Factors Associated with Early Postoperative Pain after Lateral Lumbar Interbody Fusion

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Abstract:

Introduction: Despite that lateral lumbar interbody fusion (LLIF) is a minimally invasive surgery, some patients complain of severe site pain immediately after the surgery. This study aimed to explore the extent of perioperative pain after LLIF, compare the degree of perioperative pain after LLIF with that after other surgical procedures, and evaluate the factors associated with severe pain in the early postoperative period.

Methods: In this study, 93 patients who underwent lumbar spine surgeries for lumbar degenerative diseases were analyzed. The patients were categorized into three groups based on the surgical procedure: Group L, LLIF with percutaneous pedicle screw (PPS); Group P, posterolateral fusion (PLF) or posterior lumbar interbody fusion (PLIF); and Group D, posterior decompression (fenestration). The extent of low back pain was evaluated using the visual analog scale (VAS) preoperatively and from postoperative days 1 to 14.

Results: The VAS score for postoperative pain decreased in a time-dependent manner in all three groups ($P<0.01$). Repeated measures analysis of variance (ANOVA) showed that the VAS in Group L was significantly higher than that in Group D ($P<0.01$). Time point analysis revealed that the VAS scores from postoperative days 1 to 9 in Group L were significantly higher than those in Group D ($P<0.05$). No significant difference was observed in the VAS scores of postoperative pain between Groups L and P on all postoperative days. The VAS score for early postoperative pain in Group L was significantly correlated with the change in disc height index ($P<0.05$, $r=0.43$) and tended to be associated with the grade of preoperative disc degeneration and the VAS score of preoperative low back pain ($P=0.076$-0.19).

Conclusions: This study is the first to evaluate the factors associated with pain during the early postoperative period of LLIF. Although LLIF is a minimally invasive surgery, severe pain may develop in patients with significant preoperative disc degeneration or following spinal correction surgery.

Keywords:

lateral lumbar interbody fusion, postoperative pain, disc degeneration, disc height, preoperative low back pain

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Introduction

When treating pain and neurological deficits in patients with degenerative lumbar diseases and spinal instability, lumbar interbody fusion is a common operative procedure[1]. Since its introduction in 2006 by Ozgur[2], lateral lumbar interbody fusion (LLIF) surgery has been increasingly carried out. LLIF is a minimally invasive surgical technique that allows access to the intervertebral disc space and vertebral bodies via a retroperitoneal transpsoas approach[2]. Unlike traditional posterior approaches including posterior lumbar interbody fusion (PLIF) or transforaminal lumbar interbody fusion, it does not affect the lamina, paravertebral muscles, and facet joints by LLIF. Thus, LLIF has the advantages of avoiding damage and bleeding, reducing the risk of nerve injury, and enabling faster recovery compared to traditional posterior surgery[1,3]. LLIF also has the advantage of inserting a wider intervertebral cage than other posterior approaches, which is effective in restoring intervertebral disc height and spinal correction[4].

Despite that LLIF is a minimally invasive surgery, some patients complain of severe site pain immediately after the surgery[5]. Nevertheless, the cause of severe pain immediately after LLIF is still unknown.

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Table 1. Characteristics of Patients Who Underwent Lumbar Spinal Surgeries.

	Group L	Group P	Group D	P value
Number of patients	31	18	44	
Age (years old)	68.5±10.8	70.2±12.0	63.7±17.1	0.18
Gender (M/F)	16/15	12/6	28/16	0.48
Surgery time (min)	226.0±53.8	206.4±47.1	94.7±32.7	<0.01
Blood loss (mL)	99.0±83.8 *	164.3±110.5 *	49.6±46.2	<0.01
White blood cell ($\times10^3/\mu L$)	10.0±2.7 **	10.8±2.3 *‡	9.8±2.5	<0.01
C-reactive protein (mg/dL)	11.6±7.2	11.5±5.0	5.0±3.5	<0.01
Number of operative intervertebral levels	1.8±0.7 *	1.8±0.9 *	1.4±0.6	0.054
1	11	9	30	
2	17	5	11	
3	2	3	3	
4	1	1	0	
Celecoxib/TRAMCET®	12/19	7/11	17/27	1.0

*: P<0.01 compared to Group D, **: P<0.05 compared to Group D, ‡: P<0.05 compared to Group L.

This study aimed to explore the extent of perioperative pain after LLIF, compare the degree of perioperative pain after LLIF with that after other surgical procedures, and evaluate the factors associated with severe pain in the early postoperative period.

Materials and Methods

Patients

In this study, 93 patients who underwent lumbar spine surgery for lumbar degenerative diseases at our institution between August 2015 and February 2016 were retrospectively analyzed. Those who underwent corrective fusion surgery from the thoracic spine to the pelvis for adult spinal deformities were excluded. Those in whom postoperative pain was difficult to evaluate owing to delirium or dementia were also excluded. Age, sex, fusion level, and number of patients were adjusted for (Table 1).

The patients were categorized into three groups according to the surgical procedure: Group L, LLIF with percutaneous pedicle screw (PPS); Group P, posterolateral fusion (PLF) or PLIF; and Group D, posterior decompression (fenestration). Decompression surgery was conducted on patients with lumbar spinal stenosis without instability. Fusion surgery (LLIF or PLF/PLIF) was carried out in patients with lumbar degenerative disease and spinal instability. LLIF or PLF/PLIF was performed at the discretion of the surgeons. Previous studies[3,6,7] showed that serum C-reactive protein (CRP) levels and white blood cell (WBC) counts were measured on postoperative day 1 to evaluate surgical invasion.

Postoperative analgesia protocol and pain assessment

All patients received fentanyl (0.02-0.04 mL/kg) via intravenous administration approximately 24 h after the surgery. After the intravenous administration of fentanyl, all patients received oral analgesic agents, until 2 weeks after surgery. The patients without renal impairment (estimated glomerular filtration rate: eGFR≥60), gastroduodenal ulcer, or nonsteroidal anti-inflammatory agent allergy received celecoxib (400 mg/day). The patients with renal impairment (estimated glomerular filtration rate: eGFR<60) received TRAMCET® Combination Tablets (Tramadol Hydrochloride 112.5 mg and Acetaminophen 1,125 mg/day).

On the first postoperative day, the patient was kept on bed rest. The patient then started getting out of bed and walking on postoperative day 2. Using the visual analog scale (VAS) preoperatively, the extent of low back pain was evaluated from postoperative days 1-14. The VAS score for early postoperative pain was defined as the mean VAS score on postoperative days 1 and 2.

Image evaluation

The disc height was evaluated using lateral lumbar spine radiography. The anterior disc height (Ha), posterior disc height (Hp), superior disc depth (Ds), and inferior disc depth (Di) were measured. The disc height was expressed as the disc height index (DHI), which was calculated as [(Ha+Hp)/(Ds+Di)]×1,008[8]. The degree of disc degeneration was evaluated using sagittal T2-weighted lumbar Magnetic Resonance Imaging (MRI) and graded according to Pfirrmann's classification from Grades I-V[9].

Statistical analysis

Differences in background data and VAS among the three groups were analyzed using ANOVA or two-way repeated measures ANOVA, which was followed by Bonferroni correction. Using an unpaired *t*-test or ANOVA, differences in VAS scores for early postoperative pain in Group L by sex, grade of disc degeneration, and presence or absence of spondylolisthesis were analyzed. Correlations between the VAS score for early postoperative pain in Group L and age, DHI, change in DHI, and VAS score for preoperative low back pain were evaluated using Pearson's correlation coefficient test. Statistical significance was set at P<0.05. All statistical analyses were carried out using the IBM SPSS Sta-

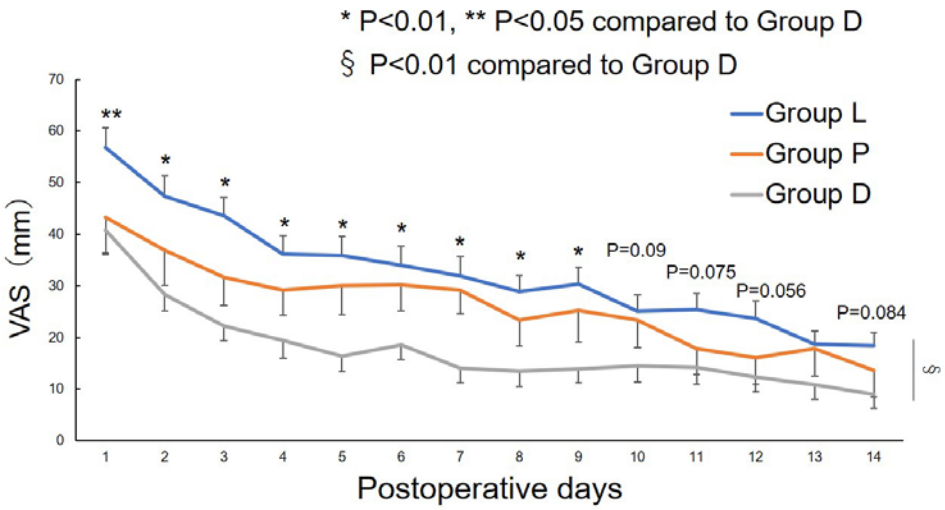

Figure 1. Change of postoperative VAS score.
The VAS score for postoperative pain decreased in a time-dependent manner in all three groups (P<0.01). Repeated-measures ANOVA showed that the VAS score in Group L was significantly higher than that in Group D (time, P<0.01; interaction, P=0.19). Time point analysis showed that the VAS scores from postoperative days 1 to 9 in Group L were significantly higher than in Group D (P<0.05). VAS: visual analog scale; *: P<0.01 compared to Group D (time point analysis); **: P<0.05 compared to Group D (time point analysis); §: P<0.01 compared to Group D (repeated measure ANOVA).

tistics software (version 28.0; IBM Japan, Tokyo).

Results

Patients' characteristics

In this study, a total of 93 patients (56 men and 37 women; mean age 66.6±14.4 years) were analyzed (Table 1), with 31 patients included in Group L, 18 in Group P, and 44 in Group D. No significant differences were found in age, sex, number of operative intervertebral levels, or oral analgesic agents among the three groups (Table 1).

The surgery times in Group L and Group P were significantly longer than those in Group D (P<0.01; Table 1); nevertheless, no significant difference was found in the surgical time between Group L and Group D. Blood loss in Group L was significantly lower than that in Group P (P<0.05, Table 1).

Among the three groups, no significant differences were observed in the number of white blood cells on postoperative day 1 (Table 1). The values of CRP in Group L and Group P were significantly higher than those in Group D (P<0.01, Table 1). Nevertheless, no significant difference was found in the CRP levels between Groups L and D.

Change in postoperative pain

In all three groups, the VAS score for postoperative pain decreased in a time-dependent manner (P<0.01) (Fig. 1). Repeated measures ANOVA revealed that the VAS in Group L was significantly higher than that in Group D (time P<0.01; interaction P=0.19); nevertheless, no significant differences were found between Groups L and P (P=0.94) or Groups P and D (P=0.20). Time point analysis showed that the VAS scores from postoperative days 1 to 9 in Group L were significantly higher than in Group D (P<0.05). On all postoperative days, no significant difference was found in the VAS scores between Groups L and P.

Factors associated with early postoperative pain after LLIF

The VAS score for early postoperative pain (mean VAS at days 1 and 2, postoperatively) in Group L was higher than that in Group D (P<0.01) (Fig. 2). The VAS score for early postoperative pain in Group L displayed no significant correlation with age (Fig. 3). No significant changes were observed in the VAS score for early postoperative pain according to sex (Fig. 4A), number of operative intervertebral levels (Fig. 4B), or presence or absence of spondylolisthesis (Fig. 4C). The VAS score for early postoperative pain in Group L was significantly correlated with the change in DHI (P<0.05, r=0.43) (Fig. 5A, B). For early postoperative pain in Group L, the VAS score tended to be associated with the grade of preoperative disc degeneration and the VAS score of preoperative low back pain (P=0.076-0.19) (Fig. 4 D, 6).

Discussion

In this study, the degree of postoperative pain after LLIF was examined and compared with that after other surgical procedures. Furthermore, the present study is the first to evaluate the factors associated with pain in the early postoperative period after LLIF. Our results showed that the VAS

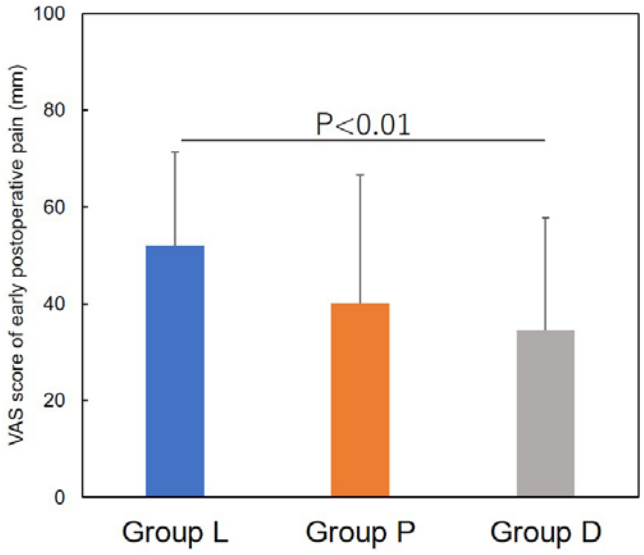

Figure 2. Comparison of VAS score of early postoperative pain among surgical procedures.
The VAS score for early postoperative pain in Group L was higher than in Group D (P<0.01). VAS: visual analog scale

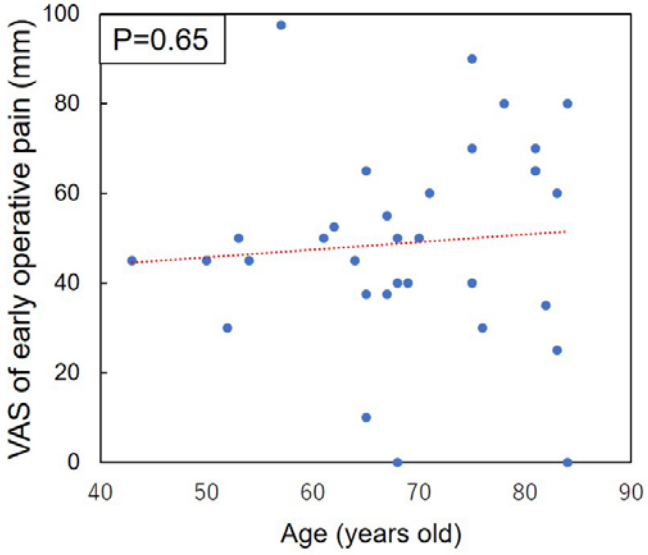

Figure 3. Correlation between early postoperative pain and age in Group L.
The VAS score for early postoperative pain in Group L showed no significant correlation with age. VAS: visual analog scale

scores of patients after LLIF were significantly higher than those after decompression surgery and that no significant difference was found in the VAS scores between patients who underwent LLIF and those who underwent posterior spinal fusion surgery. Postoperative pain after LLIF was significantly correlated with postoperative changes in disc height and tended to be associated with preoperative disc degeneration and low back pain.

Few reports have described pain during the early postoperative period after LLIF. Ohba et al. compared the invasiveness and tolerability of extreme lateral interbody fusion (XLIF) with PPS and PLIF for degenerative lumbar spondylolisthesis compared with PLIF[7]. They revealed that the XLIF/PPS group had significantly lower postoperative WBC count, CRP level, and serum creatine kinase level on postoperative days 4 and 7. Nevertheless, the level of surgical pain between the two groups did not differ significantly in the postoperative period of days 1-7. No significant differences were observed in VAS scores between Groups L and P on all postoperative days. Similarly, our results indicated no significant variation in VAS scores between Groups L and P on any postoperative day.

Furthermore, this study showed that postoperative pain after LLIF was significantly correlated with postoperative changes in disc height. It has been shown that disc height significantly increased after LLIF surgery[10] and is significantly higher than following PLIF surgery[6,11,12]. Furthermore, a significant increase in the facet joint gap has been observed after LLIF[13]. These changes after LLIF may lead to early postoperative pain.

Moreover, the results of the current study showed that no significant differences were observed in preoperative and postoperative DHI and changes in DHI between patients who underwent LLIF and PLIF surgeries (data not shown). The VAS score for early postoperative pain in patients who underwent LLIF significantly correlated with DHI changes. Nevertheless, no significant correlation was found between the VAS score and change in DHI after PLIF surgery (Fig. S1). Additionally, to the best of our knowledge, there have been no previous reports on the association between postoperative pain after PLIF and disc height. Evaluating postoperative pain after PLIF surgery may be difficult by only evaluating changes in disc height because lumbar posterior elements, including the paravertebral muscles, lamina, facet joint, or epidural space, are invaded during the PLIF procedure. Unlike PLIF, LLIF is a minimally invasive surgical technique that allows for lateral access to the intervertebral disc. Thus, the change in disc height might more closely be related to postoperative pain after LLIF surgery than after PLIF surgery.

Preoperative and postoperative disc height evaluated via DHI in Grade 3 patients was significantly higher than that in Grade 4 or Grade 5 cohorts. However, no significant difference was found in DHI among the three gradings (data not shown). That is, we considered that the major factor of early postoperative pain after LLIF was compression on the cartilage endplate and the distraction force on the annulus fibrosis (AF) tissue due to disc height recovery, regardless of the degree of disc degeneration.

The postoperative pain after LLIF tended to be associated with preoperative disc degeneration and preoperative low back pain in this study. This may be more painful after LLIF in more degenerative discs. As disc degeneration progresses, a decreased joint space leads to extreme loss of mobility, eventually rendering the disc unable to perform its biomechanical functions. The vertebra, disc, facet joint, posterior longitudinal ligament, and dura mater are innervated segmentally by the dorsal ramus and the sinuvertebral

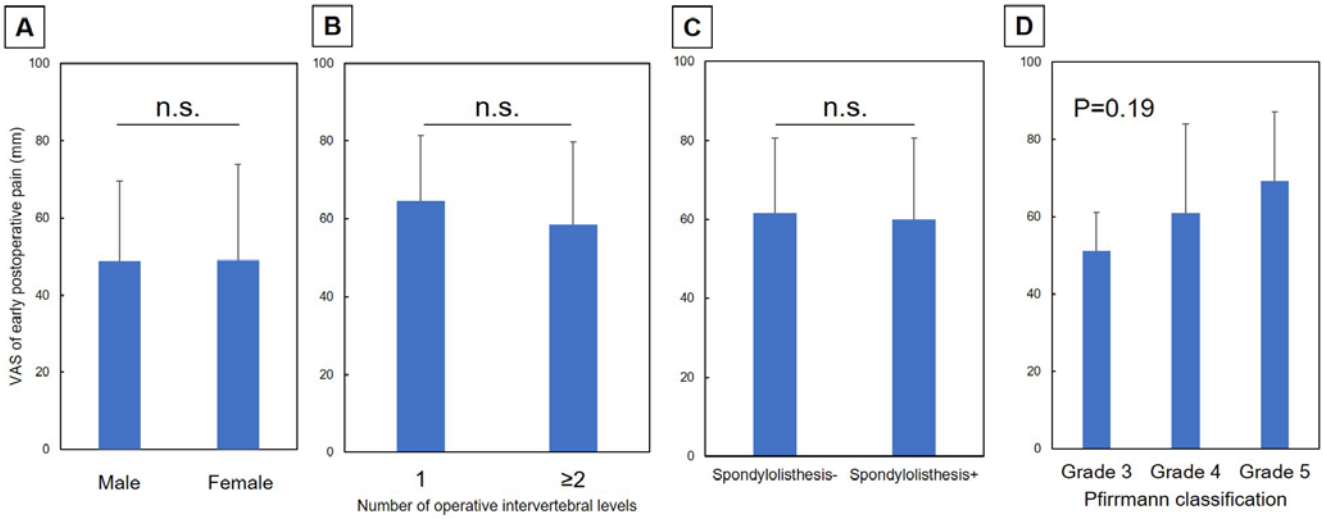

Figure 4. VAS score of early postoperative pain in Group L.
A: For early postoperative pain according to sex, no significant changes in the VAS scores were observed. B: Based on the number of operated intervertebral levels, there were no significant changes in the VAS scores for early postoperative pain. C: There were no significant changes in the VAS scores for early postoperative pain in the presence or absence of spondylolisthesis. D: The VAS score for early postoperative pain in Group L was associated with the grade of preoperative disc degeneration (P=0.19). VAS: visual analog scale

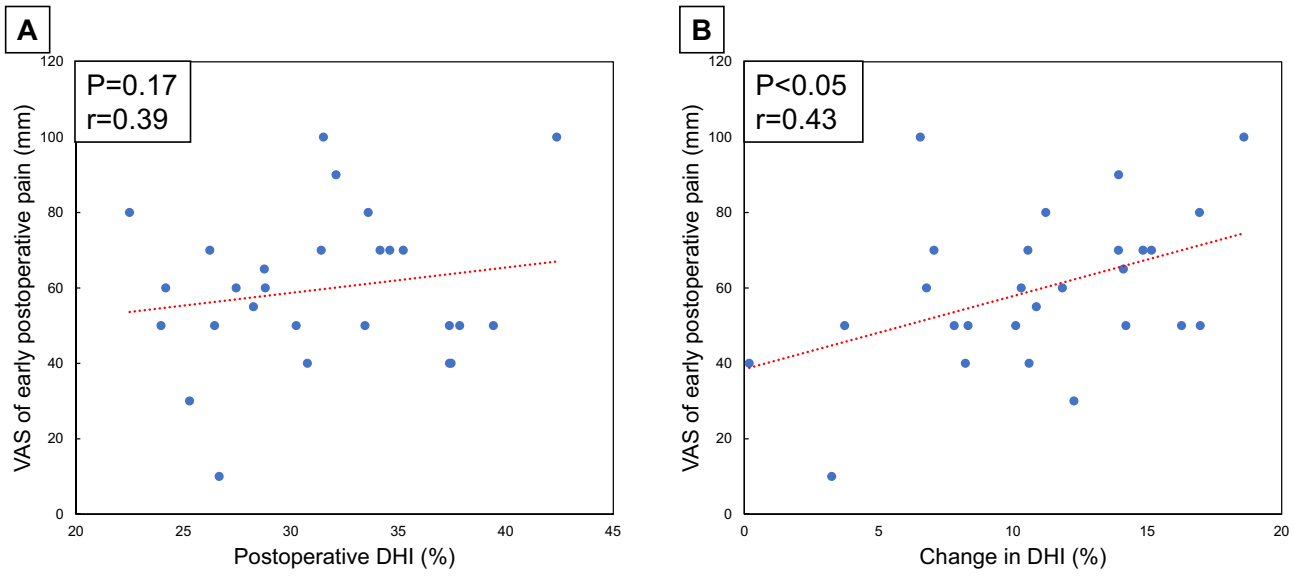

Figure 5. Correlation between early postoperative pain and DHI in Group L.
The VAS score for early postoperative pain in Group L tended to be associated with the postoperative DHI (P=0.17). The VAS score for early postoperative pain was significantly correlated with the change in the DHI (P<0.05, r=0.43). VAS: visual analog scale. DHI: disc height index

nerves, which branch from the spinal nerve of the corresponding levels[14]. Nevertheless, in the normal intervertebral disc (IVD), innervation is restricted to the outermost lamella of the annulus fibrosis (AF)[15]. Sensory nerve fibers include C-fibers and A delta-fibers[14], and in degenerated IVDs, a greater number of nerve fibers that enter the inner AF and nucleus pulposus (NP) are present. Fissures that occur in the AF cause the NP to extrude, allowing sensory nerve ingrowth and vascularization in the inner AF and NP, thereby leading to discogenic back pain[16,17]. It is believed that an increase in sensory nerve activity is the origin of chronic discogenic pain[16,18]. Furthermore, the IVD and cartilage endplate were widely removed using curettage during LLIF. In patients with severe back pain and markedly reduced disc height, proliferation of blood vessels and accompanying nerve fibers have been observed in the cartilage endplate region and subchondral bone[19]. The insertion of large-footprint cages in LLIF markedly enhanced the disc height. Severe pain may occur in the early postoperative period owing to the compression force on the cartilage endplate and distrac-

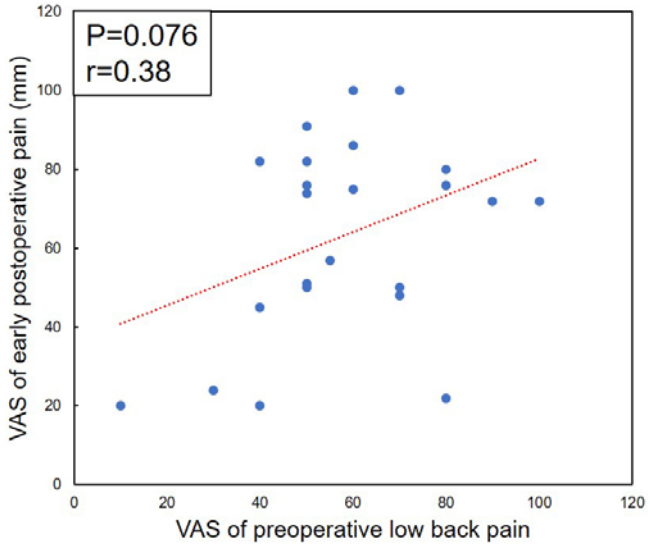

Figure 6. Correlation between early postoperative pain and preoperative pain in Group L.
The VAS score for early postoperative pain tended to be associated with that of preoperative lower back pain (P=0.076). VAS: visual analog scale

tion force on the AF tissue.

Limitations

The site of the postoperative pain was not identified. Whether postoperative pain was due to the intervertebral discs, psoas major muscle, or other types of pain was difficult to distinguish. Surgical invasion associated with pedicle screw insertion may also be a cause of early postoperative pain.

Conclusions

This study is the first to evaluate the factors that are associated with pain during the early postoperative period of LLIF. Postoperative pain after LLIF was significantly correlated with postoperative changes in disc height. Despite that LLIF is a minimally invasive surgery, severe pain may occur in patients with substantial preoperative disc degeneration or after spinal correction surgery. Adequate postoperative pain management is important even after LLIF.

Conflicts of Interest: The authors declare that there are no relevant conflicts of interest.

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Author Contributions: Norihiko Takegami: Data curation, Writing-Original draft preparation.

Koji Akeda: Writing-Review & Editing, Supervision, Projected ministration.

All of the authors had read, reviewed, and approved the manuscript.

Ethical Approval: Ethics were approved by the institutional review boards of Mie University Hospital (IRB reference number: H2020-027).

Informed Consent: Informed consent was obtained in the form of optout on the website of Mie University Hospital.

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