

Peer Review File**Article Information:** <https://dx.doi.org/10.21037/jss-22-24>**Round 1****Comment 1:**

The authors compared clinical outcomes following different fixation interventions treating degenerative lumbar spondylolisthesis. Five hundred and five patients undergoing posterior lumbar interbody fusion (PLIF) and 1333 undergoing transforaminal lumbar interbody fusion (TLIF) with six-month follow-up were compared. Both PLIF and TLIF result in clinically significant improvements in ODI, NRS back pain, and NRS leg pain, with superiority of TLIF for improvements in back and leg pain. Average theatre time and blood loss volume were higher for PLIF. I am very interested in research-based on this database. However, the follow-up period is short, and the consideration is insufficient. Please discuss the result.

Response: Thank you for your feedback and we agree that we needed to further justify our 6 months follow period. Part of the rationale is the increasing demand for shorter hospital stays, early return to work and need to reduce postoperative morbidity. The growth of new techniques attempts to shorten operative times and achieve faster recovery with reduced operative complications. Focus is also therefore importantly on short and middle term outcomes as well as long term – understanding of all timepoints being necessary for decision making regarding surgery. Previous data regarding mid-term outcomes is limited compared to the longer term and hence our focus.

Changes in the text:

The rationale for the study has been strengthened (P4/5).

Comment 2: Although the survey is based on the database, the patient's condition and the indication of each surgical method are unknown and insufficient explanation. Please indicate at least the surgical level.

Response: The table of characteristics (Table 1) has been extended to include surgical level, and the surgical level has been commented on in the results section (page 9).

Changes in the text:

‘Most patients in both the PLIF (12.2%) and TLIF group (33.5%) had interbody fusion level L4/5’.

Comment 3: The patients are 18 years old and over, but if the authors are targeting degenerative lumbar spondylolisthesis, shouldn't you survey over 50 years old?

Response: We appreciate your comment, and as indicated in Table 1 (patient characteristics), most of our patients were indeed aged 50 years and above: PLIF (80.4%) [406/505*100]; TLIF (83.7%) (1116/1333*100). However, if we had used this inclusion criterion, we would have

missed the patients in the lower age ranges including >10% patients in the 40-49.9 age range for both PLIF and TLIF.

Changes in text:

None made.

Comment 4: Line 239- 240, “The operative time was statistically higher for PLIF (200±72 minutes) compared to TLIF (184±78) [p=0.031].” It would be best if the authors used longer rather than higher.

Response: Thank you and yes, we agree.

Changes in text:

Changed as requested (see page 11] and a point added in the discussion on page 12.

Comment 5: Line 255- 258, “The results did demonstrate statistically and clinically meaningful differences between PLIF and TLIF in both back (p=0.048) and leg pain (p=0.005) at six months; with TLIF showing greater improvements in both back and leg pain.” It is a list of previous data, and please discuss the reason carefully.

Response: We have added some text as advised to carefully discuss results. This relates carefully to the key points raised in the earlier rationale for the study.

Changes in text:

We have added further details (see page 11/12).

Comment 6: Line 265-268, “In this study, PLIF was associated with significantly higher blood loss (380 mls) compared to TLIF (311 mls); consistent with Liu et al’s findings [16]. A plausible reason for the greater blood loss for the PLIF surgical technique might be the greater dissection involved.” There is a lack of evidence.

Response: Thank you for pointing this out.

Changes in text:

We have reworded to ensure our analysis is supported by evidence (see page 12).

Comment 7: Line 276-278, “When considering implant cost, there was a statistically significant difference between the groups (p<0.001). Implant cost was considerably higher in the TLIF cohort (£2668) compared to the PLIF cohort (£1298).” Why are the costs so different just because of the different approaches? Is it the difference between cages?

Response: Thank you for highlighting this point and we have linked to Kelly et al’s findings to explain further.

Changes in text:

‘..... are perhaps explained by Kelly et al’s (2019) finding that costs were higher for TLIF for implants (p<0.01) [10]’.

Reviewer A

Comment: I do not understand to difference in costs between the PLIF implants and the TLIF implant. The TILF procedure requires ONE implant and the PLIF requires TWO. In the USA the PLIF costs for implants are often close to double when compared to the TLIF costs.

Response: Thank you for highlighting this point and we have checked our data and analysis to confirm that our findings are accurate and that for our study costs were significantly higher for TLIF.

Reviewer B

Comment: The study should continue in order to also compare the fusion rate.

Response: We would be interested in continuing the study but sadly we have no further funding.

Reviewer C

Interesting database study--thanks for putting all of this together.

Comment: Line 6 (p 1) Bell D—for consistency, please use the author’s full name (assuming this is not his or her full name)

Response: Updated as requested P1.

Comment: Line 47 (p 1). You state ODI was statistically significant preoperatively for both. Please clarify? Was there a statistically significant difference preoperatively between the two?

Response: Thank you for pointing this out. We have re-structured this sentence. Please see page 2.

“There was a statistically significant difference in ODI scores preoperatively between PLIF and TLIF ($P<0.001$).”

Comment: Line 75(p 2) I would clarify here the indications for fusion (instability). Currently, this line in the intro reads as if spinal fusion is always recommended for degenerative spondylolisthesis. (Occasionally, isolated decompression is done).

Response: We have added some text as advised, clarifying the indication for fusion surgery. Please see page 4 line 96.

“Indication for spinal fusion may include discogenic/facetogenic low back pain, neurogenic claudication, radiculopathy due to foraminal stenosis, lumbar degenerative spinal deformity including symptomatic spondylolisthesis and degenerative scoliosis (7).”

Comment: Also comment on interbody fusion vs fusion without interbody)

Response: We have added a sentence to briefly describe fusion without interbody cage. Please see page 4 line 103.

“Occasionally, lumbar spine is fused without interbody cage or grafting, where fusion is attempted at the facet joint or nearby outer aspect of vertebra”

Comment: Line 81 (p 2) has fewer, not “less” complications

Response: Changed as requested. Please see page 4

Comment: Line 81 “or is more effective” (parallel structure)

Response: Sentence re-structured as requested. Please see page 4 (line 105-106)

Comment: Line 169 sign up for the registry

Response: Sentence updated as requested. Please see page 8 (line 190)

Comment: Line 204-for those who underwent PLIF

Response: Sentence re-structured as requested. Please see page 9 (line 221)

Comment: Consider commenting on why some PRO data demonstrate a difference between those undergoing PLIF and TLIF (i.e. why do you think TLIF outcomes might be better).

Response: Thank you for pointing this out. We have added a sentence clarifying why TLIF may improve health related quality of life scores post-surgery. Please see page 12-13.

“However, some of the PROMs were improved following TLIF compared to PLIF. This may be because of the minimally invasive procedure TLIF offers with equivalent postoperative fusion rates compared to PLIF; minimising the amount of iatrogenic injury to the spinal muscles. These findings are congruent with recent studies evaluating outcomes of minimally invasive spine procedures (23-25)”.

Comment: Figure 1-There appear to be a few outliers who seemed to worsen after PLIF. It would be helpful to know more about these patients and why they worsened. I assume these are the same patients who also seemed to have worse results in PLIF based on NRS scores in Figures 2 and 3

Response: Thank you for pointing this out. We have added a sentence to clarify why PLIF appears to show worse PROMS post-surgery. Some of the outliers mentioned may indicate that some of these patients may take longer than the 6 months follow-up to show any improvement. We have added some text describing the minimally invasive TLIF procedure which could be the cause of better improvement in PROMS. Please see page 12-13.

Comment: Table 1-alcohol intake, male the category goes from 1-28 and 229-49. I assume 29

was intended.

Response: Thank you for pointing this out. This should read “29-49 units”. We have rectified this in the table of characteristics.

Comment: For table 1-Is there clarification on how the surgical level are labeled? Difference between L3/4-L4/5 and L4/5-L3/4?

Response: The database did not enable labelling of the precise surgical level.

Comment: Were there any patients who had both PLIF and TLIF?

Response: No.

Comment: Line 257 “TLIP” typo

Response: Thank you, we have rectified this. Page 11.

Comment: Line 276—Are you able to comment on why you think TLIF showed greater improvements than PLIF for back and leg pain (which, as you note, differs from most of the data).

Response: Thank you for this comment. We have added a sentence to clarify why TLIF showed greater improvement in back/leg pain. Please see page 12.

“TLIF shows greater improvement in leg/back pain compared to PLIF because of effective and durable restoration of disc height and neuroforaminal height, reduction in slippage, greater lumbar lordosis, and higher union rate which might be expected to result in reduce pain scores.”

Comment: In the discussion, it would be good to more broadly discuss the other types of interbody fusion that are being used as well (XLIF, ALIF, LLIF, etc.)

Response: Thank you for your suggestion. We have added some content describing other types of fusion currently in use. Please see page 11-12.

“Lumbar interbody fusion is an established treatment for a range of spinal disorders and is performed using five main approaches; PLIF, TLIF, oblique lumbar interbody fusion (OLIF), anterior lumbar interbody fusion (ALIF) and lateral lumbar interbody fusion (LLIF). There is minimal evidence to suggest that one approach is superior to another in terms of fusion or clinical outcomes. OLIF is a surgical technique which is minimally invasive which uses a single port to access the disc space thus minimises damage to the muscles and ligaments. ALIF is similar to PLIF but is performed from the anterior (front) of the body through a small incision in the lower abdomen. This procedure requires blood vessels to be moved and the disc removed and replaced with a large cage. LLIF is another minimally invasive lumbar interbody fusion surgery in which access to the spine is gained from the side and involves removing the disc between two vertebrae and replacing it with an implant.”

Comment: Several studies already discuss degenerative spondylolisthesis techniques

and outcomes (Spiker et al GSJ, 2019—“review of techniques, indications, outcomes”; Yan et al. European Spine Journal, 2008), including with regard to PLIF/TLIF. Please elaborate on how this study will differ—would be good to note these other studies and differentiate this paper from those.

Response: Thank you for pointing this out. We have added some content exploring some differences between this study and other published studies. Please see page 14 (line 331-348). “Several studies demonstrated that surgical interventions such as PLIF/TLIF improves pain and quality of life in patients affected by degenerative lumbar spondylolisthesis (Rezk et al, 2019; Zhang et al, 2008). In a retrospective case series aiming to compare the surgical outcome of PLIF and TLIF in the treatment of degenerative spondylolisthesis, Rezk et al (2019) recruited 94 patients who underwent lumbar interbody fusion between March 2015 and May 2018. Results indicate that back pain/disability and complication rates were significantly lower in the TLIF group compared the PLIF group (29). Conversely, Zhang et al (2017) compared operative blood loss, surgical time, length of hospital stay, pain, disability, creatinine kinase (CK) level, and complications between TLIF and PLIF for spondylolisthesis. A cohort of (26 TLIF and 29 PLIF) patients were reviewed between March 2012 and March 2014, who were managed surgically for spondylolisthesis. Results show that compared with PLIF, TLIF achieved similar reduction and fusion results with improved quality of life, shorter hospital stays, less estimated blood loss, and shorter operative times (30). Our findings are consistent with other studies suggesting that TLIF provides better post-operative outcome compared to PLIF in the short-term. Compared with other studies, this study presents a very heterogeneous population with respect to age, procedure level and demographic data. Also, the large sample size allows for more precise estimate of the surgical effect and post-surgical outcome and broadly provide a good representativeness of the sample and generalisability of the results”.

Reviewer D

The authors present a retrospective cohort study using a multi-institutional database comparing characteristics of PLIF versus TLIF for treatment of lumbar spondylolisthesis. Notable findings, as reported by the authors, include:

1. Better improvement of back and leg pain for TLIF but no difference in ODI (despite worse preoperative scores for PLIF) nor QOL metrics.
2. No significant difference in intraoperative complications
3. Higher implant costs with TLIF and longer theatre time for PLIF

The study holds value in its large sample size that may be the largest of its kind to date. There are however, major concerns with regards to data granularity, interpretation of the data, and clinical relevance.

Comment: Most apparently, the author's state there was a significant difference in NRS change "with TILF showing greater improvements in both back and leg pain," yet both Table 2 and Figures 2+3 contain larger changes in NRS with PLIF. This discrepancy either needs to be corrected, or if no error exists, clarified so that other readers are not also confused by such

a central result.

Response: Thank you for this. We have added a sentence to clarify our justification indicating that NRS back/leg showed greater improvement following TLIF. Please see page 12 (line 298-300).

“Higher VAS scores (back/leg) at follow-up indicates greater pain intensity. TLIF shows greater improvement in both back and leg pain 6 months post-operatively”.

Comment: The population is also very heterogeneous with respect to procedure level and single-level versus multi-level procedure. Unsurprisingly, a plurality of surgeries were single-level L4-5 TLIFs/PLIFs. It is also unfortunate that only a small fraction were graded by Meyerding classification. While the study does benefit from large sample size, the clinical relevance is diminished with the aggregation of distinct cohorts and also introduces potential cofounders for the primary study outcomes like complications and procedure times as well as indication for PLIF versus TLIF in the first place. Table 1 is, in fact, filled with secondary demographic data (education, alcohol consumption, work status) that is often "Not reported" but not potentially relevant details such as how many were revision procedures or had other indications for surgery (canal or foraminal stenosis, trauma, adjacent segment disease, etc.). Consider subanalyses where it is possible, for example for just L4-5 fusions.

Response: Thank you for this. The only meaningful sub-group analyses associated with L4/5 fusion for both PLIF and TLIF interventions were intra-operative complication. We present a table detailing some meaningful analyses. Appendix 1

Appendix 1

Table 5: Intra-operative complications by L4/5 interbody fusion between PLIF and TLIF

Intra-operative complications	L4/5 interbody fusion- n(835)		Total
	PLIF- n(223) [26.7%]	TLIF- n(612) [73.3%]	835
Dural tear	14 (6.3)	26 (4.2)	40
Excessive bleeding	3 (1.3)	3 (0.5)	6
Implant malposition	1 (0.4)	9 (1.5)	10

Intra-operative complications in relation to L4/5 interbody fusion shows greater complication associated with PLIF intervention: dural tear 6.3% compared to 4.2% and excessive bleeding 1.3% compared to 0.5% for those undergoing TLIF.

Comment: Lastly, consider referencing and discussing the following, highly-relevant papers found while reviewing this topic on PubMed:

Response: Thank you for pointing this out. We have quoted additional papers.

- 1- Mobbs RJ, Phan K, Malham G, Seex K, Prashanth JR. Lumbar interbody fusion: techniques, indications and comparison of interbody fusion options including PLIF, TLIF, MI-TLIF, OLIF/ATP, LLIF and ALIF. *J Spine Surg.* 2015; 1:2-18.
- 2- Hee HT, Castro FP, Majd ME, Holt RT, Myers L. Anterior/posterior lumbar fusion versus transforaminal lumbar interbody fusion: Analysis of complications and predictive factors. *J. Spinal Disord.* 2001;14:533–540.
- 3- Potter BK, Freedman BA, Verwiebe EG, Hall JM, Polly DW, Kukla TR. Transforaminal lumbar interbody fusion: Clinical and radiographic results and complications in 100 consecutive patients. *J. Spinal Disord.* 2005;18:337–346.
- 4- Schwender JD, Holly LT, Rouben DP, Foley KT. Minimally invasive transforaminal lumbar interbody fusion (TLIF): Technical feasibility and initial results. *Journal of Spinal Disorders.* 2005;18:S1–S6.
- 5- Woodward J, Malone H, Witiw CD. Transforaminal lumbar interbody fusion using a novel minimally invasive expandable interbody cage: patient-reported outcomes and radiographic parameters. *J Neurosurg.* 2021; 4: 1-7
- 6- Abbasi H, Abbasi A, Oblique Lateral Lumbar Interbody Fusion (OLLIF): Technical Notes and Early Results of a Single Surgeon Comparative Study. *Cureus.* 2015; 7:e351
- 7- Allain J, Dufour T. Anterior lumbar fusion techniques: ALIF, OLIF, DLIF, LLIF, IXLIF. *Orthop Traumatol Surg Res.* 2020; 1: s149-s157.
- 8- Rabau O, Navarro-Ramirez R, Aziz M, Teles A, Mengxiao Ge S, Quillo-Olvera J, MD,2 Jean Ouellet J. Lateral Lumbar Interbody Fusion (LLIF): An Update. *Global Spine J.* 2020; 10: 17S–21S.
- 9- Rezk EMA, Elkholy AR, Shamhoot EA. Transforaminal lumbar interbody fusion (TLIF) versus posterior lumbar interbody fusion (PLIF) in the treatment of single-level lumbar spondylolisthesis. *Egypt J Neurosurg.* 2019; 34:26.
- 10- Zhang D, Mao K, Xiaojun Qiang X. Comparing minimally invasive transforaminal lumbar interbody fusion and posterior lumbar interbody fusion for spondylolisthesis. A STROBE-compliant observational study. *Medicine.* 2017; 96:e8011