Clinical and Cost-Effectiveness of Lumbar Interbody Fusion Using Tritanium Posterolateral Cage (vs. Propensity-Matched Cohort of PEEK Cage)

Inamullah Khan[1], Scott L. Parker[2], Hansen Bow[2], Ahilan Sivaganesan[2], Jacquelyn S. Pennings[1], Byron F. Stephens II[1], Anthony M. Steinle[1], Rishabh Gupta[1)2)4)] and Clinton J. Devin[1)3)]

1) Department of Orthopaedic Surgery, Vanderbilt University Medical Center, Nashville, United States
2) Department of Neurological Surgery, Vanderbilt University Medical Center, Nashville, United States
3) Steamboat Orthopaedic and Spine Institute, Steamboat Springs, United States
4) University of Minnesota Medical School, Minneapolis, United States

Abstract:

Introduction: Surgical management of degenerative lumbar spine disorders is effective at improving patient pain, disability, and quality of life; however, obtaining a durable posterolateral fusion after decompression remains a challenge. Interbody fusion technologies are viable means of improving fusion rates in the lumbar spine, specifically various graft materials including autograft, structural allograft, titanium, and polyether ether ketone. This study assesses the effectiveness of Tritanium posterolateral cage in the treatment of degenerative disk disease.

Methods: Nearest-neighbor 1:1 matched control transforaminal lumbar interbody fusion with PEEK vs. Tritanium posterior lumbar (PL) cage interbody fusion patients were identified using propensity scoring from patients that underwent elective surgery for degenerative disk diseases. Line graphs were generated to compare the trajectories of improvement in patient-reported outcomes (PROs) from baseline to 3 and 12 months postoperatively. The nominal data were compared via the χ^2 test, while the continuous data were compared via Student's t-test.

Results: The two groups had no difference regarding either the 3- or 12-month Euro-Qol-5D (EQ-5D), numeric rating scale (NRS) leg pain, and NRS back pain; however, the Tritanium interbody cage group had better Oswestry Disability Index (ODI) scores compared to the control group of the PEEK interbody cage at both 3 and 12 months (p=0.013 and 0.048).

Conclusions: Our results indicate the Tritanium cage is an effective alternative to the previously used PEEK cage in terms of PROs, surgical safety, and radiological parameters of surgical success. The Tritanium cohort showed better ODI scores, higher fusion rates, lower subsidence, and lower indirect costs associated with surgical management, when compared to the propensity-matched PEEK cohort.

Keywords:

Degenerative lumbar disease, Interbody cage, Interbody fusion, Posterolateral fusion, Spine

Spine Surg Relat Res 2022; 6(6): 671-680
dx.doi.org/10.22603/ssrr.2021-0252

Introduction

Low back pain (LBP) is a highly prevalent and disabling condition that is associated with significant healthcare costs in the United States[1-3]. Although many patients with low back and leg pain are successfully medically managed, as many as 300,000 patients per year require surgery for medically refractory back and leg pain[4]. Over the past two decades, there has been a 300% increase in the number of spinal surgeries performed and a greater increase in the incidence and prevalence of degenerative spinal disorders[5-7]. Surgical management of degenerative spinal disorders has proven to be effective at improving patient pain, disability, and, quality of life[8,9]; however, obtaining a durable posterolateral fusion after decompression of neural elements remains a challenge[10-12].

Interbody fusion technologies have emerged as a viable means of improving fusion rates in the lumbar spine includ-

Corresponding author: Byron F. Stephens II, byron.stephens@vumc.org
Received: December 14, 2021, Accepted: February 5, 2022, Advance Publication: April 12, 2022

ing various graft materials such as autograft, structural allograft, titanium, and polyether ether ketone (PEEK)[13-16]. Each material has its own pros and cons for use, with potential complications including pseudarthrosis, subsidence, and graft dislodgement[17-20]. Furthermore, the risk of such complications is increased in patients with challenging fusion environments including advanced age, osteoporosis, pseudarthrosis, obesity, and smoking history[21]. Off-label use of recombinant human bone morphogenetic protein-2 (rhBMP-2) to increase fusion rates in posterior interbody fusion procedures can be associated with increased complications such as heterotopic ossification, radiculitis, and endplate osteolysis with interbody subsidence and increased healthcare cost[22]. New interbody technologies are being introduced with the goal of improved fusion rates, decreased complications, and improved cost-effectiveness. The Tritanium PL cage (Stryker) is manufactured with 3D printing using titanium alloy (Ti-6Al-4V) and has a porous structure featuring the Tritanium In-Growth Technology. The cage's In-Growth Technology demonstrates that osteoblasts infiltrate via capillary action and attach to and proliferate on the porous Tritanium material[23]. In addition, the porous Tritanium material has a modulus of elasticity of 6.2 MPa that falls in between the modulus of elasticity for cancellous (0.14 GPa) and cortical bone (15 GPa)—the two types of bones that constitute the vertebral body[24]. On the other hand, without the porous 3D-printed structure, a block of pure titanium alloy (Ti-6Al-4V) has modulus of elasticity of 117 GPa. Navarrete et al. examined differences in cellular response to variations in surface roughness for titanium alloys and found that roughened titanium alloy demonstrates an increase in osteoblast differentiation and a reduction in osteoclastic activity[25]. The authors also reported that the osteogenic-angiogenic responses were higher for titanium alloy than for PEEK and the roughened titanium alloy surfaces demonstrated increased levels of bone morphogenetic factors, producing an osteogenic environment that may further enhance bony fusion[26-29]. In the present-day literature, there is no direct comparison of porous titanium cages to PEEK in the treatment of degenerative lumbar disk diseases.

We hypothesize that use of a Tritanium PL cage will result in improved fusion rates, which may then translate into greater durability in postoperative improvement of pain, disability, and quality of life improvement postoperatively, decreased total disease-specific healthcare expenditure, and improved cost-effectiveness of lumbar interbody fusion procedures. The results of this study will allow for a real-world assessment of quality and effectiveness for the Tritanium PL cage in the treatment of degenerative disk disease at one or two contiguous levels from L2 to S1.

Materials and Methods

Patient selection

An institutional research board waiver was granted for this study (100388). All patients undergoing elective spine surgery for lumbar degenerative diseases at a single medical center over a period from November 2010 to April 2019 were enrolled into a prospective longitudinal registry. This included the historical PEEK cohort that spanned from the beginning of the enrollment period to the end date, whereas the Tritanium patients were included from the commercial launch in 2015 (Tritanium PL cages) to the end of enrollment in April 2019. The PEEK cages used in the study included the Capstone PEEK cage by Medtronic and the AVS TL PEEK cage by Stryker. The primary inclusion criteria for this study were as follows: (1) patients that underwent lumbar interbody fusion at one or two contiguous levels using either PEEK or Tritanium PL interbody cages, (2) mechanical back pain (defined as pain arising from the spine, interverbal disks, or surrounding soft tissue) with or without neurogenic claudication/leg pain, (3) failure of at least 6 months of conservative therapy, and (4) an age of ≥18 years. Patients were excluded if they had (1) an extraspinal cause of back pain or sciatica, (2) had any pre-existing spinal pathology (infection, trauma, or tumor), (3) had previous interbody fusion surgeries with pseudarthrosis, or (4) were unwilling or unable to participate with follow-up procedures.

Surgical safety, patient-reported outcomes, fusion, and subsidence

Patient demographics, disease characteristics, treatment variables, surgical details, and all 90-day surgical morbidity were assessed for each case and entered into a Web-based portal Research Electronic Data Capture (REDCap)[30]. Baseline and 3- and 12-month patient-reported outcomes (PROs) including Oswestry Disability Index (ODI)[31], numeric rating scale (NRS) for LBP and leg pain (LP)[32], European Quality of Life-5 Dimensions (EQ-5D)[33], and return to work were prospectively assessed via email, telephone interview, or in-person during the follow-up clinic visit. In addition, an independent data coordinator reviewed the patients' electronic medical record for the assessment of surgery-related readmission or return to operating room, where any missing follow-up records were supplemented by patient interviews.

As the standard of care for surgical spine fusion, routine imaging is performed within the first postsurgical year to assess intact surgical constructs and fusion. Flexion and extension X-ray images were assessed for both groups to identify intact lumbar fusion constructs and subsidence of the interbody cages[34]. Fusion was considered successful if the following criteria were met: (1) there was less than 5 mm of interspinous motion between the flexion and extension radiographs and (2) angular motion was less than 3 to 5° between flexion and extension radiographs[34]. Interspinous motion for the lumbar level of interest was measured using change (in millimeters) in interspinous process distance between flexion and extension lumbar radiographs. The most identifiable landmark near the tip of the spinous process was used to keep measurements consistent (Fig. 1). Angular motion was defined as the angular change between flexion and

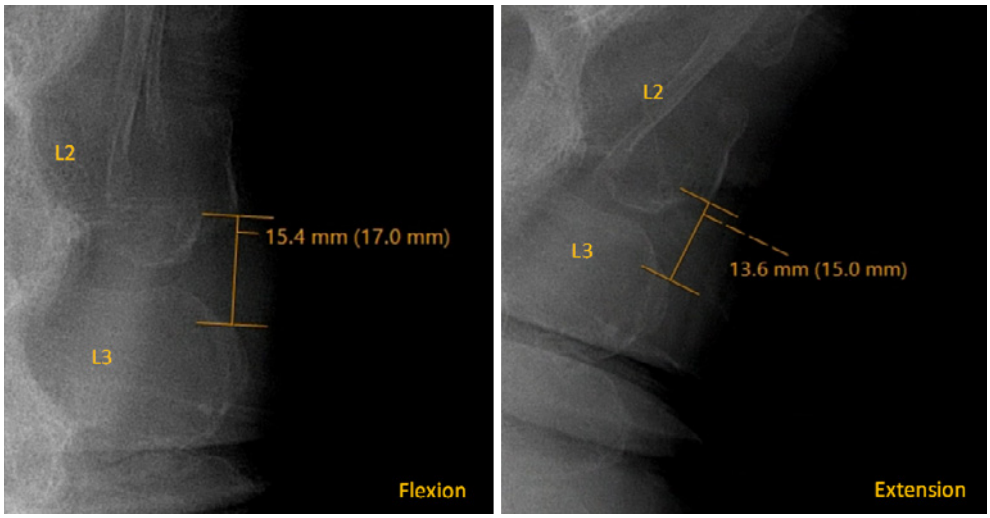


Figure 1. Flexion-extension radiographs for a patient who underwent lumbar fusion at the L2-L3 levels. Interspinous motion is 1.8 mm.

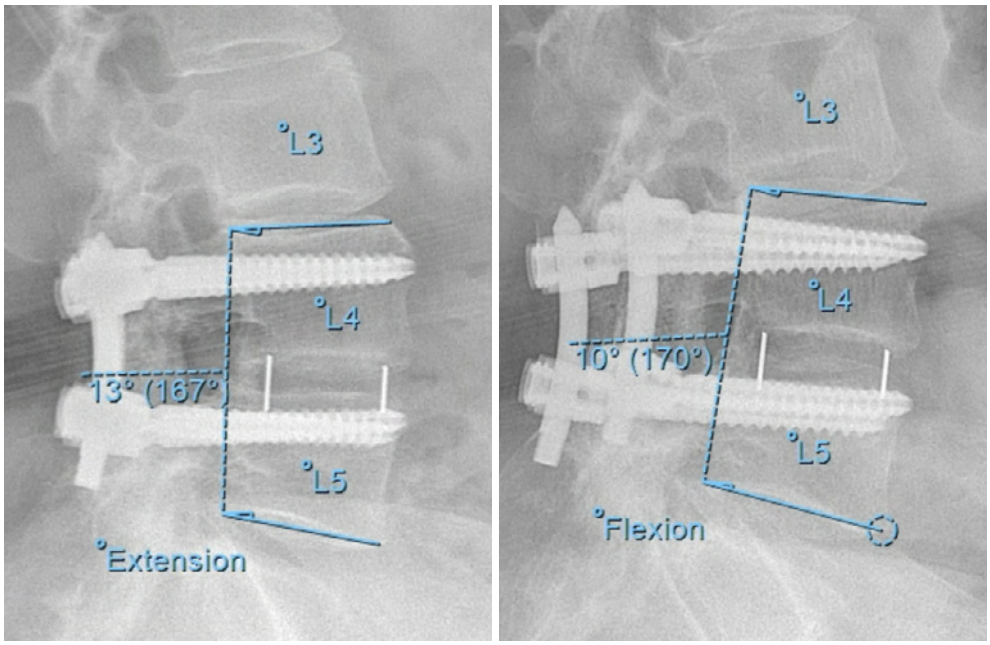


Figure 2. Lateral flexion and extension radiographs of the lumbar spine demonstrating angular motion. Across the L4-5 interspace, angular motion measures 3^0.

extension radiographs for the level of interest (Fig. 2). Subsidence was graded as the percentage of disk 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[35].

Cost data

Cost data for the study patients were retrieved from the hospital discharge and billing records for inpatient hospital stay and surgery. The direct (hospital's) and indirect (societal perspective) costs were calculated. The surgeon's professional fee was derived on the basis of Medicare payment amounts using the resource-based relative value scale, and the hospital costs were derived using the diagnosis-related group codes. Indirect costs included patient or family member's workday losses and cost of caregiver, when applied. The standard capital approach was used to estimate costs by multiplying the change in hours of work by gross-of-tax wage rate (based on the wages reported by patients at enrollment). These calculations for costs have been validated in previous studies[36-39].

Statistical analysis

Nearest-neighbor 1:1 matched control transforaminal lumbar interbody fusion (TLIF) with PEEK vs. Tritanium PL cage interbody fusion surgery patients were identified using propensity scoring from the cohort of patients that under-

went elective lumbar spine surgery for degenerative lumbar disk diseases. In the propensity-matched score generation, we adjusted for patient-specific variables of age, gender, body mass index (BMI), race, smoking status, employment, insurance status, history of comorbidities, motor deficit, ambulatory ability, and surgery-specific variable of revision surgeries and the baseline PRO scores. Frequencies for categorical variables and mean (standard deviation) for continuous variables were calculated. Line graphs were generated to compare the trajectories of improvement in the PROs from baseline to 3 and 12 months postoperatively. Horizontal bar graphs were used to plot the proportion of intact fusion and the incidence of subsidence for the two groups. The nominal data were compared via the χ^2 test, and the two-way repeated measures ANOVA test was used to compare the continuous data. A P value <0.05 was considered statistically significant. The analysis was conducted with SPSS, version 23 (IBM Corp., Armonk, New York, USA).

Results

Patient demographics

A total of 228 patients who underwent elective lumbar interbody fusion surgery for degenerative disk diseases and had completed 12-month follow-up were included in the study (Table 1). The completion rate for 12-month follow-up rate was recorded at 81%. The mean age for the 135 female and 93 male patients was 63.52±9.39 years. Preoperatively, approximately 70% (n=159) were ambulatory without any assistance and 29% (n=66) needed device assistance for ambulation, whereas 1% (n=2) were non-ambulatory. The mean BMI of the cohort was 32.71±6.96 kg/m^2. The PEEK cohort had higher proportion of patients with longer duration of symptoms (p=0.007) and had higher mean number of involved vertebrae (2.68 vs. 1.92, p=0.029) compared to the Tritanium cohort. In addition, the PEEK cohort had higher PHQ-9 scores compared to the Tritanium cohort (10.67 vs. 6.26, p<0.001). Twenty percent (n=45) of patients underwent revision surgery for previous discectomy or decompression surgery.

Patient-reported outcomes, surgical safety, fusion, and subsidence

In light of the propensity score matching, there was no significant statistical difference in the baseline PRO scores for the two groups of PEEK and Tritanium interbody cages. On average, patients in both groups improved regarding the PROs from baseline to 3- and 12-month scores in a statistically significant manner (Fig. 3). The two groups had no difference regarding either the 3- or 12-month EQ-5D (p= 0.288 and 0.450), NRS-LP (p=0.619 and 0.965), and NRS-BP (p=0.549 and 0.743); however, the Tritanium interbody cage group had better ODI scores compared to the control group of the PEEK interbody cage at both 3 and 12 months (p=0.013 and 0.048) (Table 2).

A lower proportion of patients were discharged to facility in the Tritanium interbody cage group compared to the PEEK group (9% vs. 20% [p=0.014]). However, there was no statistical difference in the readmissions or return to operating room for the two cohorts (Table 3).

Of 228 patients, 200 had radiological follow-up within the first year of the lumbar interbody fusion surgery. On review of the radiological images and electronic medical records, intact fusion of the surgical levels with no complications was seen in 90% of the Tritanium cohort, whereas a statistically significant lower proportion of patients had intact fusion in the control group of the PEEK interbody cage (73%, p=0.003) (Fig. 4). The images revealed around 40% incidences of subsidence of the cages in the PEEK cohort, while only 23.5% incidences of subsidence of the cage were identified in the Tritanium cohort (p=0.010).

Return to work and cost analysis

There was no statistical difference in the return to work for the two groups, and 90% (n=64) of the preoperatively employed patients (n=71) returned to work at 3 months postoperatively (Table 4). The direct cost of surgery and episode of care had no statistical difference (p=0.950); however, the indirect costs for healthcare resource utilizations were higher for the PEEK group than for the Tritanium group (p=0.006) (Table 5).

Discussion

In this study, we used prospectively collected data from a single institute to compare the surgical safety, PROs, cost, and radiological outcomes for two different types of lumbar interbody cages: PEEK and Tritanium. This is the first study of its nature to compare such outcomes for the two cages in propensity-matched cohorts. Our results identified that the Tritanium cage had better results regarding improvement in ODI score, lower discharge rates to facility, lower indirect cost, higher postoperative fusion, and lower rates of subsidence; however, no differences were identified in the EQ-5D, NRS-BP/LP, postoperative readmissions/return to operating room, and return to work.

In this study, there was no difference in the quality of life scores at both 3- and 12-month follow-up between the two groups. Cuzzocrea et al. demonstrated a similar trend in the quality of life scores comparing metallic cages to PEEK cages[40]. In a very similar manner, there was no difference in either the 3- or 12-month axial or extremity pain scores. However, the Tritanium cage patients had improved both the 3- and 12-month ODI scores compared to the PEEK cage. Cabraja et al. compared the cervical fusions and clinical outcomes in PEEK and solid titanium cages and identified that there were no differences in the disability or pain scores[41]. Arts et al. compared porous titanium 3D-printed cages used in cervical fusions and identified no difference in the disability or pain scores at 1-year postsurgery[42]. Titanium cages have shown comparable results in terms of pain scores, early

Table 1. Patient Characteristics.

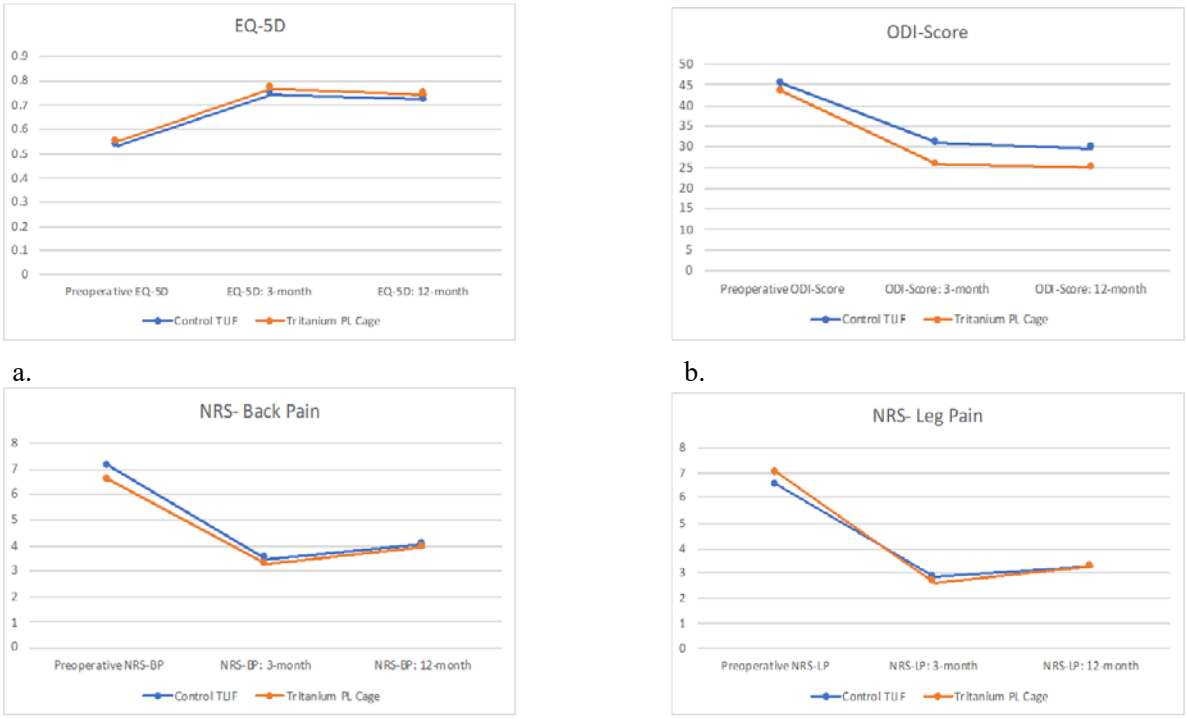
		Total (228) N (%)	Control TLIF (PEEK) (114)	Tritanium PL cage (114)	P value
Age		63.52±9.39	63.99±8.95	63.05±9.83	0.452
Gender	Female	135 (59.2%)	72 (63.2%)	63 (55.3%)	0.225
	Male	93 (40.8%)	42 (36.8%)	51 (44.7%)	
Race	African American	29 (12.7%)	17 (14.9%)	12 (10.5%)	0.502
	Caucasian	196 (86.0%)	95 (83.3%)	101 (88.6%)	
	Other	3 (1.3%)	2 (1.8%)	1 (0.9%)	
Currently employed		71 (31.1%)	32 (28.1%)	39 (34.2%)	0.317
Ambulatory preoperatively	Non-ambulatory	2 (0.9%)	2 (1.8%)	0 (0.0%)	0.111
	With assistance	66 (28.9%)	28 (24.6%)	38 (33.3%)	
	Without assistance	159 (69.7%)	84 (73.7%)	75 (65.8%)	
Duration of symptoms	<3 months	10 (4.4%)	2 (1.8%)	8 (7.0%)	0.007*
	3–12 months	58 (25.4%)	22 (19.3%)	36 (31.6%)	
	>12 months	160 (70.2%)	90 (78.9%)	70 (61.4%)	
Current smoker		22 (9.65%)	14 (12.28%)	8 (7.02%)	0.178
Any narcotic use		101 (44.30%)	58 (50.88%)	43 (37.72%)	0.046
Insurance payer	Medicare/Medicaid	123 (53.9%)	62 (54.4%)	61 (53.5%)	0.283
	Private	82 (36.0%)	41 (36.0%)	41 (36.0%)	
	Uninsured/indigent	3 (1.3%)	3 (2.6%)	0 (0.0%)	
	VA/government	20 (8.8%)	8 (7.0%)	12 (10.5%)	
Neurogenic claudication		43 (18.9%)	26 (22.8%)	17 (14.9%)	0.128
Motor deficits		49 (21.5%)	24 (21.1%)	25 (21.9%)	0.872
Primary/revision Surgery	Primary	183 (80.3%)	96 (84.2%)	87 (76.3%)	0.134
	Revision	45 (19.7%)	18 (15.8%)	27 (23.7%)	
Primary diagnosis	Deformity/scoliosis	30 (13.2%)	21 (18.4%)	9 (7.9%)	0.091
	Herniated disc	22 (9.6%)	10 (8.8%)	12 (10.5%)	
	Spondylolisthesis	121 (53.1%)	60 (52.6%)	61 (53.5%)	
	Stenosis	55 (24.1%)	23 (20.2%)	32 (28.1%)	
BMI		32.71±6.96	33.04±7.31	32.37±6.61	0.469
Number of Levels Involved		2.30±2.64	2.68±3.14	1.92±1.96	0.029*
PHQ9		8.49±6.30	10.67±6.61	6.26±5.12	<0.001*
ASA grade (>2)		191 (83.77%)	96 (84.21%)	95 (83.33%)	0.857
History of CAD		45 (19.7%)	27 (23.7%)	18 (15.8%)	0.134
History of hypertension (HTN)		163 (71.5%)	82 (71.9%)	81 (71.1%)	0.883
History of COPD		9 (3.9%)	6 (5.3%)	3 (2.6%)	0.308
History of arthritis		168 (73.7%)	88 (77.2%)	80 (70.2%)	0.229
History of diabetes		58 (25.4%)	30 (26.3%)	28 (24.6%)	0.761
History of osteoporosis		7 (3.1%)	4 (3.5%)	3 (2.6%)	0.701

mean±SD *for continuous variables and n (%) for categorical variables*

ASA, American Society of Anesthesiology grade; BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease

1:2 Nearest-neighbor match by age, gender, race, insurance, employment status, ambulation, BMI, diabetes, smoking status, motor deficits, revision surgery, and baseline ODI score

**P values <0.05 indicate a significant difference*



***** 1:2 Nearest-neighbor match by age, gender, race, insurance, employment status, ambulation, BMI, diabetes, smoking status, motor deficits, revision surgery, and baseline ODI score*

Figure 3. (a-d) Change in PRO scores for patients in Tritanium PL cage and TLIF control group (PEEK) over follow-up time points.

Table 2. Patient-reported Outcomes at the 3- and 12-month Follow-up Time Points.

	Total	Control TLIF	Tritanium PL cage	P value
Preoperative EQ-5D	0.541±0.199	0.532±0.206	0.549±0.193	0.521
EQ-5D: 3-month	0.755±0.170	0.743±0.166	0.767±0.174	0.288
EQ-5D: 12-month	0.733±0.199	0.723±0.207	0.743±0.192	0.450
Preoperative ODI score	44.29±12.96	45.16±12.79	43.41±13.11	0.309
ODI score: 3-month	28.28±16.05	30.97±15.95	25.69±15.78	0.013*
ODI score: 12-month	27.26±17.60	29.56±17.74	24.96±17.23	0.048*
Preoperative NRS-LP	6.75±2.74	6.50±2.96	6.99±2.48	0.177
NRS-LP: 3-month	2.73±3.18	2.84±3.14	2.63±3.23	0.619
NRS-LP: 12-month	3.26±3.41	3.25±3.53	3.27±3.29	0.965
Preoperative NRS-BP	6.85±2.38	7.11±2.26	6.59±2.47	0.099
NRS-BP: 3-month	3.36±2.51	3.46±2.49	3.26±2.54	0.549
NRS-BP: 12-month	3.98±2.75	4.04±2.75	3.92±2.77	0.743

mean±SD for continuous variables and n (%) for categorical variables

EQ-5D, European Quality of Life-5 Dimensions; ODI, Oswestry Disability Index; NRS, numeric rating scale; LP, leg pain; BP, back pain

1:2 Nearest-neighbor match by age, gender, race, insurance, employment status, ambulation, BMI, diabetes, smoking status, motor deficits, revision surgery, and baseline ODI score

**P values <0.05 indicate a significant difference*

or late complications when used in surgical management of thoracolumbar spine fractures[43]. PHQ-9 and ODI scores were significantly greater in the PEEK cohort. These two scores have a moderate correlation, with higher depression scores resulting in worse ODI scores[44]. Risk factors for depression include poor social support and significant life changes, such as moving[45]. The PEEK cohort had a higher rate of patients being discharged to a facility. This could have weakened social support for patients and created additional stress, leading to increasing rates of depression that then negatively impacted ODI scores[45].

The primary goal of the lumbar interbody fusion is to

Table 3. 90-day Morbidity (N=228).

	Total N (%)	Control TLIF (PEEK) (114)	Tritanium PL cage (114)	P value
Discharge to facility	33	23 (20.18%)	10 (8.77%)	0.014*
Readmission	14	9 (7.9%)	5 (4.39%)	0.270
Reasons for readmission				
Wound dehiscence/surgical site infection		2		
Pain			2	
Medication related			1	
Hardware revision		2	1 (trauma related)	
New neurologic deficits		1		
Medical (unrelated to spine)		4	1	
Return to OR	6	4 (3.50%)	2 (1.75%)	0.369
Reasons for return to OR				
Infection (SSI)		1		
Wound related		1	1	
Hardware related		2	1	

P value: Chi-square/exact test

SSI, surgical site infection

**P values <0.05 indicate a significant difference*

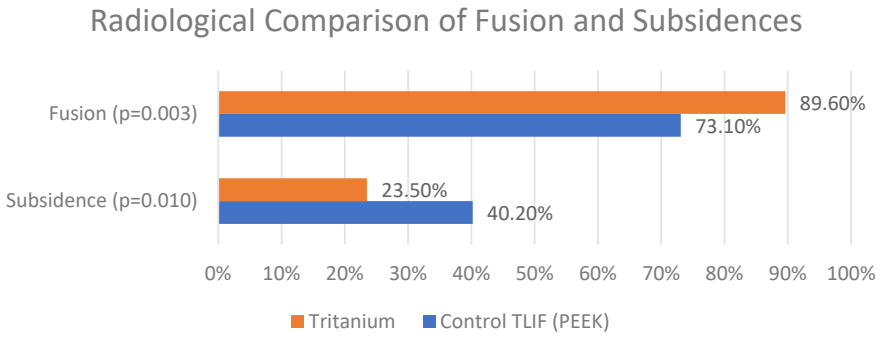


Figure 4. Comparing the radiological fusions and subsidence in the two groups.

Table 4. Return to Work.

	Total N (%)	Tritanium PL cage	Control TLIF (PEEK)	P value
Employed preoperatively	71 (31.1%)	39 (34.2%)	32 (28.1%)	0.317
Return to work	64 (90.14%)	36 (92.3%)	28 (87.5%)	0.499

Table 5. The Average Cost of Surgery and Indirect Cost during 1-year after Surgery.

	Tritanium PL cage	Control TLIF (PEEK)	P value
Cost of surgery	29,194.90±12,130.14	29,291.43±11,057.83	0.950
Indirect cost	2,474.26±2,574.31	3,706.84±4,020.52	0.006*

**P values <0.05 indicate a significant difference*

achieve union of the involved vertebral bones. The Tritanium cohort in our study had higher proportion of patients who achieved successful fusion compared to the PEEK cage. McGilvray et al. identified similar superiority in the rates of fusion and bone in-growth profile for the 3D-printed porous titanium cages in their ovine lumbar fusion model compared to PEEK cages[46]. Previous studies have reported inconclusive results regarding successful vertebral fusion with PEEK cages compared to titanium alloy[41,47]; however, we believe that the inconsistency can be explained by the

fact that the authors assessed solid titanium cages of non-porous structure. In a cervical prospective controlled trial, Nemoto et al. identified no difference in the fusion rates at 1-year postoperative images for the porous 3D-printed titanium compared to PEEK cages[42].

The literature identifies varying rates of subsidence for lumbar interbody fusion ranging from 8% to 32% for different types of interbody graft materials[35,48-51]. In our cohort, we observed an overall subsidence rate of 32.1% and the Tritanium cage had lower incidence of subsidence compared to the PEEK cage. Previously, metallic cages have been associated with higher rates of subsidence[52], which can be attributed to the higher modulus of elasticity of the solid metallic implant[53]. However, the porous 3D-printed technology reduces the modulus of elasticity of the titanium alloy, bringing it closer to that of the constituent bones of the vertebral body. Hence, the subsidence rates were lower in our cohort than in previous reports that used solid titanium cages. Zachary et al. reported a higher correlation between subsidence and a need for revision surgery[50]; even though the PEEK cages had higher incidences of subsidence, we did not observe any difference in the return to operating room during the 1-year follow-up. The lower rates of subsidence in the Tritanium cages compared to the PEEK cages could be due to the higher osteogenic-angiogenic response reported in titanium cages compared to PEEK cages [26-29]. The literature demonstrates that the mean time between index surgery and development of symptoms from non-union is 2.69 years[54-56]. Keeping in mind that our data is limited by 1-year follow-up, we believe that the higher rates of non-union will drive the cost associated with revisions for PEEK cage when compared to Tritanium cage at a time point beyond 1 year. Having said that, the PEEK cohort had higher costs related to postoperative resource utilizations, which includes cost pertaining to 90-day readmissions/complications, inpatient/outpatient physical therapy/occupational therapy, pain medications, and imaging studies. The increase in cost could potentially be explained by the higher rate of discharge to a facility in the PEEK group. Skilled nursing facilities commonly care for patients requiring additional physical and occupational therapy than those discharged home[57]. Patients who are sent to a facility will have higher therapy costs than those discharged home, which could explain why the PEEK cohort had higher indirect costs.

The findings of this study should be interpreted in light of its inherent limitations. This study represents the experience of a single institute spine center. The post-discharge resource use costs are estimated by data extracted from the electronic medical records and supplemented by patient interview to capture care outside of the facility. However, the patient interview is subject to recall bias. The one significant difference in the two population was that the number of vertebral levels involved, and the PEEK patients had more patients with two contiguous segments fused (three levels) compared to the Tritanium cage. Despite the aforementioned limitations, we adjusted for a comprehensive list of variables captured in a single-center prospective longitudinal spine registry in our propensity score matching.

Conclusion

This study represents the first real-world comparison of a porous titanium cage to a PEEK cage in the elective surgical management of degenerative lumbar disc diseases. Our results indicate that the porous titanium cage (Tritanium) is an effective alternative to the previously used PEEK cage in terms of PROs, surgical safety, and radiological parameters of surgical success. The Tritanium cohort showed better ODI scores, higher fusion rates, lower subsidence, and lower indirect costs associated with surgical management, when compared to the propensity-matched PEEK cohort. The results of this study are unique and can inform surgeons' decisions for interbody cage material in the treatment of lumbar degenerative disc diseases.

Conflicts of Interest: Financial support and industry affiliations: Dr. Devin reports a Stryker grant, Stryker consulting, Wright medical, defense expert witness, and Medtronic legal consulting outside the submitted work. The other authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper. The authors have no personal or institutional financial interest in drugs, materials, or devices described in their submissions.

Sources of Funding: This study received funding from Stryker [grant number R1160501].

Author Contributions: Inamullah Khan: Software, Investigation, Data Curation, Writing-Original Draft, and Visualization

Scott L. Parker: Validation, Conceptualization, Methodology, Writing-Review, and Editing

Hansen Bow: Conceptualization, Validation, Writing-Reviewing, and Editing

Ahilan Sivaganesan: Investigation and Writing-Original Draft

Jacquelyn S. Pennings: Formal analysis, Software, Writing-Review, and Editing

Byron F. Stephens II: Funding acquisition, Project administration, Supervision, Visualization, Writing-Review and Editing, Resources, and Methodology

Anthony M. Steinle: Visualization, Writing-Review, and Editing

Rishabh Gupta: Visualization, Writing-Review, and Editing

Clinton J. Devin: Supervision, Resources, Project Administration, and Methodology

Ethical Approval: This project was approved by Vanderbilt IRB under the IRB number 171321.

Informed Consent: Patient consent was obtained.

References

1. Shmagel A, Foley R, Ibrahim H. Epidemiology of chronic low back pain in US adults: data from the 2009-2010 National Health and Nutrition Examination Survey. Arthritis Care Res (Hoboken). 2016;68(11):1688-94. https://doi.org/10.1002/acr.22890.
2. Martin BI, Deyo RA, Mirza SK, et al. Expenditures and health status among adults with back and neck problems. Jama. 2008;299 (6):656-64. https://doi.org/10.1001/jama.299.6.656.
3. Freburger JK, Holmes GM, Agans RP, et al. The rising prevalence of chronic low back pain. Arch Intern Med. 2009;169(3):251-8. https://doi.org/10.1001/archinternmed.2008.543.
4. Hazard RG. Failed back surgery syndrome: surgical and nonsurgical approaches. Clin Orthop Relat Res. 2006;443:228-32.
5. Ragab A, Deshazo RD. Management of back pain in patients with previous back surgery. Am J Med. 2008;121(4):272-8.
6. Martin BI, Mirza SK, Comstock BA, et al. Reoperation rates following lumbar spine surgery and the influence of spinal fusion procedures. Spine. 2007;32(3):382-7.
7. Weiner DK, Kim Y-S, Bonino P, et al. Low back pain in older adults: are we utilizing healthcare resources wisely? Pain Med. 2006;7(2):143-50.
8. McGirt MJ, Parker SL, Hilibrand A, et al. Lumbar surgery in the elderly provides significant health benefit in the US health care system: patient-reported outcomes in 4370 patients from the N2 QOD registry. Neurosurgery. 2015;77(suppl_1):S125-35.
9. Parker SL, Mendenhall SK, Shau DN, et al. Minimally invasive versus open transforaminal lumbar interbody fusion for degenerative spondylolisthesis: comparative effectiveness and cost-utility analysis. World Neurosurg. 2014;82(1-2):230-8.
10. Gertzbein SD, Hollopeter MR, Hall S. Pseudarthrosis of the lumbar spine: outcome after circumferential fusion. Spine. 1998;23 (21):2352-6.
11. Kuslich SD, Danielson G, Dowdle JD, et al. Four-year follow-up results of lumbar spine arthrodesis using the Bagby and Kuslich lumbar fusion cage. Spine. 2000;25(20):2656-62.
12. Boden SD, Kang J, Sandhu H, et al. Use of recombinant human bone morphogenetic Protein-2 to achieve posterolateral lumbar spine fusion in humans: a prospective, randomized clinical pilot trial 2002 volvo award in clinical studies. Spine. 2002;27(23): 2662-73.
13. Muschler GF, Negami S, Hyodo A, et al. Evaluation of collagen ceramic composite graft materials in a spinal fusion model. Clin Orthop Relat Res. 1996;328:250-60.
14. Kozak JA, Heilman AE, O'Brien JP. Anterior lumbar fusion options. Technique and graft materials. Clin Orthop Relat Res. 1994; (300):45-51.
15. Ray CD. Threaded titanium cages for lumbar interbody fusions. Spine. 1997;22(6):667-79.
16. Xiao Y, Chen Q, Li F. Unilateral transforaminal lumbar interbody fusion: a review of the technique, indications and graft materials. Int J Med Res. 2009;37(3):908-17.
17. Vaidya R, Sethi A, Bartol S, et al. Complications in the use of rhBMP-2 in PEEK cages for interbody spinal fusions. J Spinal Disord Tech. 2008;21(8):557-62. https://doi.org/10.1097/BSD.0b013e31815ea897.
18. Le TV, Baaj AA, Dakwar E, et al. Subsidence of polyetheretherketone intervertebral cages in minimally invasive lateral retroperitoneal transpsoas lumbar interbody fusion. Spine. 2012;37(14):1268-73.
19. Choi JY, Sung KH. Subsidence after anterior lumbar interbody fusion using paired stand-alone rectangular cages. Eur Spine J. 2006;15(1):16-22.
20. Luis M, Nitamar A, Leonardo O, et al. Radiographic and clinical evaluation of cage subsidence after stand-alone lateral interbody fusion. J Neurosurg Spine. 2013;19(1):110-8. https://doi.org/10.3171/2013.4.SPINE12319.
21. Chun DS, Baker KC, Hsu WK. Lumbar pseudarthrosis: a review of current diagnosis and treatment. Neurosurg Focus. 2015;39(4): E10.
22. Chrastil J, Low JB, Whang PG, et al. Complications associated with the use of the recombinant human bone morphogenetic proteins for posterior interbody fusions of the lumbar spine. Spine. 2013;38(16):E1020-7.
23. Reza A, Conrad MM. Randomized porous titanium impacts cell morphology and induces stem cell differentiation in vitro. Orthopaedic Research Society 5th International Spine Research Symposium. 2019;5:83.
24. Stryker. TRITA-SS-1. Stryker Marketing Material. 2016. https://doi.org/http://stryker.com/builttofuse/media/assets/TRITA-SS-1%20Technical%20Sell%20Sheet%20FINAL.pdf.
25. Olivares-Navarrete R, Hyzy SL, Slosar PJ, et al. Implant materials generate different peri-implant inflammatory factors: poly-ether-ether-ketone promotes fibrosis and microtextured titanium promotes osteogenic factors. Spine. 2015;40(6):399.
26. Olivares-Navarrete R, Hyzy SL, Gittens RA, et al. Rough titanium alloys regulate osteoblast production of angiogenic factors. Spine J. 2013;13(11):1563-70.
27. Johansson CB, Roser K, Bolind P, et al. Bone-tissue formation and integration of titanium implants: an evaluation with newly developed enzyme and immunohistochemical techniques. Clin Implant Dent Relat Res. 1999;1(1):33-40. https://doi.org/10.1111/j.1708-8208.1999.tb00089.x.
28. Yamada K, Ito M, Akazawa T, et al. A preclinical large animal study on a novel intervertebral fusion cage covered with high porosity titanium sheets with a triple pore structure used for spinal fusion. Eur Spine J. 2015;24(11):2530-7. https://doi.org/10.1007/s00586-015-4047-2.
29. Fujibayashi S, Takemoto M, Neo M, et al. A novel synthetic material for spinal fusion: a prospective clinical trial of porous bioactive titanium metal for lumbar interbody fusion. European spine journal: official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 2011;20(9):1486-95. https://doi.org/10.1007/s00586-011-1728-3.
30. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42(2):377-81.
31. Fairbank JC, Pynsent PB. The Oswestry disability index. Spine. 2000;25(22):2940-53.
32. Hawker GA, Mian S, Kendzerska T, et al. Measures of adult pain: visual analog scale for pain (vas pain), numeric rating scale for pain (nrs pain), Mcgill pain questionnaire (mpq), short-form Mcgill pain questionnaire (sf-mpq), chronic pain Cain grade scale (cpgs), short form-36 bodily pain scale (sf-36 bps), and measure of intermittent and constant osteoarthritis pain (icoap). Arthritis Care Res (Hoboken). 2011;63(S11):S240-52.
33. Rabin R, Charro FD. EQ-SD: a measure of health status from the EuroQol Group. Ann Med. 2001;33(5):337-43. https://doi.org/10.3109/07853890109002087.
34. Burkus JK, Foley K, Haid R, et al. Surgical interbody research group—radiographic assessment of interbody fusion devices: fusion

criteria for anterior lumbar interbody surgery. Neurosurg Focus. 2001;10(4):1-9.

35. Marchi L, Abdala N, Oliveira L, et al. Radiographic and clinical evaluation of cage subsidence after stand-alone lateral interbody fusion. J Neurosurg Spine. 2013;19(1):110-8. https://doi.org/10.3171/2013.4.Spine12319.

36. Chotai S, Sielatycki JA, Parker SL, et al. Effect of obesity on cost per quality-adjusted life years gained following anterior cervical discectomy and fusion in elective degenerative pathology. Spine J. 2016;16(11):1342-50.

37. Adogwa O, Parker SL, Shau DN, et al. Cost per quality-adjusted life year gained of revision neural decompression and instrumented fusion for same-level recurrent lumbar stenosis: Defining the value of surgical intervention. J Neurosurg Spine. 2012;16(2):135-40.

38. Bala MM, Riemsma RP, Nixon J, et al. Systematic review of the (cost-) effectiveness of spinal cord stimulation for people with failed back surgery syndrome. Clin J Pain. 2008;24(9):741-56.

39. Parker SL, Fulchiero EC, Davis BJ, et al. Cost-effectiveness of multilevel hemilaminectomy for lumbar stenosis-associated radiculopathy. Spine J. 2011;11(8):705-11.

40. Cuzzocrea F, Ivone A, Jannelli E, et al. PEEK versus metal cages in posterior lumbar interbody fusion: A clinical and radiological comparative study. Musculoskelet Surg. 2019;103(3):237-41.

41. Cabraja M, Oezdemir S, Koeppen D, et al. Anterior cervical discectomy and fusion: Comparison of titanium and polyetheretherketone cages. BMC Musculoskelet Disord. 2012;13(1):172.

42. Arts M, Torensma B, Wolfs J. Porous titanium cervical interbody fusion device in the treatment of degenerative cervical radiculopathy; 1-year results of a prospective controlled trial. Spine J. https://doi.org/10.1016/j.spinee.2020.03.008.

43. Brandão RACS, Martins WCdS, Arantes AA, Jr., et al. Titanium versus polyetheretherketone implants for vertebral body replacement in the treatment of 77 thoracolumbar spinal fractures. Surg Neurol Int. 2017;8:191. https://doi.org/10.4103/sni.sni_113_17.

44. Bernstein DN, Greenstein AS, D'Amore T, et al. Do PROMIS physical function, pain interference, and depression correlate to the Oswestry disability index and neck disability index in spine trauma patients? Spine (Phila Pa 1976). 2020;45(11):764-9. https://doi.org/10.1097/BRS.0000000000003376.

45. Almeida OP. Prevention of depression in older age. Maturitas. 2014;79(2):136-41. https://doi.org/10.1016/j.maturitas.2014.03.005.

46. McGilvray KC, Easley J, Seim HB, et al. Bony ingrowth potential of 3D-printed porous titanium alloy: a direct comparison of interbody cage materials in an in vivo ovine lumbar fusion model. Spine J. 2018;18(7):1250-60. https://doi.org/10.1016/j.spinee.2018.02.018.

47. Nemoto O, Asazuma T, Yato Y, et al. Comparison of fusion rates following transforaminal lumbar interbody fusion using polyetheretherketone cages or titanium cages with transpedicular instrumentation. Eur Spine J. 2014;23(10):2150-5.

48. Le T, Baaj A, Dakwar E, et al. Subsidence of polyetheretherketone intervertebral cages in minimally invasive lateral retroperitoneal transpsoas lumbar interbody fusion. Spine (Phila Pa 1976). 2012;37(14):1268-73. https://doi.org/10.1097/BRS.0b013e3182458b2f.

49. Tempel Z, Gandhoke G, Okonkwo D, et al. Impaired bone mineral density as a predictor of graft subsidence following minimally invasive transpsoas lateral lumbar interbody fusion. Eur Spine J. 2015;24(Suppl 3):414-9. https://doi.org/10.1007/s00586-015-3844-y.

50. Tempel ZJ, McDowell MM, Panczykowski DM, et al. Graft subsidence as a predictor of revision surgery following stand-alone lateral lumbar interbody fusion. Journal of Neurosurgery. 2018;28(1):50. https://doi.org/10.3171/2017.5.Spine16427.

51. Bocahut N, Audureau E, Poignard A, et al. Incidence and impact of implant subsidence after stand-alone lateral lumbar interbody fusion. Orthop Traumatol-Sur. 2018;104(3):405-10. https://doi.org/https://doi.org/10.1016/j.otsr.2017.11.018.

52. Chen Y, Wang X, Lu X, et al. Comparison of titanium and polyetheretherketone (PEEK) cages in the surgical treatment of multilevel cervical spondylotic myelopathy: a prospective, randomized, control study with over 7-year follow-up. European spine journal: official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society. 2013;22(7):1539-46. https://doi.org/10.1007/s00586-013-2772-y.

53. Heary RF, Parvathreddy N, Sampath S, et al. Elastic modulus in the selection of interbody implants. Int J Spine Surg. 2017;3(2):163.

54. Adogwa O, Parker SL, Shau D, et al. Long-term outcomes of revision fusion for lumbar pseudarthrosis: Clinical article. J Neurosurg Spine. 2011;15(4):393-8. https://doi.org/10.3171/2011.4.Spine10822.

55. Etminan M, Girardi FP, Khan SN, et al. Revision strategies for lumbar pseudarthrosis. Orthop Clin North Am. 2002;33(2):381-92. https://doi.org/10.1016/s0030-5898(02)00005-6.

56. Adogwa O, Carr RK, Kudyba K, et al. Revision lumbar surgery in elderly patients with symptomatic pseudarthrosis, adjacent-segment disease, or same-level recurrent stenosis. Part 1. Two-year outcomes and clinical efficacy: clinical article. J Neurosurg Spine. 2013;18(2):139-46. https://doi.org/10.3171/2012.11.Spine12224.

57. Tijsen LM, Derksen EW, Achterberg WP, et al. Challenging rehabilitation environment for older patients. Clin Interv Aging. 2019;14:1451-60. https://doi.org/10.2147/cia.s207863.