Graft subsidence as a predictor of revision surgery following stand-alone lateral lumbar interbody fusion

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OBJECTIVE Lateral lumbar interbody fusion (LLIF) is a less invasive surgical option commonly used for a variety of spinal conditions, including in high-risk patient populations. LLIF is often performed as a stand-alone procedure, and may be complicated by graft subsidence, the clinical ramifications of which remain unclear. The aim of this study was to characterize further the sequelae of graft subsidence following stand-alone LLIF.

METHODS A retrospective review of prospectively collected data was conducted on consecutive patients who underwent stand-alone LLIF between July 2008 and June 2015; 297 patients (623 levels) met inclusion criteria. Imaging studies were examined to grade graft subsidence according to Marchi criteria, and compared between those who required revision surgery and those who did not. Additional variables recorded included levels fused, DEXA (dual-energy x-ray absorptiometry) T-score, body mass index, and routine demographic information. The data were analyzed using the Student t-test, chi-square analysis, and logistic regression analysis to identify potential confounding factors.

RESULTS Of 297 patients, 34 (11.4%) had radiographic evidence of subsidence and 18 (6.1%) required revision surgery. The median subsidence grade for patients requiring revision surgery was 2.5, compared with 1 for those who did not. Chi-square analysis revealed a significantly higher incidence of revision surgery in patients with high-grade subsidence compared with those with low-grade subsidence. Seven of 18 patients (38.9%) requiring revision surgery suffered a vertebral body fracture. High-grade subsidence was a significant predictor of the need for revision surgery ($p < 0.05$; OR 12, 95% CI 1.29–13.6), whereas age, body mass index, T-score, and number of levels fused were not. This relationship remained significant despite adjustment for the other variables (OR 14.4; 95% CI 1.30–15.9).

CONCLUSIONS In this series, more than half of the patients who developed graft subsidence following stand-alone LLIF required revision surgery. When evaluating patients for LLIF, supplemental instrumentation should be considered during the index surgery in patients with a significant risk of graft subsidence.

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KEY WORDS subsidence; osteopenia; osteoporosis; lateral lumbar interbody fusion; LLIF; vertebral body fracture

OVER the past decade, lateral lumbar interbody fusion (LLIF) has gained popularity among spine surgeons as a useful minimally invasive option in the operative management of a variety of spinal conditions.^{3,12,23,24,29,30,34,39} LLIF furthermore functions as an adjunct approach to enhance complex spinal deformity correction.^{2,4,6,9,14,25,39,43} Several studies have demonstrated that when compared with traditional open approaches to the spine, the minimally invasive LLIF procedure is asso-

ciated with decreased anesthesia time, less trauma to normal anatomical structures, and fewer complications.^{18,25,27,34} The most recent data have demonstrated that LLIF has an excellent cost-effectiveness profile and may reduce the outcome discrepancy between challenging and more routine surgically treated pathological entities.¹⁷ The LLIF thus represents an excellent alternative in the management of patients with spinal pathology and an elevated perioperative complication risk profile (e.g., the elderly).

ABBREVIATIONS ACDF = anterior cervical discectomy and fusion; BMD = bone mineral density; BMI = body mass index; DEXA = dual-energy x-ray absorptiometry; LLIF = lateral lumbar interbody fusion; PLIF = posterior lumbar interbody fusion; TLIF = transforaminal lumbar interbody fusion.

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Although the risk of major morbidity and mortality following the LLIF procedure is small, the complication profile is fairly unique and has been well documented in the literature.^{2,14,26,33,36,39} A common complication seen with LLIF surgery is subsidence of the interbody graft into one or both of the adjacent vertebral bodies, which occurs with a reported incidence range from 8% to 30%.^{19,22,40} Although the radiographic occurrence of graft subsidence has been characterized in the literature, the clinical consequence remains nebulous.

Marchi et al. performed an extensive radiographic study of graft subsidence following stand-alone LLIF, and they proposed a grading scale to describe the degree of subsidence. Grade 0 (0%–24% of the graft height) and Grade I (25%–49% of the graft height) are low grade, and Grade II (50%–74% of the graft height) and Grade III (75%–100% of the graft height) are high grade.²² The literature to date has failed to demonstrate a clear correlation between the degree of radiographic subsidence and clinical sequelae, specifically the need for reoperation.^{8,11,35} Factors that may increase the risk of graft subsidence include impaired bone mineral density (BMD), disc space overdistraction, length of construct, cage width, endplate violation, and lateral plate fixation.^{5,10,19,35,38,40}

The effectiveness of the LLIF procedure is in part related to the extension-distraction moment arm applied to the anterior and middle columns of the spine. Studies have proven that the resultant ligamentotaxis indirectly decompresses the spinal canal and neuroforamina, and serves as an effective means of relieving claudication and radicular symptoms in select patients.^{7,21,28} Subsidence of the interbody graft may compromise this indirect decompression, leading to return of symptoms, new-onset back pain, and neurological deficit, and in severe cases, fracture of the vertebral body itself.^{5,10,19,22,38} Severely symptomatic patients with subsidence, especially those who experience a vertebral body fracture, often require more extensive open posterior decompression and stabilization. The aim of this study is to further examine the correlation between severity of graft subsidence and the need for revision surgery.

Methods

A retrospective review of prospectively collected data was conducted for all patients who underwent stand-alone minimally invasive LLIF at a single institution between July 2008 and June 2015. The database identified 411 patients (844 levels) who underwent LLIF. Of those patients, 297 (623 levels) met inclusion criteria as patients who underwent elective stand-alone LLIF. Patients who underwent LLIF for corpectomy or trauma, as part of a staged deformity correction procedure, or who received supplemental instrumentation (e.g., lateral plate, facet, or pedicle screw fixation) were excluded from the study. All patients who undergo LLIF at this institution are followed with imaging studies at standard follow-up intervals. Anteroposterior and lateral radiographs are obtained immediately postoperatively and at the 6-week, 3-month, 6-month, 1-year, and 2-year follow-up. A lumbar spine CT scan is routinely obtained postoperatively and at the 1-year follow-up. Patients' radiographs were evaluated by the sur-

gical team and an independent radiologist, using standing lateral lumbar spine radiographs and CT scans according to the criteria of Marchi et al.²² A separate database query was performed to identify all patients who underwent revision surgery following stand-alone LLIF, to determine other variables that influenced the need for revision surgery. Additional data pulled from electronic medical records included body mass index (BMI), the WHO T-score on dual-energy x-ray absorptiometry (DEXA), presenting symptoms, and basic demographic information.

Subsidence grading is expressed as the percentage of disc space or vertebral body collapse around the interbody graft compared with the immediate postoperative films: Grade 0, 0%–24% collapse; Grade I, 25%–49% collapse; Grade II, 50%–74% collapse; and Grade III, 75%–100% collapse. Grades 0 and I are considered low-grade subsidence, whereas Grades II and III are considered high-grade subsidence. Chi-square analysis and logistic regression analysis were used to compare patients with subsidence who underwent revision surgery against those with subsidence who did not require revision surgery. Age, BMI, DEXA T-scores, number of levels fused, graft size, and subsidence grade were compared between the 2 groups.

Results

The indications for surgery included degenerative scoliosis, degenerative disc disease with or without foraminal stenosis, low-grade spondylolisthesis, adjacent-segment disease following prior fusion, and far-lateral disc herniation. Thirty-four of 297 total patients (11.4%) who underwent stand-alone LLIF experienced radiographic evidence of graft subsidence. Of these 297 patients, 18 (6.1%) required revision surgery between 1 and 156 weeks after the index surgery (average 35 weeks), due to return and/or progression of symptoms, new-onset neurological deficit, and/or debilitating back pain. Revision surgery consisted of open decompression and instrumented fixation at the index level in all cases. In certain patients with additional pathological entities, such as a vertebral body fracture, the arthrodesis was performed at additional adjacent levels.

The mean follow-up was 1.8 years among all patients with stand-alone LLIF and 1.52 years in the operative cohort. Eight patients were lost to follow-up entirely. The overall fusion rate, as demonstrated on lumbar spine CT scans and dynamic radiographs, was 93.9%. All but 3 patients who developed subsidence received 22-mm-wide polyetheretherketone interbody grafts filled with demineralized bone matrix allograft; the 3 patients with subsidence who received 18-mm-wide grafts all experienced high-grade subsidence and underwent revision surgery. The mean time from the index surgery to revision surgery was 35.1 weeks, ranging from 1 week to 156 weeks postoperatively; however, 10 of the 18 patients (55.6%) underwent the revision operation within 3 months of the index procedure.

The database was also queried to identify all patients with stand-alone LLIF who required revision surgery, to determine additional etiologies other than subsidence; 20 total patients were identified. The 2 additional patients underwent revision surgery due to psoas abscess and infection. Both of these events occurred within weeks of one

TABLE 1. Demographic information for stand-alone LLIF patients with subsidence requiring revision surgery and those not requiring revision surgery

Results Post-LLIF	Mean Age (yrs)	Mean Levels Fused	Mean BMI (kg/m ²)	Mean DEXA T-score	Median Subsidence Grade	Diabetes Mellitus (%)	History of Cancer (%)	Immunosuppression or Chronic Steroid Use (%)
Subsidence w/ revision surgery	67.6	1.78	30.7	-1.90	2.5	33.3	5.56	27.8
Subsidence w/o revision surgery	65.1	1.75	26.9	-1.53	1.0	29.4	5.89	29.4

another, and represent the only incidents of infection following stand-alone LLIF at this institution. Tables 1 and 2 demonstrate patient demographic and clinical information for the 2 groups. The mean age in patients requiring revision surgery was 67.6 years, compared with 65.1 years for those without a revision ($p = 0.40$). The mean BMI in patients requiring revision surgery was 30.7, compared with 26.9 in patients without a revision ($p = 0.10$). The mean levels fused in patients requiring revision surgery was 1.78, compared with 1.75 in patients without a revision ($p = 0.92$). The mean DEXA T-score at the femoral neck in patients requiring revision surgery was -1.9; of these 18 patients, 6 had osteoporosis (T-score ≤ -2.5), 11 had osteopenia (T-score -1.0 to -2.5), and 1 had a normal T-score (T-score > -1.0). By contrast, the mean DEXA T-score in patients with subsidence who did not require revision surgery was -1.53 ($p = 0.29$); of these 16 patients, 4 had osteoporosis, 6 had osteopenia, and 6 had a normal T-score.

The median subsidence grade for patients requiring revision surgery was 2.5, compared with 1 for those with subsidence without a revision ($p < 0.01$). Grades 0 and I were considered low-grade subsidence, whereas Grades II and III were considered high-grade subsidence. Chi-square analysis (Table 3) for noncontinuous variables was also performed. There was a statistically higher incidence of need for revision surgery for patients with high-grade subsidence compared with those with low-grade subsidence ($\chi^2 = 20.86$, $df = 1$, $p < 0.01$). All patients with subsidence requiring revision surgery had high-grade subsidence, whereas 4 of 16 patients (25%) without revision surgery had high-grade subsidence (Fig. 1). High-grade subsidence was a significant predictor of need for revision surgery ($p < 0.05$; OR 12, 95% CI 1.29–13.6), whereas age, BMI, T-score, and number of levels fused were not. High-grade subsidence remained a significant predictor of need for revision surgery, despite adjustment for age, BMI, and T-score (OR 14.4; 95% CI 1.30–15.9). Seven of 18 patients (38.9%) requiring revision surgery suffered a fracture of the vertebral body (for a total incidence of 2.4%), all of whom had high-grade subsidence.

TABLE 2. Stratification of subsidence occurrence based on number of levels operated on during stand-alone LLIF

No. of Levels	Total	Subsidence	No Subsidence
1	132	17	115
2	66	9	57
3	63	7	56
4	36	1	35

Of the 18 patients who underwent revision surgery for symptomatic subsidence, 14 improved to achieve $> 75\%$ symptom reduction at last follow-up, and 2 patients improved to achieve partial symptom relief. Two patients experienced worsening symptoms; one required additional revision surgery with instrumentation, whereas the other patient was offered additional revision surgery in the setting of progressive degenerative scoliosis but elected to pursue conservative treatment instead.

Discussion

Although the complication profile of minimally invasive transpoas LLIF has been widely studied, the clinical implications of graft subsidence remain unclear. Most studies of interbody graft subsidence are found in the literature on anterior cervical discectomy and fusion (ACDF). The phenomenon of subsidence following ACDF surgery has long been regarded as a potential risk factor for pseudarthrosis and treatment failure, and has generated significant debate over the use of stand-alone grafts versus supplementation with anterior plating.¹³ However, studies have failed to demonstrate a significant correlation between graft subsidence and overall clinical outcome following ACDF.^{16,42} In the lumbar spine literature, biomechanical and clinical studies have historically focused on transforaminal lumbar interbody fusion (TLIF) and posterior lumbar interbody fusion (PLIF) techniques.^{15,20,32,41} Whereas in vitro studies have demonstrated the mechanisms of graft subsidence and the risk of biomechanical failure, in vivo studies have been less definitive.^{15,32,41}

It is acknowledged that a slight degree of graft settling occurs as an arthrodesis evolves. When evaluating graft subsidence, it is important to determine at what point it

TABLE 3. Chi-square analysis demonstrating the association between subsidence grade and revision surgery after stand-alone LLIF

Grade	Subsidence w/o Revision Surgery	Subsidence w/ Revision Surgery	Row Total
Low	12 (5.65) [7.15]	0 (6.35) [6.35]	12
High	4 (10.35) [3.9]	18 (11.65) [3.47]	22
Column total	16	18	34
Chi-square test results	$\chi^2 = 20.864$, $df = 1$ $p = 0.000005$		

Values in brackets are the expected values for the chi-square test. Values in parentheses are the chi-square statistic, which was calculated using the following formula: (observed value – expected value)²/expected value. The numbers without brackets—i.e., 12, 0, 4, and 18—are the observed values.

FIG. 1. Bar graph showing distribution of subsidence grade in patients with subsidence who required revision surgery and those who did not require revision surgery. Values on the y-axis represent the number of patients. Figure is available in color online only.

represents a pathological process as opposed to settling. Tokuhashi et al. presented a series of 66 patients who underwent traditional PLIF with interbody graft and pedicle screw fixation and found that, although the size of the disc space increases in the immediate postoperative period, it tends to decrease to a greater degree over time.⁴¹ However, this subsidence did not have a significant impact on clinical outcomes, thus representing settling during arthrodesis evolution. Another study by Karikari et al. analyzed complications in 66 elderly patients who underwent 68 minimally invasive TLIF (n = 27) and LLIF (n = 41) procedures, and noted 4 patients who developed graft subsidence.¹⁵ All 4 cases of subsidence occurred in patients who underwent LLIF, and all patients required revision surgery for correlative symptoms; however, these authors did not discuss the severity of subsidence in their population.

The relationship between degree of subsidence and clinical outcomes has not been comprehensively studied to date, and what information does exist remains inconclusive and inconsistent. In a study of 145 levels of LLIF

FIG. 2. Images obtained in a 68-year-old woman who presented with radiculopathy and back pain. **A:** Preoperative MRI sequence demonstrates degenerative disc disease and retrolisthesis of L-3 on L-4. **B:** Intraoperative fluoroscopy reveals an appropriately sized LLIF graft at L3–4; however, there was concern for endplate violation intraoperatively. **C:** Sagittal CT scan performed 16 weeks postoperatively demonstrates high-grade subsidence. **D and E:** Postoperative radiographs obtained following revision surgery consisting of open decompression and pedicle screw fixation at L3–4.

FIG. 3. Images obtained in a 61-year-old woman who presented with severe progressive back and bilateral lower-extremity pain. **A:** Preoperative MRI sequence reveals Grade I spondylolisthesis with moderate stenosis at L4–5. **B:** Intraoperative fluoroscopy demonstrates appropriate graft placement without obvious endplate violation. **C:** Postoperative CT imaging reveals good positioning of stand-alone interbody graft within the L4–5 disc space without evidence of endplate violation or graft subsidence. **D:** Delayed CT imaging reveals fracture of the L-5 vertebrae with associated graft subsidence. **E:** Postoperative radiograph obtained following posterior decompression and pedicle screw and rod placement from L-4 to S-1.

in 90 patients, Alimi et al. assessed the clinical impact of graft subsidence by measuring the change in foraminal height, disc space height, and the presence of radicular symptoms over time.¹ They did not find a correlation between subsidence and return of radicular symptoms, and the rate of subsidence between patients with stand-alone LLIF and those with supplementary instrumentation was not significant. In contrast to the present study, there is a strong correlation between subsidence grade and the risk of revision surgery after stand-alone LLIF. Revision surgery after LLIF represents an undesirable outcome due to the increased cost, increased risk exposure to the patient, and increased recovery time associated with additional surgery.

The clinical effects of subsidence may be more pronounced in patients who undergo stand-alone LLIF compared with patients who undergo traditional PLIF/TLIF procedures. One biomechanical advantage of PLIF/TLIF is that pedicle screws provide anterior, middle, and posterior column support and maximize load sharing. This

may limit the degree of graft settling and protects patients from developing pathological subsidence. Conversely, the LLIF procedure, either stand-alone or supplemented with lateral plating, subjects the vertebral bodies to increased biomechanical stress due to the lack of posterior column support. In fact, lateral plating has been implicated as a risk factor for subsidence and vertebral body fracture due to destructive effects of anchoring screws on the trabecular architecture of subchondral bone.^{10,37,38} To reduce the biomechanical shortcomings of LLIF, wider grafts are used to span the entire length of the disc space and increase contact with the apophyseal ring and cortical bone to maximize contact surface area between the graft and endplate interface.³¹ Meticulous endplate preparation is of paramount importance to minimize destruction of cortical bone and maximize the ability of the vertebral bodies to resist the biomechanical forces exerted by the graft within. Endplate violation places the graft in direct contact with cancellous bone that is less capable of resisting the axial loading stresses on the vertebral bod-

ies. This phenomenon is illustrated in Fig. 2: following an L3–4 LLIF, the patient experienced recurrent symptoms 16 weeks later. Plain radiographs and CT imaging demonstrated Grade III subsidence, ultimately necessitating an open decompression and pedicle screw fixation at L3–4. Figure 3 depicts a stand-alone LLIF at L4–5 that resulted in a coronal split fracture of the L-5 vertebral body 10 days after discharge from the hospital. This patient required an open posterior decompression with pedicle screw fixation from L-4 to S-1.

One limitation of this study is the lack of patient-reported outcome measures in the different patient populations. Determining whether there is ultimately a difference in long-term clinical outcomes between patients with graft subsidence who require revision surgery and those who do not will enable clinicians to better elucidate the clinical relevance of radiographic subsidence. This study furthermore does not address subsidence in patients who received supplementary fixation at their index surgery. Additional studies comparing the grade of subsidence and symptomatology between patients with and without supplementary instrumentation would be useful in further delineating the role of posterior instrumentation in preventing symptomatic graft subsidence. Based on the current literature and extensive experience, all patients evaluated for potential stand-alone LLIF at this institution are now screened for subsidence risk factors and stratified based on age and BMD. When considering stand-alone LLIF, we recommend obtaining a DEXA scan in patients older than 50–55 years of age and in younger patients with risk factors for osteoporosis (rheumatological conditions, chronic steroid use, and so on), because impaired BMD appears to correlate strongly with the development of graft subsidence.⁴⁰ Patients with evidence of osteopenia or osteoporosis on DEXA scanning are typically offered LLIF plus supplemental percutaneous pedicle screw fixation to mitigate the negative sequelae of graft subsidence. However, contrary to past data, the T-score was not an independent predictor of subsidence requiring revision surgery when stratified by severity of subsidence. Additional stratification as a larger volume of patients is collected may better determine when patients with osteoporosis are at the highest risk of high-grade subsidence and thus would most benefit from fixation.

Conclusions

This study attempts to demonstrate the correlation between graft subsidence and need for revision surgery in patients following stand-alone LLIF. Patients with high-grade subsidence require revision surgery more often than those with low-grade subsidence. It may be advantageous to place supplementary posterior instrumentation at the time of initial surgery in patients undergoing LLIF who have an increased risk of graft subsidence, to circumvent the need for revision surgery.

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Disclosures

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Author Contributions

Conception and design: Kanter, Tempel, Okonkwo. Acquisition of data: Kanter, Tempel, Panczykowski, Gandhoke, Hamilton, Okonkwo. Analysis and interpretation of data: Kanter, Tempel, Panczykowski, Gandhoke, Hamilton, Okonkwo. Drafting the article: all authors. Critically revising the article: Kanter, Tempel, McDowell. Reviewed submitted version of manuscript: Kanter, Tempel, McDowell, Panczykowski, Hamilton. Approved the final version of the manuscript on behalf of all authors: Kanter. Statistical analysis: Tempel, McDowell, Gandhoke, Okonkwo. Administrative/technical/material support: Kanter. Study supervision: Kanter, Okonkwo.

Supplemental Information

Previous Presentations

Presented as an abstract, as a platform presentation at the 2016 Joint Spine Section meeting held in Orlando, Florida, on March 16–19, 2016.

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