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Effect of Interbody Composition on the Development of Pseudarthrosis Following Anterior Cervical Discectomy and Fusion

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Study Design: Retrospective cohort study.

Purpose: To determine if polyetheretherketone (PEEK) or titanium alloy cages increase the rate of pseudarthrosis development or revision surgery rate compared with structural allograft following anterior cervical discectomy and fusion (ACDF) and identify if the cage type results in differences in patient-reported outcome measures (PROMs) versus structural allograft.

Overview of Literature: PEEK and titanium alloy cages have become popular options for ACDF intervertebral spacers. However, while data is beginning to emerge on how cage types affect arthrodesis rates, the effect of their composition on PROMs is less clear.

Methods: All patients aged >18 years who underwent primary one- to four-level ACDF at a single institution were retrospectively identified. Propensity matching was performed to compare patients' PEEK or titanium alloy cages with structural allograft. Multivariate logistic regression analysis was performed to measure the effect of interbody spacer composition on the likelihood of pseudarthrosis development.

Results: Of the 502 patients who received structural allograft and had 1-year postoperative dynamic radiographs, 96 patients were propensity matched to 32 patients who received a PEEK cage, and 162 patients were propensity matched to 54 patients who received a titanium alloy cage. Multivariate logistic regression analysis identified that PEEK cage implants (odds ratio [OR], 3.34; p=0.007) predicted pseudarthrosis development compared with structural allograft implantation. Titanium alloy cage (OR, 1.64; p=0.156) implantation was not predictive of pseudarthrosis. One-year postoperative PROMs were not significantly different between patients who received PEEK or titanium alloy cages and those who received structural allograft (all p>0.05).

Conclusions: Compared with structural allograft, receiving a PEEK cage increased the risk of pseudarthrosis development following ACDF, whereas receiving a titanium alloy cage had no significant effect on pseudarthrosis development. One-year postoperative patient-reported outcomes were similar between patients who received structural allograft, PEEK, and titanium alloy interbody spacers.

Keywords: Anterior cervical discectomy and fusion; Polyetheretherketone; Titanium; Fusion; Pseudarthrosis

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Introduction

The Smith and Robinson approach was first described in the 1950s, and it has become the mainstay approach for patients undergoing anterior cervical discectomy and fusion (ACDF) procedures due to its high efficacy in achieving long-term clinical improvements [1-3]. Originally, iliac crest autograft was used as an intervertebral spacer; however, while it continues to be the gold-standard choice for achieving solid arthrodesis, the longer operative times and morbidity associated with iliac crest bone graft (ICBG) harvesting make it a less appealing option in patients without concerning risk factors for pseudarthrosis [4]. New technology has promoted potential alternatives to ICBG, including structural femoral ring allograft, polyetheretherketone (PEEK) cages, and titanium alloy cages, which act as a scaffold for bony ingrowth into the cage [5]. However, the fusion rate following surgery may be different given that each biomaterial has various osseointegrative properties [6].

Pseudarthrosis is a common complication following ACDF with rates potentially as high as 20% per construct level 1-year postoperatively [7-9]. While a majority of patients who develop pseudarthrosis remain asymptomatic, pseudarthrosis can present with recurrent axial neck pain or radiculopathy and is one of the primary indications for revision surgery [7-10]. The development of pseudarthrosis is often facilitated by a combination of various patient- and surgeon-specific risk factors [7]. It is expected that the type of interbody spacer may influence pseudarthrosis development considering the differences in design, biocompatibility, and biomechanics between structural allografts and PEEK or titanium alloy cages [11-13]. However, conflicting evidence exists, as some studies have reported disparate fusion rates and pseudarthrosis revision rates for PEEK and titanium alloy cages compared with structural allografts, whereas other studies have found no differences [6,12-14].

Therefore, the following were the objectives of this study: (1) investigate whether PEEK or titanium alloy cages increase the pseudarthrosis rate or pseudarthrosis revision surgery rate compared with structural allograft spacers and (2) determine if 1-year postoperative patient-reported outcome measures (PROMs) differ between patients who received PEEK or titanium alloy interbody cages and those who received structural allograft spacers.

Materials and Methods

1. Inclusion criteria

This study was approved by the Institutional Review Board (IRB) at Thomas Jefferson University (Control #19D.508) with informed patient consent waived due to the retrospective nature of the study. Following IRB approval, all patients aged >18 years who underwent primary one- to four-level ACDF at our academic medical center from 2016 to 2019 were retrospectively identified. Patients were excluded if the ACDF was performed as a revision procedure, utilized a combined anterior/posterior approach, included a concomitant cervical corpectomy, or indicated in the setting of trauma, infection, or neoplasm. Additional exclusion criteria included any patient who did not have 1 year postoperative dynamic cervical spine radiograph. Local autograft was used to augment fusion in both cases with interbody cages or structural allograft. To augment fusion, demineralized bone matrix was also utilized in the very rare instances where local autograft (endplate or anterior osteophyte shavings) provided an insufficient amount of bone. Anterior cervical plates were used for all procedures.

2. Data extraction

Patient demographics, surgical characteristics, and surgical outcomes were collected through a Structured Query Language search and manual chart review of electronic medical records. Demographic data collected included age, sex; body mass index (BMI), smoking status, and Elixhauser comorbidity index (ECI) score. Surgical characteristics collected included preoperative diagnosis, preoperative symptom duration (months), construct length, and interbody spacer composition (structural allograft, porous PEEK cage, or titanium alloy cage). Surgical outcomes included surgical readmission within 90 days (defined as a surgical site infection, wound dehiscence, or persistent postoperative pain), follow-up duration (months), fusion status, and revision for pseudarthrosis. PROMs were retrospectively collected through our institution's prospectively collected database (OBERD, Columbia, MO, USA) and were included at the preoperative and 1-year postoperative time points. PROMs extracted included the Visual Analog Scale for neck pain (VAS Neck) and arm pain (VAS Arm), Neck Disability Index

(NDI), modified Japanese Orthopaedic Association scale (mJOA), and Mental and Physical Component Scores of the Short-Form 12 Health Survey (MCS-12 and PCS-12, respectively). The change in each PROM score (Δ) at 1 year was calculated by subtracting the preoperative from the postoperative value.

3. Radiographic evaluation

Postoperative dynamic cervical spine radiographs were reviewed through our institution's Picture Archiving and Communication System (Sectra AB, Linköping, Sweden). The distance (millimeters) between the superior and inferior spinous processes at each level of the ACDF construct was measured on postoperative flexion and extension radiographs. Radiographic fusion was defined as <1 mm of interspinous motion between each instrumented level with ≥4 mm of motion at any adjacent unfused level following the guidelines published by the Cervical Spine Research Society Special Project Committee, whereas ≥1 mm of interspinous motion at any instrumented level was defined as a pseudarthrosis [15].

4. Statistical analysis

Patients were stratified into groups based on ACDF interbody spacer composition. Propensity matching, controlling for patient age, sex, BMI, smoking status, ECI, and construct length, was utilized to match patients who received structural allograft spacers with those who received PEEK interbody cages and patients who received structural femoral ring allograft spacers with those who received titanium interbody cages. Descriptive statistics, including mean and standard deviation, were used to record patient demographics, surgical characteristics, and surgical outcomes. The Shapiro-Wilk test analyzed the normality of each continuous variable, and parametric data were compared using independent *t*-tests. Nonparametric data were compared using the Mann-Whitney *U* tests. Dichotomous variables were compared using Pearson's chi-square tests. Multivariate logistic regression models measured the effect of patient demographics, interbody spacer composition, and construct length on the likelihood of achieving radiographic fusion after the index ACDF. Statistical significance was set at $p<0.05$. Data analysis was completed using R software ver. 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria).

Results

1. Structural allograft versus polyetheretherketone cages

1) Patient demographics and surgical characteristics

Of the 502 patients who received structural allograft, 96 patients were propensity matched to 32 patients who received a PEEK cage (3:1 propensity match). No significant differences in baseline demographics, including age ($p=0.796$), sex ($p=0.826$), BMI ($p=0.919$), smoking status ($p=1.000$), and ECI ($p=0.820$), between patients who received structural allograft and those who received PEEK cages were noted. Furthermore, no significant differences in preoperative diagnosis ($p=0.342$), symptom duration ($p=0.686$), or number of levels included in the construct ($p=0.697$) were observed (Appendix 1).

2) Surgical outcomes

The 90-day surgical readmission rate (1.04% versus 3.12%, $p=0.439$), average length of clinical follow-up (21.3±12.5 months versus 24.0±16.3 months, $p=0.150$), and pseudarthrosis revision rate (6.25% versus 0.00%, $p=0.336$) were not significantly different between groups. However, a significantly greater pseudarthrosis rate detected on dynamic radiographs for patients who received PEEK cages than those who received structural allograft was noted (53.1% versus 26.0%, $p=0.009$) (Table 1). Furthermore, multivariate logistic regression analysis found that receiving a PEEK cage was a significant predictor for pseudarthrosis development (odds ratio [OR], 3.34; 95% confidence in-

Table 1. Structural allograft vs. PEEK: surgical outcomes

Variable	Allograft (N=96)	PEEK (N=32)	*p*-value
Follow-up time (mo)	21.3±12.5	24.0±16.3	0.150
Radiographic fusion			0.009*
No	25 (26.0)	17 (53.1)	
Yes	71 (74.0)	15 (46.9)	
90-Day readmission			0.439
No	95 (99.0)	31 (96.9)	
Yes	1 (1.04)	1 (3.12)	
Pseudarthrosis revision			0.336
No	90 (93.8)	32 (100.0)	
Yes	6 (6.25)	0	

Values are presented as mean±standard deviation or number (%).
PEEK, polyetheretherketone.
*$p<0.05$ (statistical significance).

terval [CI], 1.40–8.19; p=0.007) compared with receiving structural allograft (Table 2).

3) Patient-reported outcomes

No significant differences in the preoperative or 1-year postoperative MCS-12, PCS-12, or NDI scores between patients who received structural allograft and those who received PEEK were observed (all p>0.05). Patients who received PEEK had significantly greater preoperative VAS Arm scores (7.19 versus 5.46, p=0.030); however, they had similar 1-year (p=0.418) postoperative VAS Arm scores. This resulted in a greater magnitude of VAS Arm improvement for patients receiving PEEK (−6.50 versus −2.89, p=0.013). Analysis of mJOA scores revealed that the 1-year postoperative Δ mJOA score (5.20 versus 1.29, p=0.043) was significantly greater in patients who received PEEK cages (Table 3).

2. Structural allograft versus titanium alloy cages

1) Patient demographics and surgical characteristics

A total of 54 patients with a titanium alloy cage were included in the study. They were propensity matched to 162 patients who received structural femoral ring allograft (3:1 propensity match). No significant differences in baseline demographics, including age (p=0.860), sex (p=0.694), BMI (p=0.744), smoking status (p=1.000), and ECI (p=0.811), between groups were observed. Moreover, no significant difference in the proportion of patients who underwent one-, two-, three-, or four-level ACDF was noted (p=0.974) (Appendix 2).

2) Surgical outcomes

Patients who received structural allograft had a longer average length of clinical follow-up (21.2±10.3 months versus 18.5±8.96 months, p=0.035) than those who received titanium alloy cages. The 90-day surgical readmission rate (1.23% versus 0.00%, p=1.000) and revision surgery rate due to pseudarthrosis (5.56% versus 0.00%, p=0.116) were not significantly different between groups. Furthermore, the pseudarthrosis rate detected on dynamic radiographs (34.0%

Table 2. Structural allograft vs. PEEK: multivariate logistic regression of radiographic pseudarthrosis

Variable	Estimate	p-value	Odds ratio (95% CI)
Age	0.03	0.072	1.03 (1.00–1.07)
Body mass index	-0.04	0.338	0.96 (0.88–1.04)
Male sex	0.23	0.618	1.26 (0.50–3.15)
Smoking status			
Never	Ref		
Former	-0.04	0.937	0.97 (0.39–2.29)
Elixhauser	0.09	0.371	1.09 (0.90–1.34)
Interbody spacer			
Allograft	Ref		
PEEK	1.21	0.007*	3.34 (1.40–8.19)
Levels fused	0.55	0.107	1.73 (0.90–3.44)

PEEK, polyetheretherketone; CI, confidence interval; Ref, reference.
*p<0.05 (statistical significance).

Table 3. Structural allograft vs. PEEK: patient-reported outcomes

Variable	Allograft (N=96)	PEEK (N=32)	p-value
MCS-12			
Preoperative	45.8±14.8	49.4±9.35	0.611
1 Year postoperative	49.7±10.2	49.2±9.31	0.866
Δ 1 Year postoperative	2.48±11.6	-2.36±3.11	0.235
PCS-12			
Preoperative	33.2±9.49	36.4±7.71	0.276
1 Year postoperative	41.6±12.0	47.5±9.21	0.176
Δ 1 Year postoperative	10.4±12.6	8.90±9.25	0.737
NDI			
Preoperative	43.4±17.7	46.4±13.2	0.445
1 Year postoperative	26.9±22.0	18.4±13.1	0.463
Δ 1 Year postoperative	-14.97±19.2	-30.40±16.5	0.109
VAS Neck			
Preoperative	5.93±2.54	6.85±2.41	0.202
1 Year postoperative	2.95±2.91	2.80±3.11	0.981
Δ 1 Year postoperative	-3.21±2.88	-3.25±4.92	0.990
VAS Arm			
Preoperative	5.46±2.84	7.19±2.37	0.030*
1 Year postoperative	2.26±2.53	1.40±1.95	0.418
Δ 1 Year postoperative	-2.89±2.88	-6.50±1.73	0.013*
mJOA			
Preoperative	15.3±2.60	13.0±4.39	0.086
1 Year postoperative	16.5±2.13	17.4±0.89	0.383
Δ 1 Year postoperative	1.29±2.37	5.20±4.27	0.043*

Values are presented as mean±standard deviation.
PEEK, polyetheretherketone; MCS-12, Mental Component Score of the Short-Form 12 Health Survey; PCS-12, Physical Component Score of the Short-Form 12 Health Survey; NDI, Neck Disability Index; VAS Neck, Visual Analog Scale for neck pain; VAS Arm, Visual Analog Scale for arm pain; mJOA, modified Japanese Orthopaedic Association scale.
*p<0.05 (statistical significance).

versus 44.4%, p=0.221) was not significantly different (Table 4). When comparing only three- and four-level fusions, no significant differences in fusion rates or revision surgery rates between groups were noted (p=0.095 and p=1.000, respectively); however, allograft was the least likely interbody material to form a pseudarthrosis (Appendix 3).

Multivariate logistic regression analysis identified that receiving a titanium alloy cage was not a significant predictor for pseudarthrosis development (OR, 1.64; 95% CI, 0.83–3.24; p=0.156) compared with structural allograft.

Table 4. Structural allograft vs. titanium alloy: surgical outcomes

Variable	Allograft (N=162)	Titanium (N=54)	*p*-value
Follow-up time (mo)	21.2±10.3	18.5±8.96	0.035*
Radiographic fusion			0.221
No	55 (34.0)	24 (44.4)	
Yes	107 (66.0)	30 (55.6)	
90-Day readmission			1.000
No	160 (98.8)	54 (100.0)	
Yes	2 (1.23)	0	
Pseudarthrosis revision			0.116
No	153 (94.4)	54 (100.0)	
Yes	9 (5.56)	0	

Values are presented as mean±standard deviation or number (%).
*p<0.05 (statistical significance).

Table 5. Structural allograft vs. titanium alloy: multivariate logistic regression of radiographic pseudarthrosis

Variable	Estimate	*p*-value	Odds ratio (95% CI)
Age	0.03	0.022*	1.04 (1.01–1.07)
Body mass index	-0.01	0.631	0.99 (0.93–1.04)
Male sex	0.85	0.006*	2.35 (1.29–4.36)
Smoking status			
Never	Ref		
Current	1.30	0.181	3.67 (0.55–30.82)
Former	0.06	0.845	1.07 (0.56–2.01)
Elixhauser	-0.09	0.311	0.91 (0.76–1.09)
Interbody spacer			
Allograft	Ref		
Titanium	0.49	0.156	1.64 (0.83–3.24)
Levels fused	0.57	0.002*	1.77 (1.24–2.57)

CI, confidence interval; Ref, reference.
*p<0.05 (statistical significance).

Patient age (OR, 1.04; 95% CI, 1.01–1.07; p=0.022), male sex (OR, 2.35; 95% CI, 1.29–4.36; p=0.006), and ACDF construct length (OR, 1.77; 95% CI, 1.24–2.57; p=0.002) were identified as significant predictors for pseudarthrosis development (Table 5).

3) Patient-reported outcomes

No significant differences in preoperative or 1-year postoperative MCS-12, NDI, VAS Neck, and VAS Arm scores between patients who received structural allograft and those who received titanium alloy cages were noted (all p>0.05). Patients who received titanium alloy cages had significantly higher preoperative PCS-12 (36.6 versus 32.8,

Table 6. Structural allograft vs. titanium alloy: patient-reported outcomes

Variable	Allograft (N=162)	Titanium (N=54)	*p*-value
MCS-12			
Preoperative	47.5±12.7	46.3±9.32	0.393
1 Year postoperative	48.1±11.6	44.0±8.68	0.158
Δ1 Year postoperative	0.49±13.5	-5.22±9.73	0.163
PCS-12			
Preoperative	32.8±9.31	36.6±8.65	0.039*
1 Year postoperative	40.0±11.6	39.6±10.3	0.882
Δ 1 Year postoperative	7.98±12.3	0.52±12.9	0.065
NDI			
Preoperative	41.1±19.8	43.8±17.2	0.450
1 Year postoperative	25.3±20.6	30.0±20.2	0.321
Δ 1 Year postoperative	-16.78±18.1	-10.67±17.4	0.353
VAS Neck			
Preoperative	5.92±2.85	6.75±2.21	0.210
1 Year postoperative	2.96±2.62	3.10±2.85	0.958
Δ 1 Year postoperative	-2.83±2.63	-2.71±3.90	0.926
VAS Arm			
Preoperative	5.28±3.18	6.17±2.58	0.283
1 Year postoperative	2.53±2.82	3.20±2.86	0.284
Δ 1 Year postoperative	-2.63±3.29	-2.86±3.18	0.837
mJOA			
Preoperative	14.6±3.21	13.0±3.16	0.006*
1 Year postoperative	15.9±2.39	15.8±1.99	0.631
Δ 1 Year postoperative	1.32±2.82	0.80±1.40	0.696

Values are presented as mean±standard deviation.
MCS-12, Mental Component Score of the Short-Form 12 Health Survey; PCS-12, Physical Component Score of the Short-Form 12 Health Survey; NDI, Neck Disability Index; VAS Neck, Visual Analog Scale for neck pain; VAS Arm, Visual Analog Scale for arm pain; mJOA, modified Japanese Orthopaedic Association scale.
*p<0.05 (statistical significance).

p=0.039) and lower mJOA (13.0 versus 14.6, p=0.006) scores; however, no significant differences in 1-year postoperative PCS-12, mJOA, Δ PCS-12, or Δ mJOA scores between groups were observed (all p>0.05) (Table 6). In a secondary analysis comparing patients with and without pseudarthroses, the majority of PROMs, including MCS-12, PCS-12, NDI, VAS Neck, and mJOA, were not significantly different between groups (p>0.05). Although the VAS Arm during the 1-year postoperative visit was lower in patients with pseudarthrosis (2.96±2.76 versus 1.44±1.92, p=0.033), no significant difference in the overall improvement between groups was noted (3.41±3.14 versus 2.94±2.86, p=0.621). This indicates that the difference in the 1-year VAS Arm score was likely due to the greater "potential for improvement" than the actual pseudarthrosis (Appendix 4).

Discussion

ACDF is a highly effective procedure for the treatment of symptomatic cervical spondylosis resulting in myelopathy or radiculopathy due to its low overall complication profile and revision surgery rate [16,17]. To date, the use of structural allograft spacers or intervertebral cages is widespread in ACDF procedures, likely due to the literature demonstrating satisfactory clinical outcomes regardless of allograft or cage usage [4,18-20]. However, additional analysis assessing the effect of interbody spacer incorporation on clinical outcomes is warranted considering that recent literature has suggested that PEEK cages may be associated with greater pseudarthrosis rates than structural allografts. Our study found that the use of PEEK cages significantly increases the risk of pseudarthrosis development following ACDF compared with structural allograft. However, most patients who developed pseudarthrosis appear to be relatively asymptomatic considering the nonsignificant difference in pseudarthrosis revision surgery between the two groups and the relatively similar postoperative PROMs. When assessing titanium alloy cages, our study did not identify differences in 1-year postoperative pseudarthrosis development, revision surgery, or PROMs compared with structural allograft.

The near-physiologic elastic modulus of PEEK is intended to optimize the mechanical load transfer through the interbody cage. Theoretically, this should promote bone formation and facilitate bony arthrodesis [5,11,21]. However, PEEK is also an inherently bio-inert material, which limits surface osseointegration and may contribute to the development of pseudarthrosis [21,22]. The findings of recent retrospective studies comparing the clinical outcomes of patients who received structural allograft with those who received PEEK cages have reported conflicting results regarding the rates of pseudarthrosis development and revision surgery following ACDF [12,13,23]. However, a recent meta-analysis comparing structural allografts and PEEK cages reported a 61% and 71% less likelihood of pseudarthrosis development and pseudarthrosis revision rate for patients who received structural allograft compared with those who received PEEK cages [12,13,23]. The results of our multivariate logistic regression analysis found that patients who received PEEK cages had a significantly greater likelihood of pseudarthrosis development than those who received structural allograft, which was consistent with the results of a previous meta-analysis. However, unlike the meta-analysis, we did not find PEEK cages increased the rate of pseudarthrosis revision. However, our results may be limited by the small sample size considering that only 32 patients were evaluated in our study (with none of the patients who received PEEK cages requiring revision surgery for pseudarthrosis). Although long-term outcomes (greater than 2-year follow-up) may elicit a greater rate of pseudarthrosis revisions or inferior clinical outcomes among patients who develop a pseudarthrosis, we only had a total of 11 patients who followed up at this time point. Therefore, patients with at least 2-year follow-up were not analyzed in our study. Although radiographic fusion may occur up to 2 years following ACDF, a meta-analysis by Shriver et al. found no significant differences in fusion rates between patients with 1- and 2-year follow-up [24].

Before the introduction of PEEK cages, titanium alloy was one of the first materials to be incorporated as an alternative to structural autografts and allografts [5]. The excellent biocompatibility of titanium alloy is attributable to the formation of a layer of titanium dioxide along the surface of the implant, which is resistant to corrosion and enhances hydroxyapatite deposition, thereby promoting fusion [21,25]. The main disadvantage of titanium alloy cages compared with other interbody spacer options is the elastic modulus mismatch between titanium and bones [25]. The increased stiffness of titanium alloy compared with bones may result in stress shielding, wherein the titanium shields the graft inside the cage from appreciating the physiologic mechanical load of the vertebral column,

potentially resulting in a failure of the bone to bridge across the vertebrae [25]. However, previous investigations assessing fusion status following ACDF with titanium alloy cages have reported largely favorable outcomes, with several retrospective studies reporting fusion rates ranging from 95% to 100% during the 6-month postoperative visit with no differences in fusion rate compared with structural allograft spacers [19,26,27]. We found no significant difference in the rate of fusion between patients who received a titanium alloy cage and those who received a structural allograft, which is consistent with the findings of previous studies. This was further substantiated by multivariate logistic regression analysis, which demonstrated that titanium alloy cages, compared with structural allografts, did not significantly increase the likelihood of pseudarthrosis development during the 1-year postoperative visit.

Very few studies have investigated the effect of interbody spacers on PROMs following ACDF [6,17]. One retrospective study found no difference in NDI, VAS Arm, and VAS Neck scores during the 1-year postoperative visit between patients who received PEEK interbody cages and those who received titanium interbody cages, whereas another retrospective analysis reported similar findings for patients who received PEEK cages and those who received structural allograft [6,17]. Other studies, primarily investigating the relationship between interbody spacer selection and PROMs in patients with cervical trauma, have reported no difference in 1-year PROMs based on interbody cage or structural autograft use [28]. Our results demonstrated that patients who received titanium alloy cages had no significant difference in PROMs compared with those who received structural allografts, whereas those who received PEEK cages had more improvement in VAS Arm and mJOA scores at 1 year. The greater improvement in VAS Arm and mJOA scores is likely due to the "more to gain" phenomenon, wherein patients who have worse baseline symptoms have a greater opportunity to have larger clinical improvements. This is substantiated by the similar postoperative clinical outcomes in patients who received PEEK cages versus those who received structural allografts. Overall, our results suggest that interbody spacer choice does not have a significant impact on patient-reported outcomes following ACDF, and surgeons can expect improvements in PROMs regardless of whether structural allografts, PEEK cages, or titanium alloy cages are used during surgery. While it may seem counterintuitive that PEEK cages did not lead to inferior PROMs, part of allograft fusion relies on graft resorption, conferring a loss in disc space height. This may translate to neuroforaminal stenosis and some recurrence of radiculopathy, which may have resulted in greater VAS Arm scores. Therefore, while an arthrodesis may be less likely with PEEK cages, it may provide sufficient disc height so that patients have an improvement in the VAS Arm score even in the absence of a bony fusion.

This study had several limitations, including those inherent to all retrospective studies. First, while we were able to review electronic medical records to confirm implantation of structural allograft, PEEK, or titanium alloy cages during surgery, documentation was not granular enough to determine the cage porosity or degree of allograft lordosis. Second, while computed tomography (CT) scans are considered the gold standard for the radiographic assessment of fusion status following ACDF, our institution does not obtain CT scans unless the patient is suspected to have a symptomatic pseudarthrosis. However, dynamic radiographs have similar sensitivity and specificity for identifying pseudarthrosis compared with CT scans [29]. Although the radiographic measurements used to determine interspinous motion (and thus pseudarthrosis) are small, the interobserver reliability for this measurement is −0.1, indicating the measurement is highly reliable [29]. Finally, our cohort had an average time interval of approximately 20 months between surgery and postoperative radiographs; therefore, we were unable to evaluate long-term improvements in PROMs. Although we would ideally evaluate outcomes during the 2-year postoperative visit, only 11 patients in our cohort had follow-up at that time; thus, our study was limited to shorter-term outcomes. Since some studies have demonstrated an increase in the rate of fusion between 1 and 2 years following ACDF, longer follow-up may have slightly altered fusion rates and postoperative PROM scores; however, this would likely not have significantly changed our results [30].

Conclusions

PEEK cages are associated with an increased likelihood of pseudarthrosis development following ACDF compared with structural allografts. However, titanium alloy cages have similar pseudarthrosis rates compared with allografts. Regardless of whether a structural allograft or

a cage is utilized, the revision surgery rate for pseudarthrosis is not significantly different, indicating that most radiographic pseudarthroses are asymptomatic. This finding is substantiated by the similar postoperative patient-reported outcome scores found between interbody cage utilization and structural allograft use.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Conceptualization: MJL; funding acquisition: not available; visualization: MJL; writing–review & editing: NDA, MJL, JH, BK, AH, AV, CK; data curation: NDA, JH, GT, GB, JB; methodology: MJL, NDA; writing–original draft: NDA, MJL, JH, GT, EB; formal analysis: NDA, JH; and final approval of the manuscript: all authors.

References

1. Smith GW, Robinson RA. The treatment of certain cervical-spine disorders by anterior removal of the intervertebral disc and interbody fusion. J Bone Joint Surg Am 1958;40-A:607-24.
2. Bohlman HH, Emery SE, Goodfellow DB, Jones PK. Robinson anterior cervical discectomy and arthrodesis for cervical radiculopathyL long-term follow-up of one hundred and twenty-two patients. J Bone Joint Surg Am 1993;75:1298-307.
3. Emery SE, Bohlman HH, Bolesta MJ, Jones PK. Anterior cervical decompression and arthrodesis for the treatment of cervical spondylotic myelopathy: two to seventeen-year follow-up. J Bone Joint Surg Am 1998;80:941-51.
4. Yoon ST, Konopka JA, Wang JC, et al. ACDF graft selection by surgeons: survey of AOSpine members. Global Spine J 2017;7:410-6.
5. Chong E, Pelletier MH, Mobbs RJ, Walsh WR. The design evolution of interbody cages in anterior cervical discectomy and fusion: a systematic review. BMC Musculoskelet Disord 2015;16:99.
6. Cabraja M, Oezdemir S, Koeppen D, Kroppenstedt S. Anterior cervical discectomy and fusion: comparison of titanium and polyetheretherketone cages. BMC Musculoskelet Disord 2012;13:172.
7. Leven D, Cho SK. Pseudarthrosis of the cervical spine: risk factors, diagnosis and management. Asian Spine J 2016;10:776-86.
8. Pennington Z, Mehta VA, Lubelski D, et al. Quality of life and cost implications of pseudarthrosis after anterior cervical discectomy and fusion and its subsequent revision surgery. World Neurosurg 2020;133:e592-9.
9. Lambrechts MJ, D'Antonio ND, Karamian BA, et al. What is the role of dynamic cervical spine radiographs in predicting pseudarthrosis revision following anterior cervical discectomy and fusion? Spine J 2022;22:1610-21.
10. Crawford CH, Carreon LY, Mummaneni P, Dryer RF, Glassman SD. Asymptomatic ACDF nonunions underestimate the true prevalence of radiographic pseudarthrosis. Spine (Phila Pa 1976) 2020;45:E776-80.
11. Heary RF, Parvathreddy N, Sampath S, Agarwal N. Elastic modulus in the selection of interbody implants. J Spine Surg 2017;3:163-7.
12. Krause KL, Obayashi JT, Bridges KJ, Raslan AM, Than KD. Fivefold higher rate of pseudarthrosis with polyetheretherketone interbody device than with structural allograft used for 1-level anterior cervical discectomy and fusion. J Neurosurg Spine 2018;30:46-51.
13. Wang M, Chou D, Chang CC, et al. Anterior cervical discectomy and fusion performed using structural allograft or polyetheretherketone: pseudarthrosis and

revision surgery rates with minimum 2-year follow-up. J Neurosurg Spine 2020;32:562-9.
14. Pirkle S, Kaskovich S, Cook DJ, Ho A, Shi LL, Lee MJ. Cages in ACDF are associated with a higher nonunion rate than allograft: a stratified comparative analysis of 6130 patients. Spine (Phila Pa 1976) 2019;44:384-8.
15. Rhee JM, Chapman JR, Norvell DC, Smith J, Sherry NA, Riew KD. Radiological determination of postoperative cervical fusion: a systematic review. Spine (Phila Pa 1976) 2015;40:974-91.
16. Veeravagu A, Cole T, Jiang B, Ratliff JK. Revision rates and complication incidence in single- and multilevel anterior cervical discectomy and fusion procedures: an administrative database study. Spine J 2014;14:1125-31.
17. Buyuk AF, Onyekwelu I, Gaffney CJ, et al. Symptomatic pseudarthrosis requiring revision surgery after 1- or 2-level ACDF with plating: peek versus allograft. J Spine Surg 2020;6:670-80.
18. Samartzis D, Shen FH, Matthews DK, Yoon ST, Goldberg EJ, An HS. Comparison of allograft to autograft in multilevel anterior cervical discectomy and fusion with rigid plate fixation. Spine J 2003;3:451-9.
19. Rohe SM, Engelhardt M, Harders A, Schmieder K. Anterior cervical discectomy and titanium cage fusion: 7-year follow-up. Cent Eur Neurosurg 2009;70:180-6.
20. Kim SH, Lee JK, Jang JW, Park HW, Hur H. Polyetheretherketone cage with demineralized bone matrix can replace iliac crest autografts for anterior cervical discectomy and fusion in subaxial cervical spine injuries. J Korean Neurosurg Soc 2017;60:211-9.
21. Levy HA, Yalla GR, Karamian BA, Vaccaro AR. Impact of porosity on interbody cage implants: PEEK and titanium. Contemp Spine Surg 2021;22:1-7.
22. Jain A, Marrache M, Harris A, et al. Structural allograft versus PEEK implants in anterior cervical discectomy and fusion: a systematic review. Global Spine J 2020;10:775-83.
23. Fatima N, Massaad E, Shankar GM, Shin JH. Structural allograft versus polyetheretherketone implants in patients undergoing spinal fusion surgery: a systematic review and meta-analysis. World Neurosurg 2020;136:101-9.
24. Shriver MF, Lewis DJ, Kshettry VR, Rosenbaum BP, Benzel EC, Mroz TE. Pseudoarthrosis rates in anterior cervical discectomy and fusion: a meta-analysis. Spine J 2015;15:2016-27.
25. Rao PJ, Pelletier MH, Walsh WR, Mobbs RJ. Spine interbody implants: material selection and modification, functionalization and bioactivation of surfaces to improve osseointegration. Orthop Surg 2014;6:81-9.
26. Moreland DB, Asch HL, Clabeaux DE, et al. Anterior cervical discectomy and fusion with implantable titanium cage: initial impressions, patient outcomes and comparison to fusion with allograft. Spine J 2004;4:184-91.
27. van Jonbergen HP, Spruit M, Anderson PG, Pavlov PW. Anterior cervical interbody fusion with a titanium box cage: early radiological assessment of fusion and subsidence. Spine J 2005;5:645-9.
28. Lee HQ, Kow CY, Ng JS, et al. Correlation of anterior interbody graft choice with patient-reported outcomes in cervical spine trauma. Global Spine J 2019;9:735-42.
29. Song KS, Piyaskulkaew C, Chuntarapas T, et al. Dynamic radiographic criteria for detecting pseudarthrosis following anterior cervical arthrodesis. J Bone Joint Surg Am 2014;96:557-63.
30. Zigler JE, Rogers RW, Ohnmeiss DD. Comparison of 1-level versus 2-level anterior cervical discectomy and fusion: clinical and radiographic follow-up at 60 months. Spine (Phila Pa 1976) 2016;41:463-9.

Appendix 1. Structural allograft vs. PEEK: demographics and surgical characteristics

Characteristic	Allograft (N=96)	PEEK (N=32)	*p*-value
Age (yr)	54.4±11.6	54.8±11.2	0.796
Sex			0.826
Female	65 (67.7)	23 (71.9)	
Male	31 (32.3)	9 (28.1)	
Body mas index (kg/m^2)	27.3±5.53	27.7±6.22	0.919
Smoking status			1.000
Never	67 (69.8)	23 (71.9)	
Current	0	0	
Former	29 (30.2)	9 (28.1)	
Elixhauser	2.15±1.95	2.47±2.66	0.820
Preoperative diagnosis			0.342
Radiculopathy	53 (55.2)	20 (62.5)	
Myelopathy	23 (24.0)	9 (28.1)	
Myeloradiculopathy	20 (20.8)	3 (9.38)	
Symptom duration (mo)	11.9±13.5	9.28±9.49	0.686
Construct length			0.697
1-Level	42 (43.8)	12 (37.5)	
2-Level	48 (50.0)	17 (53.1)	
3-Level	6 (6.25)	3 (9.38)	

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

Appendix 2. Structural allograft vs. titanium alloy: demographics and surgical characteristics

Variable	Allograft (N=162)	Titanium (N=54)	*p*-value
Age (yr)	56.6±10.9	56.9±11.8	0.860
Sex			0.694
Female	88 (54.3)	27 (50.0)	
Male	74 (45.7)	27 (50.0)	
Body mass index (kg/m^2)	30.0±6.44	29.9±4.63	0.744
Smoking status			1.000
Never	98 (60.5)	33 (61.1)	
Current	4 (2.47)	1 (1.85)	
Former	60 (37.0)	20 (37.0)	
Elixhauser comorbidity index	2.26±1.86	2.30±2.15	0.811
Preoperative diagnosis			0.007*
Radiculopathy	75 (46.3)	35 (64.8)	
Myelopathy	44 (27.2)	4 (7.41)	
Myeloradiculopathy	43 (26.5)	15 (27.8)	
Symptom duration (mo)	13.3±18.6	10.7±15.9	0.060
Construct length			0.974
1-Level	35 (21.6)	13 (24.1)	
2-Level	69 (42.6)	22 (40.7)	
3-Level	47 (29.0)	15 (27.8)	
4-Level	11 (6.79)	4 (7.41)	

Values are presented as mean±standard deviation or number (%).
*$p<0.05$ (statistical significance).

Appendix 3. Pseudarthrosis and revision rates in comparison to implant material in 3 to 4 level fusions

Variable	Allograft (N=58)	PEEK (N=3)	Titanium (N=19)	*p*-value
Pseudarthrosis				0.095
No	33 (56.9)	0	8 (42.1)	
Yes	25 (43.1)	3 (100.0)	11 (57.9)	
Pseudarthrosis revision				1.000
No	56 (96.6)	3 (100.0)	19 (100.0)	
Yes	2 (3.45)	0	0	

Values are presented as number (%).
PEEK, polyetheretherketone.

Appendix 4. Patients with a pseudarthrosis versus no pseudarthrosis: patient-reported outcome measures

Variable	No pseudarthrosis	Pseudarthrosis	*p*-value
MCS-12			
Preoperative	46.2±13.8	46.8±11.2	0.811
1 Year postoperative	47.3±10.5	48.9±8.95	0.539
Δ 1 Year postoperative	0.38±12.7	-1.22±7.49	0.577
PCS-12			
Preoperative	33.4±9.27	36.7±8.53	0.054
1 Year postoperative	40.3±11.4	44.2±10.9	0.202
Δ 1 Year postoperative	9.15±14.4	4.96±10.0	0.230
NDI			
Preoperative	44.1±16.4	43.5±18.4	0.863
1 Year postoperative	28.1±20.9	24.3±20.9	0.555
Δ 1 Year postoperative	-14.77±18.0	-17.53±20.8	0.657
VAS Neck			
Preoperative	6.40±2.36	5.89±2.73	0.349
1 Year postoperative	3.19±2.87	2.61±2.87	0.505
Δ 1 Year postoperative	-3.31±3.15	-2.75±3.51	0.605
VAS Arm			
Preoperative	5.99±2.65	5.56±3.06	0.484
1 Year postoperative	2.96±2.76	1.44±1.92	0.033*
Δ 1 Year postoperative	-3.41±3.14	-2.94±2.86	0.621
mJOA			
Preoperative	14.5±3.13	14.0±3.42	0.474
1 Year postoperative	16.1±2.26	16.8±1.58	0.254
Δ 1 Year postoperative	1.46±2.40	1.88±3.26	0.651

Values are presented as mean±standard deviation.
MCS-12, Mental Component Score of the Short-Form 12 Health Survey; PCS-12, Physical Component Score of the Short-Form 12 Health Survey; NDI, Neck Disability Index; VAS Neck, Visual Analog Scale for neck pain; VAS Arm, Visual Analog Scale for arm pain; mJOA, modified Japanese Orthopaedic Association scale.
*$p<0.05$ (statistical significance).