February 2, 2021

Liz Richter
Acting Administrator
Centers for Medicare and Medicaid Services
Department of Health and Human Services
Baltimore, MD 21244-8016

Gift Tee
Director
Division of Practitioner Services
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, Maryland 21244

**Attention: Division of Practitioner Services, Potentially Misvalued Codes**

Dear Acting Administrator Richter and Director Tee:

On behalf of LifeNet Health, I am writing to submit comments requesting agency review of **CPT 22551** (*Arthrodesis, anterior interbody, including disc space preparation, discectomy, osteophytectomy and decompression of spinal cord and/or nerve roots; cervical below C2*) **and accompanying add-on codes** as potentially misvalued services as part of its annual Medicare Physician Fee Schedule rulemaking process.

LifeNet Health has been a trusted source of transplant and surgical solutions for nearly 40 years. We have provided more than seven million allograft implants to help restore patients' wellbeing and, in many cases, save lives. We work closely with clinicians and healthcare organization to understand clinical needs and provide the resources needed for efficient, effective, economical care.

## POTENTIALLY MISVALUED SERVICES IN THE MEDICARE PHYSICIAN FEE SCHEDULE

**Request for Placement of Additional Codes on List of Potentially Misvalued Services**

As part of the CY 2021 annual rulemaking process, CMS agreed with the public nominations[1] it received that **CPT 22867** *(Insertion of interlaminar/interspinous process stabilization/distraction device, without fusion, including image guidance when performed, with open decompression, lumbar; single level)* is worthy of review as potentially misvalued and sought comment on the addition of this code to the list of potentially misvalued services.

[1] https://www.cms.gov/files/zip/cy-2021-pfs-final-rule-public-nominations-potentially-misvalued-codes.zip

The submitters nominated this code asserting that the work and malpractice relative value units (RVUs) for the procedure "significantly undervalue the procedure," and requested that CMS raise the work RVU (wRVU) in order to reflect:

- The anomalous relationship between **CPT 22867** and **CPT 63047** (*Laminectomy, facetectomy and foraminotomy (unilateral or bilateral with decompression of spinal cord, cauda equina and/or nerve root[s], [e.g., spinal or lateral recess stenosis]), single vertebral segment; lumbar*)
- The work associated with the "insertion component of the procedure" in line with the wRVUs for **CPT 22868** (*Insertion of interlaminar/interspinous process stabilization/distraction device, without fusion, including image guidance when performed, with open decompression, lumbar; second level (List separately in addition to code for primary procedure)*)
- A crosswalk with "surgical comparator," citing retina surgery code, **CPT 67108** (*Repair of RD with vitrectomy (any method), including, when performed, air or gas tamponade, focal endolaser photocoagulation, cryotherapy, drainage of subretinal fluid, scleral buckling, and/or removal of lens by same technique*)

As part of our response to the CY 2021 Medicare Physician Fee Schedule, we submitted that there are additional CPT code values related to spine procedures that are in need of contemporaneous review with CPT 22867. However, these comments were not acknowledged or responded to by CMS in the final rule. We now request that CMS evaluate these services as part of its annual potentially misvalued services review. While the code CMS finalized for the potentially misvalued services list is related to a non-fusion procedure, we believe CMS has an interest in reviewing associated anterior cervical discectomy and fusion (ACDF) procedures as well. In particular, the coding schema that results from use of primary procedure **CPT 22551** (*Arthrodesis, anterior interbody, including disc space preparation, discectomy, osteophytectomy and decompression of spinal cord and/or nerve roots; cervical below C2*) can result in cumulative RVUs that do not sufficiently reflect physician work, time, or outcomes.

Cervical degenerative disc disease is one of the most common diagnoses for patients suffering from neck and back pain. In addition to pain, patients may suffer from lack of function, immobility, and sensory loss. Initial treatments tend to be conservative, focusing on anti-inflammatory medicine and/or physical therapy. However, when these options fail, a surgical intervention may be needed. Such a procedure usually involves a discectomy and fusion, whereby the affected disc is excised, and the nerve root or spinal cord is decompressed. Following disc removal, the vertebral space is typically implanted with allograft bone or another option.

Historically, autografts, meaning implants from the patient's own body, have been a standard practice. However, autografts have several disadvantages, such as extended operating time, donor site pain, limited supply, and variable quality depending upon the patient's health. Thus, there has been a shift toward the use of alternative interbody spacers for treatment of degenerative disc disease. Two of the most common choices are structural allograft bone or synthetic cages.

Both allograft bone and synthetic cages have mechanical properties similar to autograft. However, synthetic cages may not integrate into the bone as well as autografts, which can lead the patient back to experiencing pain, immobility, and sensory loss, and potentially necessitating further surgery. By contrast,

structural allografts will integrate into the surrounding bone, which may result in superior clinical outcomes.[2,3,4]

However, the values assigned to the codes for these different implant approaches vary. The primary procedure under either clinical scenario is **CPT 22551** (*Arthrodesis, anterior interbody, including disc space preparation, discectomy, osteophytectomy and decompression of spinal cord and/or nerve roots; cervical below C2*). The table below illustrates the coding scenarios for the use of 3 devices depending on whether the device selected is PEEK or structural allograft and how it results in wRVU differentials.

| Work RVU Differentials Based on Implant Selection | |
|---|---|
| **3 synthetic cage devices with plate** | **3 structural allografts with plate** |
| **CPT 22551** (*Arthrodesis, anterior interbody, including disc space preparation, discectomy, osteophytectomy and decompression of spinal cord and/or nerve roots; cervical below C2*) (50.42) **wRVUs: 25.00** | **CPT 22551** (*Arthrodesis, anterior interbody, including disc space preparation, discectomy, osteophytectomy and decompression of spinal cord and/or nerve roots; cervical below C2*) **wRVUs: 25.00** |
| **+CPT 22552 (x2)** (*Arthrodesis, anterior interbody, including disc space preparation, discectomy, osteophytectomy and decompression of spinal cord and/or nerve roots; cervical below C2, each additional interspace (List separately in addition to code for separate procedure)*) **wRVUs (6.5 x2): 13** | **+CPT 22552 (x2)** (*Arthrodesis, anterior interbody, including disc space preparation, discectomy, osteophytectomy and decompression of spinal cord and/or nerve roots; cervical below C2, each additional interspace (List separately in addition to code for separate procedure)*) **wRVUs (6.5 x2): 13** |
| **+CPT 22846 w Modifier 59**[5] (*Anterior instrumentation; 4 to 7 vertebral segments (List separately in addition to code for primary procedure)*) **wRVUs: 12.4** | **+CPT 22846 w Modifier 59** (*Anterior instrumentation; 4 to 7 vertebral segments (List separately in addition to code for primary procedure)*) **wRVUs: 12.4** |
| **+CPT 22853 (x3)** (*Insertion of interbody biomechanical device(s) (e.g., synthetic cage, mesh) with integral anterior instrumentation for device anchoring (e.g., screws, flanges), when performed, to intervertebral disc space in conjunction with interbody arthrodesis, each* | N/A |

[2] Nigeste Carter, Elena C. Gianulis and Mark A. Moore (July 16. 2019). Allograft Structural Interbody Spacers Compared to PEEK Cages in Cervical Fusion: Benchtop and Clinical Evidence [Online First], IntechOpen, DOI: 10.5772/intechopen.88091. Available from: https://www.intechopen.com/online-first/allograft-structural-interbody-spacers-compared-to-peek-cages-in-cervical-fusion-benchtop-and-clinic

[3] Katie L. Krause, MD, PhD, James T. Obayashi, BS, Kelly J. Bridges, MD, Ahmed M. Raslan, MD, and Khoi D. Than, MD (January 2019). 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 30:46–51, 2019 (Attached).

[4] Nida Fatima, Elie Massaad, Ganesh M. Shankar, John H. Shin (April 2020). Structural Allograft versus Polyetheretherketone Implants in Patients Undergoing Spinal Fusion Surgery: A Systematic Review and Meta-Analysis. World Neurosurgery136: 101-109, 2020 (Attached).

[5] Modifier 59 (*Distinct Procedural Service*)

| | |
|---|---|
| *interspace (List separately in addition to code for primary procedure)*) **wRVUs (4.25x3): 12.75** | |
| **+CPT 20930/6** (*Allograft, morselized, or placement of osteopromotive material, for spine surgery only (List separately in addition to code for primary procedure)*) (0.00) | **+CPT 20931** (*Allograft, structural, for spine surgery only (List separately in addition to code for primary procedure)*) **wRVUs: 1.81**. |
| **Total wRVUs: 63.15** | **Total wRVUs: 52.21** |

We are concerned that the variance in the total RVUs assigned to these procedures as outlined above do not reflect a variance in work, resources, or intensity. Therefore, we urge CMS to encourage review of these services.

Sincerely,

Bud Brame
Vice-President of Strategic Product Planning and Reimbursement Services

# Structural Allograft versus Polyetheretherketone Implants in Patients Undergoing Spinal Fusion Surgery: A Systematic Review and Meta-Analysis

***Nida Fatima, Elie Massaad, Ganesh M. Shankar, John H. Shin***

**Key words**
- Allograft
- Fusion
- PEEK implant
- Spinal fusion surgery
- Subsidence

**Abbreviations and Acronyms**
CI: Confidence interval
OR: Odds ratio
PEEK: Polyetheretherketone

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OBJECTIVE: **Interbody spacers have been successfully used in spinal fusion procedures with the aim to restore disc height, provide stability, and promote bone fusion. The authors evaluated the efficacy of structural body allograft versus polyetheretherketone (PEEK) implants in patients undergoing spinal fusion surgery.**

METHODS: **A systematic review of electronic databases was conducted using different Medical Subject Headings terms from January 1970 to August 2019. Pooled and subgroup analyses were performed using random-effects and fixed-effects models based on $I^2$ heterogeneity.**

RESULTS: **The analysis included 6640 patients (structural allograft 64% and PEEK cage 36%) from 7 comparative studies. There were no statistically significant differences in age ($P = 0.27$), sex ($P = 0.31$), body mass index ($P = 0.82$), and smoking status ($P = 0.27$) between the 2 groups. Overall, the mean follow-up was 12.9 ± 1.5 months. Pooled meta-analysis revealed that patients with structural allograft had 2.59-fold higher likelihood of fusion compared with patients with PEEK cages (odds ratio [OR] 2.59, 95% confidence interval [CI] 1.02–6.57, $P = 0.05$) at last follow-up evaluation. Patients with structural allograft had 61% less likelihood of pseudarthrosis (OR 0.39, 95% CI 0.15–0.98, $P = 0.05$) and 74% lower incidence of reoperation compared with patients with PEEK implants (OR 0.26, 95% CI 0.09–0.79, $P = 0.02$). Our results suggest that patients with structural allografts had a higher subsidence rate compared with patients with PEEK implants, but this was statistically insignificant (OR 1.07, 95% CI 0.45–2.53, $P = 0.89$).**

CONCLUSIONS: **Our results corroborate that structural allografts are highly effective in promoting bony fusion compared with PEEK implants in patients undergoing spinal fusion surgery.**

## INTRODUCTION

The evolution of interbody spacers has revolutionized spinal fusion surgery, as these spacers restore disc height, provide stability, and promote bony fusion.[1] With comparable elastic modulus values and mechanical properties similar to autologous bone, structural bone allograft and polyetheretherketone (PEEK) synthetic cages have gained immense popularity over other alternatives, such as autograft.[2] The osteoconductive scaffold demonstrating osseointegration in a rat model by structural allograft has shown a long history of successful clinical use.[3] However, in vivo models of PEEK implants demonstrate lack of osseointegration as well as the growth of fibrous tissue.[4,5] Therefore, modifications of surface enhancement through titanium coating, increased surface porosity, and impregnation of PEEK with bioactive materials such as hydroxyapatite have been proposed.[6] Although the restoration and maintenance of disc space height are the main goals of fusion surgeries, literature exists regarding the failure of mechanical function in supporting the anterior column through bone graft while assuming an essential biologic role to promote bone growth.[7,8] Nonetheless, there is insufficient evidence supporting the use of structural allograft over PEEK implants in spinal fusion procedures. To evaluate the differences between these spacers, we conducted a systematic review and meta-analysis of all available literature comparing structural body allograft and PEEK implants in spinal fusion surgery and associated surgical and radiographic outcomes, including subsidence, pseudarthrosis, fusion rate, reoperation, and patient-reported outcomes.

## MATERIALS AND METHODS

### Data Source and Search Strategy

We conducted a literature search according to the guidelines provided by the Preferred Reporting Items for Systematic Review and Meta-Analysis.[9] Two reviewers (N.F. and J.H.S.) conducted a detailed systematic review of electronic databases (PubMed, Embase, Scopus, Medline, and

Google Scholar) for articles published between January 1990 and November 2019. We used different Medical Subject Headings terms (with Boolean operators "AND" and "OR") including "allograft," "structural body allograft," "polyetheretherketone," "PEEK," "femoral cortical allograft," "femoral ring allograft," "cage," "cervical fusion," "lumbar fusion," and "interbody fusion." We included only articles that were published in English.

### Eligibility Criteria

Eligible studies were of spinal fusion procedures that compared structural allograft and PEEK cages for primary diagnoses of degenerative spinal disease, trauma, herniated disc, and ossified posterior longitudinal ligament. We included only studies that reported at least 1 of the following clinical or radiographic outcomes: subsidence, pseudarthrosis, fusion rate, or patient-reported outcomes. Exclusion criteria were case reports, case series, and implantation of the cage in the setting of spinal infection.

### Data Extraction and Outcome Measures

The data were extracted by 2 authors (N.F. and J.H.S.) using a structured template form based on Cochrane Consumers and Communication Group. Any disagreement between the 2 authors was resolved by discussion. The following data were extracted from each article: 1) demographic characteristics of each cohort, 2) clinical conditions, 3) intraoperative parameters (surgical approaches and number of levels involved), 4) type of allograft used during each study, and 5) outcome parameters (subsidence rate, mean change in lordotic angle, pseudarthrosis, reoperation, fusion rates, and patient-reported outcome measures).

### Evidence Quality Assessment

The Grades of Recommendation, Assessment, Development and Evaluation protocol[10] was used to assess the quality of evidence for each study independently by the 2 reviewers. Each study was given an overall rating based on study design, limitations, and results as high, moderate, low, or very low.

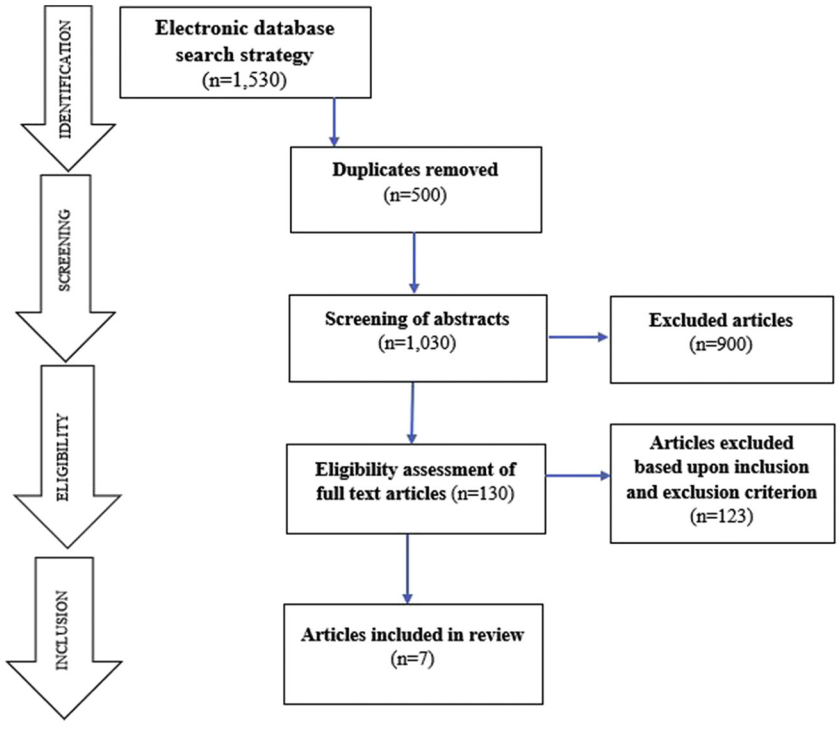


**Figure 1.** Database search strategy of the included studies according to Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines.

### Statistical Analysis

RevMan 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) was used for comparing data from the included studies. Dichotomous data were reported as odds ratio (OR) with 95% confidence interval (CI). Heterogeneity among studies was evaluated using $I^2$ statistics. A fixed-effects model was used for $I^2 < 50\%$, and a random-effects model was used for $I^2 \geq 50\%$. All tests were 2-tailed, and $P < 0.05$ was considered as statistically significant. Subsidence was defined as decrease in anterior and/or posterior disc heights by >2 mm. Radiographic fusion was defined as presence of bridging bone in front of or through the radiolucent cage or allograft incorporation into the surrounding bone. IBM SPSS Version 25 software (IBM Corporation, Armonk, New York, USA) was used to evaluate for differences between groups using independent sample t tests, and $\chi^2$ statistical analysis was used for assessment of categorical variables.

### Risk of Bias Across Studies

No randomized controlled trials were included in our analysis. Furthermore, double blindness was not achieved in any study. The high heterogeneity among studies was further analyzed using funnel plots, which showed the asymmetric distribution. This bias can be attributable to the sample size, as the removal of the smaller sized cohort significantly decreased the heterogeneity.

## RESULTS

### Literature Search

A flow diagram in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines[9] was plotted as shown in **Figure 1**. The reviewers retrieved 1530 articles from PubMed, Embase, Scopus, Medline, and Google Scholar. Of 1530 articles, 500 articles were removed owing to duplication in different electronic databases, and a further 900 articles were excluded because of data not related to spinal fusion surgery. Lastly, 123 of the remaining130 articles were excluded owing to lack of quantitative data and absence of comparison groups.

**Table 1.** Baseline Characteristics of Included Studies

| Reference | Type of Study | Levels | Patients (*N*) | Case/Control* | F/M Sex | Mean Age (years) | BMI | Smokers | Mean FU (months) | Type of Surgery | Type of Allograft | Indications of Surgery |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cutler et al., 2006[8] | Retro | Single-level | 39 | 21 (53.8)/18 (46.2) | 12 (57)/9 (23): 10 (55.5)/8 (20.5) | 45.8/50.2 | NA | 4 (19)/5 (27.7) | 15.1 | TLIF | Femoral cortical bone allograft | DDD: 27; recurrent disc herniation: 7; grade I or II degenerative spondylolisthesis: 5 |
| Wan et al., 2014[11] | Retro | Multilevel | 48 (83) | 30 (36.1)/53 (63.8) | 38 (79.2)/10 (20.8) | 56.3 | 24.3 | 1 (2.1) | 12 | ALIF | Femoral ring allografts | Spine deformities including scoliosis, kyphosis and flat-back syndrome |
| Yson et al., 2017[12] | Retro | Multilevel | 67 (117) | 19 (32)/48 (85) | 12 (63.2)/7 (36.8): 27 (56.3)/21 (43.7) | 48.6/52.5 | NA | NA | 14.7 | ACDF | Structural fibular allograft | Herniated nucleus pulposus: 24; multilevel cervical spondylosis: 24; foraminal stenosis: 7, adjacent segment disease: 5; myelopathy: 4; degenerative spondylolisthesis: 2; DDD: 1 |
| Pirkle et al., 2019[13] | Retro† | Multilevel | 6130 | 4063 (66)/2067 (34) | NA | NA | NA | 60/2195 (2.7)/69/1034 (6.7) | 12 | ACDF | Structural allograft | NA |
| Teton et al., 2019[14] | Retro | Multilevel | 62 | 31 (50)/31 (50) | NA | NA | NA | NA | NA | ACDF | Structural allograft | NA |
| Hill et al., 2019[15] | Retro | Multilevel | 167 | 39 (23.4)/128 (76.6) | 22 (56.4)/17 (43.6): 75 (58.6)/53 (41.4) | 53.8/55.0 | 31.0/29.9 | 8 (20.5)/12 (9.4) | 12 | ACDF | Structural allograft | DDD and cervical trauma |
| Krause et al., 2019[16] | Retro | Single-level | 127 | 71 (55.9)/56 (44.1) | 37 (52.1)/34 (47.8): 35 (62.5)/21 (37.5) | 53/51 | 28.4/29.1 | 17 (23.9)/15 (26.7) | 16/21 | ACDF | Structural allograft composed of composite, cortical, or cancellous materials | DDD and cervical trauma |

Numbers in parentheses are percentages.

F, female; M, male; BMI, body mass index; FU, follow-up; Retro, retrospective; TLIF, transforaminal lumbar interbody fusion; DDD, degenerative disc disease; ALIF, anterior lumbar interbody fusion; NA, not available; ACDF, anterior cervical disc fusion.

*Case: structural allograft; Control: polyetheretherketone cage.

†Pearl Driver National Database.

**Table 2.** Outcome Characteristics Including Clinical and Radiographic Factors of Included Studies

| Reference | Subsidence Rate | Mean NDI Improvement | Mean Change in Lordotic Angle (°) | Pseudarthrosis | Reoperation | Fusion Rate |
|---|---|---|---|---|---|---|
| Cutler et al., 2006[8] | 2/21:0/18 | ODI: 42.3/40.2 | 2.68/1.72 | 1/21: 0/18 | 1/21: 0/18 | 95.2%/100% |
| Wan et al., 2014[11] | NA | NA | 1.8 ± 1.7/2.5 ± 4.2 | 5/30: 3/53 | NA | 84.2%/94.9% |
| Yson et al., 2017[12] | 9/32:25/85 | Subsidence: 7.1; nonsubsidence: 16.6 | NA | 1/19: 4/48 | 1/19: 4/48 | 94.7%/91.6% |
| Pirkle et al., 2019[13] | NA | NA | NA | 80/4063: 110/2067 | NA | 98.0%/94.7% |
| Teton et al., 2019[14] | NA | NA | NA | 6/31: 20/31 | 0/31: 4/31 | 81%/35% |
| Hill et al., 2019[15] | NA | 0.4/0.6 | NA | NA | NA | NA |
| Krause et al., 2019[16] | NA | NA | NA | 7/71: 29/56 | 1/71: 7/56 | 90%/48.3% |

NDI, Neck Disability Index; ODI, Oswestry Disability Index; NA, not available.

Hence, 7 comparative studies were included in our meta-analysis.[8,11-16]

## Study Characteristics

All studies were retrospective in nature. These studies were carried out in the United States ($n = 6$), and China ($n = 1$). The baseline characteristics, outcome characteristics, and comparison of both groups are presented in Tables 1–3.

Our analysis included 6640 patients; 4250 (64.0%) underwent procedures with structural allograft, and 2390 (36.0%) underwent procedures with PEEK cages. The mean follow-up in both groups was 12.9 ± 1.5 months. The quality of evidence as assessed by the Grades of Recommendation, Assessment, Development and Evaluation assessment was deemed very low in 4 studies and low in 3 studies.

Of the available data ($n = 448$), $\chi^2$ statistical analysis was performed to look at the comparative analysis of male versus female patients in structural allograft and PEEK cage groups, with 121 female and 77 male patients in the structural allograft group and 103 female and 147 male patients in the PEEK cage group. There was no statistically significant difference in gender distribution between the structural allograft group and PEEK group ($P = 0.31$). Furthermore, the mean age (SD) for the structural allograft and PEEK groups was 51.5 (4.3) and 53.0 (2.6), respectively. There was no statistically significant difference in age between the 2 groups ($P = 0.27$).

The mean body mass index was 27.9 ± 3.4 kg/m$^2$ among patients with structural allograft and 27.8 ± 3.1 kg/m$^2$ among patients with PEEK cages. There was no statistically significant difference between the 2 cohorts ($P = 0.82$). Similarly, there was no statistically significant difference in data related to smoking between the 2 groups ($P = 0.27$).

**Table 3.** Demographic, Radiographic, and Clinical Characteristics of Included Studies Comparing the 2 Cohorts

| Parameter | Structural Allograft | PEEK Cage | *P* Value |
|---|---|---|---|
| Number of patients | 4250 | 2390 | — |
| Sex, F/M* | 121/77 | 103/147 | 0.31 |
| Age, years, mean ± SD | 51.5 ± 4.3 | 53.0 ± 2.6 | 0.27 |
| BMI, kg/m$^2$, mean ± SD | 27.9 ± 3.4 | 27.8 ± 3.1 | 0.82 |
| Smokers | 90 | 102 | 0.27 |
| Follow-up, months, mean ± SD | 12.9 ± 1.5 | 12.9 ± 1.5 | — |
| Pseudarthrosis | 120 | 213 | 0.02† |
| Reoperation | 3 | 15 | 0.13 |
| Fusion rate, mean ± SD | 90.5 ± 6.7 | 77.4 ± 28.2 | 0.24 |

PEEK, polyetheretherketone; F, female; M, male; BMI, body mass index.
*Sample size is smaller than the total number of patients owing to lack of data provided in the included studies.
†Statistically significant.

## Operative Data

The spinal fusion surgeries in our meta-analysis included anterior cervical discectomy and fusion ($n = 5$),[12-16] anterior lumbar interbody fusion ($n = 1$),[11] and thoracolumbar interbody fusion ($n = 1$).[8] Five studies[11-15] involved multilevel spinal fusion surgery, and 2 studies[8,16] involved single-level spinal fusion surgery. The structural allografts included femoral cortical bone allograft ($n = 1$), femoral ring allograft ($n = 1$), fibular allograft ($n = 1$), and unspecified ($n = 4$). Owing to the inclusion of 1 study with data from a national database,[13] there was moderate heterogeneity in terms of type and number of PEEK cages for comparative analysis. Data regarding estimated blood loss and operative time was scarce, and therefore analysis could not be performed.

## Postoperative Patient-Reported Outcomes

The study design revealed significant heterogeneity about patient-reported outcomes, and therefore clinically meaningful

**Table 4.** Patient-Reported Outcome Characteristics of Included Studies

| Reference | Mean NDI Improvement | Neck VAS | Arm VAS | Mean ODI Improvement | Mean Prolo Scale Improvement |
|---|---|---|---|---|---|
| Cutler et al., 2006[8] | — | — | — | 42.3/40.2 | — |
| Wan et al., 2014[11] | — | — | — | — | 3.1 ± 1.1/3.5 ± 0.8 |
| Yson et al., 2017[12] | 7.1/16.6* | 1.8/2.8* | 5.9/1.6* | — | — |
| Pirkle et al., 2019[13] | — | — | — | — | — |
| Teton et al., 2019[14] | — | — | — | — | — |
| Hill et al., 2019[15] | 0.4/0.6 | — | — | — | — |
| Krause et al., 2019[16] | — | — | — | — | — |

NDI, Neck Disability Index; VAS, visual analog scale; ODI, Oswestry Disability Index.
*Subsidence/nonsubsidence.

statistical analysis could not be performed. However, none of the included studies reported a significant difference between the 2 groups in Neck Disability Index, visual analog scale, Oswestry Disability Index, and Prolo Scale. Patient-reported outcome characteristics of the included studies are presented in Table 4.

### Radiologic Outcome

***Fusion Rate.*** The fusion rate at the last follow-up was 81%–98% (pooled proportion: 90.5%) in patients with structural allograft compared with 35%–100% in patients with PEEK cages (pooled proportion: 77.4%). The pooled meta-analysis revealed that patients with structural allograft had 2.59-fold higher likelihood of fusion compared with patients with PEEK cages (OR 2.59, 95% CI 1.02–6.57, P = 0.05) at the last follow-up evaluation (Figure 2). Furthermore, patients with structural allograft had 61% less likelihood of pseudarthrosis compared with patients with PEEK cages (OR 0.39, 95% CI 0.15–0.98, P = 0.05) (Figure 3). Hence patients with structural allograft had 74% less likelihood of reoperation compared with patients with PEEK cages (OR 0.26, 95% CI 0.09–0.79, P = 0.02) (Figure 4).

***Subsidence.*** Only 2 studies[8,12] had sufficient data related to subsidence. There was no statistically significant difference in terms of subsidence between the study cohorts with structural allograft and PEEK cages (OR 1.07, 95% CI 0.45–2.53, $I^2$ = 0%, P = 0.89) (Figure 5).

***Subgroup Analysis Based on Location.*** Subgroup analysis to determine the fusion rate based on the spinal location was performed. Four included studies[12–14,16] reported the comparative fusion rates in the cervical spine region, and 2 studies reported fusion rates in the lumbar spine area.[8,11] Our results corroborated the reported rates for the cervical spine region; the patients with structural allograft had 4.68-fold higher likelihood of fusion compared with the patients with PEEK cages (OR 4.68, 95% CI 2.08–10.54, P = 0.0002) (Figure 6A). In contrast, the patients with structural allograft in the lumbar spine region had 69% less likelihood of fusion at the last follow-up than the patients with PEEK cages. This was borderline statistically significant (OR 0.31, 95% CI 0.08–1.22, P = 0.09) (Figure 6B).

## DISCUSSION

This meta-analysis sought to determine 2 important outcome parameters associated with interbody spacers during spinal fusion surgery: 1) subsidence and fusion rate through radiographic evaluation, and 2) patient-reported outcomes. Furthermore, we did a comparative analysis of preoperative demographic parameters including age, sex, body mass index, and smoking status between the 2 groups.

This review included 6640 patients from 7 comparative studies. Most of the patients had structural allograft during spinal fusion surgery (n 4250; 64%), while the remaining patients (n = 2390; 36%) had PEEK implants. The studies included in our meta-analysis involved interbody spacers following anterior cervical discectomy and fusion (n = 5), anterior lumbar interbody fusion (n = 1), and

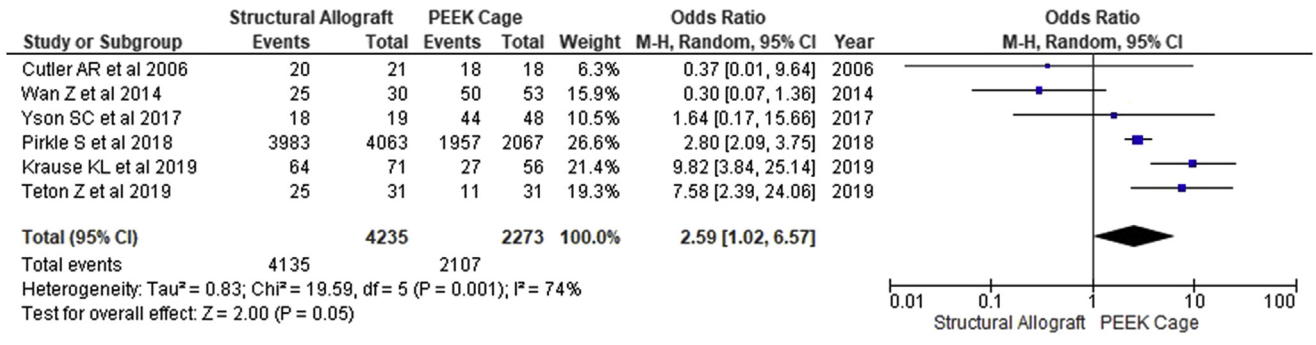


**Figure 2.** Pooled analysis of fusion rate. A statistically significant difference exists in fusion rate between the cohorts with structural allograft and polyetheretherketone cage (odds ratio 2.59, 95% confidence interval 1.02–6.57, $I^2$ 74%, P = 0.05). PEEK, polyetheretherketone; M-H, Mantel-Haenszel; CI, confidence interval.

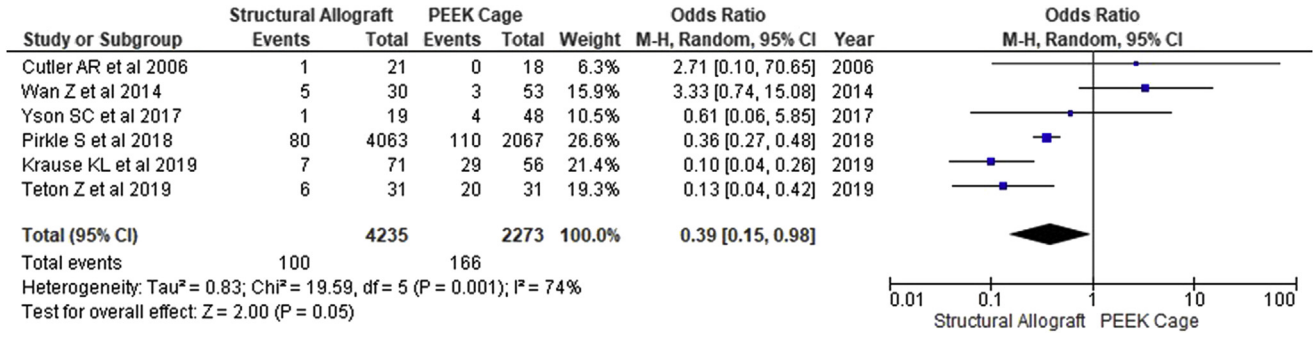


**Figure 3.** Pooled analysis of pseudarthrosis. A statistically significant difference exists in terms pseudarthrosis between the cohorts with structural allograft and polyetheretherketone cage (odds ratio 0.39, 95% confidence interval 0.15–0.98, $I^2$ 74%, $P = 0.05$). PEEK, polyetheretherketone; M-H, Mantel-Haenszel; CI, confidence interval.

transforaminal lumbar interbody fusion ($n = 1$) for degenerative disc disease and trauma. Degenerative disc disease and trauma are the most common diagnoses for patients experiencing neck and back pain.[2,17] These patients usually present with radiculopathic and myelopathic symptoms following compression of the nerve roots and spinal cord, respectively. The spinal fusion procedure involves removing the affected disc, excising the osteophytes, and decompressing the nerve root or spinal cord.[2] The residual disc space is implanted with a bone or synthetic graft for preservation and maintenance of the vertebral space height, with or without the additional support of plates and screws.[2]

Following interbody spacer placement, the fusion rate is a key determinant of success.[12] However, a standardized criterion for fusion assessment does not exist.[2] In our review, most of the surgeons subjectively assessed fusion through bridging trabecular bone and the absence of a radiolucent gap between endplates. Pooling results from our studies revealed that fusion rate was higher among patients with structural allograft by 2.59-fold compared with patients with PEEK implants ($P = 0.05$). Thus, there was 61% less likelihood of pseudarthrosis ($P < 0.05$) and 76% lower risk of reoperation among patients with structural allograft compared with patients with PEEK implants. PEEK is a nonabsorbable, semicrystalline polymer with elastic modulus similar to native bone (3.84 GPa). However, its inert nature and low surface energy affect the body's biologic response. Furthermore, the hydrophobic nature of PEEK potentially limits the protein-surface and cell-surface interactions, which eventually limit the cellular adhesions. In contrast, the structural allograft provides an osteoconductive scaffold for neovascularization and osseointegration and thus performs better. Hence PEEK is associated with lower fusion rates regardless of providing excellent mechanical stability. The modifications to improve PEEK bioactivity in terms of surface coating with synthetic osteoconductive material, increasing the surface porosity and roughness through chemical modifications, and incorporating bioactive particles have gained widespread popularity.[2,18,19] However, our review did not control for these variations owing to lack of high-quality evidence comparing these modifications.

The patients with structural allograft had significantly better fusion rates in the cervical region (OR 4.68, 95% CI 2.08–10.54, $P = 0.0002$) compared with patients with PEEK cages in the lumbar region (OR 0.31, 95% CI 0.08–1.22, $P = 0.09$). This could be explained by the fact that the strong polymer material of the PEEK cage is able to withstand the compressive load of the vertebral column in the lumbar region, thus offering a higher fusion rate

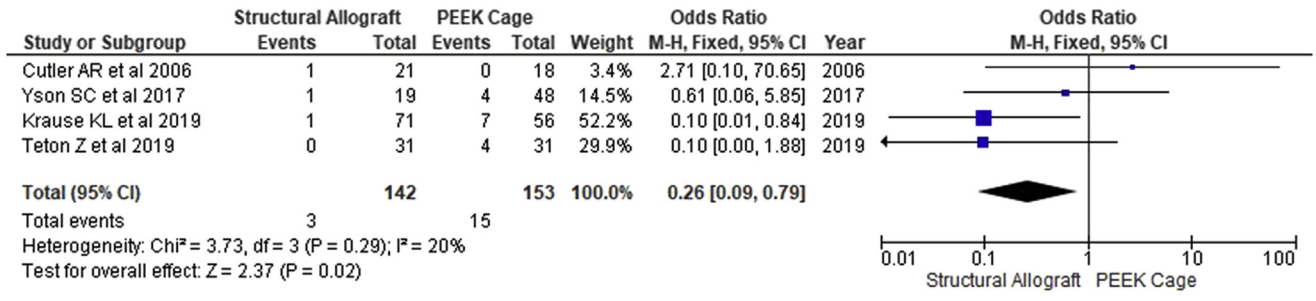


**Figure 4.** Pooled analysis of reoperation. A statistically significant difference exists in reoperation owing to nonunion between the cohorts with structural allograft and polyetheretherketone cage (odds ratio 0.26, 95% confidence interval 0.09–0.79, $I^2$ 20%, $P = 0.02$). PEEK, polyetheretherketone; M-H, Mantel-Haenszel; CI, confidence interval.

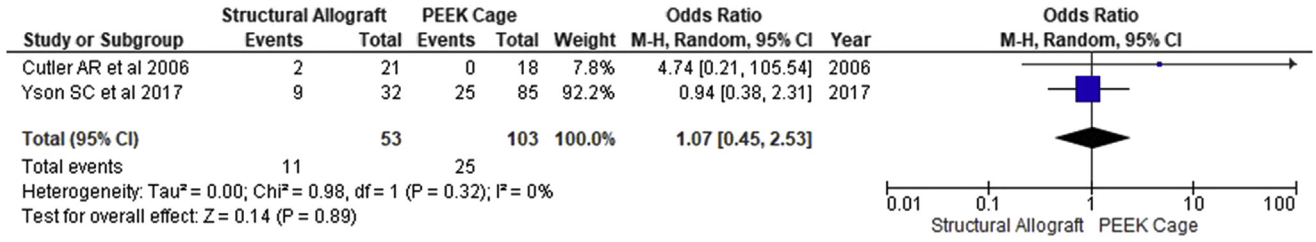


**Figure 5.** Pooled analysis of subsidence. A statistically insignificant difference exists in rate of subsidence between the cohorts with structural allograft and polyetheretherketone cage (odds ratio 1.07, 95% confidence interval 0.45–2.53, $I^2$ 0%, $P = 0.89$). PEEK, polyetheretherketone; M-H, Mantel-Haenszel; CI, confidence interval.

compared with structural allograft.[8] On the contrary, some studies suggest that the fusion rate is less with the PEEK cage in the cervical region, as it represents a mechanical block for fusion formation.[13] Furthermore, the PEEK cage provides less endplate surface area and less available intervertebral volume for arthrodesis, which is the possible cause of the lower fusion rate compared with the structural allograft.[13]

The mean radiographic follow-up after fusion in our included studies was 12.9 ± 1.5 months. All included studies reported the fusion based on plain x-ray. In general, spinal arthrodesis takes at least 3 months to 1 year to achieve a solid fusion; hence it is appropriate to repeat a plain x-ray after 1 year to determine the fusion rate.[20] However, in the assessment of patients who have undergone spinal arthrodesis, the clinical picture along with radiographic assessment should be considered for the further management plan.[21] The sensitivity and specificity of predicting the fusion rate with a plain radiograph were reported in the literature as 89% and 60%, respectively.[22] A few studies[23,24] have reported a lower fusion rate on computed tomography scans than on dynamic radiographs following spinal fusion procedures, whereas others have reported an equivalent fusion rate with computed tomography scan and plain dynamic radiographs with a positive predictive value of 100% and negative predictive value of 85%.[25]

Furthermore, our meta-analysis revealed that the subsidence rate was 1.07-fold higher among patients with structural allograft compared with patients with PEEK implants. Although the results of our pooled analysis related to subsidence were statistically insignificant ($P = 0.89$) owing to small sample sizes and lack of studies with high-quality evidence, our analysis highlights an important finding. As the structural bone allograft has an essential biologic role to promote bone growth, the disc height is mostly lost to achieve osseous fusion.[8]

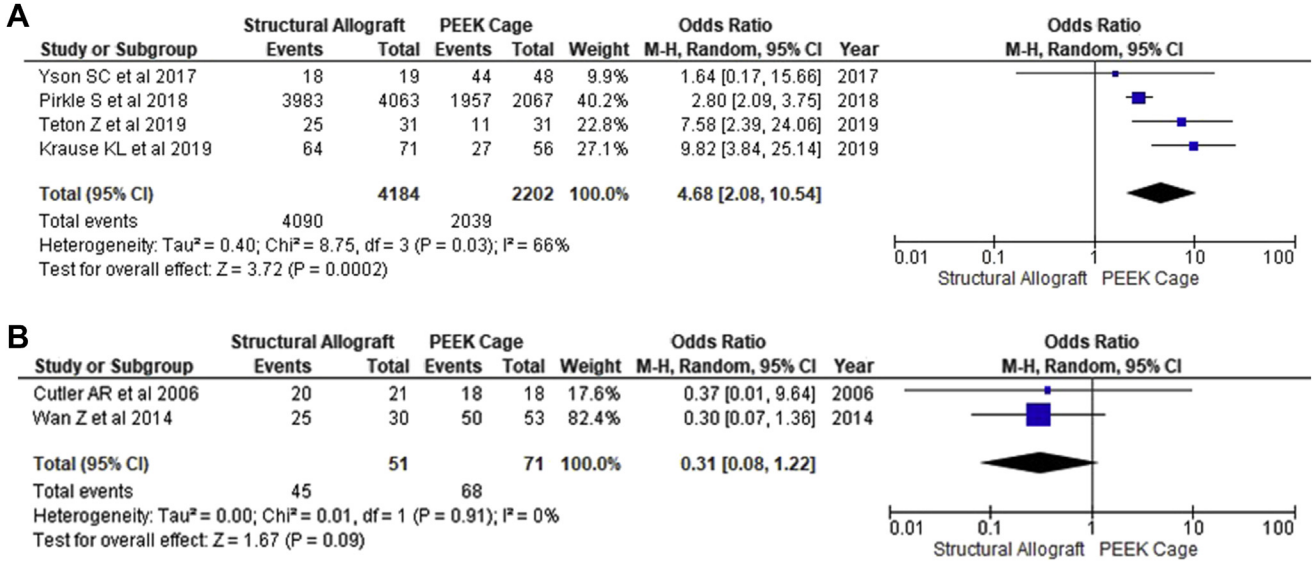


**Figure 6.** Subgroup analysis of fusion rate based on the spinal location. (**A**) Cervical spine region. A statistically significant difference exists in rate of fusion between the cohorts with structural allograft and polyetheretherketone cage (odds ratio 4.68, 95% confidence interval 2.08–10.54, $I^2$ 66%, $P = 0.0002$). (**B**) Lumbar region. A borderline statistically significant difference exists in rate of fusion between the cohorts with structural allograft and polyetheretherketone cage (odds ratio 0.31, 95% confidence interval 0.08–1.22, $I^2$ 0%, $P = 0.09$). PEEK, polyetheretherketone; M-H, Mantel-Haenszel; CI, confidence interval.

Thus, allografts are associated with more postoperative disc height loss compared with PEEK cages. This is further strengthened by McAfee et al.,[26] who reported a 66% increase in intraoperative disc space height at 2-year follow-up in patients who underwent transforaminal lumbar interbody fusion using PEEK cages.[26] However, further studies are needed to compare the subsidence rates between structural allograft and PEEK implants in patients following spinal fusion surgery.

Patient-reported outcomes were described in only 4 studies[8,11,12,15] suggesting that these clinical outcomes are often not the focus of the studies. The scales for outcome assessment were different among these studies and included Neck Disability Index, visual analog scale, Oswestry Disability Index, and Prolo Scale, and a comparative analysis could not be performed. Tracking surgical outcomes, including the patient-reported outcome, is pivotal to understanding the clinical progress and has been in increasing use in clinical practice. However, variability exists in determining the clinical outcomes through these patient-reported outcome measures in spine surgery because they depend exclusively on the patient's response. This is acknowledged by Nayak et al.,[27] who reported the limitation in comparison of clinical outcomes in spine surgery research owing to variability in patient-reported outcome measures. In addition, although the subsidence rate after spinal fusion procedures has been well studied, the effects of subsidence on the clinical outcomes and fusion rate remain unclear.[28] Further studies are needed to determine the reliability, validity, and responsiveness of these patient-reported outcome measures.

In addition to the surgical effectiveness, structural allografts are cost-effective compared with PEEK cages in spinal fusion surgeries. Our included studies did not report the cost data; however, it is of paramount importance to highlight the cost savings of these spinal implants for surgical decision making. The individual surgeon instrumentation costs varied 10-fold based on the fusion construct used.[29] However, previous literature reported that PEEK cages were much more costly than structural allograft.[29] PEEK spacers cost $4930–$5246, whereas structural allograft spacers are estimated to cost $1220–$3640.[29] Further studies are needed to determine the surgical effectiveness and cost savings related to the use of PEEK cages versus structural allograft in patients undergoing spinal fusion surgery.

Our study has several limitations. 1) No randomized controlled trials were included. 2) Only retrospective studies were included. which could be a source of selection bias. 3) The studies did not provide sufficient data regarding the different surgical approaches adopted between the 2 cohorts. 4) The indications for surgery and underlying clinical conditions were not always clear in the studies. 5) There was heterogeneity of PEEK cage assessment in one of the studies owing to inclusion of a national database.[13] 6) There were differences in the fusion assessment among the studies. 6) High-quality evidence for comparative analysis to form robust conclusions was lacking. Further prospective studies comparing structural allograft and PEEK implants following spinal fusion surgery with regard to subsidence rate, fusion assessment, and patient-reported outcome at long-term follow-up are required to better assess the effectiveness of each interbody spacer.

## CONCLUSIONS

At a mean follow-up of 12.9 months, structural body allograft provides better bony fusion compared with PEEK implants following spinal fusion surgery. However, further prospective studies are needed to compare the effectiveness of the 2 interbody spacers in patients undergoing single-level and multilevel spinal fusion procedures.

## REFERENCES

1. Patel DV, Yoo JS, Karmarkar SS, Lamoutte EHSK. Interbody options in lumbar fusion. *J Spine Surg*. 2019;5(Suppl 1):S19-S24.

2. Carter N, Gianulis EC, Moore MA. Allograft structural interbody spacers compared to PEEK cages in cervical fusion: benchtop and clinical evidence [online first]. IntechOpen. https://doi.org/10.5772/intechopen.88091. Available at: https://www.intechopen.com/online-first/allograft-structural-interbody-spacers-compared-to-peek-cages-in-cervical-fusion-benchtop-and-clinic. Accessed September 3, 2019.

3. Miller LE, Block JE. Safety and effectiveness of bone allografts in anterior cervical discectomy and fusion surgery. *Spine (Phila Pa 1976)*. 2011;36:2045-2050.

4. Phan K, Hogan JA, Assem Y, Mobbs RJ. PEEK-Halo effect in interbody fusion. *J Clin Neurosci*. 2016;24:138-140.

5. Samsell B, Softic D, Qin X, et al. Preservation of allograft bone using a glycerol solution: a compilation of original preclinical research. *Biomater Res*. 2019;23:5.

6. Chong E, Pelletier MH, Mobbs RJ, Walsh WR. The design evolution of interbody cages in anterior cervical discectomy and fusion: a systematic review orthopedics and biomechanics. *BMC Musculoskelet Disord*. 2015;16:99.

7. Brantigan JW, Steffee AD. A carbon fiber implant to aid interbody lumbar fusion: two-year clinical results in the first 26 patients. *Spine (Phila Pa 1976)*. 1993;18:2106-2107.

8. Cutler AR, Siddiqui S, Mohan AL, Hillard VH, Cerabona F, Das K. Comparison of polyetheretherketone cages with femoral cortical bone allograft as a single-piece interbody spacer in transforaminal lumbar interbody fusion. *J Neurosurg Spine*. 2006;5:534-539.

9. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol*. 2009;62:1006-1012.

10. Ansari MT, Tsertsvadze A, Moher D. Grading quality of evidence and strength of recommendations. *PLoS One*. 2009;6:e1000151.

11. Wan Z, Dai M, Miao J, Li G, Wood KB. Radiographic analysis of PEEK cage and FRA in adult spinal deformity fused to sacrum. *J Spinal Disord Tech*. 2014;27:327-335.

12. Yson SC, Sembrano JN, Santos ERG. Comparison of allograft and polyetheretherketone (PEEK) cage subsidence rates in anterior cervical discectomy and fusion (ACDF). *J Clin Neurosci*. 2017;38:118-121.

13. Pirkle S, Kaskovich S, Cook DJ, Ho A, Shi LL, Lee MJ. Cages in ACDF are associated with a higher nonunion rate than allograft. *Spine (Phila Pa 1976)*. 2019;44:384-388.

14. Teton Z, Cheaney B II, Raslan A, Than K. *Use of polyetheretherketone interbody devices for multi-level anterior cervical discectomy and fusion results in a three-fold higher rate of pseudarthrosis compared to structural allograft. Paper presented at: American Association of Neurological Surgery Annual Scientific Meeting*. April 13-17, 2019. San Diego, CA.

15. Hill CP, Strenge KB. Early clinical outcomes comparing porous PEEK, smooth PEEK, and structural allograft interbody devices for anterior cervical discectomy and fusion. *J Spine Neurosurg*. 2019;8:1.

16. 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.

17. Whitecloud TS. Modern alternatives and techniques for one-level discectomy and fusion. *Clin Orthop Relat Res*. 1999;359:67-76.

18. Almasi D, Iqbal N, Sadeghi M, Sudin I, Abdul Kadir MR, Kamarul T. Preparation methods for improving PEEK's bioactivity for orthopedic and dental application: a review. *Int J Biomater*. 2016; 2016:8202653.

19. Ma R, Tang T. Current strategies to improve the bioactivity of PEEK. *Int J Mol Sci*. 2014;15: 5426-5445.

20. Makino T, Tsukazaki H, Ukon Y, Tateiwa D, Yoshikawa H, Kaito T. The biological enhancement of spinal fusion for spinal degenerative disease. *Int J Mol Sci*. 2018;19:2430.

21. Selby MD, Clark SR, Hall DJ, Freeman BJC. Radiologic assessment of spinal fusion. *J Am Acad Orthop Surg*. 2012;20:694-703.

22. Brodsky AE, Kovalsky ES, Khalil MA. Correlation of radiologic assessment of lumbar spine fusions with surgical exploration. *Spine (Phila Pa 1976)*. 1991;16(6 Suppl):S261-S265.

23. Buchowski JM, Liu G, Bunmaprasert T, Rose PS, Riew KD. Anterior cervical fusion assessment: surgical exploration versus radiographic evaluation. *Spine (Phila Pa 1976)*. 2008;33:1185-1191.

24. Ploumis A, Mehbod A, Garvey T, Gilbert T, Transfeldt E, Wood K. Prospective assessment of cervical fusion status: plain radiographs versus CT-scan. *Acta Orthop Belg*. 2006;72:342-346.

25. Ghiselli G, Wharton N, Hipp JA, Wong DA, Jatana S. Prospective analysis of imaging prediction of pseudarthrosis after anterior cervical discectomy and fusion: computed tomography versus flexion-extension motion analysis with intraoperative correlation. *Spine (Phila Pa 1976)*. 2011;36: 463-468.

26. McAfee PC, DeVine JG, Chaput CD, et al. The indications for interbody fusion cages in the treatment of spondylolisthesis: analysis of 120 cases. *Spine (Phila Pa 1976)*. 2005;30(6 Suppl): S60-S65.

27. Nayak NR, Coats JM, Abdullah KG, Stein SC, Malhotra NR. Tracking patient-reported outcomes in spinal disorders. *Surg Neurol Int*. 2015;6(Suppl 19):S490-S499.

28. Karikari IO, Jain D, Owens TR, et al. Impact of subsidence on clinical outcomes and radiographic fusion rates in anterior cervical discectomy and fusion: a systematic review. *J Spinal Disord Tech*. 2014;27:1-10.

29. Epstein N. Iliac crest autograft versus alternative constructs for anterior cervical spine surgery: pros, cons, and costs. *Surg Neurol Int*. 2012;3(Suppl 3):S143-S156.

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# Fivefold higher rate of pseudarthrosis with polyetheretherketone interbody device than with structural allograft used for 1-level anterior cervical discectomy and fusion

Presented at the 2018 AANS/CNS Joint Section on Disorders of the Spine and Peripheral Nerves

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**OBJECTIVE** Common interbody graft options for anterior cervical discectomy and fusion (ACDF) include structural allograft and polyetheretherketone (PEEK). PEEK has gained popularity due to its radiolucency and its elastic modulus, which is similar to that of bone. The authors sought to compare the rates of pseudarthrosis, a lack of solid bone growth across the disc space, and the need for revision surgery with the use of grafts made of allogenic bone versus PEEK.

**METHODS** The authors retrospectively reviewed 127 cases in which patients had undergone a 1-level ACDF followed by at least 1 year of radiographic follow-up. Data on age, sex, body mass index, tobacco use, pseudarthrosis, and the reoperation rate for pseudarthrosis were collected. These data were analyzed by performing a Pearson's chi-square test.

**RESULTS** Of 127 patients, 56 had received PEEK implants and 71 had received allografts. Forty-six of the PEEK implants (82%) were stand-alone devices. There were no significant differences between the 2 treatment groups with respect to patient age, sex, or body mass index. Twenty-nine (52%) of 56 patients with PEEK implants demonstrated radiographic evidence of pseudarthrosis, compared to 7 (10%) of 71 patients with structural allografts ($p < 0.001$, OR 9.82; 95% CI 3.836–25.139). Seven patients with PEEK implants required reoperation for pseudarthrosis, compared to 1 patient with an allograft ($p = 0.01$, OR 10.00; 95% CI 1.192–83.884). There was no significant difference in tobacco use between the PEEK and allograft groups ($p = 0.586$).

**CONCLUSIONS** The results of this study demonstrate that the use of PEEK devices in 1-level ACDF is associated with a significantly higher rate of radiographically demonstrated pseudarthrosis and need for revision surgery compared with the use of allografts. Surgeons should be aware of this when deciding on interbody graft options, and reimbursement policies should reflect these discrepancies.

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**KEYWORDS** ACDF; anterior cervical discectomy and fusion; pseudarthrosis; PEEK; allograft

Anterior cervical discectomy and fusion (ACDF) is one of the most common neurosurgical procedures performed for the treatment of cervical myelopathy and radiculopathy.[1] Although immediate symptomatic relief is generally due to decompression of the affected neural structures, long-term success is dependent on the placement of an appropriate interbody graft within the disc space to maintain disc and foraminal height, restore cervical lordosis, and promote bone fusion.[11,13]

As surgeons continue to refine this common procedure, options for graft material have increasingly multiplied. An autograft, often obtained from the patient's anterior iliac crest, is considered to be the gold standard due to its lack of histocompatibility difference from the removed disc,

**ABBREVIATIONS** ACDF = anterior cervical discectomy and fusion; DBM = demineralized bone matrix; PEEK = polyetheretherketone; QALY = quality-adjusted life-year; rhBMP-2 = recombinant human bone morphogenetic protein–2.

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which could lead to graft rejection, and its ability to form a solid fusion construct.[17,22] Harvesting bone for an autograft, however, comes with added morbidity, including donor site pain, stress fractures, and injury to the lateral femoral cutaneous nerve, as well as increased operative time, blood loss, and rate of surgical infection.[13,19,22] Allograft substitutes, including cortical, cancellous, and composite cadaver bone, have been employed to circumvent these complications, but they come with the theoretical risk of increased disease transmission, such as hepatitis and HIV, for which the estimated risks of disease spread are reported to be 0.01% and 0.03%, respectively.[6,14]

More recently, synthetic interbody fusion devices have been developed, which are primarily made from carbon fiber, titanium, or polyetheretherketone (PEEK).[28] The PEEK cage, in particular, has gained significant popularity due to its radiolucent properties and its elastic modulus, which is similar to that of bone.[4,8,12] Furthermore, the use of PEEK cages results in increased billing per surgical level compared to allograft,[23] which may further drive graft selection. Of note, for single-level cases, if a PEEK cage is used without a plate, the number of work relative value units is fewer than if a structural allograft is used with a plate (approximately 36 vs 49, depending on the payor). It seems conceivable that PEEK, a plastic material, would promote less bone fusion than a structural cadaveric bone allograft, even if the PEEK cage were packed with bone. Thus, we performed the largest retrospective cohort study to date to examine the incidence of radiographically demonstrated pseudarthrosis and subsequent reoperations in patients who underwent a 1-level ACDF with either a PEEK or structural allograft implant.

## Methods

In this retrospective, single-center study, all consecutive 1-level ACDF procedures performed at the Oregon Health & Science University between July 2011 and July 2016 were reviewed. Thirteen different attending surgeons (9 neurological surgeons and 4 orthopedic surgeons) performed the operative procedures. Any adult patient undergoing a 1-level ACDF for degenerative disease or trauma was included. Patients who did not have at least 1 year of follow-up with either a cervical x-ray study or CT scan were excluded. Implant selection, duration of follow-up, and the acquisition of follow-up imaging were dependent on the practice pattern of the individual surgeon. The study was approved by the local institutional review board, with a waiver of consent.

Electronic medical records were reviewed for demographic data, patient smoking status, type of graft material used, and evidence of pseudarthrosis. The presence of pseudarthrosis was defined as the lack of solid bone growth across the disc space at 1 or more years of radiographic follow-up. The primary investigators and an attending neuroradiologist independently reviewed all postoperative imaging studies. Records were further reviewed for any additional surgical intervention that was warranted beyond the index surgery. All records were also reviewed for the occurrence of postoperative infection.

Statistical analysis was undertaken using SPSS Statistics version 24 (IBM Corp.), and p values were considered significant at $< 0.05$. Pearson correlation tests were used to determine whether there were statistically significant correlations between the rates of pseudarthrosis and of reoperations, and the graft materials (PEEK vs allograft materials). A Pearson correlation test was also used to determine if there was a statistically significant level of correlation between smoking history and graft material in patients in whom pseudarthrosis was confirmed. A Fisher exact test was used to determine the correlation between pseudarthrosis and the reoperation rate for PEEK grafts associated with a plate. A Student t-test was used to determine differences between the times of radiographic follow-up.

Mean results for the treatment groups are expressed as means ± standard deviations.

## Results

Four hundred eight patients underwent 1-level ACDF during the collection period; of these, 211 (51.7%) received PEEK implants, 185 (45.3%) received structural allograft implants, and 12 (2.9%) received iliac crest autografts. Of the 408 patients, 127 (31%) met the study's inclusion criteria: 56 (44%) with PEEK implants and 71 (56%) with structural allograft implants. The allograft implants included composite (61/71), cortical (8/71), or cancellous (2/71) materials. All PEEK cages were filled with nonstructural allograft in the form of demineralized bone matrix (DBM; 47/56) or a local autograft (9/56). The mean age of patients was 51 ± 14.9 years in the PEEK group and 53 ± 13.0 years in the allograft group. There was no significant difference in body mass index or smoking status between patients in the PEEK and allograft groups (Table 1). The overall 25% rate of smokers was slightly higher than the 17% rate in the overall US population.[9] In both groups, the majority of procedures were performed for degenerative changes: 1 procedure was performed for trauma in the PEEK group (2%) and 11 procedures were performed for trauma in the allograft group (15.5%) ($p = 0.009$). Excluding patients who underwent ACDF for trauma yielded similar pseudarthrosis rates: 27 (48.2%) of 56 patients in the PEEK group and 5 (8%) of 62 patients in the structural allograft group.

Patient imaging at the 1-year follow-up included x-ray studies in 110 patients (86.6%) and CT scanning in 17 patients (13.4%). In the PEEK group, 45 (80.4%) of 56 pa-

**TABLE 1. Patient demographics**

| Factor | Structural Allograft Group | PEEK Group | Total |
|---|---|---|---|
| Patients | 71 | 56 | 127 |
| Age in yrs (mean ± SD) | 51 ± 14.9 | 53 ± 13.0 | 51.7 ± 14.2 |
| Males | 34 | 21 | 55 |
| Females | 37 | 35 | 72 |
| Smokers | 17 (24) | 15 (27) | 32 (25) |
| BMI (mean ± SD) | 28.4 ± 0.6 | 29.1 ± 0.7 | 28.7 ± 0.6 |

Unless otherwise specified, values represent numbers of patients (%, if given). There was no statistically significant difference between groups in any category.

tients underwent x-ray studies compared to 65 (91.5%) of 71 patients in the structural allograft group; the difference in these values was not statistically significant ($p = 0.115$). Average radiographic follow-up was longer in the PEEK group than in the structural allograft group: 21 versus 16 months, respectively ($p = 0.02$). Of the 56 patients who received PEEK implants, 29 (51.8%) had demonstrated radiographic evidence of pseudarthrosis at 1 or more years after follow-up, as seen on a cervical x-ray film or CT scan (Fig. 1). In contrast, only 7 (10%) of the 71 patients with structural allograft implants had radiographic evidence of pseudarthrosis ($p < 0.001$, OR 9.82; 95% CI 3.8–25.1). Of patients with pseudarthrosis, 7 patients with PEEK implants (24.1%) required a revision operation for pseudarthrosis, compared to only 1 patient with a structural allograft (14.3%) ($p = 0.01$, OR 10.00; 95% CI 1.192–83.884) (Table 2). Clinical indications for revision surgery for the 7 patients with PEEK implants included persistent radiculopathy (6/7), myelopathy (2/7), or chronic, debilitating neck pain (1/7). One of the 7 patients required revision surgery to correct completely fractured hardware with radiculopathy. The types of revision surgery included a redo ACDF, a posterior instrumented fusion, and a combination of redo anterior fusion combined with posterior fusion.

The 1 patient who underwent revision ACDF surgery in the allograft group initially received a composite bone graft and displayed clinical indications of persistent radiculopathy. Interestingly, the graft for this patient was changed to a PEEK implant upon revision surgery. This was also the only patient in whom a postoperative wound infection developed after revision surgery; the infection was treated with operative washout and a course of antibiotics. There were no reports of postoperative transmission of hepatitis or HIV in either group.

The incidence of pseudarthrosis in patients who had received PEEK implants requiring plate and screw fixation was also examined. The majority of PEEK implants were stand-alone devices with no associated plate devices (46/56 implants, 82.1%). Of the 10 patients who received PEEK implants with an associated plate, there was radiographic evidence of pseudarthrosis in 3 patients, 2 of whom required revision surgery. Compared to stand-alone PEEK implants, there was no significant correlation between a PEEK implant associated with a plate and the incidence of pseudarthrosis ($p = 0.171$) or revision surgery ($p = 0.596$). In other words, PEEK implants led to higher pseudarthrosis rates than structural allografts regardless of whether the PEEK implants were stand-alone or supplemented with a plate and screws. However, the number of patients with a plated PEEK implant was very small ($n = 10$) and insufficient to draw strong conclusions.

Smoking status was further examined in patients with radiographic pseudarthrosis: 11 (37.9%) of 29 patients with pseudarthrosis in the PEEK group smoked tobacco, whereas 4 (57.1%) of 7 patients with pseudarthrosis in the allograft group smoked ($p = 0.586$) (Table 2). Of all patients with pseudarthrosis, only 1 patient in the PEEK group was on a long-term regimen of steroids for lupus.

## Discussion

This retrospective study—the largest ever in which PEEK implants have been compared with structural allografts for ACDF—demonstrates an alarmingly high rate of radiographic evidence of pseudarthrosis in patients who received PEEK grafts while undergoing a 1-level ACDF compared to those who received structural allografts. After at least 1 year of radiographic follow-up, there was a fivefold higher incidence of pseudarthrosis in patients with PEEK cages and almost a doubled rate of subsequent revision surgery.

Since their approval by the US Food and Drug Administration in 1998,[12,21] PEEK implants have been a widely accepted choice as an interbody spacer. A recent study surveying 5334 surgeons from the Global AO Spine database found that PEEK cages make up 84% of cages selected for the graft component of an ACDF.[28] PEEK implants have gained popularity because their elastic modulus is close to that of human bone, and in contrast to metallic cages, PEEK cages are composed of radiolucent material and produce less artifact on postoperative imaging.[5] Furthermore, PEEK does not come with the risk of disease transmission that allograft spacers theoretically carry. However, the inherent bio-inertness of PEEK comes with the significant disadvantage of its being less likely to integrate with organic bone tissue.[21] In vitro studies have demonstrated that when mesenchymal cells are cultured on PEEK material, they do not express known markers of bone formation, including alkaline phosphatase or osteocalcin.[15] Furthermore, mesenchymal cultures grown on PEEK have significantly higher levels of interleukin-1β, which is associated

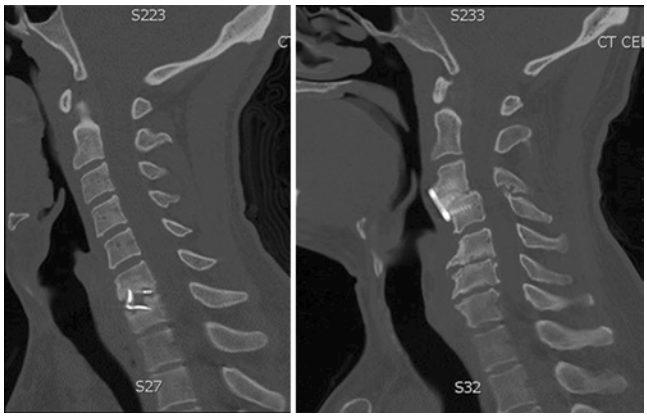


**FIG. 1.** Sagittal x-ray films obtained in a patient with a PEEK interbody graft and pseudarthrosis (**left**) and a patient with a structural allograft implant (**right**) healed 1 year after surgery.

**TABLE 2. Comparison of pseudarthrosis, need for revision surgery, and smoking status between the structural allograft and PEEK implant groups**

| Factor | Structural Allograft Group | PEEK Group | p Value |
|---|---|---|---|
| Pseudarthrosis on imaging studies | 7 (10) | 29 (52) | ≤0.001 |
| Revision surgery | 1 (14) | 7 (24) | 0.01 |
| Smokers w/ pseudarthrosis | 4 (57) | 11 (38) | 0.59 |

Unless otherwise specified, values represent numbers of patients (%).

with the formation of fibrous tissue rather than bone tissue. Cells cultured on PEEK have also been demonstrated to have significantly higher levels of necrosis, DNA damage, and apoptosis.[16] These in vitro studies are supported in an in vivo sheep model, which also demonstrated PEEK cages surrounded by fibrous connective tissue, preventing bone integration and potentially resulting in nonunion.[24]

In the clinical setting, there is little evidence for the superiority of PEEK over allograft, although studies describing well-controlled, direct comparisons between PEEK and allograft are limited. A recent meta-analysis found only 10 studies that directly compared PEEK to autograft, allograft, or other synthetic cages (titanium and carbon fiber). However, within those 10 studies there were no significant differences in fusion rates or clinical outcomes between PEEK and other graft materials.[10] In only 2 of those 10 studies did researchers directly compare PEEK to allograft. Vaidya et al.[25] performed a retrospective chart review of 46 consecutive cases of ACDF in which they compared patients treated with PEEK cages filled with recombinant human bone morphogenetic protein–2 (rhBMP-2) with patients treated with allograft interbody spacers and DBM at a single institution. Follow-up x-ray studies at 1.5–6 months postoperatively demonstrated that the PEEK cages filled with rhBMP-2 consistently exhibited 100% endplate resorption, which was said to have often been mistaken as infection by radiologists' interpretations. In contrast, there was no endplate resorption in any of the patients treated with allograft and DBM, with only "simple and progressive blurring" of the endplate junction, indicating ongoing fusion. However, at the 2-year follow-up, there was no significant difference in radiographic or clinical outcomes between the two groups, as measured by Cervical Oswestry Scale scores or visual analog scale scores. Subsequent cost analysis demonstrated that the cost of implants treated with PEEK and rhBMP-2 was more than 3 times the cost of those treated with allografts and DBM, which led the authors to ultimately abandon the use of PEEK and rhBMP-2 in lieu of the less expensive and equally effective allograft spacer. Another retrospective review[20] compared PEEK and rhBMP-2 with allograft and rhBMP-2 for both ACDF and lumbar interbody fusion. In those patients who underwent an ACDF (n = 34), the PEEK and rhBMP-2 groups had slightly higher fusion rates than the allograft group (91% vs 81%, respectively), with 1 PEEK cage displaying cage migration. Similar to the findings of Vaidya et al.,[25] there was 100% endplate resorption with the use of rhBMP-2. There was a 50% subsidence rate in all patients.[20]

This potential for subsidence is one main concern cited in the literature as a disadvantage of allografts, which can lead to loss of disc and foraminal height, increased angulation, and nonunion.[2,3,18] However, in a recent retrospective study, researchers compared subsidence rates between PEEK and allograft cages and found that there was no significant difference between the PEEK (29%) and allograft (28%) groups. Furthermore, this study by Yson et al. demonstrated that even those patients who did have subsidence did not display any clinical difference from those who did not, as measured by the Neck Disability Index and the visual analog scale.[29]

Our findings have a wider implication on a systems level, as the number of ACDF procedures performed continues to increase, and reimbursement policies continue to evolve. Between 1992 and 2005, the rate of ACDFs grew by 206% in patients older than 65 years,[27] which is in line with the significant increase in general American healthcare spending, which rose to $2.6 trillion in 2010. As such, there has been increased scrutiny regarding the cost-effectiveness of all spinal procedures.[26] In 1 study, a Markov decision model was used to determine the most effective graft (PEEK, allograft, or autograft) for a 1-level ACDF in terms of cost and quality of life. Cost was defined as the total sum of hospital, physician, and graft fees based on Current Procedural Terminology codes. The code designated for a PEEK interbody cage (22851) has a significantly higher reimbursement rate than that for a structural allograft (20931),[23] with a work relative value unit of 6.7 versus 1.8, respectively. As such, there was a significantly higher total cost for an ACDF with a PEEK cage (estimated total cost of $18,314) than for the same procedure in which an allograft cage was used (estimated total cost of $12,539). Virk et al. further examined the cost of quality-adjusted life-years (QALYs) gained by each graft type. PEEK was reported to be the most expensive, costing $3220/QALY, compared to allograft at $2358/QALY and autograft at $2413/QALY.[26] This economic discrepancy is further widened by synthetic cage billing per level of placement, while allograft billing is once per surgery, regardless of the number of levels instrumented.

As Kersten et al. described in the review accompanying their meta-analysis, data regarding clinical outcomes of PEEK cages come mostly from noncomparative cohort studies and a few randomized control trials.[10] Compared with data from previous studies, the advantage of the data we present here is that it offers a direct comparison of the incidence of radiographic pseudarthrosis between patients who received a PEEK cage and those who received a structural allograft in a 1-level ACDF. Furthermore, according to our review of previous studies, our study has the largest cohort of patients. However, our study does have limitations, which are inherent to its retrospective nature. A total of 13 different surgeons performed these procedures, making standardization of graft selection and the operative procedure difficult, although the similarity of the results across multiple surgeons does suggest generalizability of our findings. Differences between surgeons and changes in practice patterns were not evaluated. Confounders may stem from the lack of uniformity of physical graft placement, the type of structural allograft used (although the vast majority were composite), and the materials used to pack the PEEK cages (although the vast majority were packed with allograft and DBM). Many patients did not have 1 year of follow-up and thus were not included in the final analysis.

Another limitation of this study is that 2 different imaging modalities (x-ray and CT) were used to evaluate fusion. Ideally, all patients would have received gold-standard CT scanning, although the use of CT leads to increased costs as well as greater radiation exposure. One might even argue that complete bone bridging from endplate to endplate is not essential. As is the case with de-

vices covered by plasma spray or sintered beads, PEEK does not undergo creeping bone substitution, as it just needs to be anchored at the ends to bone and will continue its load-bearing support irrespective of bone growth through the cage itself. As such, another imaging modality that could have been useful for assessing pseudarthrosis in this study, and which may be considered in future studies, is the flexion-extension x-ray study, which has been shown to provide a higher level of evidence for fusion.[7]

Also, as mentioned, the rate of cigarette smoking in the patient population of this study is slightly higher than the percentage of smokers in the overall US population, which may affect the generalizability of the results. In addition, the PEEK group in the present study also had a higher percentage of cigarette smokers than the structural allograft group. Although this finding was not statistically significant, it suggests that the two groups were not ideally matched. One should note, however, that the prevalence of smoking in patients with pseudarthrosis was higher in patients with structural allografts than in those with PEEK devices. This study is also lacking objective clinical data with validated outcome surveys, which will be a focus of future prospective studies. The ideal future study would be a multicenter study with a minimum of 2 years of follow-up and a better definition of the goal of the implants.

## Conclusions

The results of this study suggest that the use of PEEK cages is associated with a significantly increased risk for bone nonunion and revision surgery compared to the use of structural allograft implants, at least at our institution. Thus, surgeons should consider these risks when deciding among the many graft choices available for an ACDF. Furthermore, reimbursement policies to reduce the cost discrepancy between PEEK and allograft should be advocated.

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## References

1. Bible JE, Kang JD: Anterior cervical discectomy and fusion: surgical indications and outcomes. **Semin Spine Surg 28:**80–83, 2016
2. Bishop RC, Moore KA, Hadley MN: Anterior cervical interbody fusion using autogeneic and allogeneic bone graft substrate: a prospective comparative analysis. **J Neurosurg 85:**206–210, 1996
3. Chau AMT, Mobbs RJ: Bone graft substitutes in anterior cervical discectomy and fusion. **Eur Spine J 18:**449–464, 2009
4. Chen F, He W, Mahaney K, Noeller J, Mhanna N, Viljoen S, et al: Alternative grafts in anterior cervical fusion. **Clin Neurol Neurosurg 115:**2049–2055, 2013
5. Cizek GR, Boyd LM: Imaging pitfalls of interbody spinal implants. **Spine (Phila Pa 1976) 25:**2633–2636, 2000
6. Delloye C, Cornu O, Druez V, Barbier O: Bone allografts: what they can offer and what they cannot. **J Bone Joint Surg Br 89:**574–579, 2007
7. Ghiselli G, Wharton N, Hipp JA, Wong DA, Jatana S: Prospective analysis of imaging prediction of pseudarthrosis after anterior cervical discectomy and fusion: computed tomography versus flexion-extension motion analysis with intraoperative correlation. **Spine (Phila Pa 1976) 36:**463–468, 2011
8. Hee HT, Kundnani V: Rationale for use of polyetheretherketone polymer interbody cage device in cervical spine surgery. **Spine J 10:**66–69, 2010
9. Jamal A, Phillips E, Gentzke AS, Homa DM, Babb SD, King BA, et al: Current cigarette smoking among adults—United States, 2016. **MMWR Morb Mortal Wkly Rep 67:**53–59, 2018
10. Kersten RFMR, van Gaalen SM, de Gast A, Öner FC: Polyetheretherketone (PEEK) cages in cervical applications: a systematic review. **Spine J 15:**1446–1460, 2015
11. Kolstad F, Nygaard ØP, Andresen H, Leivseth G: Anterior cervical arthrodesis using a "stand alone" cylindrical titanium cage: prospective analysis of radiographic parameters. **Spine (Phila Pa 1976) 35:**1545–1550, 2010
12. Kurtz SM, Devine JN: PEEK biomaterials in trauma, orthopedic, and spinal implants. **Biomaterials 28:**4845–4869, 2007
13. Maharaj MM, Phan K, Mobbs RJ: Anterior cervical discectomy and fusion (ACDF) autograft versus graft substitutes: what do patients prefer?—A clinical study. **J Spine Surg 2:**105–110, 2016
14. Ng VY: Risk of disease transmission with bone allograft. **Orthopedics 35:**679–681, 2012
15. Olivares-Navarrete R, Gittens RA, Schneider JM, Hyzy SL, Haithcock DA, Ullrich PF, et al: Osteoblasts exhibit a more differentiated phenotype and increased bone morphogenetic protein production on titanium alloy substrates than on poly-ether-ether-ketone. **Spine J 12:**265–272, 2012
16. Olivares-Navarrete R, Hyzy SL, Slosar PJ, Schneider JM, Schwartz Z, Boyan BD: Implant materials generate different peri-implant inflammatory factors: poly-ether-ether-ketone promotes fibrosis and microtextured titanium promotes osteogenic factors. **Spine (Phila Pa 1976) 40:**399–404, 2015
17. Pollock R, Alcelik I, Bhatia C, Chuter G, Lingutla K, Budithi C, et al: Donor site morbidity following iliac crest bone harvesting for cervical fusion: a comparison between minimally invasive and open techniques. **Eur Spine J 17:**845–852, 2008
18. Rhee JM, Patel N, Yoon ST, Franklin B: High graft resorption rates with dense cancellous allograft in anterior cervical discectomy and fusion. **Spine (Phila Pa 1976) 32:**2980–2984, 2007
19. Schnee CL, Freese A, Weil RJ, Marcotte PJ: Analysis of harvest morbidity and radiographic outcome using autograft for anterior cervical fusion. **Spine (Phila Pa 1976) 22:**2222–2227, 1997
20. Sethi A, Craig J, Bartol S, Chen W, Jacobson M, Coe C, et al: Radiographic and CT evaluation of recombinant human bone morphogenetic protein-2-assisted spinal interbody fusion. **AJR Am J Roentgenol 197:**W128–W133, 2011
21. Shimizu T, Fujibayashi S, Yamaguchi S, Otsuki B, Okuzu Y, Matsushita T, et al: In vivo experimental study of anterior cervical fusion using bioactive polyetheretherketone in a canine model. **PLoS One 12:**e0184495, 2017
22. Silber JS, Anderson DG, Daffner SD, Brislin BT, Leland JM, Hilibrand AS, et al: Donor site morbidity after anterior iliac crest bone harvest for single-level anterior cervical discectomy and fusion. **Spine (Phila Pa 1976) 28:**134–139, 2003
23. Singh K, Qureshi S: ISASS Policy Statement—cervical interbody. **Int J Spine Surg 8:**13, 2014
24. Toth JM, Wang M, Estes BT, Scifert JL, Seim HB III, Turner AS: Polyetheretherketone as a biomaterial for spinal applications. **Biomaterials 27:**324–334, 2006
25. Vaidya R, Carp J, Sethi A, Bartol S, Craig J, Les CM: Complications of anterior cervical discectomy and fusion using

recombinant human bone morphogenetic protein-2. **Eur Spine J 16:**1257–1265, 2007
26. Virk SS, Elder JB, Sandhu HS, Khan SN: The cost effectiveness of polyetheretheketone (PEEK) cages for anterior cervical discectomy and fusion. **J Spinal Disord Tech 28:**E482–E492, 2015
27. Wang MC, Kreuter W, Wolfla CE, Maiman DJ, Deyo RA: Trends and variations in cervical spine surgery in the United States: Medicare beneficiaries, 1992 to 2005. **Spine (Phila Pa 1976) 34:**955–963, 2009
28. Yoon ST, Konopka JA, Wang JC, Youssef JA, Meisel HJ, Brodke DS, et al: ACDF graft selection by surgeons: survey of AOSpine members. **Global Spine J 7:**410–416, 2017
29. Yson SC, Sembrano JN, Santos ERG: Comparison of allograft and polyetheretherketone (PEEK) cage subsidence rates in anterior cervical discectomy and fusion (ACDF). **J Clin Neurosci 38:**118–121, 2017

## Disclosures

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article. Dr. Raslan reports being a consultant to Abbott, and Dr. Than reports being a consultant to Bioventus.

## Author Contributions

Conception and design: Than. Acquisition of data: Krause, Bridges. Analysis and interpretation of data: Than, Krause, Obayashi. Drafting the article: Than, Krause. Critically revising the article: Than, Krause, Bridges. Reviewed submitted version of manuscript: Than, Obayashi, Bridges, Raslan. Approved the final version of the manuscript on behalf of all authors: Than. Statistical analysis: Than, Krause, Obayashi, Raslan. Administrative/technical/material support: Than. Study supervision: Than.

## Supplemental Information

### Previous Presentations

Data shown in this report were presented by Dr. Krause at the Spine Summit 2018—34th Annual Meeting of the Section on Disorders of the Spine and Peripheral Nerves (Abstract no. 122, Top Abstracts Concurrent Session), March 14–17, 2018, Orlando, Florida; and in Abstracts of the 2018 AANS/CNS Joint Section on Disorders of the Spine and Peripheral Nerves Annual Meeting. *Neurosurg Focus 44(3):*A1–A109, 2018.

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