatic spinal stenosis, and pseudoarthrosis formation. Nonetheless, PLIF surgery is contraindicated in cases involving extensive epidural fibrosis, arachnoiditis, and active infection [12]. The objective of PLIF surgery is to preserve the facet joints and necessitates neural root retraction for complete removal of the intervertebral disc and insertion of interbody grafts or fusion devices. The procedure encompasses adequate decompression, complete excision of the disc, and spinal fusion, with the possibility of utilizing pedicle screws and rods for stabilization. Fusion can be achieved through the utilization of autologous iliac bone, allograft iliac bone, or bone graft substitutes. Commonly, autologous iliac bone, allogeneic bone, or a fusion cage filled with bone grafts are used for fusion in PLIF surgeries. A recent comparative study achieved a favorable lumbar fusion rate of 88.4% (84 out of 95 patients).

One advantage of PLIF is its ability to provide extensive posterior visualization and circumferential decompression of neuronal structures. Decompression can be achieved without requiring a separate incision, as the spine is already exposed. Fusion is carried out concurrently with compression [13]. However, PLIF is associated with certain disadvantages, such as dural tears. Another drawback is the potential displacement of the fusion device, particularly when posterior fixation is not utilized. Moreover, sinking of the fusion device can lead to excessive stripping of endplates. Neurogenic membrane fibrosis can result in persistent lower back pain and/or leg pain. Additionally, neurological deficits may occur [14].

Adjacent segment degeneration (ASD) is a significant complication that impacts the long-term effectiveness of posterior lumbar interbody fusion (PLIF) technique. A study conducted by Maruenda et al. examined reoperation rates for ASD over various follow-up periods [15]. Their findings revealed reoperation rates of 9.6% at the 5-year follow-up, 24.6% at the 10-year follow-up, and 37.5% at the 15-year follow-up. These statistics highlight the progressive nature of ASD and emphasize the need for careful consideration of the long-term outcomes of PLIF technique [15].

2.2 Transforaminal LIF (TLIF)

Transforaminal lumbar interbody fusion (TLIF) is a surgical technique that combines both anterior and posterior fusion methods. Initially introduced by Blume and Rojas, TLIF was later popularized by Harms and colleagues as an alternative to PLIF [16]. TLIF is an appropriate surgical approach for various degenerative conditions, including extensive disc herniation, degenerative disc disease, recurrent disc herniation, lumbar spinal stenosis, pseudoarthrosis, and segmental spinal instability.

The TLIF technique involves accessing the intervertebral disc through the posterolateral part of the intervertebral foramen. The disc space can be expanded using pedicle screw fixation, and lumbar lordosis can be restored through intervertebral bone graft fusion [17]. The transforaminal TLIF technique requires unilateral laminectomy, resection of the inferior articular process, and proximal superior articular process. It offers a method that requires no or minimal traction through the dura mater and nerve root into the intervertebral disc, in comparison to PLIF. TLIF technology better preserves the integrity of peripheral nerve tissue compared to PLIF technology [18].

TLIF offers several advantages in spinal surgery. Firstly, it effectively preserves the area of the contralateral vertebral endplate, providing an additional surface for fusion. Secondly, TLIF exclusively

exposes the ipsilateral neural foramen, but if needed, it allows for bilateral decompression, thereby reducing the risk of unintended neural complications[19]. In addition, TLIF can be safely performed at or above the L3 level, with minimal risk of conus injury, making it particularly suitable for revision surgeries involving significant epidural fibrosis. This is due to its requirement of only ipsilateral and lateral dural exposure[20]. Nevertheless, there are several disadvantages associated with TLIF. These include incomplete removal of the intervertebral disc, inadequate preparation of the vertebral endplates, and the potential for hidden damage to the exiting nerve roots. However, it is important to note that experienced surgeons rarely encounter these issues. Furthermore, classic TLIF does not provide decompression of the contralateral nerve root.

When addressing the restoration of lumbar lordosis and sagittal spinal balance in patients with degenerative lumbar scoliosis (DLS), transforaminal lumbar interbody fusion (TLIF) proves to be more effective. TLIF achieves this by restoring anterior column height through intervertebral distraction, as well as improving lumbar physiological lordosis by removing posterior facet joints and compressions. Furthermore, TLIF offers notable advantages over posterior lumbar interbody fusion (PLIF), including reduced damage to the spinal canal, shorter operating time, and lower morbidity. Consequently, TLIF has become widely adopted for lumbar fusion procedures. Research has found that complications in TLIF surgery occur at an incidence rate of 14%, encompassing complications such as hematoma, superficial infection, nerve root injury, intraoperative dural tear, pneumothorax, and others [21].

2.3 Anterior LIF (ALIF)

In 1948, Lane and Moore introduced the concept of anterior lumbar interbody fusion (ALIF) [22]. The disc can be approached anteriorly through either the retroperitoneal or transperitoneal approach, with the retroperitoneal approach allows access to all lumbar segments from L1 to the sacrum, while the transperitoneal approach is limited to levels above L4. Traditionally, the retroperitoneal approach has been the preferred method, while the transperitoneal approach is primarily used in obese patients or those who have previously undergone retroperitoneal exposure. After performing discectomy and endplate preparation, a cage or graft is inserted to achieve the desired endplate coverage, height, and lordotic angle. ALIF can be considered a salvage technique for patients who develop painful pseudarthrosis after posterior lumbar interbody fusion (PLIF) [23]. While ALIF is a suitable surgical approach for the L5-S1 vertebral body, its effectiveness is limited for vertebral bodies at the L3-L4 level and higher. The interbody fusion rate has been reported to be higher in ALIF compared to posterior lumbar interbody fusion (PLIF). According to Jackson et al., successful ALIF fusions were reported in 41 out of 43 patients (95.3%) or 71 out of 73 patients (97%) with minimal complications.

The advantages of ALIF include direct observation and effective access to the anterior column, which facilitate easier and more thorough disc removal. Additionally, ALIF provides better distraction, increasing the volume of the neural foramen and enabling the placement of large intervertebral fusion devices[24]. This technique has a higher fusion rate, reduces iatrogenic trauma to the paraspinal muscle tissue, as well as the posterior bony elements of the spinal nerve, and improves the restoration of lumbar lordosis, coronal, and sagittal balance, thus decreasing the risk of anterolisthesis[25]. The direct compression of the graft, in contact with a larger bone endplate surface area and benefiting from a greater vascular supply, can enhance the fusion potential.

Most complications associated with the surgical approach include postoperative hernia, intestinal obstruction, iliac vein thrombosis, genitourinary system injury, and retrograde ejaculation. Major vascular complications have been reported to occur at an incidence ranging from 0.5% to 4.0%. A significant drawback of ALIF is the requirement for a separate posterior incision to decompress neural elements or perform pedicle screw fixation [26].

2.4 Extreme Lateral LIF (LLIF/XLIF)

In 2011, Berjano et al. introduced the lateral lumbar interbody fusion (LLIF) as a safe and effective alternative to anterior lumbar interbody fusion (ALIF) or posterior lumbar interbody fusion (PLIF). This approach prevents potential complications associated with anterior large vessels and posterior structures [27]. LLIF is applicable for various conditions such as degenerative disc diseases, adult scoliosis, lumbar spondylolisthesis, lumbar instability, lumbar spinal stenosis, adjacent segment diseases, revision intervertebral disc replacement, and pseudarthrosis. Additionally, the use of a large transverse interbody fusion cage during LLIF allows for the redistribution of forces in the coronal and sagittal planes of the spine. This feature makes it suitable for treating new cases of scoliosis as well [28].

The LLIF technique enables access to the anterior and middle columns of the lumbar spine through a small incision of approximately 3-4 cm, resulting in minimal intraoperative blood loss during intervertebral space access. Moreover, in the lateral position, gravitational forces effectively clear most of the abdominal contents from the surgical field. The lateral approach allows for relatively easy access to multiple levels ranging from T11 to L4, while the transposas approach preserves the integrity of the longitudinal ligament and posterior muscle tissue of the spine. In comparison to ALIF, LLIF technique avoids direct damage to the abdominal organs, peritoneum, ilio-lumbar vessels, and sympathetic chain^[29]. Notably, LLIF offers minimally invasive access to the lumbar spine, thereby reducing surgery time and hospitalization duration^[30].

The LLIF technique exhibits limitations, particularly in cases of severe central artery stenosis, where it may pose challenges^[31]. Furthermore, venous anatomical variations, tear-shaped psoas muscle, and the anteriorly located nerve plexus can impede the surgical approach to L4-5. Additionally, the presence of the iliac crest obstructs the true lateral pathway, rendering LLIF unfeasible at the L5-S1 level. It is important to note that this lateral technique directly traverses the lumbar muscle, which has been associated with reports of postoperative hip flexor weakness^[32]. Moreover, stretching or injuring the genitofemoral nerve during LLIF surgery may result in thigh and inguinal pain^[33].

Long-term follow-up data has demonstrated comparable fusion rates between LLIF and PLIF. The LLIF approach is associated with common complications, including postoperative motor and sensory disorders in the lower limbs, such as thigh numbness and weakness in hip flexion, with an overall incidence of up to 20%. However, these symptoms typically resolve over time, with a recovery rate of only 50% at 3 months post-surgery and reaching 90% at 1 year post-surgery. ^[34].

2.5 Oblique LIF (OLIF)

Phan and Mobbs were the pioneering surgeons to describe oblique lumbar interbody fusion (OLIF) surgery. This technique involves accessing the disc through the anterior oblique diameter of the psoas major muscle (ATP). They specifically employed this approach to address cases of failed bone fusion on the posterior wall during revision surgeries [35]. OLIF surgery, unlike lateral lumbar interbody fusion (LLIF) which is impeded at the L5-S1 level by the iliac crest, can be performed in the retroperitoneal plane. This procedure involves accessing the disc through the anterior iliac crest channel situated between the psoas muscle and the main abdominal vessels. OLIF surgery, in comparison to LLIF, eliminates the necessity for dissection and division of the psoas major muscle, which may potentially lead to a decrease in postoperative pain. The most common indications for OLIF surgery comprise degenerative disc disease, discitis, pseudarthrosis formation at L5-S1, and isthmic spondylolisthesis.

The tilted surgical trajectory of OLIF technique minimizes surgical trauma to the psoas major muscle and lumbosacral plexus, effectively removing intervertebral disc space obstruction, and employing a large intervertebral device for foraminal decompression[36]. Additionally, the angled approach enables distinctive observation of the extradural space (in comparison to LLIF), facilitating the decompression and extraction of ventrolateral osteophytes and herniated discs[37]. The OLIF approach is regarded as a potential resolution to the challenges presented by ALIF (iliac vessel and peritoneal injury) and LLIF (lumbosacral muscle splitting and restricted access to the lower lumbar region).

Nevertheless, Postoperative complications of OLIF encompass numbness, pain, and weakness in the lower limbs[38]. In cases where the retroperitoneal oblique corridor (ROC) is narrow, a higher degree of psoas major muscle retraction may be necessary, leading to an increased probability of postoperative neurologic complications.

Studies have indicated a fusion rate of 84% or higher with OLIF surgery. [39]. The most frequent complications after OLIF surgery were endplate fracture/collapse (18.7%), transient lumbar muscle weakness and thigh numbness (13.5%), segmental artery injury (2.6%), surgical site infection (1.9%), and the need for reoperation (1.9%). Abe et al. reported a perioperative complication rate of 48.3% for OLIF surgery. The study included 155 patients and found that only 1.9% of complications led to permanent damage. [40].

3. Bone biologics and biomaterials in LIF

3.1 Bone graft

Bone grafts are frequently employed in lumbar interbody fusion (LIF) surgery. Although autologous

and allogeneic bone can both be used, autologous iliac bone graft (ICBG) is regarded as the preferred choice due to its capability to prevent immune reactions and supply osteoblasts and biological factors that act as a framework for new bone formation. Nonetheless, the risks associated with intraoperative complications and donor-site pain during the iliac bone harvesting process restrict the extensive utilization of ICBG in LIF procedures [41].

3.2 Bone Biomaterials

Bone biomaterials, also referred to as bone substitutes, are synthetic or natural materials that facilitate bone repair and can be implanted into bone defect sites. In contrast to bone grafts or bone-induced growth factors, an ideal bone biomaterial should possess certain properties. These include biocompatibility, easy moldability, absorbability, radiological detectability, sterilizability, and accessibility. A variety of biological materials have been utilized in lumbar interbody fusion (LIF) surgeries, such as polyester, collagen scaffold, hydroxyapatite (HA), and porous β -tricalcium phosphate [42]. However, it is acknowledged that bone-conductive biomaterials alone have limitations in healing large bone defects. Therefore, combining bone biomaterials with osteoblasts and/or growth factors can lead to more favorable outcomes for spinal fusion. Bone biomaterials facilitate spinal fusion through two primary mechanisms: (1) serving as scaffolds to facilitate cell migration, capillary ingrowth, cell proliferation, and osteogenic differentiation of mesenchymal stem cells on material surfaces within the bone environment, and (2) serving as carriers for osteogenic proteins, including nanomaterials, to control or regulate their release [43].

3.3 Bone biological products based on osteoinductive proteins

Over the past 20 years, recombinant human bone morphogenetic protein 2 (rhBMP2) has become the predominant osteoinductive growth factor used in lumbar interbody fusion (LIF) procedures. Its efficacy in promoting fusion and avoiding the requirement for autologous bone grafts has contributed to its widespread adoption. Initial research has shown that utilizing collagen-1 as a carrier for rhBMP2 results in better lumbar fusion outcomes and fewer complications compared to the established gold standard of autologous bone grafts, with fusion rates of 88% and 73%, respectively. [44].

4. Prospects

As previously mentioned, although there have been advancements in recent technologies, the current spinal fusion treatment modalities have not yet achieved satisfactory rates of bone fusion and functional improvement. Various strategies exist to enhance the outcomes of spinal fusion, and we will primarily focus on developing interbody fusion devices and biologics to achieve better bone fusion and functional outcomes[45]. This involves enhancing bone fusion and improving functional outcomes. First, there is a need to develop interbody fusion devices and biologics further. This necessitates research on the advantages and disadvantages of different materials and the development of novel material processing techniques. Second, there is a need to place cortical bone trajectory screws to reduce detachment and improve clinical results[46]. Additionally, it is essential to investigate osteoinductive bone biologics, identify novel osteogenic proteins, and develop new biomaterials and controlled release technologies[47]. Moreover, Mesenchymal stem cells are seen as potential approaches for enhancing spinal fusion. Future research should concentrate on extensive, long-term clinical studies to comprehensively evaluate the effectiveness of new technologies and treatment methods.

5. Conclusions

In conclusion, the fusion rate of lumbar interbody fusion (LIF) surgeries for the treatment of low back pain associated with degenerative lumbar disease has progressively improved in recent decades. This improvement can be attributed to advancements in surgical techniques and continuous enhancements in cage design. Nevertheless, surgical complications, particularly bone fusion failure or pseudarthrosis development, continue to present significant [48]. Future research should prioritize the following areas. The success rate of surgeries can be improved and the occurrence of complications can be reduced by further enhancing the fusion cage and refining surgical techniques [49]. Furthermore, there is a need for more efficient osteogenic factors that have fewer side effects in order to promote bone fusion. In addition, the development of new biomaterials capable of regulating the release of osteogenic proteins could effectively manage the inflammatory response and prevent excessive growth of the cage and surrounding

hard tissues. Lastly, it is essential to clarify the role of mesenchymal stem cells (MSCs) in LIF in order to fully harness their potential and improve surgical outcomes[50].

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