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A longitudinal investigation of the endplate cystic lesion effect on oblique lumbar interbody fusion

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ABSTRACT

Objective: To determine longitudinal effects of changes in endplate cystic lesions on oblique lumbar interbody fusion (OLIF), the relationship between bone healing and endplate cystic lesion changes, and clinical significance of cyst formation.

Patients and Methods: A total of 107 segments in 67 patients who underwent OLIF between January 2013 and July 2016 were examined in this retrospective study. Using computed tomography, radiographic examinations of endplate cystic lesion, positive or negative cyst formation, cage subsidence, and fusion status were performed. Clinical outcomes were measured using visual analogue scale (VAS) pain scores, Oswestry disability index (ODI), and modified Macnab criteria. Outcomes were compared with preoperatively and postoperatively. A logistic regression analysis was performed to evaluate the relationship between measurements for endplate cysts.

Results: The fusion rate after OLIF was 94.4% at 2-year follow-up, with 86% of cases reporting satisfactory outcome (based on modified Macnab criteria). A significantly higher ($P < 0.01$) VAS score for back pain was observed in the cystic lesion group than non-cystic lesion group at 6-month follow-up. Cage subsidence significantly increased the risk of non-union (odds ratio [OR]: 17.24; 95% confidence interval [CI]: 1.67–178.09). Positive cyst sign was a significant risk factor for cage subsidence (OR: 8.52; 95% CI: 2.73–26.62) while cage subsidence was also a significant risk factor for positive cyst formation (OR: 8.37; 95% CI: 2.71–25.89).

Conclusions: Cystic lesion may increase back pain in the early postoperative period. However, the preoperative cystic lesion does not aggravate a positive cyst formation or affect the final clinical result. Positive cyst formation was a significant risk factor for cage subsidence. In addition, cage subsidence was a significant predictor of non-union. Thus, the authors can speculate that positive cyst sign was potentially an indirect predictor of non-union.

1. Introduction

Epidemiological evaluations have demonstrated the occurrence of endplate cystic lesions. Specific imaging findings such as cystic change account for up to 30% in asymptomatic population [1]. Although the exact cause of endplate cystic lesion is currently unclear, it might be due to ischemic necrosis beneath the cartilaginous endplate or a stress-induced bone resorption event [2,3]. Initially, the endplate cyst is formed and a disc herniation will invade into the cyst through thinned cartilaginous and damaged endplates to form the so-called Schmorl's node [4]. These endplate cystic lesions may be correlated with degenerative spinal disease, Modic changes [5], and back pain [6].

Lumbar interbody fusion surgery is effective in relieving pain, strengthening stability, and correcting balance in patients with various lumbar spinal conditions [[7] [8],]. As a useful minimally invasive surgical option, oblique lumbar interbody fusion (OLIF) has been gaining more popularity. OLIF essentially needs a retroperitoneal customized corridor (between the psoas muscle and the great vessel structure) to achieve discectomy and insert cage. OLIF omits the psoas muscle, resulting in a relative reduction of complications associated with lumbar plexus injury [9]. Moreover, OLIF has favorable clinical results, good bony fusion rates, and lower complication rates [9,10].

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To date, longitudinal assessment of the risk of endplate cyst or its clinical significance has not been reported yet. Therefore, the purpose of this study was to investigate time course effects of changes in endplate cyst on OLIF and the relationship between bone healing and cystic lesion.

2. Materials and methods

2.1. Patient data

The current study was approved by the Institutional Review Board (IRB) of our institute. We retrospectively reviewed data of 94 patients who received OLIF procedure using a single cage with supplemental pedicle screw fixation for lumbar degenerative spinal disease between January 2013 and July 2016. Of these patients, those who had infection, trauma, neoplasm, or had history of prior spinal surgery at index level, who became deceased, who used iliac bone, or who had less than 2 years of follow-up were excluded. Finally, a total of 67 patients (107 levels) were enrolled in this study, including 39 females and 28 males. Thirteen and 11 of these patients underwent additional posterior decompression at index-level and other levels, respectively. Another eleven of these patients underwent additional posterior decompression combined with minimally invasive transforaminal lumbar interbody fusion at other levels. Of these patients, eight had rheumatoid arthritis, one had dermatomyositis, and one had fibromyalgia. These 67 patients were divided into two subgroups based on the presence or absence of endplate cyst before surgery (cystic lesion and non-cystic lesion groups). Operative techniques followed those described in our previous reports [11]. All patients were implanted with 18–22 × 8–16 × 40–55 mm polyetheretherketone (PEEK) cages (80 levels with 6-degree lordotic cage and 27 levels with 12-degree lordotic cage; Clydesdale, Medtronic Sofamor Danek, Memphis, Tennessee). The patients packed with demineralized bone matrix for all single-level cases. In multilevel cases, we used demineralized bone matrix or hydroxyapatite (considering medical costs). All surgeries were performed by one senior spine surgeon.

2.2. Outcomes

Data collection included patient demographics, primary diagnosis, Charlson comorbidity index (CCI), body mass index (BMI), bone mineral density (BMD), smoking, and reports of complications. To investigate functional outcomes, we collected visual analogue scale (VAS) score for back and leg pain and Oswestry disability index (ODI). These scores were calculated preoperatively, at 6-month, 1-year, and 2-year after surgery. Outcome was evaluated according to the modified Macnab criteria. We used computed tomography (CT) images to investigate bony fusion, cage subsidence, and endplate cyst. Fusion status [12] was assessed using the modified Bridwell criteria (Table 1). Cage subsidence was expressed as more than 2 mm cage migration into either adjacent vertebral endplate. Endplate cystic lesion was defined as one or more irregular or nearly circular polycystic areas around the lesion near the vertebral endplate with irregular or diffuse bone density observed in CT images. To investigate longitudinal development of endplate cysts, we used the following methods to compared changes in endplate cysts at each follow-up visit and findings of coronal and sagittal CT images. The endplate cyst of a positive sign was determined as one that arose *de novo* or that of which became larger than previously seen. The size of the cyst was as large as it was before surgery or it gradually became smaller after it appeared. It was identified as a negative sign (Fig. 1). A lumbar spine CT scan was obtained preoperatively and postoperatively at 6-month, 1-year, and 2-year follow-up. All images were assessed by two independent observers.

Table 1
Modified Bridwell fusion criteria.

Grade	Description
I	Fused with remodeling and trabeculae present
II	Graft intact, not fully remodeled and incorporated, but no lucency present
III	Graft intact, potential lucency present at top and bottom of the graft
IV	Fusion absent with collapse/resorption of the graft

Grades I and II are considered satisfactory fusion.

2.3. Statistical analysis

Data are expressed as mean ± standard deviations. A *t*-test was used for continuous variables while Chi-square or Fisher's exact test was used for categorical variables. Logistic regression analysis was used to evaluate the correlation among variables in terms of age, gender, BMD, BMI, smoking, preoperative cystic lesion, cage subsidence, positive cyst sign, and fusion. Statistical calculations were performed using SPSS version 23 (IBM Corp., Armonk, NY, USA). Statistical significance was considered at $P < 0.05$.

3. Results

Demographic characteristics of patients are summarized in Table 2. A total of 67 patients (107 levels) received OLIF. Their mean age was 67.9 ± 7.9 years (range, 49–88 years). The mean follow-up time was 3.1 ± 0.8 years (range, 2–5 years). The most operated level was at L4-5. The most common patient diagnosis was degenerative stenosis at 49.3% (33/67). At 2 years after surgery, VAS and ODI scores were significantly decreased compared to preoperative baseline values, with 86% of cases reporting satisfactory results (based on modified Macnab criteria). The overall incidence of complications was 25.4% (17/67). None of these patients had revision surgery or persistent pain or weakness at the 2-year follow-up. The most reported complication was approach-related lumbar plexopathy (11 cases, 16.4%), followed by sympathetic chain injury-related symptoms (4 cases, 6.0%), dural tear (1 case, 1.5%), and ureteral injury (1 case, 1.5%). Both dural tear and urethral injury were repaired intraoperatively. One patient had persistent subjective left hip flexion weakness without any functional disability while another patient had persistent sympathetic chain symptoms for more than six months. Other patients who had lumbar plexopathy and sympathetic chain symptoms gradually recovered within 6 months after surgery.

There was no significant difference in age, gender, BMI, BMD, CCI, smoking, or functional outcomes between the cystic lesion group and the non-cystic lesion group (Table 3). However, fused level was significantly different between the two groups. There were more 3-level fusion cases in the non-cystic lesion group. Concurrently, the number of patients undergoing 1- or 2-level fusion surgery was significantly ($P = 0.01$) more than those undergoing 3-level fusion surgery in both groups. There were slightly higher endplate positive cyst signs in the non-cystic lesion group than those in the cystic lesion group at any follow-up point. However, the difference between the two groups was not statistically significant ($P > 0.05$). The size of the cyst gradually reduced over time. The positive cyst sign decreased from an average of 32.7% of 107 levels at 6 months to 14.8% at 2 years postoperatively ($P = 0.002$). At the 6-month follow-up, there was a significantly higher VAS score for back pain in the cystic lesion group compared to the non-cystic lesion group (Fig. 2). VAS scores for back pain were similar between the two groups at 1-year and 2-year follow-up visits. There was no significant difference in VAS score for leg pain or ODI between the two groups at any follow-up visit (Figs. 2 and 3). Overall, cage subsidence rates at 6-month, 1-year, and 2-year after surgery were 22.4% (24/107), 20.6% (22/107), and 17.8% (19/107), respectively. Fusion rates at 6-month, 1-year, and 2-year after surgery were 62.6% (67/107), 82.2% (88/107), and 94.4% (101/107), respectively. Although the cystic lesion group had slightly higher fusion rates than the non-cystic lesion group, the

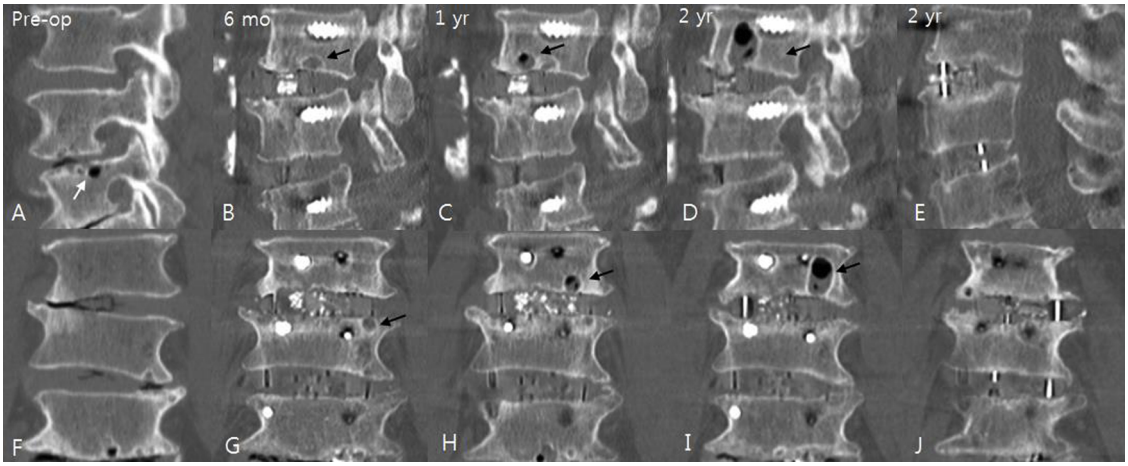


Fig. 1. A 71-year-old male who underwent oblique lumbar interbody fusion at L3-4 and L4-5 levels. Typical cystic changes in computed tomographic sagittal and coronal images before surgery and at 6-month, 1-year, and 2-year after surgery (A to D and F to I). Black arrows demonstrate endplate cyst becomes larger identified as positive cyst sign in superior level (L3-4). White arrow demonstrates endplate cyst becomes smaller then disappears which is identified as negative cyst sign in inferior level (L4-5). Typical radiologic fusion with bone union is shown in sagittal (E) and coronal (J) images at 2 years after surgery.

Table 2
Demographic and clinical data of all the patients.

Patients	67
Sex (female : male; ratio)	39 : 28
Age (years)	67.9 ± 7.9
BMI	24.9 ± 3.4
BMD	−2.5 ± 1.1
T score < -2.5	39
CCI	4.2 ± 1.9
Smoking	6
Operated level	n = 107
L2-3	23
L3-4	38
L4-5	46
No. of fusion levels	n=67
1 level	36
2 levels	21
3 levels	10
Functional outcomes	
Preoperative VAS for back	4.91 ± 1.89
Postoperative VAS for back	2.36 ± 1.86
Preoperative VAS for leg	6.26 ± 1.75
Postoperative VAS for leg	1.80 ± 1.38
Preoperative ODI	47.18 ± 9.99
Postoperative ODI	25.13 ± 12.77
Satisfaction rate (Macnab criteria)	86%
Follow-up (years)	3.1 ± 0.8
Incidence of complications	25.4% (17/67)

BMI, body mass index; BMD, bone mineral density; CCI, charlson comorbidity index; VAS, visual analogue scale; ODI, Oswestry disability index.

Table 3
Baseline demographic and clinical data between 2 groups.

	Cystic lesion group	Non-cystic lesion group	*P*
Age	67.7 ± 8.2	67.9 ± 7.7	0.86
BMI	24.9 ± 3.4	24.9 ± 3.4	0.93
BMD	−2.3 ± 1.1	−2.6 ± 1.1	0.20
CCI	4.3 ± 2.3	4.2 ± 1.6	0.71
Smoking	3	3	0.91
Operated Level	43	64	
L2-3	9	14	0.91
L3-4	19	19	0.12
L4-5	14	32	0.07
No. of fusion levels	32	35	
1 level	18	18	0.69
2 levels	13	8	0.12
3 levels	1	9	0.007*
Pre-op VAS back	5.26 ± 1.83	4.67 ± 1.90	0.11
Pre-op VAS leg	6.39 ± 1.66	6.17 ± 1.81	0.51
Pre-op ODI	46.42 ± 10.19	47.69 ± 9.91	0.53

*$P < 0.05$

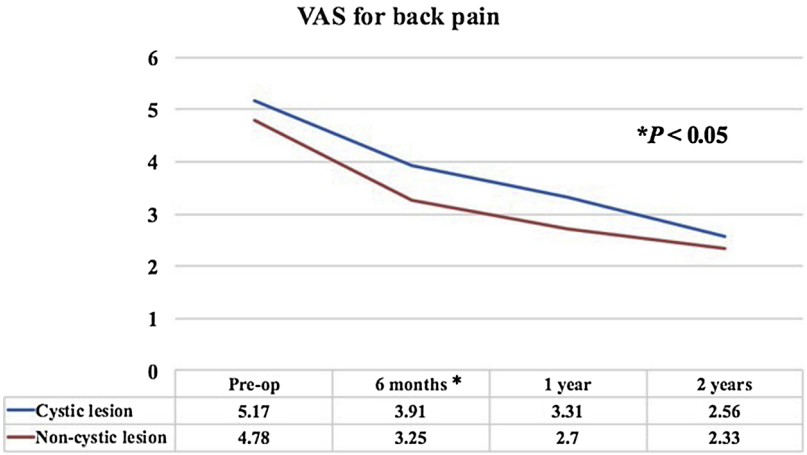
BMI, body mass index; BMD, bone mineral density; CCI, charlson comorbidity index; VAS, visual analogue scale; ODI, Oswestry disability index.

difference between the two groups at any follow-up visit was not statistically significant. Results of radiographic parameters are shown in Table 4. Multivariate logistic regression analysis showed that positive cyst sign was a significant risk factor for cage subsidence (odds ratio [OR]: 8.52; 95% confidence interval [CI]: 2.73–27.62). Cage subsidence was a significant risk factor for positive cyst sign (OR: 8.37; 95% CI: 2.71–25.89). Cage subsidence was also a significant risk factor for non-union (OR: 17.24; 95% CI: 1.67–178.09). Age, gender, BMI, T score < -2.5, preoperative cystic lesion, or multilevel fusion surgery was not a significant risk factor for fusion, subsidence, or positive cyst sign.

4. Discussion

The most important finding of the current study was that positive cyst sign was a significant risk factor for cage subsidence after OLIF. The risk of subsidence was 8.52 times greater in patients with positive cyst sign. Cage subsidence was also a significant risk factor for non-union. The risk of non-union was 17.24 times greater in subjects with cage subsidence. However, positive cyst sign was not directly related to non-union ($P = 0.22$). In other words, positive cyst sign and cage subsidence were interrelated with each other. The risk of positive cyst sign was 8.37 times greater in patients with cage subsidence.

Although cysts or cystic lesions are often found on endplates in patients with low back pain or those without symptoms, no consensus has been reached on their etiology or clinical significance. The etiology of endplate cysts is currently unclear. There has been no longitudinal investigation of cystic alteration after lumbar interbody fusion. We speculate that the formation of cyst in the vertebral endplate has similar mechanism to that leading to bone cyst around osteoarthritic joints. The intact cartilage layer can evenly distribute the load applied over the bone area. Once the cartilage at a certain part is thinned or completely deteriorated, the pressure around it will increase, subsequently causing stress-induced microfracture followed by bone resorption, eventually forming a cyst. Occasionally, vacuum phenomenon associated with gas collection within the cyst can be observed. In early postoperative



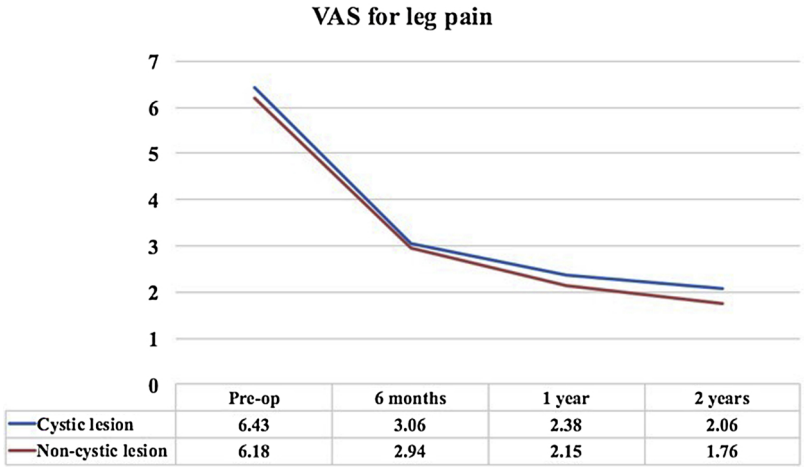


Fig. 2. Visual analog scale (VAS) of pain scores for back pain (A) and leg pain (B) with time. *P < 0.05.

period, the cage is directly in contact with the endplate where mechanical stress from the cage may cause microfracture of the contact surface, thereby leading to the development of the cyst formation. Micromotion around the cage can also lead to microfracture of the endplate which may aggravate cyst enlargement. Along with bone healing, micromotion between the endplate and the cage can reduce and the microfracture may heal or bone remodeling may occur followed by cyst becoming smaller or disappearing, thus reducing cage subsidence. On the other hand, according to our logistic analysis, there was a positive correlation between cage subsidence and endplate positive cyst sign. Subsequently, the cyst became larger and cage subsidence continued to exist, ultimately leading to non-union in the same case. The detailed development process of endplate cyst changes is shown in Fig. 4.

A few studies have reported surgical treatment for symptomatic endplate cystic lesions. An article [13] has reported a 55-year-old

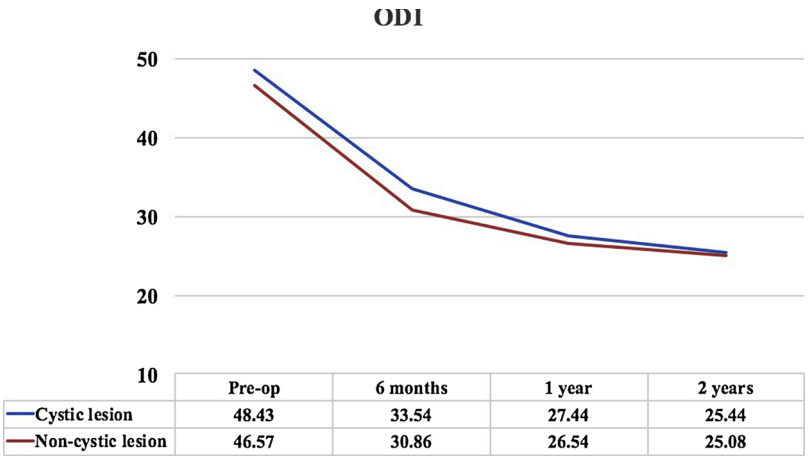


Fig. 3. Oswestry Disability Index (ODI) scores with time.

Table 4
Summary of radiographic parameters between 2 groups with time.

	Cystic lesion group (n = 43)	Non-cystic lesion group (n = 64)	*P*
	At 6 months after surgery		
Positive cyst sign	27.9% (12/43)	35.9% (23/64)	0.39
Subsidence rate	20.9% (9/43)	23.4% (15/64)	0.76
Fusion rate	65.1% (28/43)	62.6% (39/64)	0.66
	At 1 year after surgery		
Positive cyst sign	16.3% (7/43)	20.3% (13/64)	0.55
Subsidence rate	18.6% (8/43)	21.9% (14/64)	0.68
Fusion rate	83.7% (36/43)	81.3% (52/64)	0.74
	At 2 years after surgery		
Positive cyst sign	14% (6/43)	15.6% (10/64)	0.81
Subsidence rate	16.3% (7/43)	18.8% (12/64)	0.74
Fusion rate	97.7% (42/43)	92.2% (59/64)	0.23

female patient with a history of 8 years of low back pain. Her pain was successfully relieved after undergoing fusion surgery. Another recent literature [14] has reported good outcome in a 40-year-old male patient with a 4-month resistant back pain due to a giant cystic variant after undergoing a decompression procedure. At 5 years after surgery, the size of the cyst was significantly decreased. He was pain-free. A retrospective study [15] has investigated 21 cases with symptomatic low back pain originated from endplate cystic lesion who received lumbar interbody fusion surgery (14 cases through posterior approach and 7 cases through anterior approach). The authors treated the cystic lesions in En bloc procedure during operation. Finally, 20 of these 21 patients achieved complete pain relief with definite improvement in physical function after fusion surgery. In the present study, we demonstrated good clinical results and acceptable radiological outcomes at 2-year follow-up. Although preoperative existing endplate cystic lesion was not removed by aggressive curettage during the surgery, the cyst gradually became smaller or disappeared as fusion progressed. Based on longitudinal evaluation, preoperative cystic lesion was not a risk factor for cyst enlargement or bony union. However, the presence of cystic changes could correlate with back pain. Previous studies have shown that patients with endplate cystic lesions may exhibit higher incidence of back pain compared to the normal population [16,17], although such finding is not consistent in the literature [18]. In our study, the cystic lesion group had slightly higher preoperative VAS score for back pain (5.26 ± 1.83) than the non-cystic lesion group (4.67 ± 1.90). However, the difference between the two groups was not statistically significant. Interestingly, at 6-month follow-up, a significant higher VAS score for back pain was recorded for the cystic lesion group (4.28 ± 1.20) compared to the non-cystic lesion group (3.25 ± 1.49). Also, a slightly higher VAS score for back pain was shown in the cystic lesion group than the non-cystic lesion group at 1-year follow-up (3.31 ± 1.49 vs. 2.70 ± 1.65; $P = 0.15$). However, it was similar between the two groups at 2-year follow-up (2.56 ± 2.22 vs. 2.33 ± 1.80; $P = 0.70$). These findings indicate that cystic lesion enlargement might be associated with back pain. To our observation, cystic lesions were more limited to a certain area around endplate surface having contact with the cage. They then gradually evolved into positive or negative signs. In other endplate areas where there were no cysts, bony union continued and eventually patients achieved solid fusion (Figs. 1E and 1 J). With fusion of surgical segments, the effect of cystic lesion inside the segment on pain was gradually reduced. This may explain the aforementioned difference in VAS score for back pain between the two groups.

Two previous studies [3,19] have reported that postoperative endplate cystic change is closely associated with non-union after transforaminal lumbar interbody fusion. According to our investigation, cystic lesion enlargement (positive cyst sign) could increase the incidence of cage subsidence. However, it was not a direct influencing factor for non-union. In fact, the positive direct risk factor for non-union was cage subsidence in the current study. This has been demonstrated in several studies [20,21]. Therefore, positive cyst sign is a potential indirect predictor of non-union. In agreement with our previous study [22], similar logistic analysis results were found in 76 patients who underwent minimally invasive transforaminal lumbar interbody fusion.

This study has several strengths. First, all procedures were performed by a single surgeon who used the same surgical technique. Second, this was the first longitudinal evaluation of the time course of endplate cystic lesions. However, this study also has some limitations, including its retrospective nature, small sample size, and short-term follow-up. In addition, demineralized bone matrix was used for most patients and certain patients used hydroxyapatite, not iliac bone or bone morphogenetic protein-2.

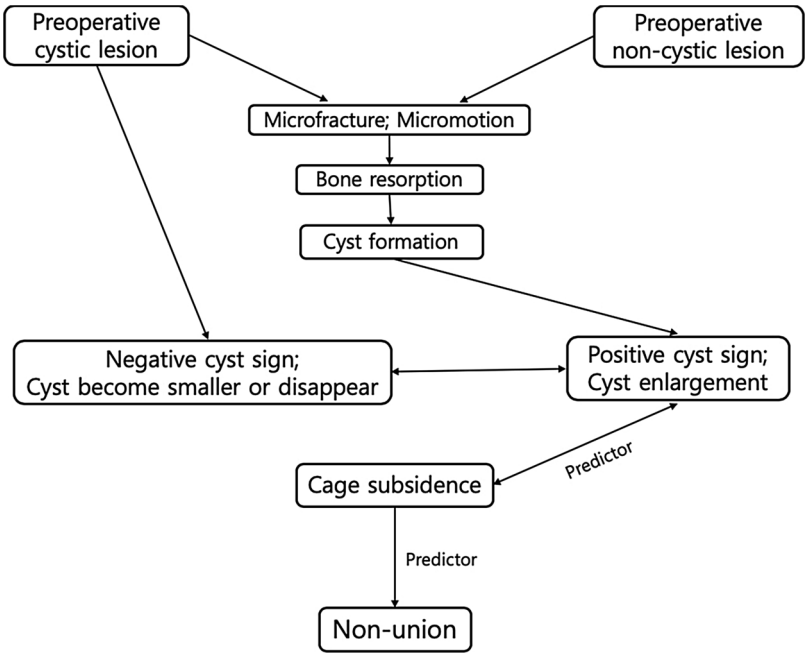


Fig. 4. General flow chart showing detailed development process of endplate cyst changes.

5. Conclusion

In the early postoperative period, preoperative cystic lesion was associated with back pain before bony fusion occurred. The presence of endplate cystic lesion before surgery did not increase the size of cyst after OLIF. It did not directly influence fusion either. In addition, the positive cyst sign was a significant risk factor for cage subsidence after OLIF and that cage subsidence was a significantly risk factor for non-union. Therefore, positive cyst sign maybe a potential indirect predictor of non-union.

Declaration of Competing Interest

All the authors declare that no actual or potential conflict of interest-associated biases in the text of the paper.

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