

Accepted Manuscript

Effects of three common lumbar interbody fusion procedures for degenerative disc disease: A network meta-analysis of prospective studies

En-Yuan Lin, Yu-Kai Kuo, Yi-No Kang



PII: S1743-9191(18)31702-3

DOI: <https://doi.org/10.1016/j.ijssu.2018.11.009>

Reference: IJSU 4792

To appear in: *International Journal of Surgery*

Received Date: 3 August 2018

Revised Date: 29 October 2018

Accepted Date: 7 November 2018

Please cite this article as: Lin E-Y, Kuo Y-K, Kang Y-N, Effects of three common lumbar interbody fusion procedures for degenerative disc disease: A network meta-analysis of prospective studies, *International Journal of Surgery*, <https://doi.org/10.1016/j.ijssu.2018.11.009>.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Effects of three common lumbar interbody fusion procedures for degenerative disc disease: A network meta-analysis of prospective studies

Running title: Lumbar interbody fusions for degenerative disc disease

En-Yuan Lin*M.D.

1 Division of Neurosurgery, Department of Surgery, Taiwan Adventist Hospital,
Taipei, Taiwan, R.O.C.

E-mail: enyuan.lin100@gmail.com

Yu-Kai Kuo*M.D.

1. School of Medicine, College of Medicine, Taipei Medical University, Taipei,
Taiwan, R.O.C.

E-mail: ken0975515036@gmail.com

Yi-No Kang**Mr., M.A.

1. Center for Evidence-Based Medicine, Department of Education, Taipei Medical
University Hospital, Taipei, Taiwan, R.O.C.

E-mail: academicnono@gmail.com

*Co-first author (equal contribution): En-Yuan Lin M.D., Yu-Kai Kuo M.D.

**Correspondence: Yi-No Kang Mr., M.A.

Center for Evidence-Based Medicine, Department of Education, Taipei Medical
University Hospital

E-mail: academicnono@gmail.com

Telephone number: +886-2-27372181 ext. 3759

32 **Contributor Statement**

33 EYL: Conception of the work, interpretation of data, revising draft critically for
34 important intellectual content, and final approval of the version to be
35 published.

36 YKK: Conception of the work, acquisition of data, drafting the work, and final
37 approval of the version to be published.

38 YNK: Design of the work, acquisition of data, analysis, interpretation of data, drafting
39 the work, and final approval of the version to be published.

41 **Word count**

42 3130

43 **Funding Statement**

44 This research received no specific grant from any funding agency in the public,
45 commercial, or not-for-profit sectors.

46 **Competing Interests**

47 The authors declare that they have nothing to disclose regarding financial or
48 nonfinancial conflicts of interest with respect to this manuscript.

49 **Abbreviations**

50 CI: confidence interval

51 LIF: lumbar interbody fusion

52 ODI: Oswestry disability index

53 RCT: randomized clinical trial

54 SE: standard error

55 SUCRA: surface under the cumulative ranking curve

56 WMD: weighted mean difference

57

Effects of three common lumbar interbody fusion procedures for degenerative disc disease: A network meta-analysis of prospective studies

Running title: Lumbar interbody fusions for degenerative disc disease

ABSTRACT

Objectives

Lumbar interbody fusion (LIF) is a treatment option for patients with degenerative disc disease (DDD). However, the effects of the most common LIF procedures—posterior LIF, transforaminal LIF, and anterior LIF—for the treatment of patients with DDD remain controversial. This study evaluated the pain and function caused by the LIF procedures for the treatment of patients with DDD.

Methods

Cochrane library, EMBASE, Ovid Medline, and PubMed were searched from inception to July 17, 2018. We only included prospective studies comparing the LIF procedures for treating patients with DDD. Pain score, Oswestry disability index (ODI) score, and operative time were analyzed in a contrast-based consistency model. Results are reported in weighted mean difference (WMD) and 95% confidence interval (CI).

23 **Results**

24 This study included eight prospective studies that recruited 503 patients for the
25 LIF procedures. Minimally invasive posterior LIF resulted in lower pain scores than
26 open transforaminal LIF (WMD: -1.45 , 95% CI: -2.27 to -0.63) and open posterior
27 LIF (WMD: -0.61 , 95% CI: -1.10 to -0.12). It also resulted in a lower ODI score
28 than open transforaminal LIF (WMD: -15.34 , 95% CI: -21.76 to -8.91), anterior LIF
29 (WMD: -15.64 , 95% CI: -26.37 to -4.91), minimally invasive transforaminal LIF
30 (WMD: -11.63 , 95% CI: -16.86 to -6.40), and open posterior LIF (WMD: -10.93 ,
31 95% CI: -16.07 to -5.79). Small study effects were not detected in any consistency
32 models.

33

34 **Conclusions**

35 Although minimally invasive posterior LIF has longer operative time than
36 anterior LIF, it is associated with lower pain and ODI scores. Therefore, minimally
37 invasive posterior LIF may be a superior LIF procedure for patients with DDD.

38

39 **Keywords**

40 Degenerative disk disease, Anterior lumbar interbody fusion, Posterior lumbar
41 interbody fusion, Transforaminal lumbar interbody fusion

1 Introduction

Degenerative disc disease is one of the most common causes of lower back pain, and lumbar interbody fusion (LIF) is a popular procedure used for treating this disease. LIF may be feasible for patients with chronic lower back pain due to degenerative disc disease [1]. Furthermore, LIF is used to treat other spinal disorders, including spondylolisthesis, scoliosis, severe disc degeneration, trauma, herniation, infection, and spinal fracture [2,3].

LIF surgery usually involves several steps. First, surgeons perform discectomy to clean out the space of the intervertebral disc and then prepare a cage that is filled with graft. After placing the cage into the space, surgeons fix the vertebrae with a pedicle screw and rods. During the surgery, the surgery team corrects the angle of the screw and checks the position of the cage using a C-Arm X-ray system. Within the surgical approach, several common methods of approaching the vertebrae exist: anterior, posterior, and transforaminal LIF. Moreover, these procedures can be performed using an open or minimally invasive approach. The minimally invasive procedure has been used as an alternative to the open approach in recent years. Each approach has its own advantages and disadvantages regarding complications, pain, Oswestry disability index (ODI) score, blood loss, surgery time, wound size, and recurrence.

Spinal fusion has become considerably more prevalent in recent years, and the relevant evidence regarding the optimal treatment method is increasing. Unfortunately, taken together, the current evidence fails to definitively support one approach over another. For instance, five systematic reviews have been performed on patients with degenerative disc disease but have only compared open transforaminal LIF with minimally invasive transforaminal LIF [4,5], anterior LIF with transforaminal LIF [6,7], and anterior LIF with posterior instrumentation with transforaminal LIF [8]. No evidence has compared all these LIF procedures (open transforaminal LIF, minimally invasive transforaminal LIF, open

posterior LIF, minimally invasive posterior LIF, and anterior LIF) for treating degenerative disc disease in a consistency model, and the effects of LIF procedures on degenerative disc disease can be further discussed.

Therefore, this study incorporated these findings into a network meta-analysis (NMA) to provide updated evidence regarding LIF procedures (open transforaminal LIF, minimally invasive transforaminal LIF, open posterior LIF, minimally invasive posterior LIF, and anterior LIF) for treating patients with degenerative disc disease.

2 Methods

This study performed evidence selection, qualitative synthesis, and meta-analysis according to the PRISMA guidelines and AMSTAR (Assessing the methodological quality of systematic reviews) Guidelines. The protocol of this study is registered on PROSPERO (CRD42018094237).

2.1 Eligibility criteria for study selection

According to the purpose of this systematic review, the inclusion criteria for study selection were as follows: (1) randomized clinical trial (RCT) or prospective study; (2) patients with degenerative disc disease; and (3) comparison of the effects of open transforaminal LIF, minimally invasive transforaminal LIF, open posterior LIF, minimally invasive posterior LIF, and anterior LIF. The exclusion criteria were as follows: (1) single-arm design; (2) patients with other diseases in addition to degenerative disc disease; or (3) comparison with other treatments that were based on open transforaminal LIF, minimally invasive transforaminal LIF, open posterior LIF, minimally invasive posterior LIF, or anterior LIF. For instance, studies have investigated the effects of robot-assisted LIF

procedures.

2.2 Search strategy and study selection

Prospective studies regarding the effects of LIF procedures for the treatment of patients with degenerative disc disease were selected from the Cochrane library database (including the Cochrane Central Register of Controlled Trials), EMBASE, Ovid MEDLINE, and PubMed (including MEDLINE). The primary search strategy was use of PubMed, and then, the search strategy was adapted to the other databases before July 17, 2018 (Supplementary File 1). The search strategy was initiated with relevant terms in free text, medical subject headings, and abbreviations with appropriate Boolean operators. We did not place restrictions on publication language or date. Two investigators (YKK and YNK) screened potential references identified from the databases after the systematic searches. There were two steps in the screening process: screening of the title and abstract of the references, and review of the full texts of the references. In the screening process, the investigators identified eligible studies according to the inclusion and exclusion criteria. The third investigator (EYL) resolved disagreement regarding study selection through discussion.

2.3 Quality assessment and data extraction

To assess biases in eligible studies and to extract relevant information and outcome data from them, two investigators (EYL and YKK) individually reviewed the studies included in this systematic review. The investigators used one of two appraisal tools for the risk of bias assessment according to the study design. The risk of bias in RCTs was assessed using the Cochrane Risk of Bias Tool (RoB). The RoB assesses six biases, namely, selection, performance, detection, attrition, reporting, and other biases. This tool comprises seven

methodological items, namely, allocation generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective report, and other bias. The risk of bias in the prospective cohort studies was assessed using the Newcastle–Ottawa Quality Assessment Scale (NOS). The NOS assesses bias in three aspects of an observational study: selection, comparability, and outcome. Regarding the solution for disagreement on quality assessment, the third investigator (YNK) resolved any disagreement through discussion.

Relevant information and outcome data were extracted by two investigators (YKK and YNK). The relevant information included country, inclusion period, study design, treatments, age, sex, and spinal level. The outcome data for network meta-analysis were pain, function, and operative time. Pain score was only analyzed when it was measured using a 10-point scale. Function was only analyzed when it was evaluated using the ODI. The operative time is reported in minutes.

2.4 Data synthesis and analysis

We conducted quantitative syntheses by using contrast-based network meta-analysis with weighted mean difference (WMD) in the random-effects model. Results are reported through the effect size (WMD) and 95% confidence interval (CI). The small study effect in NMA was assessed using an adjusted funnel plot with Egger's regression intercept. We used Lu–Ades' loop inconsistency test when we discovered any loop in NMA. $P < 0.05$ was defined as statistically significant in all analyses. All the analyses were completed using STATA version 14.

Moreover, to clarify the effects among comparators, we conducted surface under the cumulative ranking curve (SUCRA). Regarding SUCRA, a hierarchy of treatment ranking,

the probability of each treatment among the most effective treatments was estimated. Furthermore, we made a SUCRA cluster plot of the primary outcomes.

3 Results

This systematic review identified 1518 references from the Cochrane library (n = 6), Embase (n = 300), Ovid Medline (n = 752), and PubMed (n = 460). We identified 10 eligible references from eight studies. Four of the eight studies were RCTs, whereas the other four were prospective cohort studies (Fig. 1).

3.1 Characteristics and quality of included studies

The eight studies were conducted in China [9,10], Germany [11,12], Malaysia [13], Spain [14], and the United States [15,16]. The total number of recruited patients in these studies was 503. Five LIF procedures (open transforaminal LIF, minimally invasive transforaminal LIF, open posterior LIF, minimally invasive posterior LIF, and anterior LIF) were performed on these patients during January 1996 and December 2014. The number of patients who underwent each LIF procedure was as follows: 101 in open transforaminal LIF, 188 in minimally invasive transforaminal LIF, 99 in open posterior LIF, 60 in minimally invasive posterior LIF, and 55 in anterior LIF. Therefore, the consistency models involved five treatments, namely, open transforaminal LIF, minimally invasive transforaminal LIF, open posterior LIF, minimally invasive posterior LIF, and anterior LIF (Fig. 2). The mean age in each study, from 41.81 to 68 years, was determined according to the available information. A total of 212 (42.15%) men were included in the studies. Other information is shown in Table 1. Overall, the quality of the studies was acceptable, except for one conference report (Supplementary Files 2–3).

3.2 Primary outcome: Pain and ODI scores

Five studies with five treatments are included in the network meta-analysis of pain score (Fig. 2A) [9,10,13-15]. The result showed that with open transforaminal LIF as the reference, minimally invasive transforaminal LIF (WMD: -0.94 , 95% CI: -1.57 to -0.31), open posterior LIF (WMD: -0.84 , 95% CI: -1.50 to -0.18), and minimally invasive posterior LIF (WMD: -1.45 , 95% CI: -2.27 to -0.63) were associated with lower pain score. With open posterior LIF as the reference, minimally invasive posterior LIF (WMD: -0.61 , 95% CI: -1.10 to -0.12) was associated with lower pain score (Fig. 3A; Supplementary File 4). In ranking the best pain score probability, minimally invasive posterior LIF had the best pain score (89.3%), and open transforaminal LIF (0.0%) had the worst (Supplementary File 5). In SUCRA, minimally invasive posterior LIF had the highest value (Mean rank = 1.1; SUCRA = 96.9) and open transforaminal LIF had the lowest value (Mean rank = 4.6; SUCRA = 8.9). Because network meta-analysis of pain score had no loop among comparisons, inconsistency detection was not required. No evidence was discovered of small study effects ($t = -0.78$, 95% CI: -0.50 to 0.30 ; Supplementary File 6).

Five studies provided data on ODI score among the five treatments (Fig. 2A) [9,10,13-15]. The result of network meta-analysis for ODI score showed that with open transforaminal LIF as the reference, open posterior LIF (WMD: -4.41 , 95% CI: -8.26 to -0.56) and minimally invasive posterior LIF (WMD: -15.34 , 95% CI: -21.76 to -8.91) were associated with lower ODI score. Moreover, minimally invasive posterior LIF was associated with lower ODI score than anterior LIF (WMD: -15.64 , 95% CI: -26.37 to -4.91), minimally invasive transforaminal LIF (WMD: -11.63 , 95% CI: -16.86 to -6.40), and open posterior LIF (WMD: -10.93 , 95% CI: -16.07 to -5.79 ; Fig. 3B; Supplementary

File 7). Overall, in ranking the best ODI score probability, minimally invasive posterior LIF had the highest ODI score (99.8%) whereas open transforaminal LIF (0.0%), minimally invasive transforaminal LIF (0.0%), and open posterior LIF (0.0%) had the lowest ODI score (Supplementary File 8). In SUCRA, minimally invasive posterior LIF had the highest value (Mean rank = 1.0; SUCRA = 99.9) and open transforaminal LIF had the lowest value (Mean rank = 4.4; SUCRA = 14.2). No inconsistency detection for network meta-analysis of ODI score was required because the network meta-analysis had no loop among comparisons. Small study effects were not detected in this result ($t = -0.24$, 95% CI: -1.08 to 0.92 ; Supplementary File 9).

A cluster plot for pain and ODI scores demonstrated that the best balance was achieved by minimally invasive posterior LIF (Fig. 4). Therefore, minimally invasive posterior LIF may be recommended for treating patients with degenerative disc disease. By contrast, open transforaminal LIF and anterior LIF exhibited poor performance in the cluster plot. These two LIF procedures should be cautiously recommended for treating patients with degenerative disc disease because they resulted in relatively worse pain and ODI scores.

3.3 Secondary outcome: Operative time

Five studies provided data on operative time among the five treatments (Fig. 2B) [9,10,12,13,16]. The result from network meta-analysis of operative time indicated that open posterior LIF was associated with longer operative time than anterior LIF (WMD: 71.88, 95% CI: 15.55–128.21) and minimally invasive transforaminal LIF (WMD: 57.48, 95% CI: 4.18–110.79). No statistically significant difference was observed in other comparisons (Fig. 3C; Supplementary File 10). In ranking the best operative time probability, anterior LIF required the most time (53.6%), whereas open posterior LIF (0.0%)

required the least time (Supplementary File 11). In SUCRA, anterior LIF had the highest value (Mean rank = 1.7; SUCRA = 83.1) and minimally invasive posterior LIF had the lowest value (Mean rank = 4.5; SUCRA = 11.5). However, a significant result was obtained in the Lu–Ades inconsistency test (chi-square = 14.07, $P < 0.05$; Supplementary File 12), and it indicated that inconsistency was due to open posterior LIF. Two adjusted indirect comparisons existed between open posterior LIF and open transforaminal LIF. Open posterior LIF was compared with open transforaminal LIF through anterior LIF and open posterior LIF was compared with open transforaminal LIF through minimally invasive transforaminal LIF. Therefore, we examined the direct and indirect effects of open posterior LIF through side-splitting. In the side-splitting model, we observed significant differences between direct and indirect comparisons of the two paths that compared open posterior LIF with open transforaminal LIF through anterior TLIF and minimally invasive transforaminal LIF. However, in one of the two side-splitting tests, we observed similar trends, a positive value of WMD, in both direct comparison [WMD: 54.10, standard error (SE): 13.74] and indirect comparison (WMD: 118.09, SE: 10.12). We also discovered that the effect size of direct comparison was far lower than that of indirect comparison. A similar phenomenon was observed in the other side-splitting model. A similar trend was found in the direct comparison (WMD: 72.70, SE: 4.59) and indirect comparison (WMD: 8.70, SE: 16.43), but the effect size of direct comparison was far higher than that of indirect comparison (Supplementary File 13). Thus, the inconsistency in the network meta-analysis for operative time may not severely violate the transitivity assumption according to the direction of the WMD. Moreover, no small study effects ($t = 0.28$, 95% CI: $-5.01e^{-7}$ to $5.99e^{-7}$; Supplementary File 14) were detected in the result of network meta-analysis of operative time.

4 Discussion

4.1 Key findings

Compared with other lumbar fusion procedures (open transforaminal LIF, minimally invasive transforaminal LIF, open posterior LIF, minimally invasive posterior LIF, and anterior LIF), minimally invasive posterior LIF resulted in superior outcomes of pain and function based on the pain and ODI scores, according to effect size and SUCRA. The poorest procedures may be open transforaminal LIF and anterior LIF. Minimally invasive posterior LIF and anterior LIF have the longest and shortest operation time, respectively.

In our study, minimally invasive posterior LIF was discovered to have the best outcome regarding pain and ODI scores. Our result indicated that regardless of whether minimal access or an open approach is used, posterior LIF results in a lower pain score than transforaminal LIF. However, this result is inconsistent with a previous study [17]. The inconsistent result is probably explained by some limitations in that study, including few enrolled patients and a significantly lower rate of spondylolytic spondylolisthesis in the transforaminal LIF group than in the other groups [17]. Few studies have compared minimally invasive posterior LIF and other LIF procedures. A preliminary report from Korea indicated that minimally invasive approaches may effectively reduce unnecessary tissue damage, decreasing the incidence of complications. In the article, the pain score decreased rapidly from a mean of 5.5 on the first day after surgery to 3.0 on the third day and to 2.0 at the first week [18]. Nevertheless, more RCTs are required to obtain a specific conclusion about minimally invasive posterior LIF.

According to the ranking probability and SUCRA of ODI score, open transforaminal LIF and anterior LIF have similar poor outcomes among the five LIF procedures. This can probably be explained by their disadvantages. The limitations of the anterior LIF technique

include approach-related complications such as retrograde ejaculation, visceral injury, and vascular injury [3,7,19]. Open transforaminal LIF is associated with severe paraspinal iatrogenic injury and prolonged muscle retraction. Correcting coronal imbalance and restoring lordosis may also be difficult [20]. Hence, both anterior LIF and open transforaminal LIF result in poor ODI outcomes.

4.2 Minimally invasive versus traditional open approach

The other notable finding of our study concerns the comparison between minimally invasive and open approaches of LIF procedures. Regarding pain and ODI scores, minimally invasive transforaminal LIF was discovered to be superior to open transforaminal LIF, and minimally invasive posterior LIF superior to open posterior LIF. However, similar effects were observed between minimally invasive transforaminal LIF and open posterior LIF. These findings are not difficult to understand because of the advantage of minimal access. Minimally invasive transforaminal LIF results in lower morbidity because it uses smaller skin incisions, less paraspinal muscle dissection, and reduced soft tissue retraction [21]. It also causes less perioperative blood loss and pain, earlier rehabilitation, and a shorter hospitalization [22]. Similarly, compared with open posterior LIF, minimally invasive posterior LIF uses a paramedian approach, which results in less intraoperative hemorrhage, less postoperative back pain, fewer functional disabilities, and less change in multifidus [23,24]. In conclusion, regardless whether posterior LIF or transforaminal LIF is used, minimal access is less invasive of the multifidus muscle and other causes than an open approach.

The operative time for minimally invasive transforaminal LIF and open transforaminal LIF is similar, but minimally invasive posterior LIF requires more time than open posterior

LIF. In fact, the issue of operative time differences between the minimally invasive approach and open approach has been controversial for some time. Thus, the operative time is longer in the minimally invasive transforaminal LIF group. For posterior LIF, few studies have compared minimally invasive posterior LIF and open posterior LIF based on operative time.

4.3 Limitations and future direction

Our study had several limitations. First, the small sample size in each treatment arm may have reduced the statistical robustness of the results because we selected prospective studies only. An inadequate sample size may have led to imprecise results, but systematic error from the study design may have given misleading results. To avoid systematic error, we excluded retrospective studies that had more serious effects from inherent biases than limited sample size. In our analysis, however, we could not overcome the problem of underpowered findings caused by the small sample size. Thus, our results should be translated to clinical practice cautiously. Second, surgeon experience is always a critical issue in surgical topics. For instance, minimally invasive posterior LIF was developed earlier than minimally invasive transforaminal LIF, and surgeons may thus be more experienced in minimally invasive posterior LIF than minimally invasive transforaminal LIF. In our study, operative time was the variable most affected by surgeon experience. Thus, the result of operative time in our study should be interpreted carefully, and the true effect of LIF procedures on degenerative disc disease should clearly report surgeon experience in future studies. Third, network meta-analyses of pain and ODI scores were all without loops, and many comparisons were adjusted to indirect comparisons. More prospective studies are required to guarantee the effects among LIF procedures through

direct comparisons.

5 Conclusions

In conclusion, our network meta-analysis discovered that minimally invasive posterior LIF may be a superior procedure for treating patients with degenerative disc disease according to the available data from prospective studies. By contrast, open transforaminal LIF may not be recommended for this population. Minimally invasive LIF procedures were associated with lower pain and ODI, but anterior LIF was associated with shorter operative time. Based on the current prospective studies, the network meta-analysis provides the best evidence and an overview through adjusted indirect comparison on this topic. However, more trials are needed to obtain robust results by comparing the LIF procedures directly.

Provenance and peer review

Not commissioned, externally peer-reviewed

Reference

- [1] F.M. Phillips, P.J. Slosar, J.A. Youssef, G. Andersson, F. Papatheofanis. Lumbar spine fusion for chronic low back pain due to degenerative disc disease: a systematic review. *Spine*. 38 (2013) E409-422.
- [2] R. Dunn. Lumbar fusion - indications and surgical options. *SA Orthopaedic Journal*. 7 (2008) 8-12.
- [3] R.J. Mobbs, K. Phan, G. Malham, K. Seex, P.J. Rao. Lumbar interbody fusion: techniques, indications and comparison of interbody fusion options including PLIF, TLIF, MI-TLIF, OLIF/ATP, LLIF and ALIF. *Journal of Spine Surgery*. 1 (2015) 2-18.
- [4] K. Phan, P.J. Rao, A.C. Kam, R.J. Mobbs. Minimally invasive versus open transforaminal lumbar interbody fusion for treatment of degenerative lumbar disease: systematic review and meta-analysis. *European Spine Journal*. 24 (2015) 1017-1030.
- [5] Z.J. Sun, W.J. Li, Y. Zhao, G.X. Qiu. Comparing minimally invasive and open transforaminal lumbar interbody fusion for treatment of degenerative lumbar disease: a meta-analysis. *Chinese medical journal*. 126 (2013) 3962-3971.
- [6] G.D. Schroeder, C.K. Kepler, P.W. Millhouse, A.N. Fleischman, M.G. Maltenfort, D.K. Bateman et al. L5/S1 Fusion Rates in Degenerative Spine Surgery: A Systematic Review Comparing ALIF, TLIF, and Axial Interbody Arthrodesis. *Clinical Spine Surgery*. 29 (2016) 150-155.
- [7] K. Phan, G.K. Thayaparan, R.J. Mobbs. Anterior lumbar interbody fusion versus transforaminal lumbar interbody fusion--systematic review and meta-analysis. *British journal of neurosurgery*. 29 (2015) 705-711.
- [8] P.M. Udby, R. Bech-Azeddine. Clinical outcome of stand-alone ALIF compared to posterior instrumentation for degenerative disc disease: A pilot study and a literature review. *Clinical Neurology and Neurosurgery*. 133 (2015) 64-69.
- [9] S.W. Fen, X. Zhao, F.D. Zhao, X.Q. Fang. Minimally invasive transforaminal lumbar

- interbody fusion for the treatment of degenerative lumbar diseases. *Spine*. 35 (2010) 1615-1620.
- [10] B. Lin, Q.Y. Lin, M.C. He, H. Liu, Z.M. Guo, K.S. Lin. [Clinical study on unilateral pedicle screw fixation and interbody fusion for the treatment of lumbar degenerative diseases under Quadrant system]. *China Journal of Orthopaedics and Traumatology*. 25 (2012) 468-473.
- [11] T. Hartwig, P. Strube, E. Hoff, C. Groß, C. Perka, M. Putzier. Prospective randomized comparison between single-level transforaminal (TLIF), posterior (PLIF) and anterior stand alone (ALIF) lumbar interbody fusion regarding qualitative and quantitative radiologic changes of the paraspinal muscles and clinical parameters. *European Spine Journal*. 19 (2010) 1977.
- [12] E.K. Hoff, P. Strube, M. Pumberger, R.K. Zahn, M. Putzier. ALIF and total disc replacement versus 2-level circumferential fusion with TLIF: a prospective, randomized, clinical and radiological trial. *European Spine Journal*. 25 (2016) 1558-1566.
- [13] L.Y. Lee, Z. Idris, T.B. Beng, T.Y. Young, W.C. Chek, J.M. Abdullah et al. Outcomes of Minimally Invasive Surgery Compared to Open Posterior Lumbar Instrumentation and Fusion. *Asian journal of neurosurgery*. 12 (2017) 620-637.
- [14] J. Rodríguez-Vela, A. Lobo-Escolar, E. Joven, J. Muñoz-Marín, A. Herrera, J. Velilla. Clinical outcomes of minimally invasive versus open approach for one-level transforaminal lumbar interbody fusion at the 3- to 4-year follow-up. *European Spine Journal*. 22 (2013) 2857-2863.
- [15] D. Crandall, J. Revella. Transforaminal Lumbar Interbody Fusion Versus Anterior Lumbar Interbody Fusion as an Adjunct to Posterior Instrumented Correction of Degenerative Lumbar Scoliosis: Three Year Clinical and Radiographic Outcomes. *Spine*. 34 (2009) 2126-2133.

- [16] P. Klara, S. Freidank, S. Rezaiaimiri. Comparison of Lumbar Interbody Fusion Techniques Using Ray Threaded Fusion Cages and Pedicle Screw Fixation Systems. *Neurosurgery Quarterly*. 13 (2003) 20-29.
- [17] N. Lee, K.N. Kim, S. Yi, Y. Ha, D.A. Shin, D.H. Yoon et al. Comparison of Outcomes of Anterior, Posterior, and Transforaminal Lumbar Interbody Fusion Surgery at a Single Lumbar Level with Degenerative Spinal Disease. *World Neurosurgery*. 101 (2017) 216-226.
- [18] K.-T. Kim, K.-S. Suk, Y.-H. Lee, Y.-W. Kim, S.-H. Lee. The posterior decompression and posterior lumbar interbody fusion using a mini-open technique. *Journal of Korean Orthop Assoc*. 38 (2003) 492-497.
- [19] G.M. Malham, R.M. Parker, N.J. Ellis, C.M. Blecher, F.Y. Chow, M.H. Claydon. Anterior lumbar interbody fusion using recombinant human bone morphogenetic protein-2: a prospective study of complications. *Journal of Neurosurgery Spine*. 21 (2014) 851-860.
- [20] S.C. Humphreys, S.D. Hodges, A.G. Patwardhan, J.C. Eck, R.B. Murphy, L.A. Covington. Comparison of posterior and transforaminal approaches to lumbar interbody fusion. *Spine*. 26 (2001) 567-571.
- [21] H.W.D. Hey, H.T. Hee. Open and Minimally Invasive Transforaminal Lumbar Interbody Fusion: Comparison of Intermediate Results and Complications. *Asian Spine Journal*. 9 (2015) 185-193.
- [22] K.H. Lee, W.M. Yue, W. Yeo, H. Soeharno, S.B. Tan. Clinical and radiological outcomes of open versus minimally invasive transforaminal lumbar interbody fusion. *European Spine Journal*. 21 (2012) 2265-2270.
- [23] S.W. Fan, Z.J. Hu, F.D. Zhao, X. Zhao, Y. Huang, X.Q. Fang. Multifidus muscle changes and clinical effects of one-level posterior lumbar interbody fusion: minimally invasive

procedure versus conventional open approach. *European Spine Journal*. 19 (2010) 316-324.

- [24] T. Tsutsumimoto, M. Shimogata, H. Ohta, H. Misawa. Mini-Open Versus Conventional Open Posterior Lumbar Interbody Fusion for the Treatment of Lumbar Degenerative Spondylolisthesis: Comparison of Paraspinal Muscle Damage and Slip Reduction. *Spine*. 34 (2009) 1923-1928.

TABLES

Table 1. Characteristics of the included prospective studies

Study	Region	Inclusion period	Study design	Treatments	Sample size	Age	Sex (male/female)	Level
Crandall et al. (2009)	Phoenix, America	NR	Prospective cohort	1 OTLIF	20	67, 49–81	2/18	NR
Fan et al. (2010)	Hangzhou, China	May/2005–December/2006	Prospective cohort	2 ALIF	20	68, 47–85	3/17	1LF L3-S1
Hartwig et al. (2010)	Berlin, Germany	NR	RCT	1 OTLIF	30	52 ± 6.4	14/16	NR
				2 MTLIF	32	51.4 ± 7.2	18/14	
				3 ALIF	25	NR	NR	
Hoff et al. (2016)	Berlin, Germany	June/2007–November/2010	RCT	1 OTLIF	25	47.6, 36–61	10/14	1LF L4-S1
				2 ALIF	31	45.4, 38–57	14/12	2LF L4-S1
Klara et al. (2003)	Norfolk, America	January/1996–August/1998	Prospective cohort	1 OPLIF(TFC)	22	47.0 ± 16.0	11/11	1LF L3-S1
				3 ALIF(TFC)	10	51.6 ± 11.7	4/6	3LF L3-S1
Lee et al. (2017)	Sarawak, Malaysia	January/2010–December/2014	Prospective cohort	1 OPLIF	29	52.9 ± 9.67	16/13	1LF L3-S1
				2 MPLIF	60	55.88 ± 11.37	26/34	
Lin et al. (2012)	Fujian, China	October/2008–October/2010	RCT	1 OPLIF	52	52.5 ± 16.4	35/17	NR
				2 MTLIF	50	50.5 ± 13.7	32/18	
Rodríguez-Vela et al. (2013)	Zaragoza, Spain	January/2007–June/2008	RCT	1 OTLIF	20	43.15 ± 7.3	13/7	NR
				2 MTLIF	21	41.81 ± 8.7	14/7	

RCT, randomized controlled trial; 1LF, single-level fusion; 2LF, two-level fusion; 3LF, three-level fusion

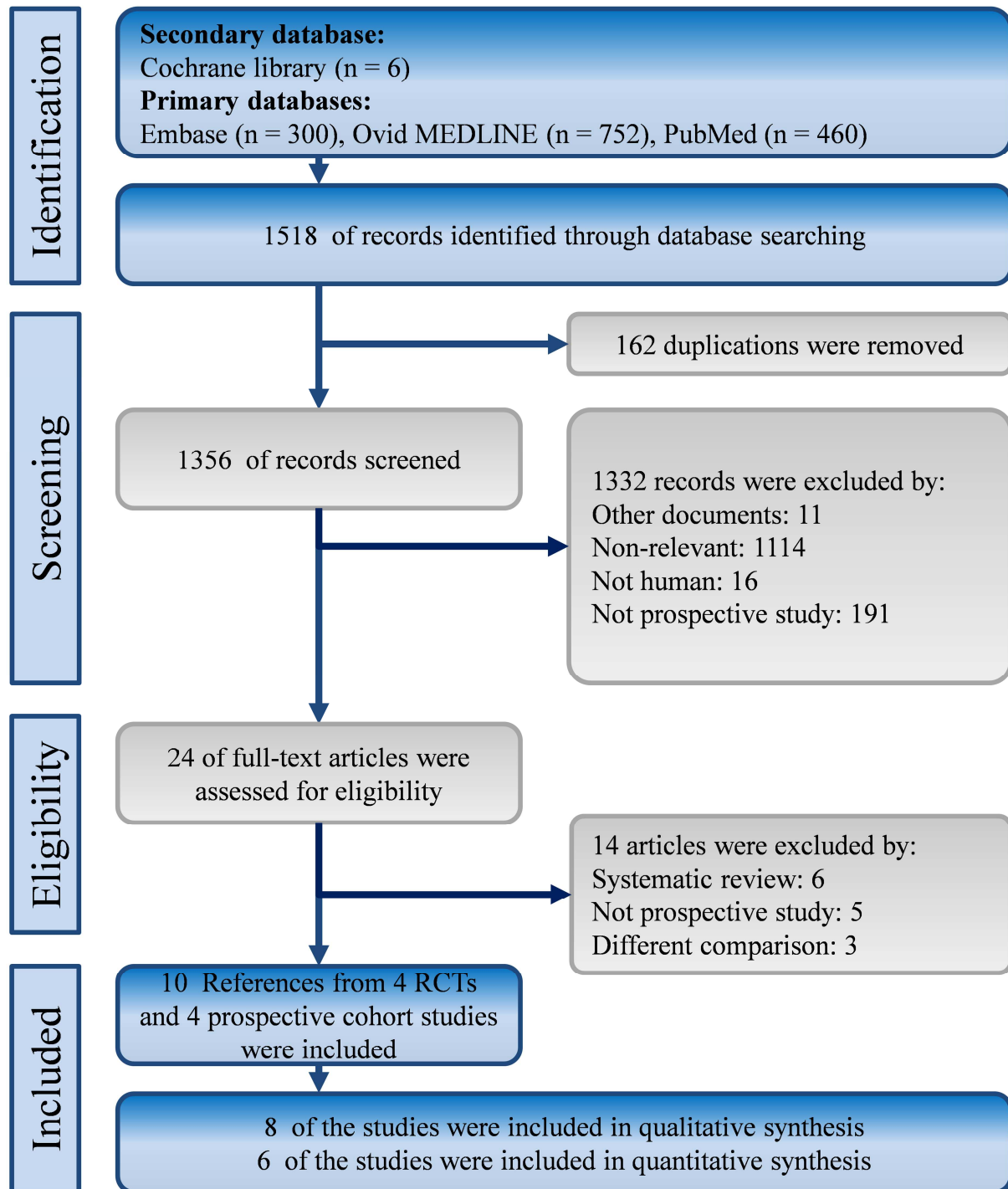
FIGURE CAPTIONS

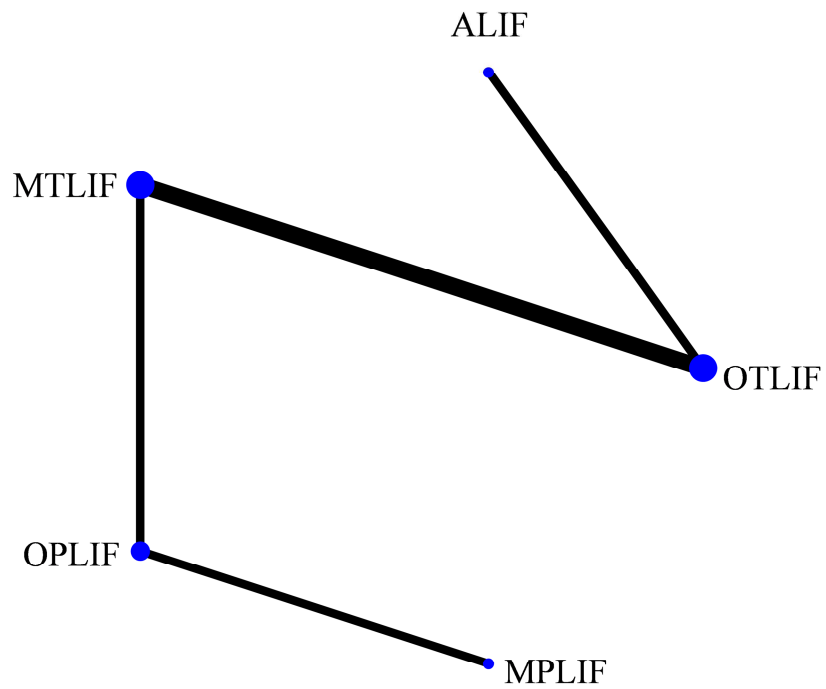
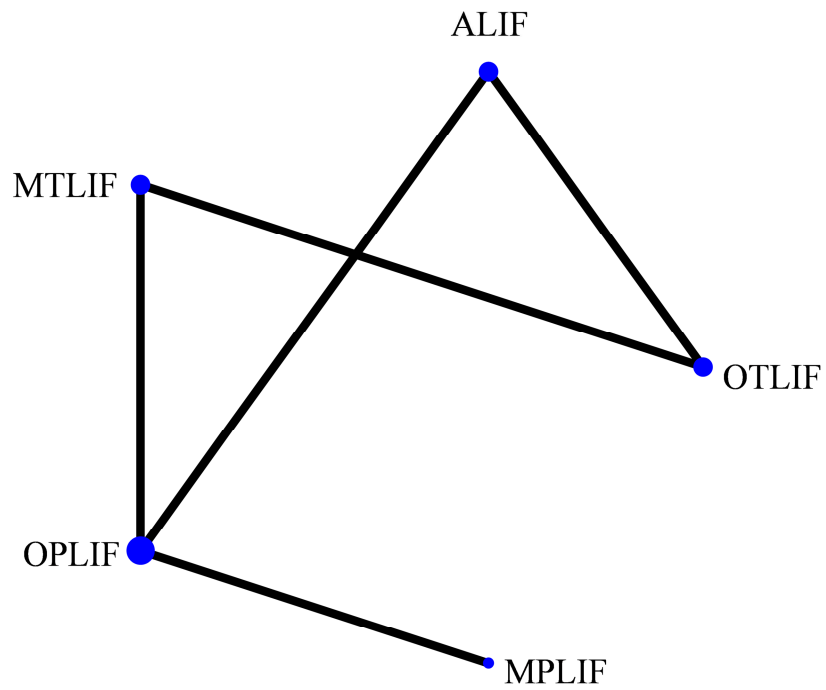
FIG. 1. Flowchart of the systematic review with network meta-analysis of prospective studies.

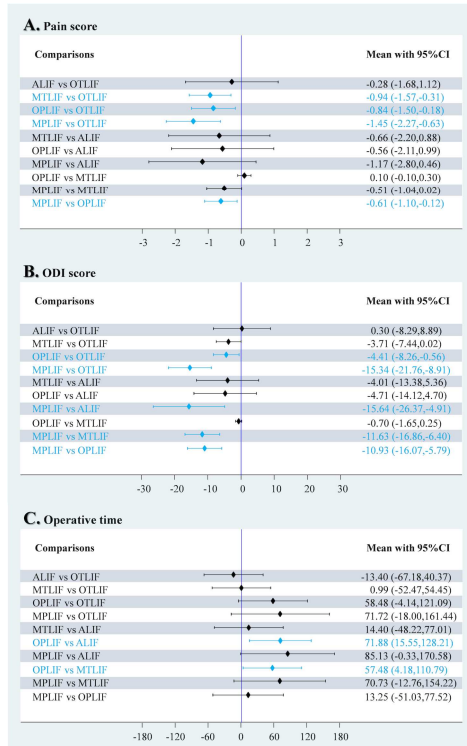
FIG. 2. Network geometry of the consistency model.

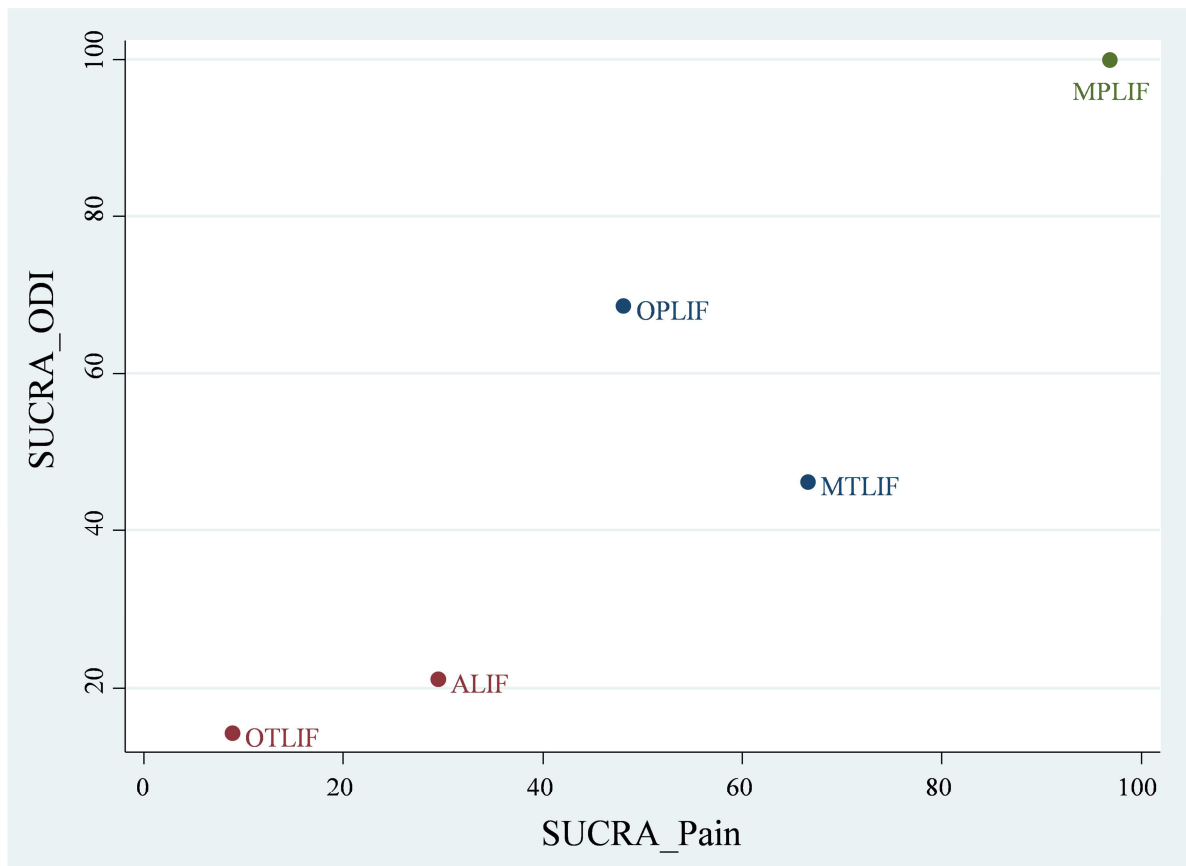
FIG. 3. Forest plot of pairwise comparisons.

FIG. 4. SUCRA cluster plot of pain score and ODI score.



A. Pain score and ODI score**B. Operative time**





Highlights

1. This is the first network meta-analysis for lumbar interbody fusion (LIF).
2. This study focused on degenerative disc disease (DDD).
3. Minimally invasive posterior LIF may be a better procedure for DDD.
4. Open transforaminal LIF may not be recommended for DDD.
5. Anterior LIF was associated with shorter operative time.

International Journal of Surgery Author Disclosure Form

The following additional information is required for submission. Please note that failure to respond to these questions/statements will mean your submission will be returned. If you have nothing to declare in any of these categories then this should be stated.

Please state any conflicts of interest

The authors declare that they have nothing to disclose regarding financial or non-financial conflicts of interest with respect to this manuscript.

Please state any sources of funding for your research

This network meta-analysis does not received funding.

Please state whether Ethical Approval was given, by whom and the relevant Judgement's reference number

No ethical approval is needed for this network meta-analysis, because we used published data.

Research Registration Unique Identifying Number (UIN)

Please enter the name of the registry and the unique identifying number of the study. You can register your research at <http://www.researchregistry.com> to obtain your UIN if you have not already registered your study. This is mandatory for human studies only.

PROSPERO (CRD42018094237)

Author contribution

Please specify the contribution of each author to the paper, e.g. study design, data collections, data analysis, writing. Others, who have contributed in other ways should be listed as contributors.

E.Y.L.: Conception of the work, interpretation of data, revising draft critically for important intellectual content, and final approval of the version to be published.

Y.K.K.: Conception of the work, the acquisition of data, drafting the work, and final approval of the version to be published.

Y.N.K.: Design of the work, the acquisition of data, analysis, interpretation of data, drafting the work, and final approval of the version to be published.

Guarantor

The Guarantor is the one or more people who accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

En-Yuan Lin, Yu-Kai Kuo, Yi-No Kang

Data Statement

Due to this study used published data from the included randomized controlled trials investigating the topic of lumbar interbody fusion for degenerative disc disorder, the raw data would not be shared.