Transforaminal versus posterior lumbar interbody fusion for symptomatic single-level spondylolisthesis (LIFT): a multicentre controlled, patient blinded, randomised non-inferiority trial

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Summary

Background The effectiveness of transforaminal lumbar interbody fusion (TLIF) compared to posterior lumbar interbody fusion (PLIF) in patients with single-level spondylolisthesis has not been substantiated. To address the evidence gap, a well-powered randomized controlled non-inferiority trial comparing the effectiveness of TLIF with PLIF, entitled the Lumbar Interbody Fusion Trial (LIFT), was conducted.

Methods In a multicenter randomized controlled non-inferiority trial among five Dutch hospitals, 161 patients were randomly allocated to either TLIF or PLIF (1:1), stratified according to study site. Patients and statisticians were blinded for group assignment. All patients were over 18 years old with symptomatic single-level degenerative, isthmic or iatrogenic lumbar spondylolisthesis, and eligible for lumbar interbody fusion surgery through a posterior approach. The primary outcome was change in disability measured with the Oswestry Disability Index (ODI) from preoperative to one year postoperative. The non-inferiority limit was set to 7.0 points based on the MCID of ODI. Secondary outcomes were change in quality-adjusted life years (QALY) assessed with EuroQol 5 Dimensions, 5 Levels (EQ-5D-5L) and Short Form Health Survey (SF-36), as well as back and leg pain (Numerical rating scale, NRS), anxiety and depression (Hospital Anxiety Depression Scale; HADS), perioperative blood loss, duration of surgery, duration of hospitalization, and complications. Trial registration: Netherlands Trial Registry, number 5722 (registration date March 30, 2016), Lumbar Interbody Fusion Trial (LIFT): A randomized controlled multicenter trial for surgical treatment of lumbar spondylolisthesis.

Findings Patients were included between August 2017 and November 2020. The total study population was 161 patients. Total loss-to-follow-up after one year was 16 patients. Per-protocol analysis included 66 patients in each group. In the TLIF group (mean age 61.6, 36 females), ODI improved from 46.7 to 20.7, whereas in the PLIF group (mean age 61.9, 41 females), it improved from 46.0 to 24.9. This difference (−4.9, 90% CI −12.2 to +2.4) did not reach the non-inferiority limit of 7.0 points in ODI. A significant difference in the secondary outcome measurement, QALY (SF-36), was observed in favor of TLIF ($P < 0.05$). However, this was not clinically relevant. No difference was found for all other secondary outcome measurements; PROMs (EQ-5D, NRS leg/back, HADS), perioperative blood loss, duration of surgery, duration of hospitalization, and perioperative and postoperative complications.

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Interpretation For patients with single-level spondylolisthesis, TLIF is non-inferior to PLIF in terms of clinical effectiveness. Disability (measured with ODI) did not differ over time between groups.

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Keywords: Lumbar fusion surgery; Transforaminal lumbar interbody fusion; Posterior lumbar interbody fusion; Spondylolisthesis; Effectiveness; Multicenter; Randomized controlled trial

Research in context

Evidence before this study

Our research team conducted two systematic reviews to compare Transforaminal Lumbar Interbody Fusion (TLIF) and Posterior Lumbar Interbody Fusion (PLIF). The first focused on effectiveness of TLIF versus PLIF. Searches were conducted in six databases, using the eligibility criteria; TLIF, PLIF, lumbar spondylolisthesis, disability, pain, complications, duration of surgery, blood loss. The search was conducted in September 2016.

After the full-text review, nine studies were included. The decrease in ODI scores was significantly larger in patients who underwent TLIF (pooled mean difference was −3.46 points in TLIF; $P \leq 0.001$). There was no significant difference in the change is VAS scores, with a pooled mean difference in postoperative VAS scores of −0.05 ($P = 0.480$). A pooled odds ratio for complications was 0.47 ($P = 0.006$), indicating a significantly lower complication rate for TLIF. The average duration of surgery was 169 min for TLIF and 190 min for PLIF ($P = 0.003$). All included studies had an overall high risk of bias.

The second focused on cost-effectiveness of TLIF versus PLIF. Searches were conducted in eight databases, using the eligibility criteria; TLIF, PLIF, lumbar spondylolisthesis, lumbar instability, cost. This search was conducted in July 2020. Sixteen studies were included for final analysis. None of these studies directly compared TLIF with PLIF, which resulted in only indirect comparison. The overall risk of bias was high, except for one prospective study. Due to heterogeneity of the studies, a meta-analysis could not be performed and it was not possible to discern which technique was more cost-effective.

Added value of this study

The incidence of symptomatic spondylolisthesis increases with age due to spinal degeneration. In an aging population, the demand for spinal fusion surgery will also increase. Specific indication for the use of TLIF or PLIF is unknown, therefore the choice of technique is frequently based on the surgeon's preference. Although these techniques are assumed to be equally effective, nonrandomized studies and one small randomized controlled trial (RCT) comparing TLIF and PLIF suggest that TLIF is associated with fewer complications, less blood loss, and shorter length of surgical procedure and hospital stay.

It is evident that there is a need for high-quality comparative data to develop evidence-based treatment recommendations for this increasing health problem. Therefore, a well-powered non-inferiority randomized controlled trial comparing the effectiveness of TLIF and PLIF in patients with single-level lumbar spondylolisthesis, entitled the Lumbar Interbody Fusion Trial (LIFT), was conducted.

Implications of all the available evidence

Effectivity analyses of previous studies and the LIFT, showed a non-inferiority of TLIF compared to PLIF. Potential future differences in cost-effectiveness between TLIF and PLIF may be a decisive factor for employing either technique. With an increasing demand of spinal fusion surgery because of the aging population, this will be of interest for both clinicians, as well as hospitals and insurance companies. Until then, the choice will remain left to the surgeons' preference.

Introduction

Lumbar spondylolisthesis with subsequent central or foraminal stenosis is a common cause of neurogenic leg pain [1]. The incidence of symptomatic spondylolisthesis increases with age due to spinal degeneration. Spine disorders are responsible for the highest burden of disease in terms of years lived with disability (YLD), and in this perspective, contributes to disability more than cancer, cardiovascular diseases, or mental disorders.[1]

For patients with symptomatic spinal stenosis, surgical treatment is inevitable in most cases. As the incidence continues to rise, the need for lumbar fusion surgery also increases.[2–8]

When decompression and fusion are indicated, transforaminal lumbar interbody fusion (TLIF) and posterior lumbar interbody fusion (PLIF) are commonly used. Both procedures include pedicle screw placement and intervertebral cage insertion. In the TLIF procedure, this is achieved by placement of one cage in the intervertebral space, using a unilateral transforaminal approach. The PLIF procedure involves placing two identical cages bilaterally in the intervertebral space,

using a bilateral central approach. Specific indication for the use of either technique is unknown, therefore the choice of technique is frequently based on the surgeon's preference. Although these techniques are assumed to be equally effective, nonrandomized studies and one small randomized controlled trial (RCT) comparing TLIF and PLIF suggest that TLIF is associated with fewer complications, less blood loss, and shorter length of surgical procedure and hospital stay.[9–12] It is evident that there is a need for high-quality comparative data to develop evidence-based treatment recommendations. Therefore, a well-powered non-inferiority randomized controlled trial comparing the effectiveness of TLIF and PLIF in patients with single-level lumbar spondylolisthesis, entitled the Lumbar Interbody Fusion Trial (LIFT), was conducted.

Methods

Trial design

For this multicenter randomized controlled non-inferiority trial, patients were randomly assigned in a 1:1 ratio to undergo either TLIF or PLIF. This study was approved by the local institutional medical ethical committee (Medical Research Ethics Committee Zuyderland, METC 16-T-36) and previously registered within the International Clinical Trials Registry Platform (ICTRP, Main ID NTR5722).

Study population

Patients were included from five Dutch hospitals between August 2017 and November 2020. Inclusion and exclusion criteria of patients are listed in Table 1. Eligibility was assessed in the outpatient clinic. When eligible to participate, informed consent was acquired.

Patients were excluded from the one-year effectiveness analyses if loss to follow-up occurred before completion of the one-year questionnaires.

Randomization

Patients were randomized into one of two parallel groups[1] TLIF and[2] PLIF in a 1:1 ratio, using web-based computer-generated block randomization with sizes of 4, 6, 8, stratified by designated hospital.

Blinding

The outcome of randomization was revealed to the surgeons preoperatively by IC and RD. Patients were blinded during the entire follow-up period. The statistician performing the final analyses was blinded as well.

Outcome measurements

The primary outcome measurement was change in disability, measured with the Oswestry Disability Index (ODI), a score of 0 indicates no disability and a score of 50 indicates complete disability. Secondary outcome measurements were quality-adjusted life years (QALY) assessed with EuroQol 5 Dimensions, 5 Levels (EQ-5D-5L) and Short Form 36 Health Survey (SF-36), pain assessed with the Numerical Rating Scale (NRS) for back pain and leg pain, and presence of anxiety or depression assessed with Hospital Anxiety Depression Scale (HADS). All patients were asked to complete patient reported outcome measurements (PROMs) questionnaires (web-based or on paper) preoperatively and at three, six and twelve months postoperatively. Questionnaires were unrelated to any hospital visit, and were completed without assistance of medical personnel or any other professionals involved in the trial.

Perioperative morbidity was determined based on intraoperative blood loss, duration of surgery, and duration of hospitalization. Direct and indirect surgical complications, including dural tears, postoperative infection, deep venous thrombosis, hematoma, hardware failure, neurological deficits, and other complications such as pneumonia or urinary tract infection were collected.

Inclusion criteria	Exclusion criteria
Indication for LIF through posterior approach	Previous radiotherapy at the intended surgical level
Clinical single-level, uni- or bilateral, lumbar radiculopathy or intermittent neurogenic claudication	(Progressive) motor failure and/or anal sphincter disorders which urges instant intervention
Single-level isthmic, degenerative, or iatrogenic spondylolisthesis	Active infection
Spondylolisthesis Meyerding classification grade I, II or III	Immature bone (ongoing growth)
Spondylolisthesis at level L3L4, L4L5 or L5S1	Active malignancy
Central or foraminal stenosis on MRI (or CT) of which the anatomical level is corresponding to the clinical syndrome	Pregnancy
Age over 18 years	Symptomatic osteoporosis (defined on DEXA-scan or the use of bisphosphonates)
Psychosocially, mentally, and physically able to fully comply with this study protocol	Contra-indications for anaesthesia or surgery
	Inadequate command of the Dutch language

Abbreviations: LIF, lumbar interbody fusion, DEXA, Dual Energy X-ray Absorptiometry.

Table 1: **Inclusion and exclusion criteria of the LIFT study.**

Interventions

General

Antibiotic prophylaxis according to local hospital protocol was administered. Subsequently, the patient was brought under general anesthesia and positioned prone. After preparing, disinfection and draping, a midline posterior approach was performed, exposing the posterior lumbar elements including facet joints. Poly-axial pedicle screws were inserted bilaterally, using fluoroscopic guidance or navigation, based on the surgeons' preference. In case of central spinal canal stenosis, a laminectomy was performed to decompress the neural structures. In both approaches, a titanium rod interconnected the screws on each side. The wound was thoroughly irrigated and closed in several layers without suction drainage.

Either TLIF or PLIF was subsequently performed according to randomization. Type and material of rods and cages, used during surgery, were based on local agreements, and can differ between participating centres.

TLIF

Unilateral exposure to the intervertebral disc was achieved by total unilateral facetectomy, decompressing the descending and leaving roots. In case of bilateral symptomatic leg pain, the side of the unilateral approach was based on the most symptomatic side; in case of equal distribution, it was based on the surgeons' preference. Unilateral facetectomy was performed to gain access to the intervertebral disc. Discectomy was performed. Endplate cartilage was prepared to provide a host bed of bleeding subchondral bone for placement of the cage. The TLIF cage size was determined by a trial cage under fluoroscopic guidance. Cages were not intended to increase disc height. Dural retraction was minimal to nothing because of the more lateral approach during the TLIF surgery. The definitive cage was packed with autologous bone or allograft, and tamped into place. Its position was checked radiologically. After placement of the TLIF cage, the remainder of the disc space was filled with autologous bone obtained from the laminectomy.

PLIF

Bilateral access to the intervertebral disc was assured by medial facetectomy. Bilateral discectomy was performed. Subsequently, endplate cartilage was prepared to provide a host bed of bleeding subchondral bone for placement of the cages. The size of the PLIF cages was determined by a trial cage under fluoroscopic guidance. Before placement of the definitive cages, the disc space was partially filled with autologous bone, obtained from decompression. The definitive cages were also packed with autologous bone or allograft, and tamped into place with dural retraction during both cage insertions. Their position was checked radiologically. Cages were not intended to increase disc height.

Postoperative care

Patients were encouraged to mobilize, initially with guidance of a physiotherapist, and to resume daily activities as soon as possible. No additional physical therapy was routinely advised. Patients were administered postoperative pain medication according to the local hospital protocol.

Sample size

Change in ODI, defined as the difference between preoperative and postoperative ODI, was the primary endpoint and used for calculating the sample size. The hypothesis are as follows: H0: $\mu^{PLIF}-\mu^{TLIF} => 7$, Ha: $\mu^{TLIF}-\mu^{PLIF} <7.0$. Assuming that there were no differences in the change in ODI after one year, the non-inferiority limit was set to 7.0 points based on the MCID described by Parker et al.[13] Based on our own retrospective data set, the response data from the ODI within each subject group was normally distributed, with standard deviation of 16.[14] This resulted in a total of 64 experimental subjects and 64 control subjects needed to be able to reject the null hypothesis that TLIF is inferior to PLIF with probability (power) of 0.8. The Type I error probability associated with one-sided null hypothesis is 0.05. A loss-to-follow-up rate of 10% was initially accounted for. However, long waiting times for surgery during the COVID-19 pandemic resulted in patients seeking care elsewhere, hence drop-out was higher than anticipated and accordingly adjusted to 20%. When accounting for a 20% loss-to-follow-up, 160 patients (80 patients per group) needed to be enrolled in this study. As inclusion occurred simultaneously in the participating centers, a total of 161 patients were included. Sample size calculation was performed using R and the TrialSize package, that is based on the book by Chow et al.[15]

Statistical analysis

Clinical effectiveness data were analyzed according to the per-protocol principle. Differences in PROMs between baseline and the twelve-month follow-up were analyzed using generalized linear mixed models (for non-normally distributed baseline data), with time, type of surgery and time*type of surgery interaction as fixed factors. Change in ODI, defined as the difference between preoperative and postoperative ODI, was the primary endpoint. Assuming that there were no differences in the change in ODI after one year, the non-inferiority limit was set to 7.0 points based on the MCID. A 90% confidence interval will be computed around the mean difference, using the estimates from the linear mixed effects model. The upper bound of the confidence interval will be compared to the non-inferiority limit of 7.0. Baseline and surgical

characteristics were compared between groups using Student's T-test, Median Tests or Chi–Square tests for continuous, normally distributed data, for continuous, non-parametric data or categorical data, respectively. The level of significance was set at $P < 0.05$. Statistical analyses were performed using IBM SPSS Statistics 28.

Results

Study population

The total study population of the LIFT study was 161 patients. Total loss-to-follow-up after one year was 16 patients. Of these, ten had refrained from filling out postoperative PROMs without a specific reason, three withdrew from the study before randomization, two died because of unrelated causes, and one patient developed severe cognitive impairment. Thirteen patients required different surgery than the outcome of the dictated randomization process. In five of these patients, cage insertion was impossible; four patients required multi-level surgery, two underwent minimally invasive TLIF, one PLIF-group patient underwent a TLIF, and one TLIF patient underwent a PLIF. In total, 132 patients were included in the per-protocol analyses, of which 66 patients received TLIF and 66 patients received PLIF (Fig. 1). Patients' characteristics are described in Table 2. In the PLIF group, significantly more patients were diagnosed with Diabetes. PEEK cages were used in 126 patients and titanium cages were used in six patients. Size was chosen-0 according the preoperative disc height. Cages height ranged from 7 to 15 mm: three patients with height 7, eight patients with height 8, five patients with height 9, 49 patients with height 10, 22 patients with height 11, 33 patients with height 12, ten patients with height 13, one patient with height 14 and one patient with height 15.

Primary outcome

The primary outcome—disability measured with ODI—improved significantly over time after lumbar interbody

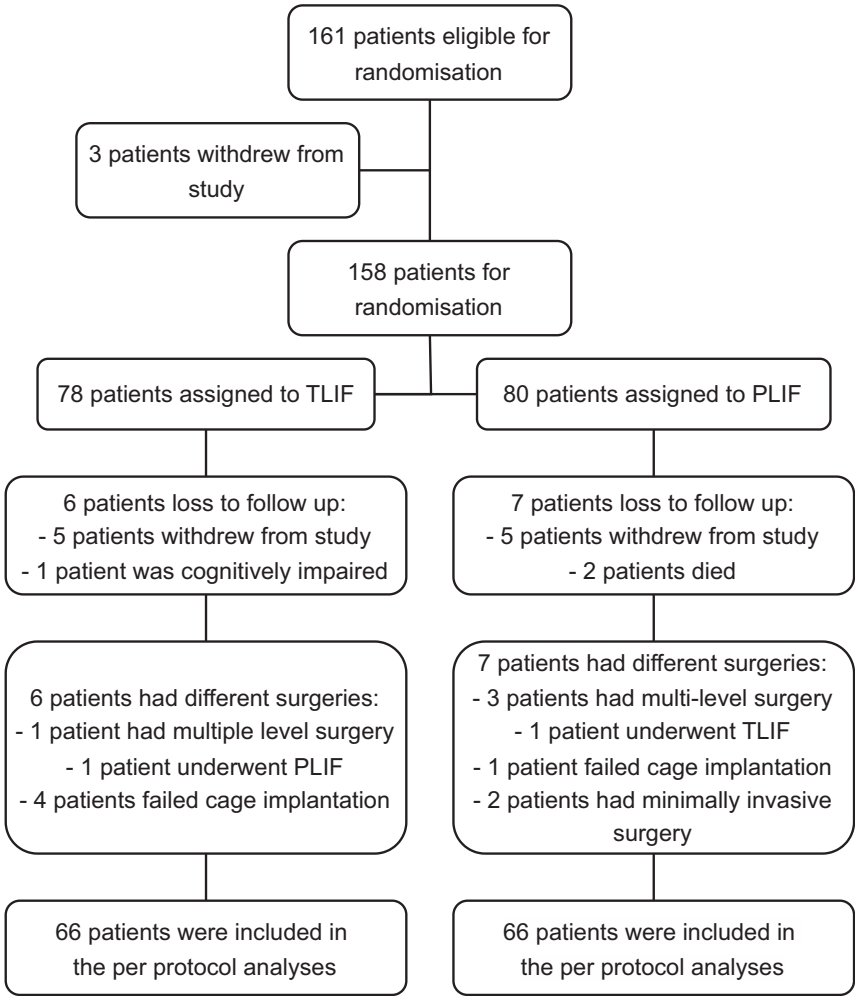

Fig. 1: **Flowchart of study population of the LIFT-study.**

Variable	TLIF (N = 66)	PLIF (N = 66)	P-value
Age in years, mean (SD)	61.6 (12.0)	61.9 (9.7)	0.85
Sex (% (N) female)	54.5% (36)	62.1% (41)	0.38
BMI, mean (SD) $kg.m^{-2}$	27.7 (4.7)	27.6 (5.1)	0.91
Diabetes (% (N) yes)	4.5% (3)	15.7% (10)	**0.03***
Smoking status (% (N) yes)	25.8% (17)	18.2% (12)	0.29
Number of Pack years, mean (SD)	25.0 (17.9)	26.6 (17.1)	0.78
Mean duration of complaints in months, median	17	16	
Indication of surgery (% (N))			
Degenerative spondylolisthesis	59.1% (39)	75.8% (50)	0.09
Iatrogenic spondylolisthesis	6.1% (4)	1.5% (1)	–
Lytic spondylolisthesis	34.8% (23)	22.7% (15)	–
Grade of spondylolisthesis (% (N))			
I	80.3% (53)	83.3% (55)	0.65
II	19.7% (13)	16.7% (11)	–
ASA classification (% (N))			
I	7.6% (5)	15.2% (10)	0.08
II	81.8% (54)	60.6% (40)	–
III	10.6% (7)	24.2% (16)	–
Level of surgery (% (N))			
L3L4	7.6% (5)	9.1% (6)	0.27
L4L5	62.1% (41)	72.7% (48)	–
L5S1	30.3% (20)	18.2% (12)	–

Abbreviation: TLIF, Transforaminal Lumbar Interbody Fusion, PLIF, Posterior Lumbar Interbody Fusion, SD, Standard Deviation, BMI, Body Mass Index, ASA classification, American Society of Anaesthesiologists classification. P-value <0.5 indicates statistical significance, marked with *.

Table 2: **Baseline characteristics of included patients divided between the TLIF and PLIF groups.**

fusion in both the TLIF and PLIF group. For TLIF, the ODI changed from 46.7 preoperatively to 20.7 (–26.0, CI –30.1; –22.2) at twelve months after surgery, while for PLIF the ODI changed from 46.0 to 24.9 (–21.1, CI –25.1; –17.1). The difference in change over time between groups in ODI was –4.9 (upper bound of the 90% CI for non-inferiority testing: 2.4), indicating non-inferiority compared to PLIF non-significantly in favor of TLIF. Moreover, the point-estimate suggests superiority, but the null-hypothesis was not rejected. Changes in ODI score over time are visualized in Fig. 2A. Possible influences on the primary outcome due to differences in Diabetes, ASA classification and indications for surgery, were calculated. There was no difference in ODI between the stated results and after corrections of multiple covariates (Supplementary File 1).

Secondary outcome

All secondary outcomes improved significantly over time after surgery for both groups. A significant, but not clinically relevant difference, in change over time in QALY, measured with SF-36, was observed in favor of TLIF compared to PLIF ($P < 0.05$). For all other PROMs, (EQ-5D-5L, NRS back and leg, HADS), a non-significant difference was observed twelve months postoperatively (Fig. 2B–G). Surgical characteristics are described in Table 3. There were no significant differences in intraoperative blood loss, duration of surgery, duration of hospitalization, and occurrence of dural tears or complications during hospitalization.

Within one year, 12 complications occurred. Five complications were hardware related; pedicle screw malposition (n = 2, TLIF), pedicle screw breakage (n = 1, PLIF), and rod extrusion (n = 1, TLIF). Reoperation was required for four of these. Furthermore, there was one patient with asymptomatic screw migration (n = 1, TLIF). In both groups, two patients developed adjacent segment disease, one of which in the TLIF group required extension of the fusion. In the PLIF group, one patient suffered an atraumatic fracture of the vertebral body, which required extension of the spinal construct. In the TLIF group, two patients developed wound infection early after hospital discharge.

Discussion

The LIFT is the first well-powered randomized controlled non-inferiority trial to determine effectiveness of TLIF and PLIF in patients with single-level lumbar spondylolisthesis. The most important finding of this study is that TLIF is non-inferior to PLIF. Both procedures are equally effective in reducing disability (ODI), as they both reached the pre-defined MCID of 7.0.

Secondary outcome measurements showed that quality of life (EQ-5D-5L), back and leg pain (NRS), and

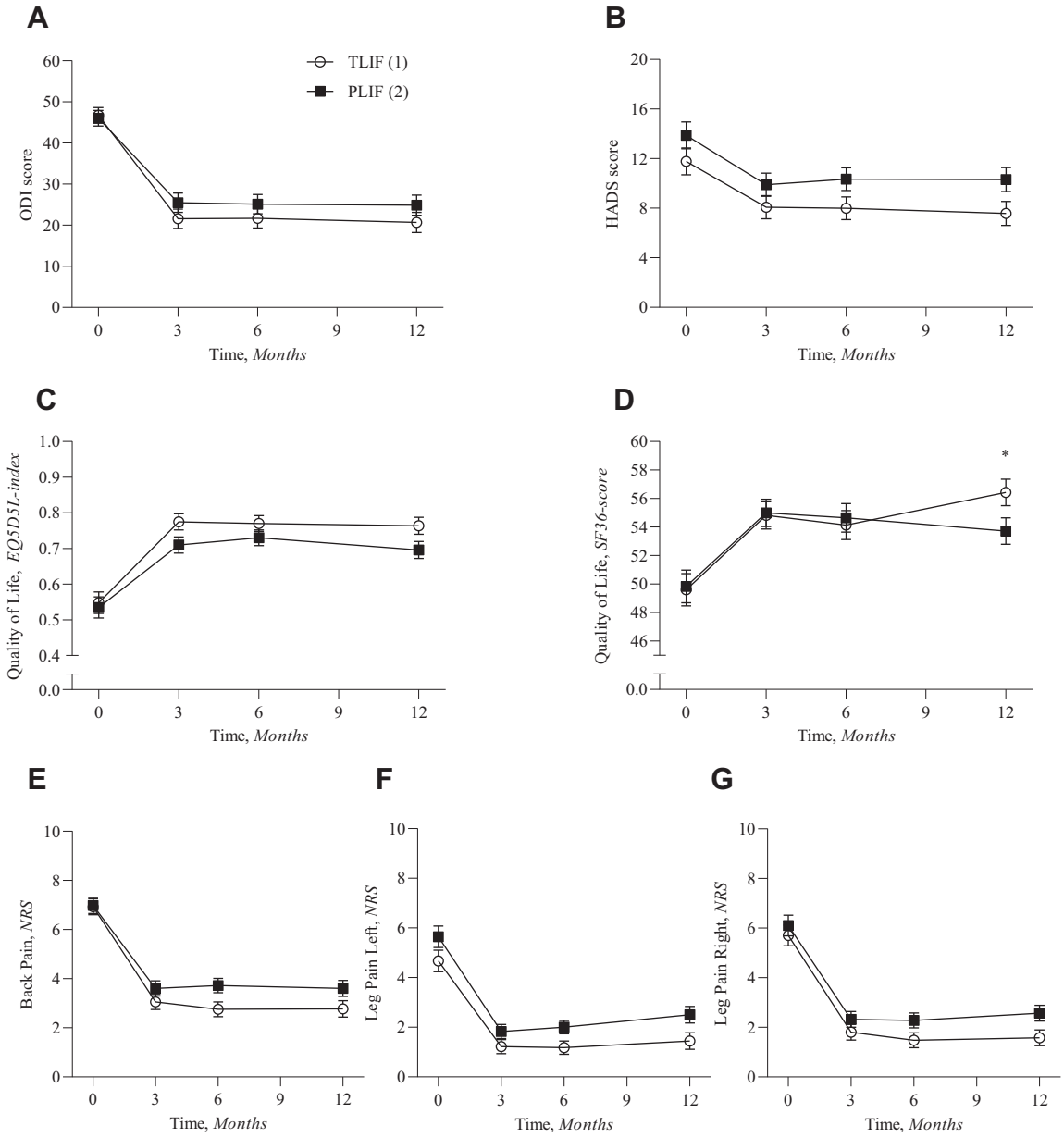

Fig. 2: **PROMs results including 95% confidence interval at baseline, and at three, six and twelve months postoperatively of TLIF and PLIF**. A. ODI, Oswestry Disbility Index; B. HADS, Hospital Anxiety and Depression Scale; C. EQ5D5L, EuroQol 5 Dimensions, 5 Levels; D. SF-36, Short Form 36 Health Survey; E. Back Pain NRS, Numeric Rating Scale; F. Leg Pain Left NRS; G. Leg Pain Right NRS. Abbreviation: TLIF, Transforaminal Lumbar Interbody Fusion; PLIF, Posterior Lumbar Interbody Fusion.

anxiety and depression (HADS) did not differ between TLIF and PLIF groups. Furthermore, results showed that both interventions are comparably safe, as reflected by the amount of intraoperative blood loss, duration of surgery, duration of hospitalization, and complications rate.

The results of this study are similar to a previously published systematic review with meta-analyses, which described comparable results in ODI for PLIF and TLIF.[9] This was also suggested in a low-powered study that described no significant difference in ODI.[10]

In our study, a significant difference in change over time in quality of life (SF-36) was observed in favor of the TLIF. However, this difference did not exceed the non-inferiority limit of 3.0 points based on the study of Hays et al.[16] Subdomains of the SF-36 and EQ-5D were

Variable	TLIF (N = 66)	PLIF (N = 66)	P-value
Duration of surgery in minutes, mean (SD)	153.0 (44.6)	158.4 (40.8)	0.47
Blood loss in cc, mean (SD)	348.1 (197.5)	357.2 (198.6)	0.79
Dural tear (% (N) yes)	7.6% (5)	10.6% (7)	0.55
Duration of hospitalization in days, mean (SD)	4.8 (4.8)	4.9 (5.0)	0.85
Complications during hospitalization (% (N) yes)	21.1% (14)	22.7% (15)	0.83
Wound infection	1.5% (1)	0	–
Hematoma	6.1% (4)	4.5% (3)	–
Neurological complaints	4.5% (3)	3.0% (2)	–
Other complications (e.g., UTI, pneumonia)	9.1% (6)	18.2% (12)	–

Abbreviation: TLIF, Transforaminal Lumbar Interbody Fusion, PLIF, Posterior Lumbar Interbody Fusion, SD, Standard Deviation, UTI, Urinary Tract Infection. P-value <0.5 indicates statistical significance, marked with *.

Table 3: **Surgical characteristics of included patients divided between the TLIF and PLIF groups.**

assessed to evaluate if this difference was driven by large differences in a specific domain. However, subdomains of SF-36 and EQ-5D were similar. In a previous analysis by McDonough et al. comparing the SF-36 and EQ-5D, it was apparent that outcomes of quality of life cannot be compared accurately between both scores among spine patients.[17] We used both questionnaires, while EQ-5D is the golden standard for QALY-outcomes and SF-36 is a broader questionnaire, which can give more information per subdivision.

Although, the difference between TLIF and PLIF for other outcome measures did not reach the non-inferiority limit, it is remarkable that all studied PROMs still showed a difference over time in favor of TLIF. It is uncertain whether these small differences are the result of coincidences, or whether outcome parameters are not sensitive enough to detect existing differences. It can be postulated that success of surgery is defined by adequate decompression instead of the superiority of one technique over another, as both techniques have the same objective: decompression of the nerve roots and stabilization of the spine. It is possible that the slightly better primary and secondary outcomes were in favor of TLIF, because of less extensive iatrogenic damage during surgery. This could possibly result in less fibrous tissue over time. However, these were deemed to be clinically irrelevant.

On the contrary, it is suggested that unilateral decompression and cage insertion, with only limited and unilateral dural retraction, could result in less iatrogenic radiculopathy or dysfunction, and dural tears.[9,18] In our study, the difference in occurrence of dural tears was not significant. Most dural tears occurred during decompression and not during cage insertion. Decompression in TLIF can be more extensive in case of central spinal stenosis, which limits the advantages regarding dural tears.

It is notable that there were no significant differences in intraoperative blood loss, or duration of surgery or hospitalization. Duration of surgery was evaluated in several previous trials and reviews. No differences were described in the systematic review of Teng et al.,[18] while in the RCT of Yang et al., duration of surgery was 113 min for TLIF and 125 min for PLIF, resulting in a significant difference with a P-value below 0.05.[10] Although we believe that a difference of 12 min is not clinically relevant, it could nevertheless be relevant in the cost-effectiveness analysis. In LIFT, it is possible that surgeons might have chosen a broader decompression in patients with lumbar spinal stenosis undergoing TLIF, which could have reduced the advantage in duration of surgery of the unilateral TLIF approach. Insertion of two cages in PLIF (instead of one cage in TLIF) might explain the non-clinically relevant difference of 5 min between groups. The similarity in blood loss and duration of hospitalization could be explained by using a midline approach in both groups, which resulted in less difference in muscle dissection and therefore muscle recovery. Another reason for comparable duration of hospitalization is the use of standardized rehabilitation protocols on the wards.

This is the first well-powered randomized controlled trial that compares effectiveness of TLIF and PLIF in patients with lumbar spondylolisthesis. The methodological implementation of this study was of high quality due to its multicenter nature, the number of loss-to-follow-up remaining within the range of the pre-calculated 20%, adequate randomization, and blinding of patients and the statistician to minimize bias. To reach the aim of our study, which was primarily to compare change of disability score after PLIF and TLIF, a per-protocol analysis was performed.

The study could be influenced by possible limitations. The study protocol described a detailed surgical approach for both TLIF and PLIF.[19] Nevertheless, it is possible that surgeons determined that more bony decompression was needed during surgery, mostly in the case of TLIF patients, if the surgeons believed indirect decompression of the contralateral neuroforamen would not be sufficient. This could have led to a less unilateral approach, resulting in a smaller difference between TLIF and PLIF in surgical variables. TLIF

procedures can be performed using less invasive approaches. For example, the paramedian approach with percutaneous screw fixation on the contralateral side, potentially leading to less paravertebral muscle dissection, compared to the midline approach without percutaneous screw fixation. For reasons of blinding of participants in this study, a paramedian approach was not investigated.

Furthermore, it is possible that the results are skewed because of a disproportional dominance in inclusions of one of the participating centers.

In previous literature, there is a lot of debate whether radiographic fusion rate should be an outcome measurement in spinal fusion surgery. Multiple studies showed no correlation between fusion or non-fusion and clinical outcome measurements.[20–22] Moreover, multiple hospitals in north-western Europe are not performing any postoperative radiological imaging after lumbar fusion surgery. Postoperative imaging is only performed if there is a clear indication, such as neurological symptoms or axial pain. The main reason not to perform postoperative imaging routinely, is that findings of imaging will not have surgical consequences for patients with good clinical outcome. It is deemed unnecessary to expose all patients to radiation. As radiological follow-up is not standard of care in the participating hospitals, additional data on radiological parameters cannot be provided in this trial. However, we understand that radiographs are routinely performed in, for example, the United Stated and the absence in this study can be notable. Furthermore, disc heights were not measured preoperative and postoperative. However, cages were not intended to increase disc height.

The primary outcome measurement of this trial is change in ODI one year postoperative. To be able to answer the question on long-term sequelae as material failure, painful pseudoarthrosis or adjacent segment disease, a longer follow-up period than one year is required. The literature overview of Epstein showed studies on adjacent segment disease ranging from two to 20 years follow up.[23] Since, this was not the scope of the study, which was clinical effectiveness, a follow-up time of one year was deemed sufficient to state an adequate conclusion about the clinical effectiveness of TLIF and PLIF.

The number of lumbar fusion surgeries has increased rapidly in the past decade.[6] Moreover, this number will continue to rise, since an aging population is correlated with degenerative diseases of the spine.[24] This rising number also means higher healthcare costs for lumbar fusion surgery.[7,8] Due to the lack of high-quality studies, surgeons greatly base their choice of surgical method on experience and preference, instead of scientific evidence on effectiveness and cost-effectiveness. Recent reviews could not fill this knowledge gap due to low quality of included studies and heterogeneity in the reported results.[9,12] The 12-month results of the LIFT, which is a high-quality randomized controlled trial, fills this knowledge gap on effectiveness. Recently, a newer minimally invasive variation of TLIF has started gaining popularity; the minimally invasive transforaminal lumbar interbody fusion (MI-TLIF). In this approach, decompression and cage insertion are performed through tubular retractors, followed by percutaneous posterior pedicle screw fixation.[25] Previous literature described varying results on the clinical superiority of MI-TLIF over TLIF. However, there are no proper comparisons between MI-TLIF and the most favorable open technique. Furthermore, new techniques keep on coming. For this reason, it is important that spine surgeons should continue to look critical at these new techniques and perform adequate high-quality research to determine effectiveness and cost-effectiveness.

It would also be interesting to follow the patients, that were included in this study, over a longer period of time. Recently, Chan et al. published a database study with five years results after TLIF and MI-TLIF to be able to know about long term QALY's and sequelae after fusion surgery.[26] A longer follow-up time in this high quality study would be interesting to better understand the consequences of TLIF and PLIF surgeries in the long run.

This multicenter randomized controlled trial has proven that TLIF is non-inferior to PLIF regarding clinical effectiveness. Potential future differences in cost-effectiveness between TLIF and PLIF may be a decisive factor for employing either technique. Until then, it will remain left to the surgeons' preference.

Contributors

Conceptualisation was performed by IC, SdK, KR, RdB and HvS. Data curation was performed by IC and RD. The methodology was checked by IC, SdK and RdB. Project administration was performed by IC, RD and SdK. Supervision was performed by KR, WvH, RdB and HvS. Formal analysis was performed by JM. Software was provided by JM. Resources were provided by RB, JK, MH, WvH and HvS. Writing of the original draft was performed by IC and RD. Reviewing and editing of the manuscript was performed by IC, RD, SdK, JM, KR, RB, JK, MH, WvH, RdB and HvS.

Data sharing statement

Methodologically sound proposals to receive individual participant data that underlie the results reported in this article, after de-identification (text, tables, figures and appendices), or the study protocol, statistical analysis plan and analytic code, should be directed to inge.caelers@mumc.nl. Requestors will need to sign a data access agreement.

Declaration of interests

There are no disclosures.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanepe.2024.100964.

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