Comparison of Clinical Outcomes Between Stand-Alone Oblique Lumber Interbody Fusion and Posterior Lumbar Interbody Fusion for Treatment of Degenerative Lumbar Diseases

Run Peng Guo
Hebei Medical University Third Affiliated Hospital

Xian Da Gao
Hebei Medical University Third Affiliated Hospital

Pei Yu Du
Hebei Medical University Third Affiliated Hospital

Wen Yuan Ding
Hebei Medical University Third Affiliated Hospital

Lei Ma (✉ maleidsyd@163.com)
Hebei Medical University Third Affiliated Hospital

Research article

Keywords: Oblique, Posterior, lumber, interbody fusion, Clinical outcomes, Radiological outcomes

DOI: https://doi.org/10.21203/rs.3.rs-129865/v1

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Abstract

Background: This study evaluated the clinical and imaging results of oblique lumber interbody fusion (OLIF) and posterior lumbar interbody fusion (PLIF) in the treatment of degenerative lumbar diseases.

Methods: The clinical data of 99 patients with degenerative lumbar diseases in the Third Hospital of Hebei Medical University from January 2016 to January 2018 were analyzed retrospectively. 49 cases were dealt with by OLIF (stand-alone) (OLIF group) and 50 cases with PLIF (PLIF group). Clinical and imaging data were collected before surgery and at each follow-up visit. Clinical data included operation time, blood loss, incision length, length of hospital stay, visual analogue score (VAS), Oswestry dysfunction index (ODI), Japanese orthopaedic association (JOA) scores and complications. Imaging measurement included the height of segmental intervertebral space, lumbar lordotic angle, operative segmental lordotic angle and fusion rate. The relationship between clinical results and radiology was assessed by comparing the radiological results before and after operation.

Results: 99 cases of interbody fusion were performed successfully, and all patients had clinical improvement. The follow-up time was 24-38 months. The operation time, intraoperative blood loss, incision length and hospital stay in OLIF group were significantly less than those in the PLIF group (p<0.05). The intervertebral disc height, lumbar lordotic angle and operative segmental lordotic angle in the two groups were significantly enhanced compared with those before operation, and the difference was statistically significant (p<0.05). All of them achieved satisfactory fusion effect. Complications were found in 5 cases in OLIF group and 13 cases in PLIF group.

Conclusion: Both OLIF and PLIF are effective in the treatment of degenerative lumbar diseases. Compared with PLIF, OLIF has a lot advantages in early stage after operation, However, similar clinical outcomes were achieved in the two approaches at mid-term follow-up visit.

Background

In recent years, degenerative disease of the lumbar spine is one of the most common diseases in aging population [1, 2]. Lumbar interbody fusion is a classic surgical procedure for the treatment of lumbar degenerative diseases, and its efficacy had been clinically proven for many years and is accepted by most surgeons. It provides nerve decompression, immediate stability and restoring the height of the intervertebral space. Lumbar interbody fusion procedure, including posterior approach, anterior approach or lateral approach, relieve symptoms caused by spinal stenosis [3–5].

PLIF is a traditional interbody fusion procedure that allows full exposure of the nerve roots through the posterior approach. Moreover, PLIF allows for direct decompression of the nerve and proper restoration of the height of the intervertebral space, while posterior approach supports stability during the surgical phase, which has been accepted by most surgeons [6, 7]. In recent years, OLIF has gained widespread popularity, first proposed by Mayer [8] in 1997 and first named oblique lateral lumbar interbody fusion (OLIF) by Silvestre [9] in 2012. It exposed the intervertebral disc space through the retroperitoneum via the
space between main vessels and the anterior border of the psoas muscle as an access route. The oblique approach has the advantages of less trauma, less bleeding, and shorter operative time [10]. Several studies have shown favorable results of OLIF in the treatment of degenerative lesions of the lumbar spine [11, 12]. However, each procedure has its advantages and disadvantages in terms of fusion rate, disc height recovery, and lumbar lordotic angle [4, 5]. As a rapidly developing surgical technique, OLIF shows more pronounced surgical advantages over PLIF, without the need for destruction of posterior spine related structures [13]. It also allows correction of spinal deformities, high fusion rates and complete removal of the disc [14].

Currently, there are only a few reports on the clinical efficacy and learning curve of the OLIF technique for the treatment of lumbar degenerative disc disease. We conducted a retrospective study of patients who underwent OLIF for lumbar degenerative disease at our institution with the aim of exploring the advantages of OLIF in the treatment of degenerative lumbar spine disease by comparing the postoperative clinical outcomes and imaging results of two different procedures, OLIF and PLIF.

**Materials And Methods**

**Patients population**

All protocols of the study was approved by the Ethics Committee of the Third Hospital of Hebei Medical University and informed consent was obtained from all individual participants for using their imaging data and questionnaire scores.

We retrospectively analyzed the medical records of patients who underwent surgery for the lumbar degenerative diseases at our institution from January 2016 to January 2018. The inclusion criteria were as follows, 1. Mild lumbar spinal stenosis with or without lumbar instability 2. Mild degenerative lumbar slippage (Meyerding score I°) 3. Discogenic low back pain 4. Mild lumbar disc herniation 5. Single-segment lumbar degenerative disease 6. With complete data and perioperative records, as well as radiographic follow-up data.

Exclusion criteria: 1. Severe lumbar disc herniation and spinal stenosis 2. Moderate to severe degenerative lumbar slippage (Meyerding score I° or higher) and spondylolisthesis 3. Severe osteoporosis 4. Previous history of abdominal surgery 5. The follow-up period is less than 24 months.

**Surgical approaches**

**OLIF**

Patients in the OLIF group were immobilized in the right lateral decubitus position on the surgical bed. The preoperative C-arm was fluoroscopically positioned, and the incision was mostly located about 4–6 cm in front of the vertebral space positioning to cut the skin. The skin and subcutaneous tissues were incised and the external oblique, internal oblique, and transverse abdominal muscles were bluntly
separated in turn to enter the retroperitoneal space and reveal the anterior border of the psoas major muscle. The vertebral bodies and intervertebral spaces were located between the psoas major muscle and the abdominal aorta. After fluoroscopic positioning to confirm the surgical segment, the working channel is placed and secured. Under direct vision, the intervertebral fibrous annulus was incised from the lateral side, and the intervertebral tissue and upper and lower endplates were adequately scraped off, taking care to avoid damaging the bony endplates during the operation. After trial molding, the appropriate size of the intervertebral fusion is placed perpendicular to the intervertebral space, taking care to avoid damaging the dural sac. Finally, after the fluoroscopic view of the position of the fusion device is satisfactory, the surgical incision is closed layer by layer.

**PLIF**

Patients in the PLIF group were placed in the prone position under general anesthesia, and a median incision was made. The paravertebral muscles were dissected from the spine to the sides, exposing the disc, lamina and facet joint. The pedicle screws were placed into the pedicle. A C-arm was used for fluoroscopy to check the position of the pedicle screws. The diseased disc and lamina and inferior facet joint were removed. The lateral crypt and nerve root canal were fully decompressed and the fibrous annulus was incised, the nucleus pulposus was removed, and the cartilage end plate was scraped. Autologous bone and a suitable Cage was implanted in intervertebral space. A titanium rod of appropriate length is placed and fixed with pressure. Finally, the wound is flushed with normal saline, a drain is placed, and the incision is closed in layers.

**Clinical and imaging assessment**

We assessed the improvement of low back pain in both groups of patients according to the VAS score [15] and the JOA score [16] at preoperative, 7 days postoperative, and final follow-up. Improvements in lumbar spine function were assessed using the ODI score [17] at preoperative, 7 days postoperative, and last follow-up visits. Patients were evaluated via office visits or telephone. Obtain clinical data such as operative time, bleeding, incision length, length of hospital stay, etc. Document perioperative complications.

X-rays are taken of all patients before surgery, immediately after surgery, and at the last follow-up visit, measurements are evaluated. Measurements on lumbar spine X-rays: Calculate intervertebral space height, lumbar lordotic angle, and operative segmental lordotic angle at preoperative, postoperative, and final follow-up surgical segments. The intervertebral gap height is the average of the anterior and posterior gaps between two adjacent vertebrae in the lateral X-ray fusion segment; the lumbar lordotic angle is the angle between the upper terminal plate of the first lumbar vertebra and the upper terminal plate of the sacrum; the operative segmental lordotic angle is the angle between the upper terminal plate of the upper vertebra and the lower terminal plate of the lower vertebra in the surgical segment. A loss of at least 2 mm of intervertebral space height is generally considered Cage subsidence on X-ray [18]. Bony fusion was defined as trabeculation between adjacent vertebrae on CT scans [19].

**statistical analysis**
All statistical analyses were performed using the SPSS 21.0 statistical software program. Measures were showed as mean ± standard deviation. Paired t-test was used for within-group comparisons and independent samples t-test was used for between-group comparisons. Technical data were showed as percentages using chi-square test. p < 0.05 was considered a statistically significant difference.

Results

Clinical data

The surgery was completed successfully in both groups (Fig. 1). 99 patients were followed up for 24–38 months. In the OLIF group, there were 21 males and 28 females, with an average age of 57.92 ± 10.20 years and an average follow-up time of 26.86 ± 2.92 months; in the PLIF group, there were 24 males and 26 females, with an average age of 59.02 ± 9.48 years and an average follow-up time of 27.90 ± 3.33 months. Statistically different were not in Follow-up time, age, gender and BMI between the OLIF and PLIF groups. A statistical difference was found in the number of fused segments between the two groups, with fewer patients in the OLIF group undergoing L5/S1 surgery because of higher risk[20] (Table 1). Operative time in the OLIF group was 80–111 min, mean (91.69 ± 8.62) min; intraoperative bleeding 60–110 ml, mean (90.00 ± 11.23) ml; incision length 4.0-5.1 cm, mean (4.57 ± 0.29) cm and hospital stay 5–12 days, mean (7.90 ± 1.78) days. In the PLIF group, the operative time was 90–180 min, mean (132.43 ± 20.98) min; intraoperative bleeding 250–500 ml, mean (390.82 ± 71.21) ml; incision length 7.6–14.6 cm, mean (10.09 ± 1.61) cm and hospital stay 6–14 days, mean (7.90 ± 1.78). The OLIF group was superior to the PLIF group in abovementional dates, with a statistically significant difference (p < 0.05) (Table 2).

| Table 1       | Baseline characteristics |
|---------------|--------------------------|
|               | OLIF(n = 49)             | PLIF(n = 50) | t/z  | P      |
| Follow-up time (months) | 26.86 ± 2.92            | 27.90 ± 3.33 | 1.857 | P = 0.066 |
| Age (years)   | 57.92 ± 10.20           | 59.02 ± 9.48 | 0.640 | P = 0.524 |
| Gender (male/female) | 21/28                   | 24/26 | 0.264 | 0.607 |
| BMI (kg/m)    | 22.77 ± 2.45            | 22.14 ± 2.54 | 0.184 | 1.339 |
| Fused segments|                         | 11.999 | 0.002 |
| 3/4           | 8                        | 5       |
| 4/5           | 38                       | 28      |
| 5/1           | 3                        | 17      |
### Table 2
Comparison of intraoperative and situation between the two groups of patients

|                      | OLIF (n = 49) | PLIF (n = 50) | t/z   | P      |
|----------------------|--------------|--------------|-------|--------|
| Operation time (min) | 91.69 ± 8.62 | 132.43 ± 20.98 | 12.713 | P < 0.001 |
| intraoperative bleeding (ml) | 90.00 ± 11.23 | 390.82 ± 71.21 | 29.053 | P < 0.001 |
| incision length (cm)  | 4.57 ± 0.29  | 10.09 ± 1.61  | 23.823 | P < 0.001 |
| hospital stay (days)  | 7.9 ± 1.78   | 9.49 ± 1.82   | 4.451  | P < 0.001 |

### Imaging data

There was no statistically significant difference in the preoperative intervertebral space height between the two groups (p = 0.572). Post-operative intervertebral space height was significantly higher than preoperative in both groups, OLIF (p < 0.001), PLIF (p < 0.001). The postoperative intervertebral height in the OLIF group was better than that in the PLIF group, and there was a statistical difference in the postoperative intervertebral height between the two groups (p = 0.001). At the final follow-up, there was statistical difference in loss of height of the intervertebral space between the two groups (p = 0.011) (Table 3).
Table 3

Comparison of radiological outcomes between OLIF and PLIF

|                          | OLIF (n = 49) | PLIF (n = 50) | t/z   | P    |
|--------------------------|--------------|---------------|-------|------|
| Intervertebral height (mm) |              |               |       |      |
| Preoperative             | 10.48 ± 1.50 | 10.34 ± 1.40  | 0.568 | 0.572|
| Post-operative           | 12.84 ± 1.49*| 11.79 ± 1.33* | 3.365 | 0.001|
| The last follow-up       | 11.64 ± 1.34*| 10.95 ± 1.34* | 2.587 | 0.011|
| Lumbar lordosis angle (º) |              |               |       |      |
| Preoperative             | 40.82 ± 11.19| 37.23 ± 10.68 | 1.592 | 0.115|
| Post-operative           | 47.37 ± 8.78*| 43.35 ± 7.82* | 2.374 | 0.020|
| The last follow-up       | 44.73 ± 8.15*| 42.08 ± 7.58* | 1.648 | 0.102|
| Operative segmental lordotic angle (º) |        |               |       |      |
| Preoperative             | 16.32 ± 3.78 | 16.61 ± 4.05  | 0.240 | 0.811|
| Post-operative           | 19.60 ± 3.36*| 17.95 ± 4.00* | 2.319 | 0.022|
| The last follow-up       | 17.94 ± 3.18*| 17.29 ± 3.98* | 0.988 | 0.326|

* There was statistically significant compared with preoperative

There was no statistically significant difference in the lumbar lordotic angle between the two groups preoperatively (p = 0.115), and the lumbar lordotic angle improved significantly after surgery. There were statistically significant differences between the two groups before and after surgery, OLIF (p < 0.001), PLIF (p < 0.001). The postoperative lumbar lordotic angle in the OLIF group was greater than that in the PLIF group, and there was a statistically significant difference between the two groups (p = 0.020). There was no statistically significant difference in the lumbar lordotic angle between the two groups (p = 0.102) (Table 3).

There was no statistically significant difference between the two groups in the preoperative operative segmental lordotic angle (p = 0.811), and the postoperative operative segmental lordotic angle improved in both groups. There was a statistically significant difference between the two groups before and after surgery, OLIF (p < 0.001), PLIF (p < 0.001). The operative segmental lordotic angle was more significant in the OLIF group than in the PLIF group, and there was a statistically significant difference between the two groups after surgery (p = 0.022). There was no statistically significant difference in the operative segmental lordotic angle between the two groups (p = 0.326) (Table 3).

All patients achieved bony fusion at last follow-up. 4 patients in the OLIF group had mild Cage subsidence, and none of the patients in the PLIF group had significant Cage subsidence.
Quality of life

There was no statistical difference between the OLIF and PLIF groups in preoperative lumbar and leg VAS scores (p > 0.05). VAS scores for back pain and leg pain decreased significantly in both groups 7 days after surgery. 7-day postoperative back pain VAS scores were lower in the OLIF group than in the PLIF group, with a statistically significant difference (p < 0.001). Leg pain VAS scores were lower in the OLIF group than in the PLIF group 7 days postoperatively, with a statistically significant difference (p < 0.001).

At the final follow-up, there was no statistical difference in the back and leg pain VAS scores between the two groups (p > 0.05). Preoperative JOA scores were 16.88 ± 1.93 and 16.29 ± 2.12 in the OLIF and PLIF groups, respectively, with no statistical difference (p = 0.144). The 7-day postoperative JOA scores of both groups were significantly improved compared to the preoperative period, 20.65 ± 2.05 and 18.14 ± 2.12 respectively, which were statistically different from the preoperative period, OLIF (p < 0.001), PLIF (p < 0.001). The JOA score was higher in the OLIF group than in the PLIF group at 7 days after surgery, and the difference was statistically significant (p < 0.001). At the final follow-up, there was no statistically significant difference in JOA score between the two groups (p = 0.581). The preoperative ODI scores were 58.53 ± 8.99 and 59.39 ± 9.34, respectively, with no statistical difference between the two groups (p = 0.652). The ODI scores decreased by 24.1 ± 8.7 and 34.3 ± 10.3 on 7 days after surgery, which were statistically different from the preoperative levels, OLIF (p < 0.001) and PLIF (p < 0.001). Furthermore, the ODI score was lower in the OLIF group than in the PLIF group at 7 days after surgery, and the difference was statistically significant (p < 0.001). At the final follow-up, there was no statistical difference in ODI scores between the two groups (p = 0.437). The OLIF group showed satisfactory clinical efficacy at an early stage (Table 4).
|                          | OLIF (n = 49) | PLIF (n = 50) | t/z       | P        |
|--------------------------|--------------|---------------|-----------|----------|
| **VAS of low back pain** |              |               |           |          |
| Preoperative             | 6.53 ± 0.85  | 6.48 ± 0.82   | 0.195     | P = 0.846|
| 7 days after operation   | 1.94 ± 0.79* | 3.37 ± 0.86*  | 8.705     | P < 0.001|
| The last follow-up       | 1.48 ± 0.66* | 1.67 ± 0.63*  | 1.588     | P = 0.116|
| **VAS of leg pain**      |              |               |           |          |
| Preoperative             | 5.40 ± 0.74  | 5.50 ± 0.75   | 0.845     | P = 0.400|
| 7 days after operation   | 2.04 ± 0.69* | 3.67 ± 0.82*  | 10.761    | P < 0.001|
| The last follow-up       | 1.40 ± 0.61* | 1.47 ± 0.58*  | 0.765     | P = 0.446|
| **ODI**                  |              |               |           |          |
| Preoperative             | 58.53 ± 8.99 | 59.39 ± 9.34  | 0.452     | P = 0.652|
| 7 days after operation   | 24.12 ± 8.74*| 34.33 ± 10.33*| 5.307     | P < 0.001|
| The last follow-up       | 17.55 ± 6.66*| 18.61 ± 6.26* | 0.780     | P = 0.437|
| **JOA**                  |              |               |           |          |
| Preoperative             | 16.88 ± 1.93 | 16.29 ± 2.12  | 1.472     | P = 0.144|
| 7 days after operation   | 20.65 ± 2.05*| 18.14 ± 2.12* | 5.976     | P < 0.001|
| The last follow-up       | 23.04 ± 2.07*| 22.78 ± 2.27* | 0.554     | P = 0.581|

* There was statistically significant compared with preoperative

**Complications**

In the OLIF group, four patients had fusion subsidence at the last follow-up; one patient had a vascular injury, which was repaired intraoperatively, and no other significant abnormalities were seen after surgery.

In the PLIF group, one patient developed fusion apparatus subsidence; two patients developed wound redness and swelling and poor healing, which healed well after dressing change; two patients developed dural sac rupture and cerebrospinal fluid leakage during the operation, which were repaired, and no cerebrospinal fluid leakage after the procedure; five patients developed intermuscular vein thrombosis after the system, which was treated with anticoagulant drugs. After PLIF surgery, due to long bedtime and late activities, intermuscular vein thrombosis was prone to occur; infection occurred in one case, which was treated with anti-infection after surgery without severe consequences; one case of lung infection occurred, which may be related to older age and long bedtime, which was treated with antibiotics promptly without severe effects; one case of wound hematoma occurred, which was treated with surgery...
again and recovered well after surgery with a total of complications (Table 5). No severe complications such as displacement of the fusion and loosening of the internal fixation were found during the follow-up period.

### Table 5
Comparison after OLIF and PLIF

|                     | OLIF \(n = 49\) | PLIF \(n = 50\) | \(t/z\) | \(P\) |
|---------------------|------------------|-----------------|---------|-------|
| Cage subsidence     | 4                | 1               | 4.151   | 0.042 |
| Vascular injury     | 1                | 0               |         |       |
| Poor healing        | 0                | 2               |         |       |
| Dural rupture       | 0                | 2               |         |       |
| venous thrombosis   | 0                | 5               |         |       |
| infection           | 0                | 1               |         |       |
| lung infection      | 0                | 1               |         |       |
| hematoma            | 0                | 1               |         |       |

### Discussion

The occurrence of lumbar degenerative diseases is on the rise in the global society with the advancement of the society and the phenomenon of aging population of the society [21]. Obviously, as the incidence increases, it seriously affects the quality of life of patients and is a major source of chronic disability [22–24]. Therefore, lumbar fusion is becoming increasingly common as an adjunct in the surgical treatment of lumbar degenerative diseases [25]. Interbody fusion is an effective treatment for a variety of spinal conditions, including degenerative disc disease, spinal stenosis, lumbar slippage, degenerative scoliosis, traumatic changes, infections, and tumors. However, with the development of interbody fusion, the frequency and complications of the procedure have increased [4, 21]. Our goal is to reduce complications and increase the success of the procedure. In between, a number of minimally invasive interbody fusions have emerged, and for many surgeons, minimally invasive surgical approaches have become a safe alternative to traditional open techniques.

In this study, we report the safety and efficacy of OLIF compared to the PLIF technique in treating degenerative lumbar spondylosis, which has the advantages of shorter operative time, more temporary hospital stays, less bleeding, and lower incidence of postoperative low back pain. We found that the back VAS score, ODI score, and JOA score were lower in the OLIF group than in the PLIF group 7 days after surgery. Furthermore, intraoperative bleeding was lower, the incision was smaller, and the operative time was shorter in the OLIF group. This may be related to the entry route of the OLIF procedure, where the disc is entered through the natural gap between the abdominal aorta and the anterior border of the psoas.
major muscle in the abdomen, with a smaller incision, preserving the posterior structures of the spine and reducing the risk of damage to the surrounding tissues \[26, 27\]. PLIF is a classic and effective surgical procedure for treating lumbar degenerative spine disease and is suitable for most patients with lumbar degenerative disease. The stability of the posterior column structures in the three columns of the spine is compromised due to an extensive dissection of the paravertebral tissue during the procedure. As a result, the incidence of intraoperative complications associated with PLIF is higher than with OLIF, and the short-term effects of PLIF are slightly lower than those of OLIF; in particular, postoperative symptoms may worsen in the short term, or they may not be relieved. Compared to PLIF, the OLIF group did not have a dissection of the paravertebral muscles of the back, as well as damage to the back muscles, avoiding posterior scar tissue, thus reducing bleeding, shortening the operative time, and effectively reducing the incidence of postoperative low back pain \[28\]. This resulted in a better back VAS score in the OLIF group than in the PLIF group in the early postoperative period. Also, leg VAS scores were lower in the OLIF group than in the PLIF group 7 days after surgery, which may be due to the avoidance of direct stimulation and nerve roots pulling during the OLIF procedure.

In previous analyses, it has been found that the occurrence and progression of degenerative lumbar spine disease are strongly associated with loss of lumbar curvature and intervertebral space height. Indirect decompression is achieved through the OLIF procedure by inserting a larger area and volume fusion in the vertebral body's lateral aspect, increasing the lumbar lordotic angle and gap height, and pulling on the ligaments. According to Sato \[14\] et al., there was a significant improvement in the intervertebral space's size after OLIF compared to preoperatively. In the present study, the immediate postoperative intervertebral space height was significantly higher than the preoperative space height in both groups, and the OLIF group had a statistically significant difference in postoperative intervertebral space height compared to the PLIF group. The loss of the lumbar lordotic angle is a fundamental cause of lower back pain. It is crucial to restore the lumbar lordotic angel and the lumbar lordotic angel of the surgical segment for symptom recovery and prevent degeneration of the adjacent phases \[29\]. It has been shown \[30\] that OLIF surgery has a significant improvement in lumbar lordotic at the surgical stage. In the present study, both the OLIF and PLIF groups showed a substantial recovery of lumbar lordotic angle and operative segmental lordotic angle, with a statistically significant difference between the OLIF and PLIF groups in the immediate postoperative period, which may be related to the insertion of a larger fusion device. At the final follow-up, there was a statistically significant difference between the lumbar lordotic and the operative segmental lordotic angle between the two groups and the preoperative period, but not between the two groups. This means that the OLIF group achieved the same surgical results as the PLIF group. No fusion was observed in any of the patients by CT and X-ray at the final follow-up. In the OLIF group, four patients found fusion subsidence, and the loss of vertebral space was less than 25%, which is considered mild \[31\], and all patients with subsidence had no clinical symptoms during the follow-up. Osseous fusion was obtained in both groups at the final follow-up, with no difference in infusion rate. We believe that the more extensive fusion apparatus used in the OLIF procedure increases the contact area with the last plate, which contributes to a higher fusion rate and a lower settling rate \[30\].
Intraoperative complications of OLIF include vascular injury, nerve injury, ureteral injury, and cerebrospinal fluid leakage [9, 32, 33], which did not occur in the present study. Postoperative complications included transient thigh and groin sensory deficits and hip flexor weakness, fusion settling, pseudarthrosis, and postoperative infection [32, 34, 35], none of which were serious complications in the present study.

**Conclusions**

Both OLIF and PLIF are effective in the treatment of degenerative lumbar diseases. Compared with PLIF, OLIF has a lot advantages in early stage after operation, However, similar clinical outcomes were achieved in the two approaches at mid-term follow-up visit.

**Abbreviations**

OLIF= oblique lumber interbody fusion, PLIF=posterior lumbar interbody fusion, VAS= visual analogue score, ODI=oswestry dysfuction index, JOA= Japanese Orthopaedic Association.

**Declarations**

Conflict of Interest: The authors declare that they have no conflict of interest.

Funding: There is no funding source.

Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors.

Availability of data and materials: The datasets generated and analysed during the current study are availabled from the corresponding author on reasonable request.

Authors’ contributions: LM and RPG conceived and designed the study, RPG and XDG collected, RPG, PYD and WYD analyzed and interpreted the patient data. RPG wrote the paper. All authors read and approved the final manuscript. All authors have read the journal policies and have no issues relating to journal policies.

All authors have seen the manuscript and approved to submit to your journal.

The work described has not been submitted elsewhere for publication, in whole or in part.

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