



# Evaluation of cage subsidence in standalone lateral lumbar interbody fusion: novel 3D-printed titanium versus polyetheretherketone (PEEK) cage

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## Abstract

**Purpose** This study aims to compare the early subsidence rate (6–12 months) of standalone novel 3D-printed titanium (Ti) versus polyetheretherketone (PEEK) interbody cages after lateral lumbar interbody fusion (LLIF).

**Method** A retrospective study of 113 patients (186 levels) who underwent LLIF surgery with Ti or PEEK cages was conducted. Early subsidence was measured in each treated level using the Marchi et al. classification in radiographs or CT scans acquired at 6–12 months follow-up. Multivariate logistic regression analyses with generalized mixed models, setting subsidence as the outcome variable and including cage type (Ti vs PEEK) as well as significant and trending variables ( $p < 0.10$ ) in univariate analyses, were conducted.

**Results** In total, 51 female and 62 male patients were analyzed. The median [IQR] age at surgery was 60.0 [51.0–70.0] years. Of the 186 levels, 119 levels were treated using PEEK and 67 levels with Ti cages. The overall subsidence rate for Grades I–III was significantly less in the Ti versus the PEEK group ( $p = 0.003$ ). For high-grade subsidence (Grade II or III), Ti cages also demonstrated a subsidence rate (3.0%) that was significantly less compared to PEEK cages (18.5%) ( $p = 0.002$ ). Multivariate analysis showed that patients treated with Ti cages were less likely to develop severe subsidence compared to those treated with PEEK (OR = 0.05, 95% CI = 0.01, 0.30) ( $p = 0.001$ ).

**Conclusion** Our study demonstrated that 3D-printed novel Ti cages had a significantly lower early subsidence rate compared to PEEK cages in standalone LLIF patients.

**Keywords** LLIF · Standalone · Cage subsidence · Titanium · PEEK · Lumbar fusion

## Introduction

One surgical treatment strategy for interbody fusion in the lumbar region is lateral lumbar interbody fusion (LLIF), also known as extraforaminal lumbar interbody fusion (ELIF) or eXtreme lateral interbody fusion (XLIF), which has been

increasingly used in the past couple decades [1–3]. This minimally invasive retroperitoneal transpsoas approach has grown in popularity due to its safe and effective treatment with reports of lower risk of visceral and major vascular injuries compared to an open, classic anterior approach. Also, there are reports of less muscle injury and fewer wound infections with LLIF than posterior techniques [1, 4]. Moreover, preservation of the anterior and posterior longitudinal ligament is possible in addition to the use of larger cages that can span the apophyseal ring bilaterally. These LLIF characteristics are advantageous for maintaining segmental stability [1, 2, 5]. Consequently, LLIF can be performed as a standalone LLIF (SA-LLIF) procedure without any additional instrumented stabilization for a broad range of spinal disorders [2, 6].

Despite the advantages of minimally invasive LLIF, there are also several possible complications such as cage

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subsidence and approach-related anterior thigh symptoms. Severe cage subsidence is associated with malalignment, nonunion and loss of disk height correction that can result in possible revision surgery [3, 7, 8]. In SA-LLIF especially, the subsidence risk is reportedly higher than LLIF with posterior fusion [8].

In March 2017, a novel 3D-printed titanium (Ti) cage with a porous architecture was cleared by the U.S. Food and Drug Administration [9]. In laboratory settings, these new Ti cages with their unique architecture demonstrated a substantial decrease in stress at the bone–hardware interface [10, 11]. In addition, Ti cages are reported to be more osteoconductive, maximize bone-to-implant contact and have more compressive shear strength under physical force than polyetheretherketone (PEEK) [5, 12–14].

Nevertheless, the subsidence rate of these new Ti cages compared to cages made out of commonly used material such as PEEK has not been investigated in SA-LLIF. This study aims to compare the early subsidence rate (6–12 months) of Ti versus PEEK interbody cages after SA-LLIF.

## Material and methods

### Study population

This study was approved by our hospital's Institutional Review Board, and informed consent was waived due to the retrospective nature of this study. Between November 2016 and May 2020, data of patients undergoing SA-LLIF at a single academic institution were reviewed. The inclusion criteria consisted of I) patients above the age of 18 years old, II) standalone LLIF from L1/L2 to L4/L5 without previous fusions in adjacent or non-adjacent levels, III) a minimum of six-month post-operative radiological imaging availability, IV) preoperative CT scans for BMD assessment within 6 months prior to surgery and V) patients with degenerative pathology. The surgical indications for SA-LLIF were documented.

### Data collection

As potential contributing factors for cage subsidence, data including age, body mass index (BMI), gender, race, history of smoking, diabetes mellitus, surgical diagnosis, usage of recombinant human bone morphogenetic protein-2 (rhBMP2) or demineralized allograft, level(s) of fusion and cage information such as length (AP) and height were collected. Additionally, bone mineral density (BMD) using quantitative computed tomography (QCT) was calculated retrospectively in the vertebral body (vBMD) of L1 and L2 with Mindways QCT Pro Software (Mindways Software,

Inc., Austin, TX, the USA) with preoperative CTs. The average of the vBMD for the L1 and L2 levels was used as the BMD value [15]. We utilized the phantomless synchronously calibrated QCT method to convert Hounsfield Units to vBMD using a specific conversion factor for each CT model [16]. As in previous studies, normal BMD was considered  $> 120 \text{ mg/cm}^3$ , osteopenic between 80 and  $120 \text{ mg/cm}^3$  and osteoporotic below  $80 \text{ mg/cm}^3$  [2].

Cage subsidence was assessed using standing lumbar spine radiographs and/or CT scans from the 6 to 12 month postoperative follow-up period. For instance of mutual availability, both examinations were reviewed. Cage subsidence was graded based on the Marchi et al. [8] classification as Grade 0: 0%–24% loss of postoperative disk height; Grade I: 25–49%; Grade II: 50–74% or Grade III: 75%–100%. Severe subsidence was defined as Grade II or III according to the original report [8]. Subsidence assessment was independently performed by two trained orthopedic residents in a blinded manner and was reviewed by a third independently trained physician in instances of disagreement.

### Surgical technique and implants

All patients underwent SA-LLIF at a single spine center performed by one of four fellowship-trained orthopedic spine surgeons with at least 5 years of experience using the mini-open single-incision technique. Surgery was performed by a mini-open single-incision technique according to the surgeon's preference. All patients were placed in a true lateral position, and a horizontal (for single level) or vertically oriented (for multilevel) skin incision was performed. Blunt dissection was carried out until reaching the vertebra body. Endplate preparation for fusion was done to preserve the osseous structure of the endplate, and cartilaginous endplates were removed using rasps and curettes. The appropriate cage size was determined based on the preoperative imaging in combination with intraoperative cage template findings. All cages in both groups were lordotic cages, and no parallel cages were used. Moreover, all cages were packed with either recombinant human bone morphogenetic protein-2 (rhBMP2), demineralized allograft fibers or both. The implants were positioned to span the apophyseal ring bilaterally. During the surgical procedure, intraoperative neuromonitoring was performed.

We defined the cage material categories as 1) a PEEK group that included pure PEEK and PEEK-based combined material cages, such as the Cougar (carbon fiber reinforced PEEK) cage, as well as 2) a Ti group that included 3D printed titanium cages. No conventional Ti cages were used in this study period. Hence, during the study period, two PEEK cage systems [XLIF (Nuvasive, Inc., San Diego, CA, the USA)] & the COUGAR system (Depuy Spine Inc., Raynham, MA, the USA) or two Ti cage systems [(Modulus

XLIF (Nuvasive, Inc., San Diego, CA, the USA)] & Lateral Spine Truss System (4WEB Medical, Inc., Frisco, TX, the USA) were utilized.

## Statistical analysis

Proportions were used for categorical variables to summarize the distributions. Comparisons between categorical variables were performed utilizing the Fisher exact test and comparisons between normally distributed continuous variables were performed using the Student t test or analysis of variance. The Mann–Whitney U test was used for the comparisons between non-normally distributed continuous variables. Weighted Kappa values were calculated for the reliability of subsidence assessment. To adjust for the influence of low bone mineral density on subsidence, we conducted a multivariable logistic regression analysis with generalized mixed models, setting severe subsidence (Grade II or III) as the outcome variable and included cage type (Ti vs PEEK), QCT-vBMD, cage height a priori and other significant and trending variables ( $p < 0.10$ ) in simple comparisons. Since the incidence of severe cage subsidence was low, we created another multivariable model including only cage material and vBMD as a sensitivity analysis. The statistical significance was set as  $p \leq 0.05$ .

## Results

### Patient demographics

The data of 173 patients who underwent primary SA-LLIF were reviewed. 52 had a follow-up of less than 6 months, 7 had planned anterior–posterior staged surgeries, and one was below the age of 18 years old. All patients had a preoperative CT within 6 months prior to surgery. This resulted in 113 patients (186 levels) who met our study inclusion criteria who underwent SA-LLIF using either 3D-printed novel Ti cages or PEEK cages.

The average duration between surgery and subsidence assessment imaging was 29.5 weeks, ranging from 24 to 57 weeks after the initial SA-LLIF (Ti  $29.0 \pm 6.4$ ; PEEK  $29.7 \pm 7.3$  weeks). In total, 51 female and 62 male patients were analyzed. The median [IQR] age at surgery was 60.0 [51.0–70.0] years. Of the 113 patients, 75 patients (119 levels) were treated using PEEK and 38 patients (67 levels) using Ti cages. The median [IQR] L1/L2 trabecular vBMD was 127.2 [99.5–150.5] mg/cm<sup>3</sup> and 65 patients (57.5%) were retrospectively classified as normal bone status and 48 patients (42.5%) as osteopenic or osteoporotic. Demographic characteristics are summarized in Table 1.

Regarding preoperative diagnoses, there were significantly more degenerative disk disease patients in the Ti

group. A summary of preoperative diagnoses is provided in Table 2.

### Cage type and fused levels

For both cage types, 21 patients (55.3%) in the Ti cage group and 36 patients (48.0%) in the PEEK cage group underwent a single-level procedure. Ti cages were used more frequently in upper-level surgeries such as L1/2 or L2/3 ( $p < 0.001$ ).

Operative characteristics are summarized in Table 3.

### Subsidence rate

Early subsidence was measured in each treated level using the Marchi et al. [8] classification. The subsidence assessment was conducted using radiographs in 50 (74.6%) levels in the Ti group and 88 (73.9%) levels in the PEEK group. CT was used for subsidence assessment in 0 (0.0%) levels in the Ti group and 2 (1.7%) levels in the PEEK group. Both CT and X-ray were used for subsidence evaluation in 17 (25.4%) levels in the Ti group and 29 (24.4%) levels in the PEEK group ( $p = 0.75$ ).

Weighted Kappa values of subsidence assessment were used to calculate reliability. The two-raters' reliability of subsidence grading was excellent with a weighted Kappa value of 0.948 (95% CI 0.908, 0.987). The distributions of the grading according to the Marchi's classification are shown in Table 4. According to our results, the overall subsidence rate for Grades 0–III was significantly less in the Ti versus the PEEK group ( $p = 0.003$ ). For severe subsidence (Grade II or III), Ti cages also demonstrated significantly less severe subsidence (3.0%) compared to PEEK cages (18.5%) ( $p = 0.002$ ).

In multivariate analysis, factors including cage material, QCT-vBMD, degenerative disk disease, cage height and all significant or trending ( $p < 0.10$ ) variables from our simple comparisons were included. According to the multivariable analysis results, patients treated with Ti cages were less likely to develop severe subsidence compared to those treated with PEEK (OR = 0.05, 95% CI = 0.01, 0.30) ( $p = 0.001$ ) (Table 5). The effect of Ti cage was the same in the sensitivity analysis ( $p = 0.001$ ).

## Discussion

To the authors' knowledge, this is the first study to investigate cage subsidence in novel 3D-printed Ti versus PEEK cages after standalone lateral lumbar interbody fusion. In our study, we demonstrated that the overall cage subsidence rate is significantly less in new generation Ti cages compared to PEEK.

**Table 1** Patient demographics

Variables	Total	Titanium	PEEK	<i>p</i> value
No. of Patients	113	38	75	
Median age at surgery [IQR]	60 [51.0–70.0]	59.5 [50.0–69.0]	60 [53.0–72.0]	0.506
<i>Gender</i>				
Males, <i>n</i> (%)	62 (54.9)	27 (71.1)	35 (46.7)	<b>0.017</b>
Females, <i>n</i> (%)	51 (45.1)	11 (28.9)	40 (53.3)	
<i>Race</i>				
White/Caucasian, <i>n</i> (%)	100 (88.5)	35 (92.1)	65 (87.8)	0.886
Black/African-American, <i>n</i> (%)	6 (5.3)	1 (2.6)	5 (6.8)	
Others, <i>n</i> (%)	6 (5.3)	2 (5.3)	4 (5.4)	
Unknown, <i>n</i> (%)	1 (0.9)	0 (0.0)	1 (100.0)	
Median body mass index (BMI) (kg/m <sup>2</sup> ), [IQR]	26.6 [24.0–30.5]	26.3 [24.5–30]	27.2 [22.9–30.7]	0.644
Median L1/L2 trabecular vBMD (mg/cm <sup>3</sup> ), [IQR]	127.2 [99.5–150.4]	127.8 [105.4–141.1]	127.2 [95.9–159.3]	0.932
<i>Bone status</i>				
Normal, <i>n</i> (%)	65 (57.5)	23 (35.4)	42 (64.6)	0.691
Osteopenic, <i>n</i> (%)	41 (36.3)	15 (36.6)	26 (63.4)	0.681
Osteoporotic, <i>n</i> (%)	7 (6.2)	0 (0.0)	7 (100.0)	0.093
<i>Smoking history</i>				
Never Smoked, <i>n</i> (%)	62 (54.9)	22 (57.9)	40 (53.3)	0.999
Former smoker, <i>n</i> (%)	43 (38.0)	13 (34.2)	30 (40.0)	
Current smoker, <i>n</i> (%)	8 (7.1)	3 (7.9)	5 (6.7)	
<i>Diabetes mellitus status</i>				
No Diabetes, <i>n</i> (%)	106 (93.8)	35 (92.1)	71 (94.7)	0.686
Diabetes mellitus, <i>n</i> (%)	7 (6.2)	3 (7.9)	4 (5.4)	

Significant variables in bold

**Table 2** Preoperative diagnosis; some cases had multiple diagnoses

Variables, <i>n</i> (%)	Titanium	PEEK	<i>p</i> value
Degenerative disk Disease	34 (89.5)	23 (31.1)	<b>&lt;0.001</b>
Spinal stenosis	31 (81.6)	52 (69.3)	0.184
Foraminal stenosis	23 (60.5)	47 (62.7)	0.840
Spondylolisthesis	33 (86.8)	53 (70.7)	0.065
Herniated disk	1 (2.6)	7 (9.3)	0.264
Neurogenic Claudication	3 (7.9)	2 (2.7)	0.333
Scoliosis	13 (34.2)	34 (45.3)	0.314

Significant variables in bold

A lack of disk height restoration due to cage subsidence can negatively affect patient outcomes [8, 17, 18]. Reportedly, multiple factors are involved in the pathophysiology of cage subsidence after interbody fusion. Besides patient and surgical factors such as endplate bone strength, cage size and intraoperative endplate injury, the material features of the cage are also important [2, 3, 7, 10, 13, 19].

Both PEEK and Ti are the most common materials used as interbody cages in lumbar fusion [11, 20]. PEEK has been

widely used as a spinal fusion implant material in the past decades because it has good mechanical and chemical properties [19, 21]. The material stiffness, described as Young's modulus (*E*), is the amount a specific material will deform under given stress. The *E* for PEEK is 1000–4000 MPa and more closely resembles the values of trabecular bone compared to other metal materials [10]. A finite element study also demonstrated that PEEK cages showed less stress on adjacent endplates, which is potentially beneficial for subsidence prevention [22]. Furthermore, PEEK allows for better assessment of fusion because of its radiolucent properties and is therefore a suitable implant for spinal fusion [19, 20, 23]. However, one main disadvantage of PEEK cages is their relatively low osseointegration properties due to a biofilm layer around the surface of the implant, which is known as the PEEK-halo effect [5, 20, 24]. Therefore, bone needs to grow around the cage in order to bind to the host bone [19].

Titanium is another commonly used material for interbody cages. Many studies showed that Ti implants have good bone-to-implant contact with osteoconductive properties. [19, 25, 26] In contrast to PEEK, however, Ti cages have a higher material stiffness (*E* 100,000 MPa) that causes a

**Table 3** Operative characteristics

Variables	Titanium	PEEK	<i>p</i> value
No. of Patients	38	75	
No. of Levels	67	119	
Levels treated, <i>n</i> (%)	38 (100)	75 (100)	<b>0.007</b>
1	21 (55.3)	36 (48.0)	
2	8 (21.0)	34 (45.3)	
3 or more	9 (23.7)	5 (6.7)	
Spinal levels, <i>n</i> (%)	67 (100)	119 (100)	
L1/L2	5 (7.5)	2 (1.7)	<b>&lt; 0.001</b>
L2/L3	11 (16.4)	11 (9.2)	<b>&lt; 0.001</b>
L3/L4	20 (29.8)	46 (38.7)	0.728
L4/L5	31 (46.3)	60 (50.4)	0.551
Cage height in mm, <i>n</i> (%)	67 (100)	119 (100)	0.093
8	13 (19.4)	31 (26.1)	
10	50 (74.6)	69 (58.0)	
12	4 (6.0)	17 (14.3)	
14	0 (0)	2 (1.6)	
Cage width in mm, <i>n</i> (%)	67 (100)	119 (100)	<b>&lt; 0.001</b>
18	0 (0)	9 (7.6)	
22	67 (100)	89 (74.8)	
26	0 (0)	21 (17.6)	
Cage length in mm, <i>n</i> (%)	67 (100)	119 (100)	0.244
40	0 (0.0)	1 (0.8)	
45	7 (10.4)	19 (16.0)	
50	20 (29.9)	41 (34.5)	
55	34 (50.7)	40 (33.6)	
60	6 (9.0)	17 (14.3)	
65	0 (0.0)	1 (0.8)	

Significant variables in bold

**Table 4** Incidence of cage subsidence

		Titanium	PEEK	<i>p</i> value
Subsidence grade	Number of levels	67	119	
0	<i>n</i> (%)	59 (88.1)	77 (64.7)	<b>0.003</b>
I	<i>n</i> (%)	6 (9.0)	20 (16.8)	
II	<i>n</i> (%)	1 (1.5)	15 (12.6)	
III	<i>n</i> (%)	1 (1.5)	7 (5.9)	
Severe subsidence	<i>n</i> (%)	2 (3.0)	22 (18.5)	<b>0.002</b>

Significant variables in bold

stress-shielding effect. The bone–implant interaction plays a significant role because changes in the bone are affected by the material stiffness of the implant. Consequently, in order to minimize negative bone changes, the material stiffness of a given implant should be close or similar to physiological stiffness [10, 27, 28].

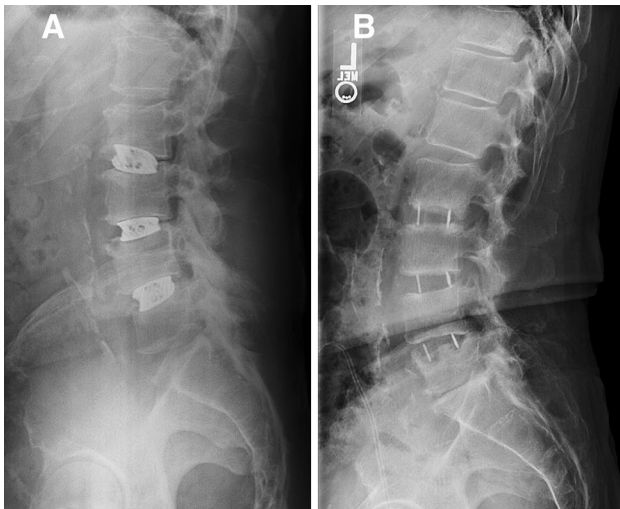
**Table 5** Results of multivariate analysis for severe subsidence

Factors	Odds Ratio (95% CI)	<i>p</i> value
Gender		
Female	Reference	0.530
Male	0.72 (0.26, 2.03)	
Average QCT-vBMD	0.99 (0.97, 1.00)	<b>0.050</b>
Degenerative disk disease		
No	Reference	<b>0.034</b>
Yes	3.73 (1.11, 12.62)	
Spondylolisthesis		
No	Reference	0.375
Yes	1.89 (0.46, 7.86)	
Number of levels treated		
1	Reference	0.764
2	1.11 (0.23, 5.45)	
3	2.42 (0.22, 26.72)	
Spinal level		
L1/L2	7.59 (0.31, 185.66)	0.764
L2/L3	7.95 (0.51, 123.08)	
L3/L4	6.06 (0.50, 73.87)	
L4/L5	Reference	
Cage height	1.13 (0.85, 1.51)	0.404
Cage width	0.99 (0.97, 1.00)	0.183
Material		
PEEK	Reference	<b>0.001</b>
Titanium	0.05 (0.01, 0.30)	

Significant variables in bold

To overcome these drawbacks, the novel 3D-printed Ti cages with porous architecture were created. The fully interconnected porous architecture of the Ti cage decreases the material stiffness from an *E* of 100,000 MPa to *E* 2,500 MPa. While this *E* value is still slightly higher than that of PEEK, it is closer to that of human bone [27]. A recent biomechanical study showed that cages with a porous architecture had considerably less stress at the bone–hardware interface [10]. Other laboratory studies also demonstrated that porous architecture of cages had more bone-to-implant contact surface, made the cages more osteoconductive and increased the compressive shear strength under physical force compared to non-porous cages [11, 29, 30]. Furthermore, due to increased friction created by the porous surface, the cage has improved stability from greater cell adhesion that leads to bony on-/in-growth [11, 31].

In general, there are a limited number of clinical studies investigating cage subsidence in the new Ti cages using the LLIF approach. Campbell et al. [5] investigated the results of LLIF with additional posterior instrumentation using new Ti versus PEEK cages. In their work, Ti cages showed a significantly less overall subsidence rate compared to PEEK cages at 8 to 12 weeks and at 12-month follow-up. The high-grade



**Fig. 1** Cage subsidence examples; **a** titanium cage multilevel SA-LLIF (L2/L3 Grade III, L3/L4 Grade 0, L4/L5 Grade 0); **b** PEEK cage multilevel SA-LLIF (L2/L3 Grade 0, L3/L4 Grade 0, L4/L5 Grade III)

subsidence rate at the latest follow-up was 2.2% for Ti compared to 20.4% for PEEK cages in their study [5]. Regarding SA-LLIF, there is only one study that investigated cage subsidence of the novel Ti cages [9]. The researchers conducted a single-arm study without a control group using the new Ti cage in 29 patient treated with either SA-LLIF or LLIF plus posterior pedicle screw fixation and compared their results to historical results of LLIF with PEEK cages. The authors showed that the rate of cage subsidence using new Ti cages was 3.4% per implant, which was lower than previously reported PEEK implant subsidence rates that ranged from 10.0 to 16.1% [9]. Similar to the previous study results, our results suggest that new 3D-printed Ti cages show lower rates of early cage subsidence after SA-LLIF compared to PEEK cages (3.0% compared to 18.5%). Considering higher subsidence rates being reported in SA-LLIF cases, new Ti cages might be more beneficial in this patient population.

A very recently published meta-analysis comparing clinical outcomes between PEEK and Ti cages, however, demonstrated opposite results. Ti cages were associated with a higher subsidence rate. In the meta-analysis, the authors collected articles published by 2018. However, all Ti cages used in the studies were conventional titanium cages and not 3D-printed novel ones. Additionally, there were no LLIF studies included in the meta-analysis. These factors might explain the discrepancy and also highlight the potential benefit of 3D printed Ti cages shown in our study [14].

There are several limitations in this study. First, this is a retrospective study with a relatively small sample size at a single center. Consequently, there might have been

unmeasured factors that led to selection bias for implant usage despite multivariate adjustment. Furthermore, we limited the inclusion criteria to patients without previous fusion. Thus, it is still unknown if our results can be applied in revision fusion cases such as in patients with adjacent segment disease. Moreover, this study only focused on the early postoperative cage subsidence and other outcomes such as long-term fusion rates were not examined. Furthermore, long-term follow-up studies to assess subsidence were not available in all cases since postoperative imaging for fusion was not standardized among surgeons. However, recent studies demonstrated that most subsidence occurred within 6 months [8, 32, 33], and longer-term follow-up might be unnecessary for subsidence assessment. Additionally, we utilized Marchi et al.'s classification which is based on the size of intervertebral disk space and did not include absolute values of subsidence. Thus, care must be taken to compare our study results to other subsidence studies. Although there were no significant differences in the distribution in modalities used for subsidence assessments between the Ti and PEEK groups, the overall incidence of subsidence in both groups might have been over- or under-estimated compared to assessments using radiographs or CT only. Additionally, due to the small study sample size and relatively low incidence of severe subsidence, especially in Ti group, we could not conduct subgroup analyses such as comparisons between single-level procedures. In addition, other cage materials such as titanium-coated PEEK cages were not taken into consideration in this study. Lastly, our study did not assess patient satisfaction or patient-reported outcome measures. These issues should be addressed in future studies.

## Conclusion

Our study demonstrated that 3D-printed novel Ti cages had a significantly lower early subsidence rate compared to PEEK cages in standalone LLIF patients.

**Authors' contribution** DAA performed all measurements and grading, collected all the data and wrote the manuscript. IO analyzed the data and reviewed and edited the manuscript. LO help validating the grade of subsidence and reviewed and edited the manuscript. EC reviewed and edited the manuscript. JZ analyzed the data. JS wrote the research plan for IRB approval and was in charge of the clinical research process and the project administration. AAS designed the study and reviewed and edited the manuscript. FPC designed the study and reviewed and edited the manuscript. FPG designed the study and reviewed and edited the manuscript. APH designed the study, reviewed and edited the manuscript and supervised all aspects of the study. All authors have read and approved the final submitted manuscript.

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**Code availability** N/A.

**Availability of data and material** The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

**Conflict of interest** DAA, IO, LO, JZ, EC, JS have no relevant financial or non-financial interests to disclose. AAS declares financial interests: Royalties: Ortho Development Corp; Private investments: Vestia Ventures MiRUS Investment LLC, ISPH II LLC, ISPH 3 LLC, VBros Venture Partners X Centinel Spine; Consulting: Clariance Inc, Kuros Bioscience AG, Medical Device Business Services Inc.; Speaking and Teaching Arrangements: DePuy Synthes Products Inc.; Trips/Travel: Medical Device Business Services Inc; Research Support: Spinal Kinetics Inc. FPC declares financial interests: Royalties: NuVasive Inc; Private investments: Bonovo Orthopedics Inc, Healthpoint Capital Partners LP, ISPH II LLC, Ivy Healthcare Capital Partners LLC, Medical Device Partners II LLC, Medical Device Partners III LLC, Orthobond Corporation, Spine Biopharma LLC, Tissue Differentiation Intelligence LLC, VBVP VI LLC, Woven Orthopedics Technologies; Consulting: 4Web Medical/4Web Inc, Spine Biopharma LLC, Research Support: 4Web Medical/4Web Inc, Beatrice & Samuel A. Seaver Foundation; Non-financial interests: Scientific Advisory Board: Healthpoint Capital Partners LP, Orthobond Corporation, Spine Biopharma LLC, Woven Orthopedic Technologies. FPG declares financial interests: Royalties: NuVasive Inc, Ortho Development Corp, Zimmer Biomet Holdings INC; Stock Ownership: Bonovo Orthopedics Inc, Liventa Bioscience (AF Cell Medical), Paradigm Spine LLC, Healthpoint Capital Partners LP, Alphatec Holdings LLC, LANX Inc, Centinel Spine Inc (fka Raymedica LLC), Tissue Differentiation Intelligence LLC, Spine Kinetics Inc; Consulting: DePuy Synthes Spine, NuVasive Inc, Non-financial interests: Consulting: EIT Emerging Implant Technologies, Spineart USA Inc, Ethicon Inc., APH declares financial interests: Research Support: 4Web Medical; Fellowship Support: NuVasive Inc, Kuros Bioscience B.V. (Fig. 1)

Ethics approval, Consent to participate and Consent for publication This study was approved by our hospital's Institutional Review Board, and informed consent was waived due to the retrospective nature of this study. (IRB# 2014–097).

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