

Minimally Invasive Transforaminal Lumbar Interbody Fusion Ameliorates Persistent Pain After Lumbar Fusion Surgery

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Research article

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Abstract

Background:

Approximately 4-20% patients with degenerative lumbar diseases showed persistent pain after lumbar fusion surgery that may develop into failed back surgery syndrome (FBSS), and this persistent pain may be related to the postoperative increased release of inflammatory mediators. Minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF) can obviously reduce the intraoperative soft tissue trauma. The aim of this study is to investigate the persistent pain in the patients with degenerative lumbar diseases undergoing MIS-TLIF compared with conventional-invasive TLIF.

Material and methods:

This study retrospectively included 146 patients (MIS-TLIF vs. conventional-invasive TLIF: 56 vs. 90), and the incidence of persistent pain were evaluated. Furthermore, inflammation related markers in both blood and drainage fluid samples, including white blood cell (WBC) count, C-reactive protein (CRP), creatine kinase (CK), interleukin-6 (IL-6) and IL-1 β , were tested before and after operation.

Results:

Significantly larger number of patients undergoing conventional-invasive TLIF showed postoperative persistent pain compared to those undergoing MIS-TLIF (4/56, 7.1% vs. 20/90, 22.2%; $P < 0.05$). In both treatment groups, the patients with postoperative persistent pain showed increased IL-6 and IL-1 β in drainage fluid, as well as increased IL-6 in blood samples ($P < 0.05$), and there is significant correlation between the inflammation markers in drainage fluid and the extent of postoperative persistent pain in patients with postoperative persistent pain ($P < 0.05$).

Conclusions:

Local inflammatory substance accumulation may be potential cause for postoperative persistent pain, and MIS-TLIF may reduce this inflammatory accumulation at the surgical site and subsequently reduce the risk of persistent pain.

Background:

Transforaminal lumbar interbody fusion (TLIF) is a routine and effective operation for degenerative spinal diseases [1]. While TLIF usually has excellent clinical outcomes, serious complications can occur [1–3]. Among these, postoperative persistent pain of low back/lower limbs after TLIF is a devastating complication that may develop into failed back surgery syndrome (FBSS) [4–6], which lead to higher morbidity/mortality rates and greater healthcare costs. Given the clinical outcomes and economic impact of both postoperative persistent pain and subsequent FBSS, efforts to minimize persistent pain in the early postoperative period have a high priority. Therefore, many previous studies have investigated potential mechanism of this postoperative persistent pain of low back/lower limbs [7–10], and recent

studies demonstrated that increased release of inflammatory mediators caused by surgical trauma may be one of the possible reasons for this persistent pain [9, 10], which was further supported by intraoperative application of the epidural steroid can effectively reduce postoperative persistent pain since steroid can reduce the surgical local inflammatory substances accumulation.

In the last few decades, an increasing interest in that minimally invasive spine surgery has been observed [11–14]. The advantages of the minimally invasive TLIF (MIS-TLIF) include smaller incisions, less blood loss, less damage to the dorsal musculature, shorter hospitalization times, reduced perioperative morbidity and better rehabilitation, thus providing a beneficial alternative to conventional surgical approaches to treat degenerative lumbar diseases [11, 12]. However, fewer studies involving the impact of MIS-TLIF on the postoperative persistent pain in patients with degenerative lumbar diseases have been conducted, although this type of study may guide clinicians to explore better treatment that allow better prognoses in patients with degenerative lumbar diseases.

The aim of this study was to investigate the incidence of the postoperative persistent pain in patients undergoing MIS-TLIF compared with those undergoing conventionalinvasive TLIF, and the potential possibilities of persistent pain after lumbar fusion surgeries were also analyzed in this study.

Methods:

Subjects:

This retrospective cohort analysis included a total of 146 patients with lumbar spinal stenosis and/or lumbosacral disc herniation. In the present study, fifty-six patients underwent MIS-TLIF [15, 16], and the other 90 patients underwent conventionalinvasive TLIF [1] (Table 1). All patients were recruited in SongJiang district central Hospital from October 2016 to September 2019. The study protocol was approved by Human Ethics Committees (Songjiang district central hospital, Shanghai, China; SJ2020-KY014). All subjects gave informed consent.

Table 1
Characteristic of patients undergoing MIS-TLIF and conventionalinvasive TLIF

	MIS-TLIF	Conventionalinvasive TLIF
Number of subjects	56	90
Age (years)	55.5 ± 10.0	55.8 ± 9.9
Gender (male vs. female)	29 vs. 27	51 vs. 39
Duration (months)	17.4 ± 6.6	16.6 ± 6.6
BMI	23.5 ± 3.5	23.5 ± 3.4
Alcohol consumption	14/56 (25.0%)	17/90 (18.9%)
Current smoking	8/56 (14.3%)	13/90 (14.4%)
Preoperative complications		
Hypertension	19/56 (33.9%)	27/90 (30.0%)
Diabetes mellitus	8/56 (14.3%)	11/90 (12.2%)
Heart disease	4/56 (7.1%)	5/90 (5.6%)
Chronic renal dysfunction	4/56 (7.1%)	4/90 (4.4%)
Involved lumbosacral level		
L2-3	3/56 (5.4%)	8/90 (8.9%)
L3-4	22/56 (39.3%)	26/90 (28.9%%)
L4-5	22/56 (39.3%)	33/90 (36.7%)
L5-S1	9/56 (16.1%)	23/90 (25.6%)
Operative time (min)	140.4 ± 27.6	149.0 ± 38.9
Intraoperative blood loss (ml)	316.1 ± 83.1*	450.9 ± 77.3*
Drainage time (day)	1.9 ± 0.8	2.1 ± 0.8
Total amount of drainage	94.5 ± 48.4*	118.5 ± 56.3*
Measurements are expressed as the mean ± SD		
*Statistically significant difference MIS-TLIF and conventionalinvasive TLIF		
MIS-TLIF: Minimally invasive TLIF; TLIF: Transforaminal lumbar interbody fusion; BMI: Body mass index;		

The inclusion criteria for patients in this study included (1) low back discomfort with referral of pain/paresthesias into lower limb and/or neuronal intermittent claudication (2) lumbosacral magnetic resonance imaging (MRI) or computer tomography (CT) that demonstrated single-level herniated disc, spinal stenosis or spondylolisthesis; (3) 6 months of regular conservative treatment without relief of symptoms; and (4) postoperative drain for at least one day. The exclusion criteria included previous spinal surgery, polyneuropathies, plexopathies, focal neuropathies, muscle disorders, cauda equina syndrome, scoliosis, spondylolisthesis, vertebral fractures, and other spinal pathologies. Furthermore, patients with incomplete medical records or lost to follow-up were excluded.

Surgical procedures:

Procedure for minimally-invasive TLIF

In the present study, the MIS-TLIF was performed by the same spine surgeon experienced in this technique. After the general anesthesia, the patient is placed in a knee-chest position, and intervertebral segment to treat is located by a positioning needle under the C-arm fluoroscopy. After performing a 2- to 3-cm skin incision approximately 3 cm away from spinous process, the guidewire was inserted along the wiltse approach into the facet joint, followed by placement of the expansion sleeve and assembly of the minimally invasive access system. The inferior and superior facets were resected under direct visualization, and then a discectomy was performed. A polyetheretherketone (PEEK) cage filled with harvested local was placed after endplate preparation. Bilateral pedicle screws were inserted through wiltse approach by minimally invasive access system, and both compression and fixation over the intervertebral space was completed afterward.

Procedure for conventionalinvasive TLIF

During the conventionalinvasive TLIF procedure [1], a midline incision was made. The soft tissues were cut in layers, and the paraspinal muscles were stripped from both sides of the spinous process to expose the lamina and the articular process. After the pedicle screw was implanted, the inferior and superior facets of the intended levels were resected under direct visualization, and then a discectomy was performed. A polyetheretherketone (PEEK) cage filled with harvested local was placed after endplate preparation, and compression over the intervertebral space was completed afterward.

Postoperative Management:

Antibiotics were given at postoperative 48 hours to prevent infection, and both hormone and non-steroidal anti-inflammatory drugs were not used in all patients in this study after operation. After one day of bed rest, the patients were allowed to walk with the protection of a waist brace. When the patients presented with postoperative persistent pain, the non-steroidal anti-inflammatory drugs were used until the Numerical Rating Scale(NRS)scores are lower than 3. A drainage tube was placed for 1–2 days. Patients were usually discharged from hospital 5–10 days after operation

Perioperative assessment:

Assessment of pain:

Both low back and lower limb pain in all patients were measured by NRS scores before, 3 days, 2 weeks and 6 months after operation. In this study, the persistent pain was defined as similar or more serious pain at the primary site or other sites in low back/lower limbs after operation. NRS scores is a continuous scale composed anchored by a score of zero, indicated no pain, and a score of 10, represented the worst pain.

Assessment of venous blood and drainage fluid samples:

Venous blood samples were obtained before, 1 day, 3 days and 6 days after operation, and the wound drainage fluid was collected from 1-3 days after operation according to the drainage time. For the blood samples, white blood cell (WBC) count, interleukin-6 (IL-6), C-reactive protein (CRP) and creatine kinase (CK) were measured. In the drainage fluid samples, both interleukin (IL)-1 β and IL-6 were measured.

Statistical methods:

The measurements were analyzed using SPSS version 18.0 (IBM, USA). Measurements between the cases in two patient groups were compared by the independent t-tests, and the same statistical method was also used to analyze the measurements between the cases with or without persistent pain in both patient groups. The frequencies of postoperative persistent pain between two patient groups were compared by chi-square tests. The correlations between the extent of persistent pain and inflammation related markers in both blood and drainage fluid samples were analyzed by Pearson correlation coefficient analysis. In all instances, a P-value < 0.05 was considered significant.

Results:

There was no statistical difference in patient characteristics between patients who accepted MIS-TLIF or conventionalinvasive TLIF (Table 1, P > 0.05), and both NRS scores and all measurements of blood samples were similar between these two patient groups before operation (Fig. 1, P > 0.05).

Compared with the patients accepting conventionalinvasive TLIF, those undergoing MIS-TLIF showed obviously less intraoperative bleeding and total amount of postoperative drainage (Table 1, P < 0.05). In contrast, there was no difference of operative time and drainage time between these two groups (Table 1, P > 0.05). Obviously lower CK and IL-6 in the blood samples were observed in the patients undergoing MIS-TLIF than those in the patients accepting conventionalinvasive TLIF in all postoperative assessments (Fig. 1, P < 0.05), and the patients undergoing MIS-TLIF also presented with significantly lower IL-6 and IL-1 β in the drainage fluid samples compared to those undergoing open discectomy (Fig. 2, P < 0.05). Furthermore, similar measurements of both WBC and CRP were observed in both patient groups in all postoperative assessments (Fig. 1, P > 0.05).

Importantly, significantly larger number of the patients who underwent conventionalinvasive TLIF presented with postoperative persistent pain compared to the patients undergoing MIS-TLIF (4/56, 7.1% vs. 20/90, 22.2%; $P < 0.05$), and both 16 patients accepting conventionalinvasive TLIF (16/20, 80.0%) and 3 patients undergoing MIS-TLIF (3/4, 75.0%) presented with more severe and extensive lumbar/lower limb pain compared to the pre-operative pain. In both treatment groups, the patients with persistent pain presented with higher IL-6 and IL-1 β in the drainage fluid samples, as well as the greater IL-6 in the venous blood samples, compared with those without persistent pain (Table 2, $P < 0.05$). In addition, in the postoperative third day, there is significant correlation between the IL-6 and IL-1 β in drainage fluid at the and the extent of the persistent pain in all 24 patients with postoperative persistent pain (lower limb pain: $R_{IL-6 \text{ and NRS}} = 0.70$, $R_{IL-1\beta \text{ and NRS}} = 0.55$; low back pain: $R_{IL-6 \text{ and NRS}} = 0.61$; $P < 0.05$).

Table 2
Characteristic of patients with or without postoperative persistent pain in both patient groups

	MIS-TLIF		Conventionalinvasive TLIF	
	With persistent pain	Without persistent pain	With persistent pain	Without persistent pain
Number of subjects	4	52	20	70
Interleukin-6 in venous blood (pg/ml)				
Before operation	2.9 ± 2.2 (4/4)	3.4 ± 1.5 (52/52)	3.7 ± 1.0 (20/20)	3.3 ± 1.4 (70/70)
First day after operation	39.9 ± 6.9 (4/4)*\$	26.3 ± 12.5 (52/52)*	54.7 ± 15.7 (20/20)*\$	40.1 ± 17.7 (70/70)*
Third day after operation	16.0 ± 0.5 (4/4)*\$	12.5 ± 2.5 (52/52)*	23.1 ± 3.6 (20/20)*\$	19.2 ± 5.8 (70/70)*
Sixth day after operation	6.1 ± 1.1 (4/4)\$	5.5 ± 2.1 (52/52)	7.7 ± 1.4 (20/20)\$	7.1 ± 2.4 (70/70)
Interleukin-6 in drainage fluid (pg/ml)				
First day after operation	19.3 ± 1.0 (4/4)*\$	14.9 ± 3.9 (52/52)*	26.9 ± 4.5 (20/20)*\$	16.9 ± 9.5 (70/70)*
Second day after operation	23.2 ± 0.6 (4/4)*\$	16.3 ± 4.6 (36/52)*	29.6 ± 5.1 (20/20)*\$	19.7 ± 5.7 (48/70)*
Third day after operation	26.0 ± 1.3 (4/4)*\$	17.6 ± 6.6 (16/52)*	37.1 ± 5.1 (11/20)*\$	23.0 ± 10.2 (22/70)*
Interleukin-1β in drainage fluid (pg/ml)				
First day after operation	13.4 ± 0.1 (4/4)*	10.8 ± 1.4 (52/52)*	13.7 ± 1.1 (20/20)	13.2 ± 1.5 (70/70)
Second day after operation	15.7 ± 0.2 (4/4)*	13.3 ± 1.5 (36/52)*	16.0 ± 2.1 (20/20)*	14.3 ± 2.6 (48/70)*
Third day after operation	17.8 ± 0.5 (4/4)*\$	14.2 ± 1.9 (16/52)*	19.7 ± 2.0 (11/20)*\$	16.0 ± 2.5 (22/70)*
Measurements are expressed as the mean ± SD				
(a/b): where a is the number of patients who accepted laboratory test, and b is the number of patients included in corresponding groups				
MIS-TLIF: Minimally invasive TLIF; TLIF: Transforaminal lumbar interbody fusion;				
*: Statistical difference between the patients with and without persistent pain (P < 0.05)				
\$: Statistical difference of the patients with persistent pain between the different patient groups (P < 0.05)				

Discussion:

The results of this study demonstrated a significant difference in the incidence of postoperative persistent pain between the patients who accepted MIS-TLIF or conventionalinvasive TLIF, and an obvious correlation between this persistent pain and surgical local inflammatory substances accumulation was also identified in this study.

Consistent with previous studies [17–19], both less intraoperative bleeding and postoperative drainage, as well as lower CK, were observed in patients undergoing MIS-TLIF compared to those undergoing conventionalinvasive TLIF, suggesting less surgical trauma in the MIS-TLIF group. Previous studies demonstrated that nerve root edema caused by intraoperative traction injury may be possible reason for postoperative lower limb pain[20, 21]. However, most patients in this study showed obviously more extensive coverage of postoperative pain than those supplied by intraoperative decompressed nerve root. Furthermore, recently published studies demonstrated that postoperative persistent pain and the resulting FBSS even may occur at the other sites, not the preoperative involved site, in both low back and lower limbs [4–6]. These results collectively argued against the intraoperative over traction of nerve root is the main cause for the postoperative persistent pain and FBSS.

These are increasing evidences that inflammatory stimulation presented with greater correlation with the radicular and low back pain compared to the mechanical stimulation [22–26]. Although inflammatory substances in the blood sample are similar between two patient groups in this study, the patients undergoing MIS-TLIF presented with obviously fewer inflammatory substances in the drainage fluid than those in the conventionalinvasive TLIF patient group. These findings suggested that postoperative persistent pain may be mainly ascribed to the stimulation of local inflammatory substance accumulation rather than systemic inflammatory response caused by surgical trauma, which was further supported by significant correlation between the inflammatory markers in drainage fluid and the extent of postoperative persistent pain in postoperative third day in this study. Therefore, difficulty in aggregating of inflammatory substances around the nerves after operation may be the main reason for the low incidence of persistent pain after MIS-TLIF.

According to the previous studies, inflammatory substances may be released by the locally damaged tissue around the surgical site [27, 28], that may stimulate the nerve roots and cause persistent pain. Different from the conventionalinvasive TLIF, MIS-TLIF is performed under the minimally invasive access system during the operation[15, 16], which may effectively prevent the aggregation of local inflammatory substances thorough protecting surrounding tissues. Therefore, less inflammatory exudation at the surgical site caused by smaller surgical wounds in MIS-TLIF may be another reason for reduced aggregation of local inflammatory substances around nerve roots.

The findings of this study should be interpreted with caution. The half-life of IL-6 or IL-1 β is quite short that may affect the analysis results, and inflammatory substances in the drainage fluid can only indirectly reflect the local inflammation. Another clinical limitation of this study is low sample size.

Therefore, more significant results might be achieved in future study with establishment of both more suitable marker and an increased number of cases.

Conclusion:

The results of the current study support the view that local inflammatory substance accumulation is a potential cause for postoperative persistent pain in patients with degenerative lumbar diseases. Therefore, perioperative management in patients with degenerative lumbar diseases should account for local inflammatory response. Importantly, differences in postoperative results between the MIS-TLIF and conventionalinvasive TLIF groups suggested that MIS-TLIF may effectively reduce the local inflammatory substances at the surgical site, reduce the risk of postoperative persistent pain and resulting FBSS.

List Of Abbreviations:

MIS-TLIF	Minimally invasive transforaminal lumbar interbody fusion
TLIF	Transforaminal lumbar interbody fusion
WBC	White blood cell
CK	Creatine kinase
CRP	C-reactive protein
IL-6	Interleukin-6
IL-1 β	Interleukin-1 β
MRI	Magnetic resonance imaging
CT	Computer tomography
NRS	Numerical Rating Scale

Declarations:

Ethics approval and consent to participate

The study protocol was approved by Human Ethics Committees (Shanghai Songjiang District Central Hospital). All subjects gave informed consent.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

DEGUO WANG have made substantial contributions to conception and design; JUN LI and KAI LIU have made substantial contributions to acquisition of data, or analysis and interpretation of data; YANG LI have been involved in drafting the manuscript or revising it critically for important intellectual content; all authors have given final approval of the version to be published

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Figures

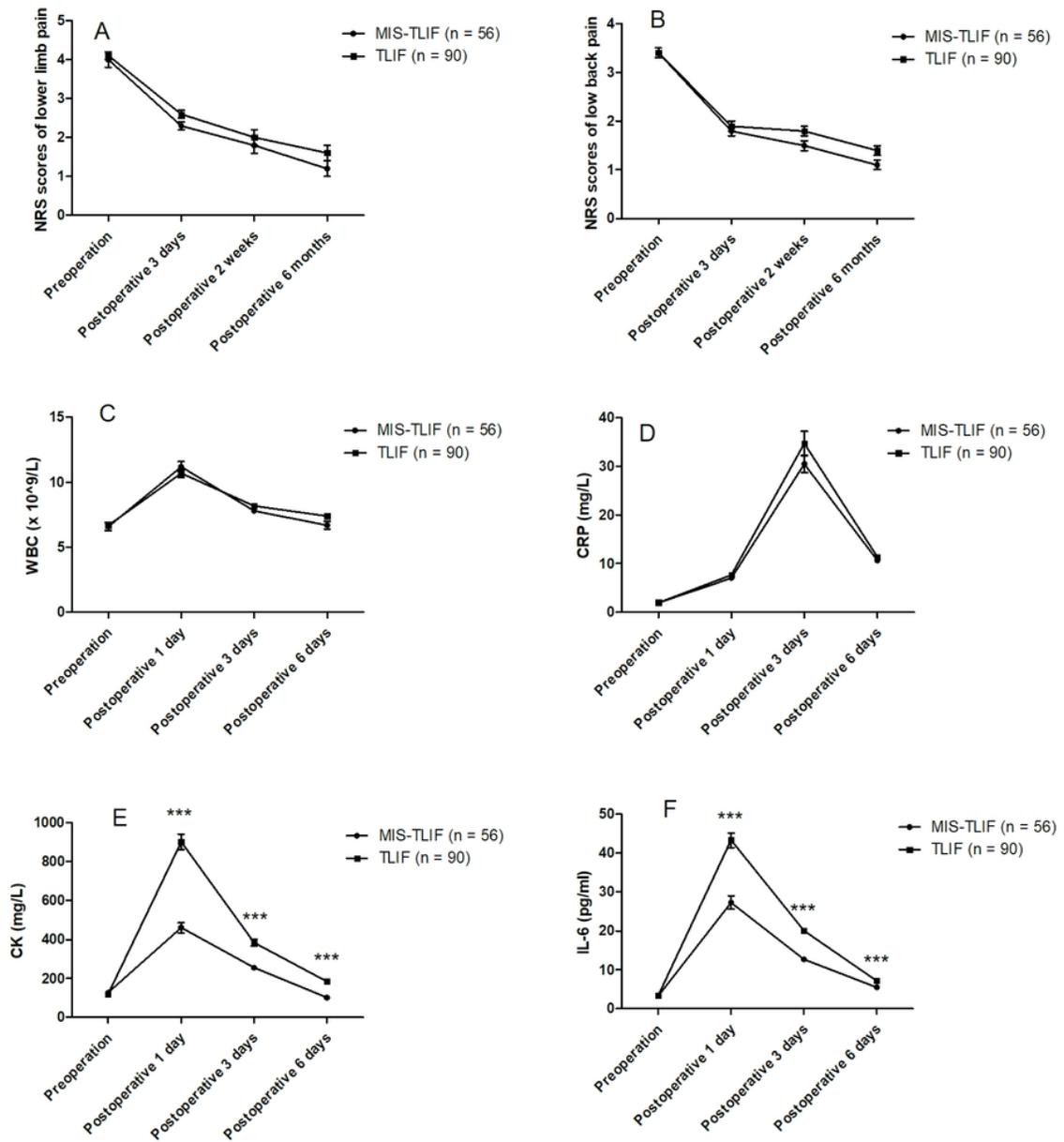


Figure 1

Measurements of both inflammation related markers in the blood sample and NRS scores between the patients undergoing MIS-TLIF (n = 56) and TLIF (n = 90). The figure shows there are significant difference of CK (E) and IL-6 (F) between the patients undergoing MIS-TLIF and TLIF ($P < 0.05$). In contrast, there was no difference of NRS scores (A and B), WBC (C) and CRP (D) between these two patient groups ($P > 0.05$). NRS: Numerical Rating Scale; MIS-TLIF: Minimally invasive transforaminal lumbar interbody fusion; TLIF: Transforaminal lumbar interbody fusion; WBC: White blood cell count, CRP: C-reactive protein; CK: Creatine kinase; IL-6: Interleukin-6; n: number. * $P < 0.05$, ** $P < 0.01$, and *** $P < 0.001$.

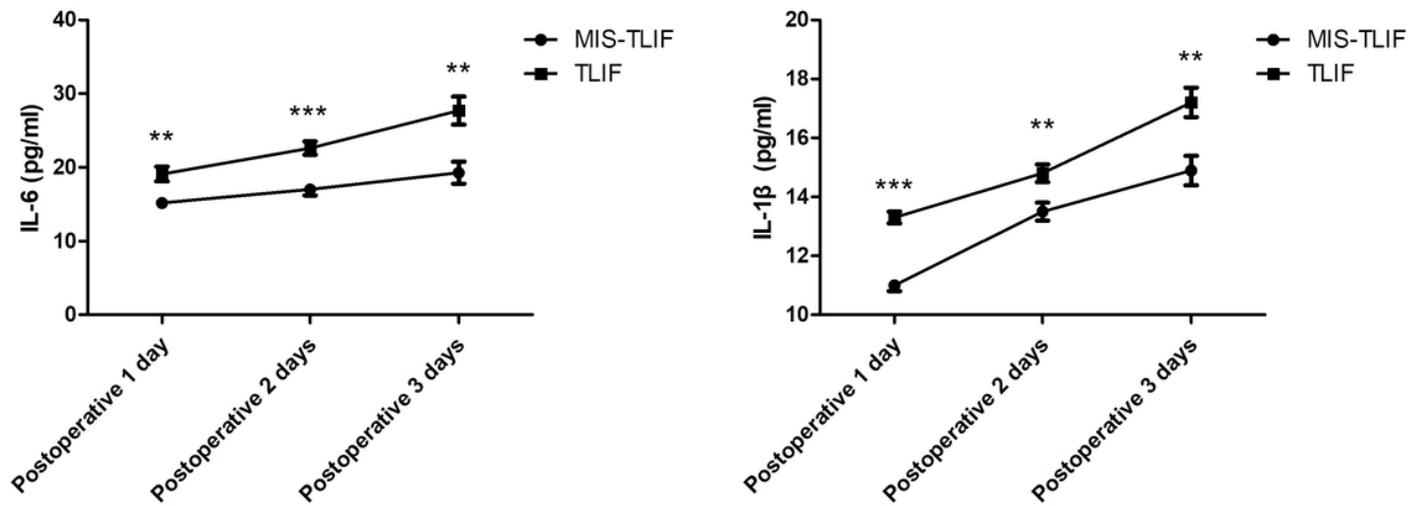


Figure 2

Inflammation related markers in the drainage fluid sample in both patient groups after operation. The figure shows that patients in the TLIF group presented with significantly increased IL-6 and IL-1β compared to the MIS-TLIF patient group. MIS-TLIF: Minimally invasive transforaminal lumbar interbody fusion; TLIF: Transforaminal lumbar interbody fusion; IL-6: Interleukin-6; IL-1β: Interleukin-1β; n: number. *P < 0.05, **P < 0.01, and ***P < 0.001.