



Anterior Thigh Pain Following Minimally Invasive Oblique Lateral Interbody Fusion: Multivariate Analysis from a Prospective Case Series

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Background: Oblique lateral interbody fusion (OLIF) involves the antepsoas approach and psoas major muscle (PMM) retraction to insert the interbody cage orthogonally. Therefore, OLIF is often associated with postoperative anterior thigh pain (ATP) on the approach side. However, there is limited evidence on the nature and risk factors of ATP following OLIF.

Methods: Consecutive patients who planned to undergo minimally invasive OLIF and percutaneous pedicle screw instrumentation for lumbar degenerative diseases were prospectively enrolled. The visual analog scale (VAS) for ATP was recorded, and a pain map was drawn daily from the operation day to postoperative day 7 in all patients. We also prospectively collected the preoperative and intraoperative data to identify the risk factors associated with ATP. Radiologically, the total cross-sectional area (CSA), retraction length, and retraction CSA of PMM were measured from the preoperative T2-weighted axial magnetic resonance imaging scans at the L4–5 intervertebral disc level. The patients were stratified into two groups based on the experience of ATP with a VAS score of ≥ 7 at any time point. Additionally, a binary logistic regression analysis was performed to identify the associated factors.

Results: The current prospective study included 92 patients (31 men, 61 women) with a mean age of 70.4 years (range, 56–86 years), who underwent OLIF at our institution. The left-side approach was used in 73 patients (79.3%), while 19 (20.7%) underwent a right-side approach. Sixty-five of the total patients (70.6%) experienced approach-side ATP to any extent during postoperative 0–7 days following OLIF. The mean pain VAS (4.4 ± 2.1) and the prevalence (57.6%) were highest at postoperative 2 days. On postoperative day 7, there were 19 patients (20.7%) who complained of residual ATP with a mean VAS of 2.6 ± 1.8 . In the multivariate analysis, the PMM retraction length was significantly associated with ATP of VAS ≥ 7 (adjusted odds ratio, 2.316; $p = 0.044$).

Conclusions: In this study, we prospectively collected and analyzed the ATP and associated factors following OLIF and identified the PMM retraction length as a potential independent risk factor for severe ATP in the immediate postoperative period following OLIF.

Keywords: Anterior thigh pain, Psoas major muscle, Antepsoas, Oblique lateral interbody fusion, Genitofemoral nerve

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Lateral interbody fusion (LIF) using a lateral access is a widely used surgical technique for various lumbar degenerative diseases, with proven efficacy and safety.¹⁾ In spinal stenosis, LIF can indirectly decompress the spinal canal by restoring the disc height and reducing spondylolisthesis.²⁾ LIF is also a powerful surgical tool for adult spinal deformity correction.³⁾ Several authors have reported favorable results in these conditions, with a relatively low complica-

tion rate.^{4,5)}

Among the various possible complications, transient hip flexor weakness and anterior thigh pain (ATP) on the surgical approach side are very common following LIF.⁶⁾ Previous meta-analyses and large-scale cohort studies have shown that the risks of these adverse symptoms are lower in oblique lateral interbody fusion (OLIF) using the antepsoas approach than lateral lumbar interbody fusion (LLIF) using the transpsoas approach.⁷⁻¹⁰⁾ The direct visualization and avoidance of penetration of the psoas major muscle (PMM) during the antepsoas approach seem to be associated with a lower risk of ATP following OLIF, which obviates the need for intraoperative neuromonitoring.¹¹⁾ However, OLIF still involves psoas muscle retraction to insert an interbody cage orthogonally and can often cause ATP in the immediate postoperative period, although it is less frequent than LLIF (Fig. 1).

In the literature, postoperative ATP has been primarily investigated in LLIF patients, and limited evidence exists on the nature and risk factors of ATP following OLIF. The incidence of pain or sensory deficit following OLIF was 1.3% to 13.5%.^{4,11)} However, these studies tend to underestimate the incidence of ATP because the occurrence of a complication is not recorded unless a patient complains of such symptoms in retrospective studies. In addition, although these symptoms do not cause significant morbidity, they may exert an adverse impact on the clinical outcomes and patient satisfaction, especially during the immediate postoperative period. Therefore, we conducted this prospective case series study to describe ATP following OLIF and identify the clinical and radiological risk factors associated with severe ATP.

METHODS

The Institutional Review Board of Seoul National University Hospital approved this study (IRB No. H-2004-

105-1118), and all participants provided written informed consent.

Study Design and Participants

In this prospective case series study, we enrolled consecutive patients who underwent OLIF for lumbar spinal stenosis in a single tertiary institution. Patients with central and/or foraminal stenosis from L2 to S1 and scheduled to undergo minimally invasive OLIF were eligible for study participation. Following patients were excluded from the study: patients who had ATP preoperatively, those who were planned to undergo simultaneous posterior direct decompression, and those who had a history of previous retroperitoneal surgery. Patients with radiologically confirmed hip disorders, such as avascular necrosis and degenerative arthritis, or a history of hip joint surgery were also excluded from this study because of the possibility of a complaint of inguinal pain or ATP. Finally, the patients with a history of infectious spondylitis and previous radiotherapy in the spine, pelvis, and hip joints were excluded.

Surgical Procedure and Postoperative Assessment

Three surgeons from a single orthopedic department (BSC, HK, and SYC) performed OLIF using a minimally invasive oblique retroperitoneal antepsoas approach as described in previous studies.¹²⁾ The approach side (right or left) was determined preoperatively based on the vascular anatomy and coronal deformity of the lumbar spine. The patient was carefully positioned in a right or left decubitus position with the hip joint ipsilateral to the approach side kept slightly flexed. No intraoperative neuromonitoring was performed in any patient.

A minimal skin incision of two fingerbreadths was made over the intervertebral disc (IVD) level under fluoroscopic guidance. Three layers of abdominal muscles (external oblique, internal oblique, and transversalis) were longitudinally split, and any neurovascular structures en-

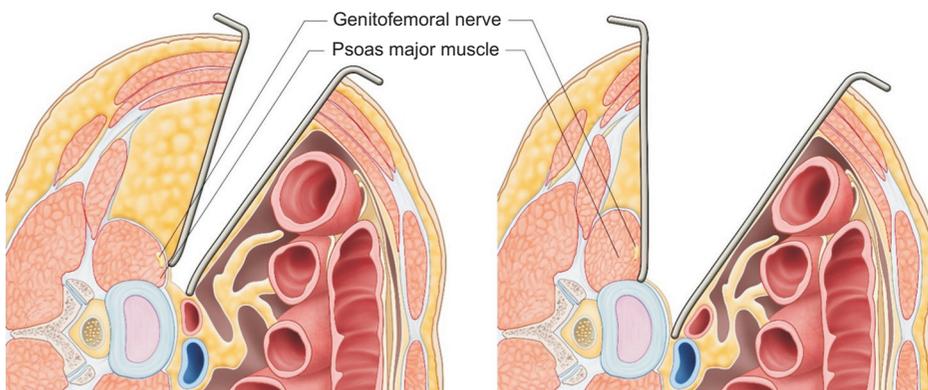


Fig. 1. Retraction of psoas major muscle and genitofemoral nerve during the antepsoas approach.

countered in the muscular layer were mobilized and preserved. Subsequently the PMM under the retroperitoneal fat was approached and gently retracted in the posterior direction to expose the IVD. When the genitofemoral nerve (GFN) was encountered during PMM exposure, no additional mobilization was performed. For PMM retraction, handheld retractors without any docking to the vertebral column were used to enable intermittent release. After removing the IVD, the subchondral bone of adjacent vertebral bodies was exposed by removal of the cartilaginous endplate. For interbody fusion, a polyetheretherketone cage filled with allogeneic cancellous bone and demineralized bone matrix was inserted orthogonally into the prepared disc space. No closed suction drainage was inserted into the retroperitoneal space. The patient was subsequently placed in a prone position, and percutaneous pedicle screw instrumentation was performed. All patients attempted to stand upright and ambulate with a lumbar corset on postoperative day 1.

The visual analog scale (VAS) for ATP was recorded, and a pain map of ATP was drawn daily from the day of the operation to postoperative day 7 in all the patients, using an organized case report form. The VAS was recorded, and pain maps were drawn separately for preoperative lower extremity radiating pain to avoid confusion. All participants were followed up until postoperative 1 year and surveyed for any ATP at postoperative 3, 6, and 12 months.

Data Collection and Radiological Measurement

We also prospectively collected preoperative and intraoperative data to identify the risk factors associated with ATP. Clinically, we collected the data on demographics (age, sex, height, weight, and body mass index), T-score in dual-energy X-ray absorptiometry, operative level, and the approach side. The comorbidities were assessed using the Charlson comorbidity index, and the weighted index score was calculated.¹³⁾ Radiologically, (1) the PMM total

cross-sectional area (CSA), (2) PMM retraction CSA, and (3) PMM retraction length were measured from the preoperative T2-weighted axial MRI scans at the L4–5 IVD level only in patients whose L4–5 level was included in the operative level (Fig. 2). In addition, the presence of an inadvertent endplate breakage and the location of the interbody cage (anterior, middle, and posterior) was identified from the immediate postoperative lateral radiographs. The radiological measurements were performed by one of the authors, who was unaware of the patients' clinical information (WSL).

Statistical Analysis

We performed a power analysis using G-Power 3.1¹⁴⁾ on the PMM retraction length, one of the key findings in this study, to determine the sufficient sample size for the current prospective study. The mean and standard deviation of the PMM retraction length were adopted from a previous study,¹⁵⁾ and the rate of ATP following OLIF was chosen to be 25%, based on our clinical experience. The analysis with a two-sided alpha of 0.05, a statistical power of 0.90, and a dropout rate of 15% yielded a sample size of 100 patients.

Group comparisons were performed to determine any differences between the patients with and without persistent ATP using Student *t*-test for continuous variables and the chi-square test or Fisher's exact test for categorical variables. For patients who had L4–5 level operated, univariate analyses were performed for all factors individually, using a binary logistic regression analysis. A multivariate binary logistic regression was applied to identify independent risk factors, using variables with a *p*-value less than 0.2 by univariate analysis. The adjusted odds ratios (aORs) and 95% confidence intervals were calculated for all variables. All statistical analyses were performed using IBM SPSS ver. 25.0 (IBM Corp., Armonk, NY, USA). The statistical significance was set at $p < 0.05$.

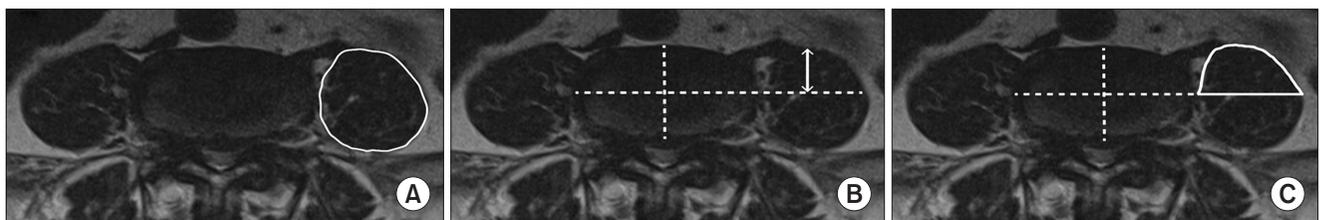


Fig. 2. Radiological measurements. (A) The cross-sectional area (CSA) of the psoas major muscle (PMM) was measured at the L4–5 intervertebral disc (IVD) level in T2-weighted axial magnetic resonance imaging. (B) The presumed retraction length of PMM was measured as the distance between the anterior margin of PMM and the line bisecting the IVD into anterior and posterior halves. (C) The presumed CSA of PMM retraction was measured as the area anterior to the IVD-bisecting line.

RESULTS

Study Participants

Initially, a total of 100 patients were enrolled in this prospective study. However, patients who underwent simultaneous posterior decompression ($n = 2$) or surgery other than OLIF ($n = 2$) and were lost to follow-up ($n = 4$) were excluded from the study. As a result, a total of 92 patients (31 men and 61 women) with a mean age of 70.4 years (range, 56–86 years) were included in the analysis. The mean number of levels operated was 2.1 ± 1.0 , and the most common level was L4–5, which was included in 77 patients (83.7%). The left-side approach was used in 73 patients (79.3%), while 19 patients (20.7%) underwent the right-side approach.

Description of ATP Following OLIF

A total of 65 patients (70.6%) experienced ATP on the approach side to any extent during the postoperative period of 0–7 days following OLIF. Twenty-three patients (25.0%) complained of an ATP of VAS ≥ 7 at any point during the period. The mean pain VAS (4.4 ± 2.1) and the prevalence (57.6%) were highest on postoperative day 2. On postoperative day 7, there were 19 patients (20.7%) who complained of residual ATP with a mean VAS of 2.6 ± 1.8 . Among these 19 patients, 8 patients (8.7%) had an ATP level of VAS ≥ 3 . The distribution and the mean VAS for ATP on the approach side during the postoperative days 0 to 7 are depicted in Fig. 3. The rate of ATP was 4.3% (4/92) and 2.2% (2/82) at postoperative 3 months and 6 months, respectively. No patient complained of ATP 1 year postoperatively.

Risk Factors for ATP Following OLIF

The patients were stratified into two groups based on the experience of ATP with a VAS ≥ 7 at any time point during postoperative day 0 to 7. As for the total cohort ($n = 99$), a

direct group comparison showed that the ATP group had a larger number of fusion levels; however, the difference was not statistically significant (2.3 ± 1.3 vs. 2.0 ± 0.9 , $p = 0.176$) (Table 1). When the radiological parameters were measured and compared in patients whose L4–5 level was included in their operative level ($n = 77$), the PMM retraction length was significantly larger in the ATP group than in the non-ATP group (29.6 ± 4.5 vs. 24.9 ± 7.8) (Table 2). The total and retraction CSA of the PMM also tended to be larger in the ATP group; however, the differences were not statistically significant. Inadvertent endplate breakage was more frequently observed in the ATP group; however, the difference was not statistically significant (27.5% vs. 11.9%, $p = 0.103$).

A logistic regression analysis of the clinical and radiological risk factors for ATP was performed in patients who had the L4–5 level included in their operative level ($n = 77$). The number of levels fused, endplate breakage, and the PMM retraction length showed a p -value of less than 0.2 in the univariate analysis, and a multivariate analysis was conducted on these factors (Table 3). The multivariate analysis showed that the PMM retraction length was significantly associated with ATP (VAS ≥ 7) following OLIF (aORs, 2.316; $p = 0.044$) (Table 4).

DISCUSSION

The most common adverse event following LIF is anterior thigh symptoms (pain, sensory deficit, and hip flexor weakness) for both LLIF and OLIF.^{10,11,16} Anterior thigh symptoms occur at a reported rate of 30% to 40% for LLIF and 1.3% to 21.4% for OLIF.^{6,17} These symptoms are generally transient and resolve at postoperative 3 to 6 months.^{18,19} Therefore, some surgeons often consider these symptoms as approach-related side effects rather than actual surgical complications. Although these symptoms do not cause significant morbidity, they can often be

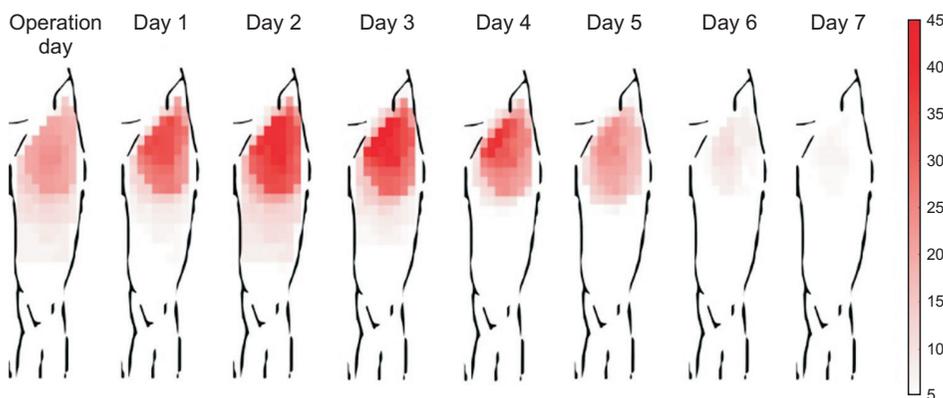


Fig. 3. The distribution and prevalence of anterior thigh pain on the approach side following oblique lateral interbody fusion from the day of operation to the postoperative day 7 (pain on the right anterior thigh in patients who received right-side approach was added onto the left anterior thigh in the pain maps).

Table 1. Comparison of Baseline Characteristics between Patients with and without Severe ATP (Total Patients, n = 92)

Variable	ATP group* (n = 23)	Non-ATP group (n = 69)	p-value
Age (yr)	70.6 ± 6.4	70.4 ± 7.2	0.891
Sex			0.373
Male	6	25	
Female	17	44	
Height (m)	1.55 ± 6.8	1.57 ± 8.2	0.323
Body weight (kg)	61.1 ± 9.9	61.7 ± 8.0	0.794
Body mass index (kg/m ²)	25.2 ± 2.5	25.0 ± 2.9	0.732
Charlson comorbidity index	3.7 ± 1.5	3.6 ± 1.4	0.902
DEXA (T-score)	-0.8 ± 1.4	-0.6 ± 1.6	0.688
Number of levels fused	2.3 ± 1.3	2.0 ± 0.9	0.176
Inclusion of L4–5 level	18 (78.3)	59 (85.5)	0.415
Surgical approach side			0.656
Left side	19 (82.6)	54 (78.3)	
Right side	4 (17.4)	15 (21.7)	

Values are presented as mean ± standard deviation or number (%).

ATP: anterior thigh pain, DEXA: dual energy X-ray absorptiometry.

*Patients with ATP of visual analog scale 7 or more at any timepoint during postoperative 0 to 7 days.

Table 2. Comparison of Radiological Measurements between Patients with and without Severe ATP (L4–5 Included Patients, n = 77)

Variable	ATP group* (n = 18)	Non-ATP group (n = 59)	p-value
PMM total CSA (mm ²)	972.8 ± 250.2	959.7 ± 276.7	0.858
PMM retraction length (mm)	29.6 ± 4.5	24.9 ± 7.8	0.018
PMM retraction CSA (mm ²)	630.3 ± 219.6	616.1 ± 259.8	0.835
Endplate breakage	5 (27.8)	7 (11.9)	0.103
Interbody cage location			0.903
Anterior 1/3	4 (22.2)	14 (23.7)	
Middle 1/3	13 (72.2)	40 (67.8)	
Posterior 1/3	1 (5.6)	5 (8.5)	

Values are presented as mean ± standard deviation or number (%).

ATP: anterior thigh pain, PMM: psoas major muscle, CSA: cross-sectional area.

*Patients with ATP of visual analog scale 7 or more at any timepoint during postoperative 0 to 7 days.

considerably disturbing to patients and have an adverse impact on the clinical outcomes and patient satisfaction, especially during the immediate postoperative period.²⁰⁾

There are several possible mechanisms for the development of anterior thigh symptoms following an LIF. For LLIF using the transpsoas approach, the direct penetration

or excessive retraction of neural structures, especially the lumbar plexus, is the leading cause of anterior thigh symptoms.²¹⁾ Numerous previous anatomical and clinical studies have extensively investigated this pathomechanism.²²⁻²⁴⁾ In contrast, the risk of direct neural injury is relatively lower in OLIF using the antepsoas approach because it does

Table 3. Univariate Analysis of Risk Factors for Severe Anterior Thigh Pain* in L4–5 Included Patients (n = 77)

Variable	Crude odds ratio	95% CI	p-value
Age	0.971	0.900–1.047	0.446
Sex (male)	1.333	0.416–4.269	0.628
Height (m)	0.972	0.906–1.043	0.427
Body weight (kg)	1.012	0.952–1.076	0.699
Body mass index (kg/m ²)	1.098	0.907–1.330	0.336
Charlson comorbidity index	0.981	0.673–1.430	0.921
DEXA (T-score)	1.004	0.720–1.401	0.981
Number of levels fused	1.434	0.869–2.366	0.158
Surgical approach side (left)	0.989	0.278–3.523	0.987
PMM total CSA (cm ²)	1.018	0.837–1.238	0.856
PMM retraction length (cm)	2.560	1.135–5.778	0.024
PMM retraction CSA (cm ²)	1.023	0.827–1.267	0.833
Endplate breakage	2.857	0.780–10.469	0.113
Posterior cage location	1.138	0.318–4.072	0.843

CI: confidence interval, DEXA: dual energy X-ray absorptiometry, PMM: psoas major muscle, CSA: cross-sectional area.

*Patients with anterior thigh pain of visual analog scale 7 or more at any timepoint during postoperative 0 to 7 days.

Table 4. Multivariate Analysis of Risk Factors for Severe Anterior Thigh Pain* in L4–5 Included Patients (n = 77)

Variable	Adjusted odds ratio	95% CI	p-value
Number of levels fused	1.161	0.668–2.019	0.597
Endplate breakage	2.301	0.548–9.658	0.255
PMM retraction length (cm)	2.316	1.021–5.254	0.044

CI: confidence interval, PMM: psoas major muscle.

*Patients with anterior thigh pain of visual analog scale 7 or more at any timepoint during postoperative 0 to 7 days.

not require dissection of the PMM. However, stripping the anterior margin of the PMM from the vertebral column and retracting the PMM posteriorly can cause damage to the GFN and sympathetic chain.⁶⁾ As possible pathomechanisms differ between the LLIF and OLIF, the two surgical techniques show different rates and clinical features of anterior thigh symptoms. In OLIF, apparent sensorimotor deficits are rare, and pain in the proximal anterior thigh is the predominant complaint. Therefore, we focused on the pain in the anterior thigh following OLIF in this study.

In our study, 65 of the 92 patients (70.6%) experienced ATP on the approach side to any extent during postoperative 0–7 days following OLIF. On postoperative day 7, there were 19 patients (20.7%) who complained of

residual ATP with a mean VAS of 2.6 ± 1.8 . Among these 19 patients, 8 (8.7%) had an ATP level of VAS ≥ 3 . The rate of ATP in our study was higher than that reported in previous studies.^{10,11)} Such a high rate in the current study seems to be due to the prospective study design, in which we actively surveyed for any symptoms in the anterior thigh in the immediate postoperative period. The previous studies that reported the rate of ATP following OLIF were primarily retrospective and may have underestimated the actual rate of ATP. However, only 4 patients (4.3%) and 2 patients (2.2%) had ATP at postoperative 3 months and 6 months, respectively. No patient complained of ATP 1 year postoperatively. The self-limited nature of ATP in the current study was consistent with the results of previous

studies.^{6,16)}

The following neural structures have a risk of injury during LIF: (1) the lumbar plexus, (2) ilioinguinal and iliohypogastric nerves, (3) sympathetic nerves, and (4) GFN. Among these neural structures, GFN has the most significant implication in the development of ATP in the OLIF procedure. The importance of GFN in OLIF using the antepsoas approach is supported by the findings from our study and the previous literatures. First and most importantly, the pain distribution depicted in our pain map corresponds to the dermatome of GFN, which is innervated by the femoral branch of the GFN. The area is also well matched with the location of GFN neuralgia caused by other etiologies, such as surgical procedures in the inguinal region (e.g., appendectomy, vasectomy, and herniorrhaphy).²⁵⁾ Second, since the GFN is located in the anterior portion of the PMM, the distance for retraction during the antepsoas approach is the longest among the abovementioned neural structures, especially at the L4–5 level, where ATP most commonly occurs (Fig. 1).¹⁵⁾ Third, none of the patients who underwent L5–S1 single level OLIF in our study ($n = 4$) complained of ATP during postoperative 0 to 7 days. This result signifies that the ilioinguinal and iliohypogastric nerves, which can be injured while separating the abdominal muscles, have little effect on the development of ATP following OLIF, not to mention the discrepancy between their dermatome and our pain map.

The significance of GFN in the occurrence of ATP following OLIF led us to measure the PMM dimensions as a potential risk factor. Some authors have investigated the association between the size of the PMM and ATP in the transpsoas LLIF procedure and showed conflicting results. In a retrospective series of 29 patients, Buric reported that the PMM dimension in the lateral-latero direction was significantly smaller in patients with postoperative sensory changes in the anterior thigh following LLIF.²⁶⁾ More recently, Yingsakmongkol et al. found no statistical differences in the total three-dimensional PMM volume between patients with or without ATP following transpsoas LLIF.²⁰⁾ These two studies significantly differ in their methodology (measurement method and statistical analysis), and no meaningful conclusions can be drawn from these studies. To the best of our knowledge, the current study is the first to evaluate the association between ATP and the measures of the PMM in OLIF, which has a different pathomechanism for ATP.

In this study, the retraction length of the PMM at the L4–5 level was significantly larger in the ATP group ($VAS \geq 7$) than in the non-ATP group in the Student *t*-test

(29.6 ± 4.5 vs. 24.9 ± 7.8). In addition, in the multivariate logistic regression analysis, the retraction length of the PMM at the L4–5 level was the only factor significantly associated with severe ATP (aORs, 2.316; $p = 0.044$). Our findings suggest that the degree of and time for PMM retraction should be minimized, except for the essential surgical steps, such as an orthogonal insertion of the interbody cage. In contrast to the retraction length, the total and retraction CSA of the PMM showed no statistically significant association with severe ATP in our study. Our theoretical explanation is that the retraction length better reflects the degree of PMM retraction and stripping than the retraction CSA. More specifically, the mediolateral width of the PMM, which contributes to the CSA, is less related to retraction of the PMM and GFN required for orthogonal cage insertion than the anteroposterior distance. However, because the ATP group had larger CSAs of the PMM, albeit not significant, future studies with a larger sample size may provide a more apparent conclusion on the significance of the CSA of the PMM on the development of ATP following OLIF.

As previously mentioned, the radiological measurements and logistic regression analysis were performed for 77 patients whose L4–5 level was included in the operative level. The L4–5 level is where neural structures are most abundant; additionally, the CSA of the PMM is the largest among the lumbar levels. Therefore, the L4–5 level is anticipated to be the most responsible surgical level for ATP development following OLIF. In addition, the L4–5 level was most frequently associated with anterior thigh symptoms after transpsoas LLIF in previous studies.^{26,27)} For these reasons, we focused on the L4–5 level in this study to identify risk factors for ATP following OLIF.

This study has several limitations. First, we focused only on the pain in the anterior thigh and did not evaluate hip flexor weakness or sensory deficit without pain. We were reluctant to measure the hip flexor power manually in the immediate postoperative period because most patients experience pain during voluntary hip flexion following OLIF. Another reason for not investigating the hip flexor power is that hip flexor weakness in the immediate postoperative period following OLIF is considered to be due to pain rather than the true paresis. Second, we did not measure the actual retraction length of the PMM or GFN intraoperatively. Although these measurements can be more accurate than magnetic resonance imaging (MRI) measurements, we considered that these intraoperative measurements were not essential surgical procedures for the patients and were unethical to perform. We also did not measure the cage location using postoperative MRI,

which may be a better radiological indicator of actual PMM retraction than the preoperative measurements. Future studies should consider intraoperative or postoperative measurements in the evaluation of the PMM retraction. Third, we did not measure the retraction time, which was suggested as a potential risk factor for developing ATP after LIF in previous studies. It was challenging to measure retraction time in our series because we used handheld retractors that were not docked and released intermittently. Instead, the number of operated levels seems to be a better reflection of the degree of PMM retraction in our study. Fourth, although we performed a power analysis to determine a sufficient sample size, heterogeneity in the operative levels may have lowered the statistical significance. Finally, because there was no control group in this study, we could not compare the incidence of ATP directly between different surgical procedures (e.g., OLIF vs. LLIF). Despite these limitations, the current study is the first to evaluate the association between the ATP and the measures of the PMM in OLIF, which is valuable information for the improvement of patient satisfaction.

In this study, we prospectively collected and analyzed the ATP and associated factors following OLIF and identified the PMM retraction length as a potential

independent risk factor for severe ATP in the immediate postoperative period following OLIF. The results suggest surgeons should minimize psoas muscle retraction during minimally invasive OLIF.

CONFLICT OF INTEREST

The current study was funded by Jeil Pharmaceutical Co., LTD. (Seoul, Korea). No other potential conflicts of interest relevant to this article were reported.

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