

Percutaneous transforaminal endoscopic discectomy ameliorates postoperative reactive pain in patients with lumbar disc herniation

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Research article

Keywords: Postoperative reactive pain, Percutaneous transforaminal endoscopic discectomy, Open discectomy, Inflammatory substances, Local inflammatory response

Posted Date: September 16th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-35700/v2>

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Abstract

Background:

Approximately one-third patients with lumbar disc herniation (LDH) showed postoperative reactive pain, and this reactive pain may be related to the postoperative increased release of inflammatory mediators. Percutaneous transforaminal endoscopic discectomy (PTED) can obviously reduce the intraoperative soft tissue trauma. The aim of this study is to investigate the reactive pain in LDH patients undergoing PTED compared with open discectomy.

Material and methods:

This study retrospectively included 72 patients (PTED vs. open discectomy: 41 vs. 31), and the incidence of reactive pain, as well as both the extent and duration of reactive 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 greater number of patients undergoing open discectomy showed reactive pain compared to those undergoing PTED (13/31, 41.9% vs. 7/41, 17.0%; $P < 0.05$), and the duration of reactive pain is mildly longer in the former ($P < 0.05$). In both patient groups, the patients with reactive 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 both duration and extent of reactive pain in both patient groups ($P < 0.05$).

Conclusions: Local inflammatory substance accumulation may be potential cause for postoperative reactive pain, and PTED may reduce this inflammatory accumulation at the surgical site and subsequently reduce the risk of reactive pain.

Trial registration: This retrospective cohort analysis was retrospectively registered at September 9, 2020.

Background

Lumbar disc herniation (LDH) is a degenerative pathology, and it was estimated that approximately 70-80% of the adult population will be affected by this disease during their lifetime [1, 2]. Lumbosacral radiculopathy caused by LDH always carries a series of signs and symptoms and often leads to surgical intervention when conservative management fails [2-4]. Traditional open discectomy through unilateral interlaminar approach has obtained satisfactory results [5, 6]. However, approximately one-third patients who accepted traditional discectomy presented with reactive pain few days after operation [7]. Reactive pain is defined as the patients with LDH presented with the initial pain relief after surgery followed by the recurrence of similar or more severe pain at the primary site or other sites in lower limbs [7]. Although it

will gradually ease and disappear approximately 2 weeks after it appears [7, 8], reactive pain may affect short-term clinical outcomes and postoperative early functional exercise. The true mechanism of this reactive pain is unclear, and recent studies demonstrated that increased release of inflammatory mediators caused by surgical trauma may be one of the possible reasons for this reactive pain [7, 8], which was further supported by intraoperative application of the epidural steroid can effectively reduce the postoperative reactive pain since steroid can reduce the surgical local inflammatory substances accumulation [9, 10].

Percutaneous transforaminal endoscopic discectomy (PTED), one of the minimal invasive spinal surgical techniques, provides a beneficial alternative to conventional surgical approaches to treat LDH [11, 12]. Previous studies have demonstrated that PTED is obviously associated with less soft tissue trauma, preservation of dorsal musculature, shorter hospitalization times, reduced perioperative morbidity, and earlier return to work [11, 12]. However, fewer studies involving the impact of PTED on the postoperative reactive pain in patients with LDH have been conducted, although this type of study may guide clinicians to explore better treatment that allow better prognoses in patients with LDH.

The aim of this study was to investigate the incidence of the postoperative reactive pain in LDH patients undergoing PTED compared with those undergoing traditional discectomy, and the potential possibilities of reactive pain after discectomy were also analyzed in this study.

Methods

Subjects:

This retrospective cohort analysis included a total of 72 patients with unilateral lumbosacral radiculopathy caused by single-level LDH. In the present study, forty-one patients with LDH underwent PTED, and the other 31 patients underwent traditional discectomy described by Caspar with or without laminotomy (Table 1) [5]. All patients were recruited in SongJiang district central Hospital from December 2017 to March 2019. The study protocol was approved by Human Ethics Committees (Songjiang district central hospital, Shanghai, China; SJ2017-KY032). All subjects gave informed consent.

The inclusion criteria for patients with LDH includes [13, 14] (1) low back discomfort with referral of pain or paresthesias into a single lower limb following an L4/L5/S1 distribution pattern; (2) lumbosacral magnetic resonance imaging (MRI) or computer tomography (CT) that demonstrated unilateral L4/L5/S1 nerve root compression by herniated disc at the L3/4, L4/L5 or L5/S1 level; (3) conventional electrophysiologic studies including normal sensory nerve conduction studies and a needle EMG revealing the presence of disease only on the involved side of abnormal spontaneous activity and/or changes in motor unit action potential in muscles that were innervated by the involved L4/L5/S1 root. (4) Surgical findings of unilateral compressed herniated discs at the L4/L5/S1 root on the involved side. (5) Postoperative drain for 3 days. The exclusion criteria for patients with LDH includes 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:

Open discectomy

All patients underwent open discectomy 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 paramedian 3- to 4-cm skin incision, a unilateral interlaminar approach is used, and the superior facet is partially removed if needed to provide a good view of the involved nerve root. A small annular incision is performed to remove the herniated disc part before smoothly extracting the mobile disc fragments. The intervertebral space is cleaned by suction without any excessive curettage. Afterwards, the canal is inspected to ensure that there is no more detached disc fragment and that the nerve root is freely mobile after decompression.

Percutaneous transforaminal endoscopic discectomy:

All patients underwent PTED performed by the same spine surgeon experienced in this technique. The PTED procedure was performed in the prone position using C-arm fluoroscopy under general anesthesia, and the positioning needle trajectory was planned on the preoperative MRI/CT to target the intervertebral foramen. The needle was introduced 10-13 cm lateral to the midline, with the transit corridor in Kambin's triangle, and C-arm fluoroscopy was used during needle introduction to validate correct positioning. Then, Sequential reamers (joimax, Irvine, California, USA) were used to enlarge the neural foramen by removing the ventral aspect of the superior facet. The cannula and endoscope were then introduced, and herniated disc material was removed using endoscopic forceps under cold saline irrigation.

Postoperative Management:

A drainage tube was placed for 72 hours. 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 reactive pain, the non-steroidal anti-inflammatory drugs were used until the Numerical Rating Scale (NRS) scores are lower than 3.

Postoperative assessment:

Assessment of pain:

Lower limb pain in all patients with LDH were measured by NRS scores before and 1 day after operation, and the NRS scores was further evaluated in the patients with reactive pain. In this study, the reactive pain was defined as preoperative pain relief after surgery followed by the recurrence pain at the primary site or other sites in lower limbs, and NRS score of this recurrence pain should increase at least 2 points compared to postoperative initial pain. 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 surgery and on the first, third, and sixth days after operation, and the wound drainage fluid was collected from first to third day after operation. The blood samples were collected and immediately centrifuged at 3000rpm for 10min, and they were then stored at -20°C until assayed. The drainage fluid samples were collected and immediately centrifuged at 1500rpm for the first 15min and 3000rpm for the second 15min, and they were then stored at -80°C until assayed. 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.

Both IL-1 β and IL-6, as well as CRP, were analyzed by the enzyme-linked immunosorbent assay (ELISA) according to the protocol provided by the manufacturer (R&D Systems, Inc., USA). Take out the EP tube and thaw at room temperature. The kit includes sample hole, standard sample hole and blank hole. The standard holes were continuously dripped with 50 μ L of standards with different concentrations, and the sample hole first add 10 μ L of the sample to be tested, then add 40 μ L of sample diluent. Except for the blank hole, first drop 100 μ L of detection antibody labeled with horseradish peroxidase (HRP) into the standard hole and sample hole, seal the reaction hole with a sealing film, and incubate in a constant temperature box (37 °C, 60 min); after discarding the liquid, blot dry with absorbent paper, fill up the washing liquid in each well, let stand for 1 min, shake off the washing liquid, blot dry with absorbent paper, repeat 5 times, wash buffer and distilled water Prepared at a ratio of 1:19; add 50 μ L of A and B substrates to each well, and incubate in the dark at 37°C for 15 min. After adding 50 μ L of stop solution to each well, measure the optical density of each well at the wavelength of 450 nm within 15 minutes, and obtain the concentration according to the kit instructions. The detection limits of this assay were 0.19 pg/ml for IL-6, 0.3 pg/ml for IL-1 β and 0.10 mg/dl for CRP.

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 reactive pain in both patient groups. The frequencies of postoperative reactive pain between two patient groups were compared by chi-square tests. The correlations between both duration and extent of reactive 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 either age or disease duration between patients who accepted PTED or open discectomy (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 and 2, $P > 0.05$).

Compared with the patients accepting open discectomy, those undergoing PTED showed obviously less intraoperative bleeding and drainage (postoperative first and second days) (Fig 1, $P < 0.05$). In contrast, there was no difference of operative time and drainage (postoperative third day) between these two patient groups (Fig 1, $P > 0.05$), and all patients with LDH in both treatment groups presented with similar immediate pain relief after operation (PTED group: 5.3 ± 1.4 vs. 1.6 ± 1.0 ; Open discectomy group: 5.1 ± 1.1 vs. 1.6 ± 1.2 ; $P < 0.05$).

Obviously lower CK and IL-6 in the blood samples were observed in the patients undergoing PTED than those in the patients accepting open discectomy in all postoperative assessments (Fig 2, $P < 0.05$), and the patients undergoing PTED also presented with significantly lower IL-6 and IL-1 β in the drainage fluid samples compared to those undergoing open discectomy (Fig 3, $P < 0.05$). Furthermore, similar measurements of both WBC and CRP were observed in both patient groups in all postoperative assessments (Fig 2, $P > 0.05$).

Importantly, significantly greater number of the patients who accepted open discectomy presented with postoperative reactive pain compared to the patients undergoing PTED (13/31, 41.9% vs. 7/41, 17.0%; $P < 0.05$), and duration of the reactive pain is mildly longer in the open discectomy group than that in the PTED group (Table 2, $P < 0.05$). Furthermore, both five patients undergoing open discectomy (5/13, 38.5%) and 2 patients undergoing PTED (4/7, 57.1%) presented with reactive pain at the primary site, and the range of postoperative reactive pain was significantly wider than the preoperative pain in the other patients in this study. In addition, in both treatment groups, the patients with reactive pain presented with increased IL-6 and IL-1 β in the drainage fluid samples, as well as the increased IL-6 in the venous blood samples, compared with those without reactive pain (Table 2, $P < 0.05$), and there is correlation between the IL-6 and IL-1 β in drainage fluid at the postoperative third day and the duration and extent of the reactive pain in both patient groups (PTED: $R_{IL-6 \text{ and NRS}} = 0.81$, $R_{IL-6 \text{ and duration}} = 0.79$, $R_{IL-1\beta \text{ and duration}} = 0.81$; Open discectomy: $R_{IL-1\beta \text{ and NRS}} = 0.58$, $R_{IL-1\beta \text{ and duration}} = 0.80$; $P < 0.05$).

Discussion

The results of this study demonstrated a significant difference in the incidence of reactive pain between the patients who accepted PTED or open discectomy, and an obvious correlation between the reactive pain and surgical local inflammatory substances accumulation was also identified in this study.

Consistent with previous studies [11, 12, 15], both less intraoperative bleeding and postoperative drainage, as well as lower CK, were observed in patients undergoing PTED compared to those undergoing open discectomy, suggesting less surgical trauma in PTED patient group. Previous studies demonstrated that nerve root edema caused by intraoperative traction injury may be possible reason for postoperative lower limb pain [16, 17]. However, some patients in this study showed obviously more extensive coverage of reactive pain than those supplied by intraoperative decompressed nerve root. Furthermore, recently published studies demonstrated that postoperative reactive pain even may occur at the other sites, not the preoperative involved site, in lower limbs [7, 8]. These results collectively argued against the intraoperative over traction of nerve root is the main cause for the postoperative reactive pain.

These are increasing evidences that inflammatory stimulation presented with greater correlation with the radicular pain compared to the mechanical stimulation [1, 2, 18-20]. Although inflammatory substances in the blood sample are similar between two patient groups in this study, the patients undergoing PTED presented with obviously fewer inflammatory substances in the drainage fluid than those in the open discectomy patient group. These findings suggested that postoperative reactive 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 both the duration and extent of the reactive pain in both patient groups in this study. Therefore, difficulty in aggregating of inflammatory substances around the nerve roots after operation may be the main reason for the low incidence of reactive pain after PTED.

According to the previous studies [19, 20], there are abundant inflammatory substances in the nucleus pulposus of lumbar intervertebral disc. When the herniated nucleus pulposus is removed, the surrounding annulus tissue around the nucleus will also be destroyed. As a result, the inflammatory mediators of the nucleus pulposus are released and gather around the nerve roots. Different from the open discectomy, PTED is performed under the water boundary during the operation [9, 21, 22], which may effectively prevent the aggregation of local inflammatory substances thorough continuous irrigation. Furthermore, previous studies demonstrated that inflammatory substances may also be released by the locally damaged tissue around the surgical site [23, 24], that may also stimulate the nerve roots and cause reactive pain. Therefore, less inflammatory exudation at the surgical site caused by smaller surgical wounds in PTED 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. However, it is difficult to collect the patients in PTED group who accepted postoperative drainage for 3 days. Therefore, more significant results might be achieved in future study with establishment of both more suitable marker and an increased number of cases, and microdiscectomy should also be included

in comparison as another treatment group in the future study since microdiscectomy always is considered to be standard of care for LDH.

Conclusion

The results of the current study support the view that local inflammatory substance accumulation is a potential cause for postoperative reactive pain in patients with LDH. Therefore, perioperative management in patients with LDH should account for local inflammatory response. Importantly, differences in postoperative results between the PTED and open discectomy patient groups suggested that PTED may effectively reduce the local inflammatory substances at the surgical site, reduce the risk of postoperative reactive pain and improve patients' perioperative satisfaction.

Abbreviations

LDH	Lumbar disc herniation
PTED	Percutaneous transforaminal endoscopic discectomy
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

Funding

Financial support from the Foundation of science and Technology Commission of Songjiang District, Shanghai (18sjgg9931)

Authors' contributions

DEGUO WANG have made substantial contributions to conception and design; JUN LI 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

Acknowledgements

Not applicable.

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Tables

Table 1 Characteristic of patients undergoing PTED or open discectomy		
	PTED	Open discectomy
Number of subjects	41	31
Age (years)	41.8 ± 15.8	44.6 ± 18.7
Gender (male vs. female)	25 vs. 16	17 vs. 14
Duration (months)	8.2 ± 5.6	8.7 ± 6.0
Involved lumbosacral level		
L3-4	18/41 (43.9%)	9/31 (29.0%)
L4-5	18/41 (43.9%)	16/31 (51.6%)
L5-S1	5/41 (12.2%)	6/31 (19.4%)
Measurements are expressed as the mean ± SD		
PTED: Percutaneous transforaminal endoscopic discectomy		

Table 2 Characteristic of patients with or without postoperative reactive pain in both patient groups				
	PTED		Open discectomy	
	With reactive pain	Without reactive pain	With reactive pain	Without reactive pain
Number of subjects	7	34	13	18
Age range (years)	40.1 ± 16.4	42.1 ± 15.9	44.2 ± 18.3	44.9 ± 19.5
Starting time# (days)	4.4 ± 1.0	/	4.5 ± 0.7	/
Maximal NRS scores	5.0 ± 1.3	/	4.6 ± 1.4	/
Duration of reactive pain (days)	6.1 ± 1.6\$	/	8.5 ± 2.8\$	/
Interleukin-6 in venous blood (pg/ml)				
Before operation	3.0 ± 0.8	2.7 ± 1.0	3.1 ± 1.3	3.2 ± 1.1
First day after operation	43.8 ± 4.4*	21.5 ± 8.9*	47.6 ± 17.4*	25.1 ± 7.0*
Third day after operation	15.9 ± 0.7*\$	11.8 ± 2.2*	22.3 ± 2.7*\$	17.3 ± 4.0*
Sixth day after operation	4.9 ± 1.9	5.4 ± 2.0	5.7 ± 2.4	7.0 ± 1.7
Interleukin-6 in drainage fluid (pg/ml)				
First day after operation	17.3 ± 2.8\$	14.5 ± 4.0	24.9 ± 8.3*\$	16.5 ± 7.4*
Second day after operation	21.0 ± 4.4*\$	15.9 ± 4.3*	25.0 ± 2.8*\$	20.1 ± 2.6*
Third day after operation	24.9 ± 4.5*\$	16.9 ± 6.3*	32.9 ± 7.0*\$	24.3 ± 10.4*
Interleukin-1β in drainage fluid (pg/ml)				
First day after operation	11.8 ± 0.6*	10.0 ± 1.4*	11.4 ± 1.8	10.9 ± 1.9
Second day after operation	14.0 ± 0.9*\$	11.7 ± 1.3*	15.7 ± 2.1\$	14.3 ± 2.2
Third day after operation	17.3 ± 1.0*	13.4 ± 2.4*	17.9 ± 1.8*	15.1 ± 2.1*
Measurements are expressed as the mean ± SD				
PTED: Percutaneous transforaminal endoscopic discectomy				
NRS: Numerical Rating Scale				
#: The day after operation				
*: Statistical difference between the patients with and without reactive pain (P < 0.05)				
\$: Statistical difference of the patients with reactive pain between the different patient groups (P < 0.05)				

Figures

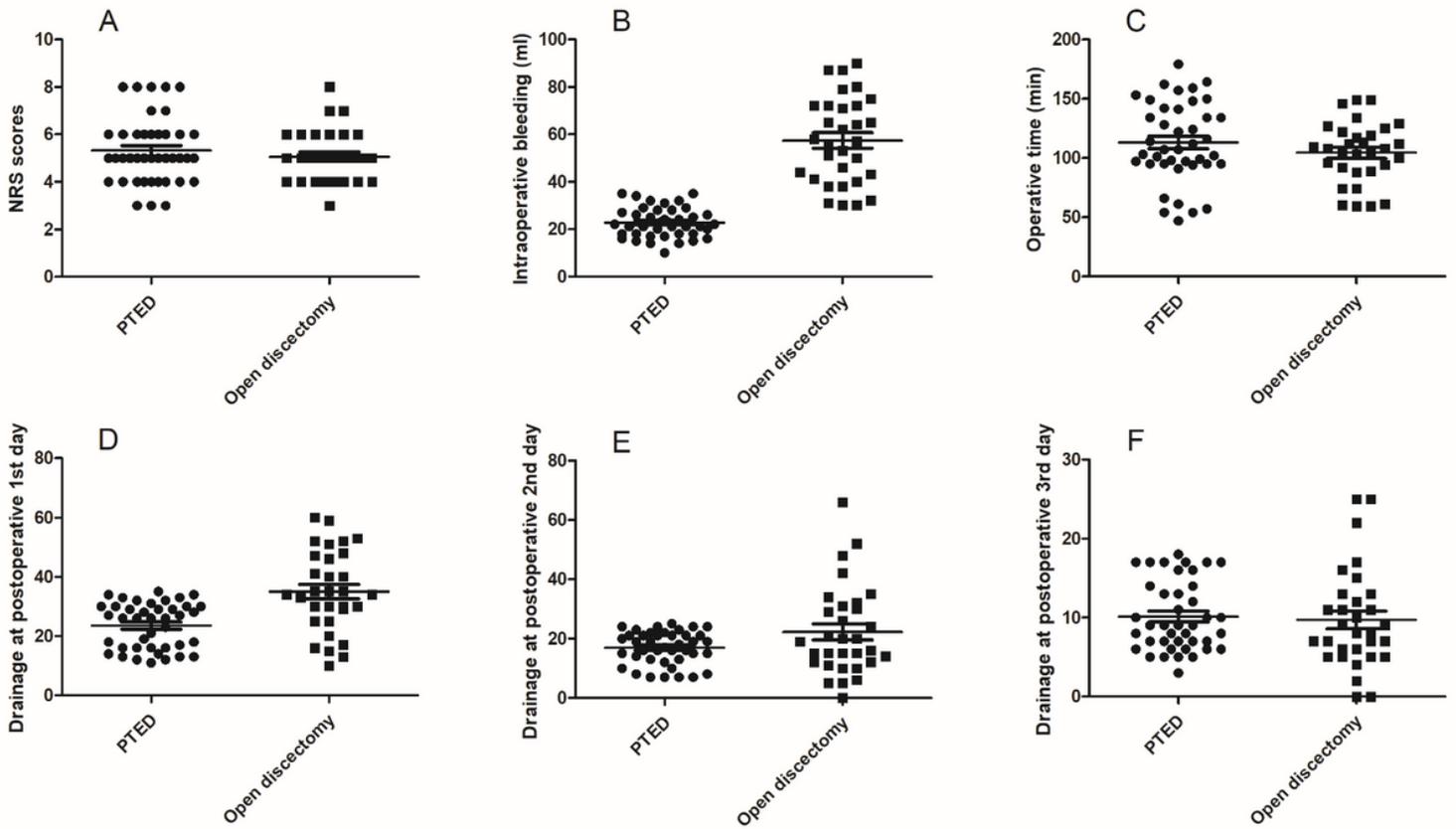


Figure 1

Measurements of both disease severity and surgical trauma between the patients undergoing PTED (n = 41) and open discectomy (n = 31). The figure shows there are significant difference of intraoperative bleeding (B) and drainage (postoperative first and second days, D and E) between the patients undergoing open discectomy and PTED ($P < 0.05$). In contrast, there was no difference of preoperative leg pain (A), operative time (C), postoperative drainage (third day, F) between these two patient groups ($P > 0.05$). NRS: Numerical Rating Scale; PTED: Percutaneous transforaminal endoscopic discectomy; n: Number.

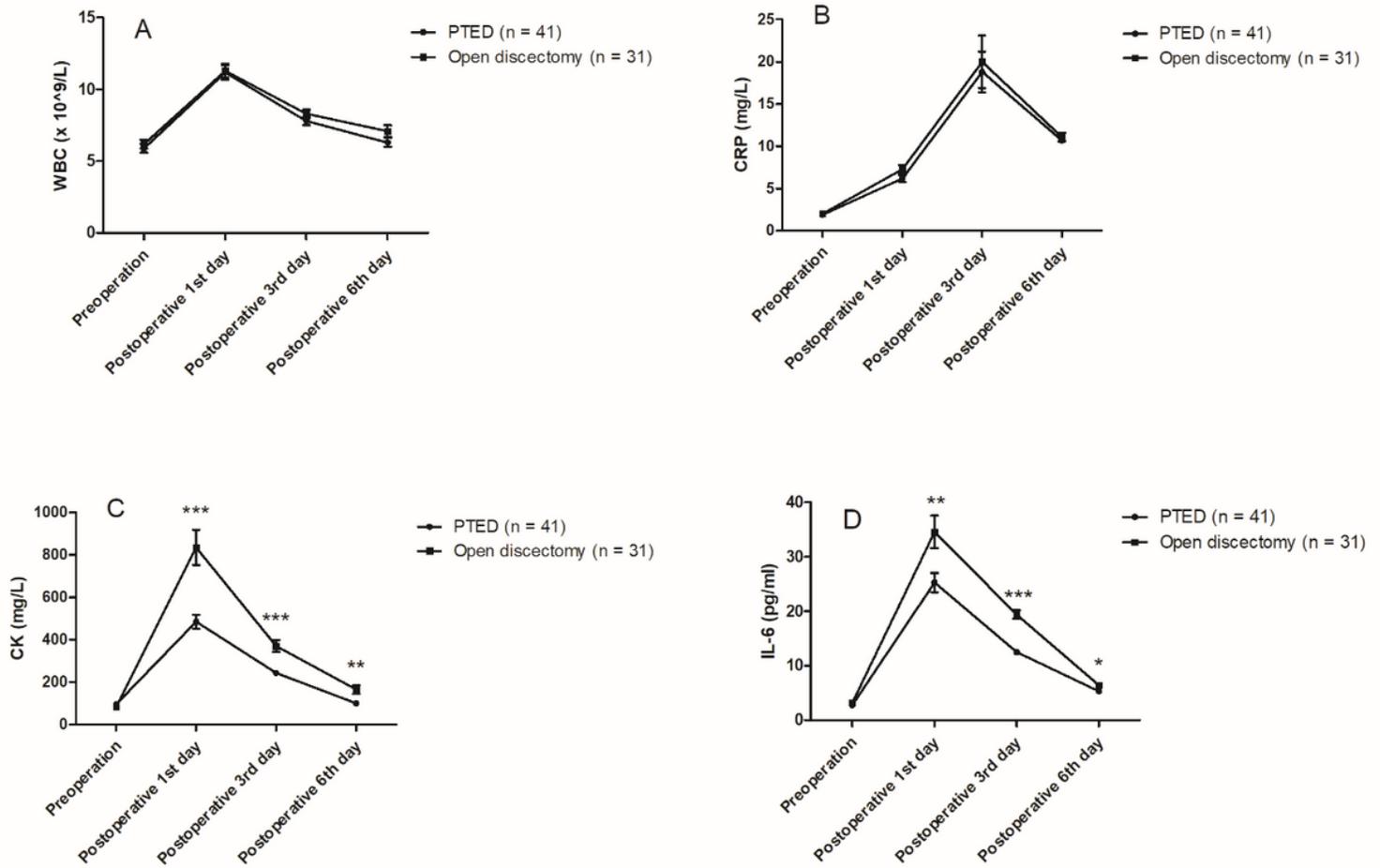


Figure 2

Inflammation related markers in the blood sample in both patient groups before and after operation. The figure shows that obviously higher CK (C) and IL-6 (D), as well as similar measurements of both WBC (A) and CRP (B), were observed in the patients undergoing open discectomy compared to the patients accepting PTED in all postoperative assessments. PTED: Percutaneous transforaminal endoscopic discectomy; 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 *** $P < 0.001$.

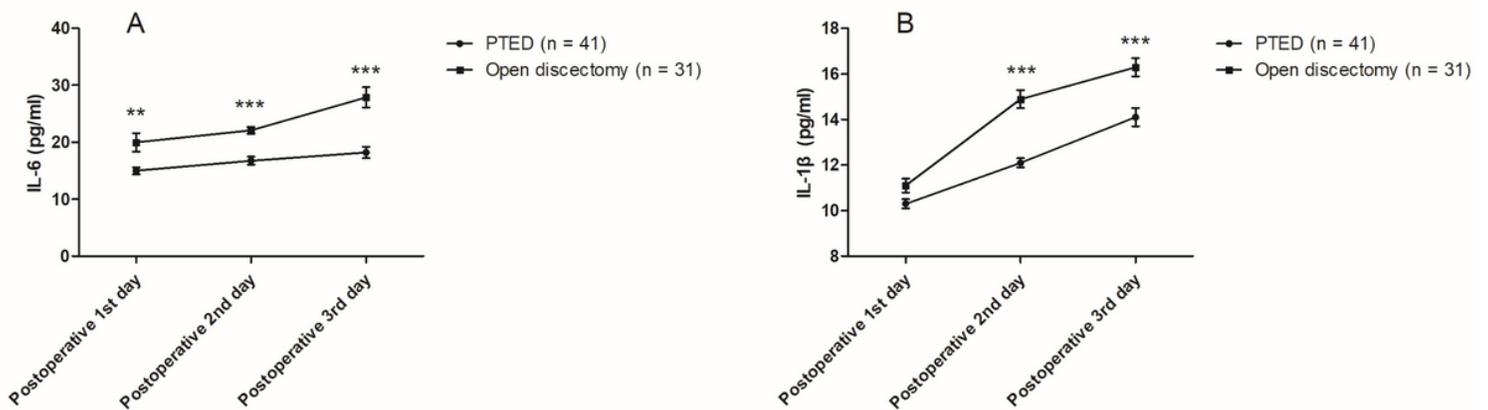


Figure 3

Inflammation related markers in the drainage fluid sample in both patient groups after operation. The figure shows that patients in the open discectomy group presented with significantly increased IL-6 and IL-1 β compared to the PTED patient group. PTED: Percutaneous transforaminal endoscopic discectomy; IL-6: Interleukin-6; IL-1 β : Interleukin-1 β ; n: number. *P < 0.05, **P < 0.01, and ***P < 0.001.