

Structural Allograft Versus PEEK Implants in Anterior Cervical Discectomy and Fusion: A Systematic Review

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Amit Jain, MD^{1*}, Majd Marrache, MD^{1*}, Andrew Harris, BS¹,
Varun Puvanesarajah, MD¹, Brian J. Neuman, MD¹, Zorica Buser, PhD²,
Jeffrey C. Wang, MD², S. Tim Yoon, MD³, Hans Jörg Meisel, MD⁴,
and AOSpine Knowledge Forum Degenerative

Abstract

Study Design: Systematic literature review.

Objective: Our primary objective was to compare reported fusion rates after anterior cervical discectomy and fusion (ACDF) using structural allograft versus polyetheretherketone (PEEK) interbody devices in patients with cervical spine degeneration. Our secondary objectives were to compare differences in rates of subsidence and reoperation and in patient-reported outcomes between the 2 groups.

Methods: Through a systematic review of the English-language literature using various databases, we identified 4702 articles. After we applied inclusion and exclusion criteria, 14 articles (7 randomized controlled trials, 4 prospective studies, and 3 retrospective studies) reporting fusion rates of structural allograft or PEEK interbody devices were eligible for our analysis. No randomized controlled trials compared outcomes of structural allograft versus PEEK interbody devices. Extracted data included authors, study years, study designs, sample sizes, patient ages, duration of follow-up, types of interbody devices used, fusion rates, definition of fusion, reoperation rates, subsidence rates, and patient-reported outcomes.

Results: Fusion rates were 82% to 100% for allograft and 88% to 98% for PEEK interbody devices. The reported data were insufficient to perform meta-analysis. Structural allograft had the highest reported rate of reoperation (14%), and PEEK interbody devices had the highest reported subsidence rate (18%). Patient-reported outcomes improved in both groups. There was insufficient high-quality evidence to compare the associations of various PEEK modifications with fusion rates.

Conclusion: Fusion rates were similar between structural allograft and PEEK interbody devices when used for ACDF for cervical spine degeneration. Currently, there is insufficient high-quality evidence to assess associations of PEEK modifications with fusion rates.

Level of Evidence: II.

Keywords

allograft, anterior cervical discectomy and fusion, cervical spine degeneration, fusion rate, interbody device, patient-reported outcome, polyetheretherketone interbody device, structural allograft, systematic review

Introduction

Anterior cervical discectomy and fusion (ACDF) is a common surgical treatment for cervical spine degeneration and associated cervical nerve root or spinal cord compression.^{1,2} Indications for ACDF include cervical radiculopathy or myelopathy secondary to degenerative disc disease, disc herniation, spondylosis, and spinal stenosis. Interbody devices used in ACDF facilitate fusion, correct kyphosis, and restore foraminal height.^{3,4} When ACDF was initially described by Cloward⁵

¹ Department of Orthopaedic Surgery, The Johns Hopkins University School of Medicine, Baltimore, MD, USA

² Department of Orthopaedic Surgery, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

³ Department of Orthopaedics, Emory University, Atlanta, GA, USA

⁴ Department of Neurosurgery, BG-Clinic Bergmannstr. Halle, Germany

* Amit Jain and Majd Marrache contributed equally toward this study.

Corresponding Author:

Amit Jain, Department of Orthopaedic Surgery, The Johns Hopkins University, 601 North Caroline Street, JHOC 5223, Baltimore, MD 21287, USA.
Email: amitjain@jhmi.edu.



in 1958, structural autograft bone was used for interbody support. However, during the past several decades, various alternatives to structural autograft have gained popularity, including structural cadaveric allograft, polyetheretherketone (PEEK) interbody devices, and metal interbody devices.⁶

A 2017 survey of AOSpine members found that PEEK interbody devices were commonly used world-wide and structural allografts were commonly used in North America.⁷ PEEK has multiple theoretical advantages, including biocompatibility, radiolucency, favorable elasticity, and ease of procurement and storage.⁸⁻¹⁰ The major drawback of PEEK is that it is bio-inert and limits host bone integration.¹¹ Various strategies have been proposed to improve the biologic integration of PEEK, including augmenting PEEK devices with graft extenders, such as demineralized bone matrix or cellular products, as well as modifications to the PEEK device.^{12,13} Proposed modifications include surface enhancements, such as increased surface porosity or titanium coating, and impregnation of PEEK with bioactive materials such as hydroxyapatite.¹⁴ The effects of these modifications on fusion success and clinical outcomes are unclear.

Structural allograft, including cortical allograft, corticocancellous or composite grafts, and dense cancellous grafts, is an effective alternative to autograft to achieve bony fusion in ACDF.^{15,16} Among surgeons who use allograft, cortical and corticocancellous composite grafts are more popular because they provide additional structural support and resistance against subsidence,¹⁷ whereas dense cancellous grafts have been reported to have high rates of resorption.¹⁸

Our primary objective was to compare reported fusion rates after ACDF using structural allograft versus PEEK interbody devices in patients with cervical spine degeneration. Our secondary objectives were to compare differences in the rates of subsidence and reoperation and in patient-reported outcomes between the 2 groups.

Methods

Our study used publicly available information and thus was not subject to review by our institutional review board.

Search Strategy

We designed our literature search in accordance with the Preferred Reporting Items of Systematic Reviews and Meta-Analyses guidelines.¹⁹ With the assistance of a clinical informationist, we performed a comprehensive literature search using PubMed, Embase, The Cochrane Library, Web of Science, Scopus, ClinicalTrials.gov, and CINAHL Plus databases in October 2018 (see Appendix 1 in the online version of the article). We identified 4702 articles (Figure 1).

Inclusion and Exclusion Criteria

We included studies that reported results of ACDF using structural allograft, PEEK interbody devices, or modified PEEK

interbody devices; analyzed patients aged ≥ 18 years; included results of >20 patients; were published in 1993 or later; were written in English; were randomized controlled trials or retrospective, prospective, or observational cohort studies; and reported 2-year radiographic follow-up. (For comparative studies in which only 1 of the study groups met the eligibility criteria, we limited our data abstraction and analysis to that group.)

We excluded studies that reported on ACDF using zero-profile or stand-alone devices; ACDF performed without anterior cervical plating; cervical corpectomy; circumferential (360° or 540°) fusion; interventions to facilitate fusion in addition to the interbody device (eg, bone morphogenic protein, stem cells, autograft, platelets); ACDF for nondegenerative conditions; ACDF for adjacent-segment disease (adjacent to previous ACDF); or revision ACDF for nonunion or other conditions. We also excluded animal studies, cadaveric studies, case reports, correspondence, letters to the editor, technical notes, abstracts, and poster presentations. Level of evidence of the articles included in this systematic review was assessed using the Oxford Centre for Evidence-Based Medicine.²⁰

Study Selection

Two independent reviewers screened the studies for eligibility. A third reviewer served as an arbitrator when there was disagreement between the 2 primary reviewers. Each article's title and abstract were reviewed. Articles that could not be excluded on the basis of this review were retrieved for full-text review ($n = 101$). Covidence Systematic Review Software (Veritas Health Innovation, Melbourne, Victoria, Australia) was used to facilitate the screening and selection process. Fourteen articles (7 randomized controlled trials, 4 prospective studies, and 3 retrospective studies) met our eligibility criteria and were included in the review (Table 1).

Data Extraction and Analysis

Using a standardized data extraction form, we extracted the following information: authors, study years, study designs, sample sizes, patient ages, duration of follow-up, types of interbody device used, fusion rates, definitions of fusion, reoperation rates, subsidence rates, and patient-reported outcomes (ie, visual analogue scale [VAS] for pain, Neck Disability Index [NDI], Patient-Reported Outcomes Measurement Information System, and Odom's criteria). Descriptive statistics were calculated and reported as appropriate. There were insufficient data to perform a meta-analysis.

Results

Fusion Rates

In 11 studies, fusion was assessed by an independent or blinded physician.²¹⁻³¹ Criteria for fusion success differed slightly among studies, although motion (commonly defined as $<2^\circ$ or $<4^\circ$ change in angulation between the spinous processes)

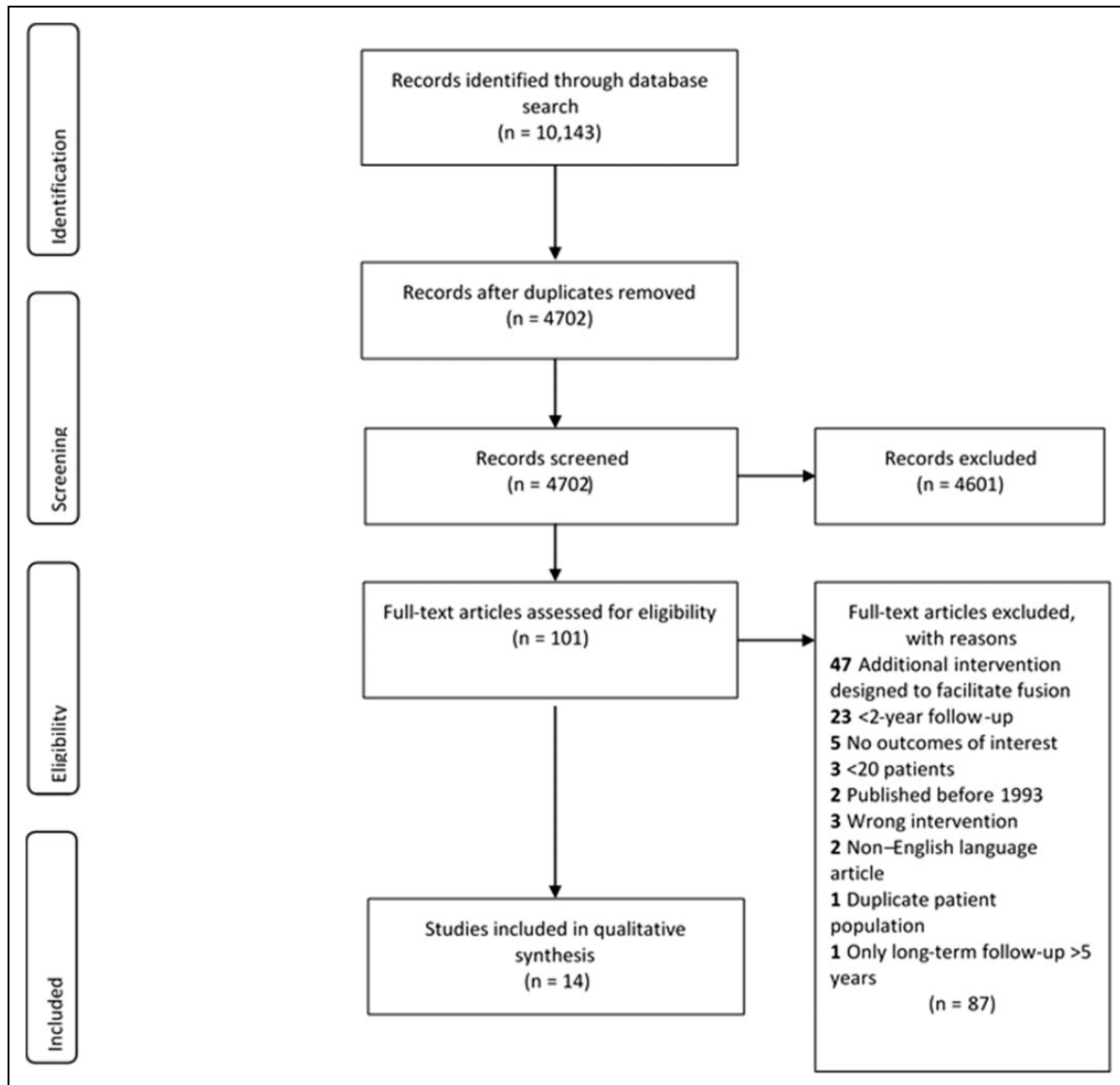


Figure 1. Literature search performed using PubMed, Embase, The Cochrane Library, Web of Science, Scopus, ClinicalTrials.gov, and CINAHL Plus databases in October 2018. The purpose was to compare the fusion rates of structural allograft versus polyetheretherketone interbody devices in patients who underwent anterior cervical discectomy and fusion for cervical spine degeneration.

on flexion-extension radiographs is the commonly used method to determine fusion success (Table 2).

Structural Allograft. Nine studies (1354 patients) reported fusion data with the use of structural allograft: 5 used corticocancellous allograft,^{21,24,26,28,31} 2 used unspecified cortical allograft,^{22,25} 1 used fibular allograft,³⁰ and 1 did not report the type of allograft used.²³ The fusion rates among these 9 studies were 82% to 100%. Among the 5 studies that used corticocancellous allograft, fusion rates at 2 years or more were 82% to 97% (Table 1).

A prospective comparison of 1-level and 2-level ACDF using corticocancellous allograft reported fusion rates of 89% and 79%, respectively, at 2 years, and 93% and 86%, respectively, at 5 years.²⁸ The reported fusion rates for unspecified

cortical grafts at 2 years were 82%²² to 97%.²⁵ In a prospective study, Suchomel et al³⁰ assessed fusion rates of fibular allograft versus structural autograft and found that the fibular allograft group had fusion rates of 85.5% at 1 year and 93.4% at 2 years.

PEEK Interbody Devices. Five studies using PEEK interbody devices (146 patients) were included in our final analysis, including 1 randomized controlled trial,²⁷ 2 prospective studies,^{29,32} and 2 retrospective studies.^{33,34} Rates of fusion for PEEK interbody devices in these 5 studies were 88% to 98%.

In a prospective study by El-Tantawy,³² 10 patients underwent 2-level fusion, 10 underwent 3-level fusion, and 8 underwent 4-level fusion with stand-alone PEEK cage. Fusion was achieved at a mean of 14.9 weeks for 2-level, 15.2 weeks for

Table 1. Studies of Fusion Rates in Patients Who Underwent Anterior Cervical Discectomy and Fusion for Cervical Spine Degeneration.

First Author, Year	Study Characteristics						Outcomes (%)			
	Design	Study Groups	Sample Size	Mean Age (Years)	Follow-up (Years)	Indications (No. of Patients)	Levels (No. of Patients)	2-Year Fusion	Reoperation	Subsidence
Feiz-Erfan, ²⁴ 2007	RCT	Allograft: with vs without platelets	50	46	2	DDD (29); herniated disc (21)	1 (18); 2 (29)	85	4	NR
Campbell, ²³ 2009	RCT	Allograft: with vs without cervical collar	257	44	2	Radiculopathy or myelopathy	1 (257)	96 (braced); 100 (nonbraced)	0.7	NR
Feng, ²⁷ 2018	RCT	PEEK with vs without tricalcium phosphate	23	64	2	Radiculopathy (12); myelopathy (5); radiculomyelopathy (6)	1 (5); 2 (12); 3 (6)	98	NR	0
Coric, ²⁶ 2011	RCT	Allograft vs arthroplasty	133	44	2	Radiculopathy or myelopathy	1 (133)	82	5	NR
Gornet, ²² 2017	RCT	Allograft vs arthroplasty	188	47	2	Radiculopathy or myelopathy	2 (188)	82	8	4
Hisey, ²¹ 2015	RCT	Allograft vs arthroplasty	81	44	4	Radiculopathy or myelopathy	1 (81)	94 ^a	NR	NR
Mummaneni, ²⁵ 2007	RCT	Allograft vs arthroplasty	265	44	2	Radiculopathy or myelopathy	1 (265)	98	8.6	NR
Suohomei, ³⁰ 2004	PC	Allograft vs autograft	NA ^b	48	2	Spondylosis and/or cervical disc prolapse/protrusion	1 or 2 (NA ^b)	93	NR	0
Zigler, ²⁸ 2016	PC	1- vs 2-level allograft	186	45	5	Radiculopathy or myelopathy	1 (81); 2 (105)	89 (1-level); 79 (2-level)	14	NR
Schlosser, ³¹ 2006	RC	Allograft	219	52	6	Unknown	1 (80); 2 (57); 3 (53); 4 (29)	98 ^c	8	NR
El-Tantawy, ³² 2015	PC	2- vs 3- vs 4-level PEEK implant	28	40	2	Neck pain and radiculopathy	2 (10); 3 (10); 4 (8)	93	0	2
Niu, ²⁹ 2010	PC	PEEK vs titanium implant	25	52	2	Radiculopathy or myelopathy	1 (16); 2 (9)	100 ^d	0	0
Cabraja, ³⁴ 2012	RC	PEEK vs titanium implant	42	58	2	Radiculopathy (34); myelopathy (8)	1 (42)	88 ^e	NR	14
Dufour, ³³ 2010	RC	PEEK implant	28	48	2.7	Radiculopathy or myelopathy	1 (19); 2 (9)	94	NR	0

Abbreviations: ACDF, anterior cervical discectomy and fusion; DDD, degenerative disc disease; NA, not available; NR, none reported; PC, prospective cohort; PEEK, polyetheretherketone; RC, retrospective cohort; RCT, randomized controlled trial.

^a Fusion rate reported at 4 years.

^b Eighty patients were included in the study. The number of patients allocated to each group was not reported.

^c Fusion rate reported at unknown time period.

^d Fusion rate reported at 1 year.

^e Fusion rate reported at 2.4 years.

Table 2. Definitions of Fusion in Studies of Structural Allograft and PEEK Interbody Devices in Patients With Cervical Spine Degeneration Who Underwent Anterior Cervical Discectomy and Fusion.

First Author, Year	Definition of Fusion
Feiz-Erfan, ²⁴ 2007	Absence of major angular motion ($\leq 2^\circ$) on flexion/extension radiographs and <50% lucency at each potential fusion surface.
Campbell, ²³ 2009	"The presence of bridging trabecular bone as evidenced by continuous bony connection of the vertebral bodies above and below in at least one of the following areas: lateral, anterior, posterior, and/or through the allograft ring implant; angulation of less than 4° on flexion-extension radiographs; and absence of radiolucency covering more than 50% of either the superior or inferior surface of the graft."
Feng, ²⁷ 2018	"(1) rotation $< 4^\circ$ and < 1.25 mm translation with the absence of motion adjacent to interspinous processes (> 3 mm) in the flexion-extension view and (2) the presence of continuous trabecular bone bridging was revealed by CT scan in at least one of the following locations: anterior, within, or posterior to the PEEK cage."
Coric, ²⁶ 2011	"(1) bridging trabecular bone; 2) angular motion less than 5° ; 3) translational motion less than 3 mm; and 4) less than 50% radiolucency along the bone-implant interface."
Gornet, ²² 2017	"(1) angulation $\leq 4^\circ$, 2) bridging bone as a continuous bony connection with the vertebral bodies above and below, and 3) no radiolucency covering more than 50% of either the superior or inferior surface of the graft."
Hisey, ²¹ 2015	"Bridging bone across the disk space, < 2 degrees angular motion measured from flexion to extension, and $< 50\%$ radiolucent lines at the graft vertebral endplate interfaces."
Mummaneni, ²⁵ 2007	"(1) bone spanning the two VBs in the treated segment; 2) less than 4° of motion on dynamic radiographs; and 3) radiolucencies covering no more than 50% of the implant surface."
Suchomel, ³⁰ 2004	According to criteria of Brown et al ⁴⁸ : "Complete: Complete bridging of trabeculae between adjacent vertebral bodies and bone graft; Partial: Less than 50% bridging trabeculae; Non-union: Lack of trabecular bridging."
Zigler, ²⁸ 2016	Unknown
Schlosser, ³¹ 2006	No radiolucency within the construct and no evidence of instrumentation failure.
Niu, ²⁹ 2010	"Lack of a radiolucent line between the cage and endplate as well as the lack of translation or angulation change in the lateral cervical flexion-extension radiographs at the 1-year follow-up."
Cabraja, ³⁴ 2012	"Movement of less than 2° was measured, and by the absence of motion between the spinous processes on lateral flexion-extension radiographs."
El-Tantawy, ³² 2015	"...continuity of the trabeculae between end-plates with the absence of lucency at the cage/end-plate interface. This was confirmed by stability on

(continued)

Table 2. (continued)

First Author, Year	Definition of Fusion
	dynamic views (not more than 2 mm widening of the inter-spinous distance) or by CT in suspected fusions."
Dufour, ³³ 2010	On CT scan, "excellent fusion," bone continuity on ≥ 1 image in both planes; "good fusion," bone continuity on ≥ 1 image in 1 plane; "no fusion," no visible bone continuity in any plane.

Abbreviations: CT, computed tomography; PEEK, polyetheretherketone; VB, vertebral body.

3-level, and 16.1 weeks for 4-level fusion, with no significant differences. The authors reported a fusion rate of 93% at 2-year follow-up (Table 2). Dufour et al³³ reported a fusion rate of 94% for 28 PEEK patients at a mean follow-up of 32 months.

Subsidence Rates

Structural Allograft. Among the studies of structural allograft, only 2 reported subsidence rates. Gornet et al²² reported the highest subsidence rate (4.3%, 6/138 patients) at 2-year follow-up. In the study by Suchomel et al,³⁰ none of the patients developed subsidence at 2-year follow-up.

PEEK Interbody Devices. High subsidence rates were reported in the study of PEEK interbody devices by El-Tantawy,³² occurring at 7 fusion levels in 5 patients (18%); however, no patient underwent revision surgery. Cabraja et al³⁴ reported a subsidence rate of 14% (6/42), with no reoperations. The remaining articles discussing PEEK fusion rates did not report any subsidence among their patients.^{27,29,33}

Reoperation Rates

Structural Allograft. In studies using structural allograft interbody, the incidence of reoperation for all reasons was 0.7% (1/149 patients) to 13.9% (26/186 patients) (Table 1).^{23,28} Overall, the rates of reoperation for pseudarthrosis with structural allograft interbody were 1.8% to 6.4%.^{28,31}

PEEK Interbody Devices. Among the 5 studies involving PEEK devices, 2 reported no reoperations^{29,32} and 3 did not monitor for reoperation^{27,33,34} (Table 1).

Patient-Reported Outcomes

Eleven studies reported patient-reported outcomes, with VAS and NDI being the most frequently used measures.^{21-29,32,34}

Structural Allograft. Seven studies described patient-reported outcomes, with an overall significant improvement in clinical outcomes assessed by VAS and NDI scores.^{21-26,28} Feiz-Erfan et al²⁴ reported subjective improvements overall. In VAS scores ranging from 3 to 30, the mean VAS score at baseline

Table 3. Power Calculation, Sample Size, and Reporting of Patients Lost to Follow-up.

First Author, Year	OCEBM Level of Evidence	Who Assessed Fusion	Power Calculation and Sample Size	Follow-up Rate, % (Follow-up duration, y)
Feiz-Erfan, ²⁴ 2007	II	Physician not in study	NR	85 (2)
Campbell, ²³ 2009	I	Physician not in study	NR	NR
Feng, ²⁷ 2018	II	2 Blinded physicians	NR	NR
Coric, ²⁶ 2011	II	Physician not in study	NR	87 (2)
Gornet, ²² 2017	I	Physician not in study	Reported	85 (2)
Hisey, ²¹ 2015	II	Physician not in study	Reported	79 (4)
Mummaneni, ²⁵ 2007	II	Physician not in study	NR	75 (2)
Suchomel, ³⁰ 2004	III	Treating surgeon and independent radiologist	NR	99 (2)
Zigler, ²⁸ 2016	III	Physician not in study	NR	I-level: 82 (5); 2-level: 90 (5)
Schlosser, ³¹ 2006	IV	Physician not in study	NR	94 (2)
Niu, ²⁹ 2010	IV	Physician not in study	NR	NR
Cabraja, ³⁴ 2012	IV	NR	NR	NR
El-Tantawy, ³² 2015	IV	NR	NR	100 (2)
Dufour, ³³ 2010	IV	NR	NR	100 (1)

Abbreviations: NR, not reported; OCEBM, Oxford Centre for Evidence-Based Medicine.

for all patients was 15.5; at 2-year follow-up the mean score had improved to 7.0.²⁴ Similarly, Coric et al²⁶ showed a >20% improvement in NDI scores at 2-year follow-up. The methods used for assessing patient-reported outcomes were heterogeneous, limiting quantitative analysis of association of allograft interbody with clinical outcomes.

PEEK Interbody Devices. Overall outcomes improved among the 4 studies that reported patient-reported outcomes.^{27,29,32,34} The success rate of surgery as measured by Odom's criteria was 64% in the study by Cabraja et al.³⁴ In the randomized controlled trial comparing an empty PEEK cage with PEEK packed with β -tricalcium phosphate, patients in both groups showed improvements in VAS, NDI, and Japanese Orthopaedic Association scores.²⁷

Discussion

We conducted a systematic review of the literature to compare fusion rates of structural allograft versus PEEK interbody devices in patients with cervical spine degeneration who underwent ACDF. Of the 14 studies included in our review, the overall fusion rates were 82% to 100%^{21-26,28,30,31} for structural allograft and 88% to 98%^{27,29,32-34} for PEEK interbody devices. The lack of randomized controlled trials comparing these 2 interbody devices, in addition to the variability in methodology to assess fusion, sample sizes, and other methods among studies, precluded meta-analysis.

Because fusion is a key determinant of success after ACDF,³⁵ a standard for determining fusion rate is needed in cervical spine fusion studies. Several widely varying criteria for determining radiographic fusion were reported (Table 2). The most common components of the definitions included <50% radiolucency along the bone-implant surface and a specified degree of angular motion on dynamic radiographs (<2° or <4°). Most studies classified fusion as a binary variable;

however, some studies classified fusion as “complete,” “partial,” and “nonunion”³⁰ or “excellent,” “good,” and “no fusion.”³³ Most studies used multiple observers to determine radiographic fusion, and none of the 14 studies reported intraobserver differences in determination of fusion. In 2008, it was presumed that a consensus definition of cervical fusion was beginning to form.³⁶ In a recently published systematic review by Oshina et al,³⁷ 10 criteria were described for fusion assessment in ACDF. Most commonly, the surgeon's subjective assessment of bridging trabecular bone between endplates and the absence of a radiolucent gap were used to assess fusion. The problem of heterogeneity in fusion assessment is commonly described in systematic reviews and meta-analyses reporting fusion rates in ACDF.³⁸⁻⁴⁰ A universally accepted criterion for fusion assessment is needed to standardize studies and allow for comparison.³⁶

Patient-reported outcomes were reported in only 10 of the 14 studies, indicating that patient-reported outcomes are often not the focus of studies that describe interbody devices, even among those with 2-year follow-up. In the studies that described patient-reported outcomes, the results were not always directly comparable, further illustrating the need for reporting and standardizing outcomes in cervical spine surgery studies. A recent review by Nayak et al⁴¹ also acknowledged that the numerous patient-reported outcome measures and the variability in minimal clinically important differences between these measures limit comparisons of clinical outcomes in spine surgery research.

We required minimum radiographic follow-up of 2 years for inclusion in our review (Table 3). The 1 high-quality study excluded because of a lack of 2-year radiographic follow-up was the PIERCE-PEEK Study (Prospective International Multicenter Evaluation of Radiological and Clinical Effects of Stand-Alone PEEK Intervertebral Spacers for ACDF) by Suess et al.⁹ The authors followed a cohort of 356 patients who underwent ACDF with PEEK interbody devices without any

osteopromotive fillers and without additional anterior instrumentation. Complete radiographic fusion occurred for 43% of patients at 6 months, 73% of patients at 12 months, and 83% of patients at 18 months. The authors recommended against using PEEK interbody devices alone without fillers because of delayed fusion. It is unclear whether delayed fusion was the result of a lack of osteopromotive fillers or a lack of anterior instrumentation to provide additional stabilization to support fusion.

The use of bone graft extenders or biologic materials in addition to PEEK cages has been reported and advocated to improve fusion success.⁴² However, the reported fusion rates with materials such as hydroxyapatite are approximately 85%, which is similar to the rate achieved with structural allograft or PEEK alone.³⁸ Future studies examining the influence of interbody devices on fusion rates should adjust for use of bone graft extender and fusion augmentation materials.

Although PEEK provides good biocompatibility and strength, it is unable to bond directly to bone and to osseointegrate.^{11,43} Modifications to PEEK designed to address the issue of osseointegration have gained popularity. These modifications include hydroxyapatite-coated PEEK, porous PEEK, titanium plasma-coated PEEK, carbon fiber-reinforced PEEK, and polyetherketone.⁴⁴ Our study did not control for these variations because there is insufficient high-quality evidence comparing these modifications. We hypothesize that modifications to PEEK result in superior biomechanical properties and superior osseointegration compared with unmodified, legacy PEEK devices.

Although we excluded patients who underwent ACDF without anterior plating, the use of stand-alone interbody devices without anterior plating is common in Europe. Studies of autograft report that use of an anterior cervical plate improved fusion rates from 93.5% to 98%.⁴⁵ To our knowledge, no high-quality studies have compared the outcomes of plated versus unplated 1- and 2-level ACDF with modern implants, indicating an important area for future research.

In addition to the potential differences in fusion rates between structural allograft and PEEK interbody devices, these devices may differ greatly in cost. Although studies comparing costs between structural allograft and PEEK devices are limited, a 2015 study by Virk et al¹⁶ estimated the costs per quality-adjusted life-year for ACDF using PEEK (\$3328), allograft (\$2492), and autograft (\$2492). However, they did not account for regional variations in cost. In some regions, because of storage, regulatory, and cultural reasons, obtaining structural allograft can be difficult or cost prohibitive. Future studies focusing on cost differences among interbody devices are needed.

When pooling results from the studies we analyzed, the subsidence rate was higher in patients who had PEEK versus allograft devices; however, none of the studies included in this review directly compared subsidence rates of PEEK versus allograft. It is important to note that although structural allograft had lower reported subsidence rates, it is difficult to assess for subsidence on radiographs because of the resemblance of allograft to native bone on imaging. In contrast, PEEK cages

have embedded radiopaque markers, which potentially allow for better visualization of subsidence. In a direct comparative study that did not meet criteria for inclusion in our review, no significant difference in subsidence rates was seen between allograft and PEEK interbody devices used in ACDF.⁴⁶ It is also important to consider that although subsidence after ACDF procedures has been well studied, the effects of subsidence on clinical outcomes and fusion rates after ACDF remain unclear.⁴⁷

Limitations are inherent in systematic reviews. In our study, heterogeneity of fusion assessment, stringent inclusion and exclusion criteria, and possible missed cases contribute to the limitations. The discrepancy in fusion assessment prevented us from performing a meta-analysis. In addition, the lack of level-I evidence with a direct comparison of structural allograft versus PEEK makes it difficult to form robust conclusions. Further high-quality evidence is required to provide evidence-based treatments for patients with cervical spine degeneration undergoing ACDF. A thorough search and review of the literature, as well as strict adherence to the Preferred Reporting Items of Systematic reviews and Meta-Analyses guidelines contributed to the strengths of this systematic review.

Conclusions

Similar fusion rates have been reported for structural allograft and PEEK interbody devices for ACDF in patients with cervical spine degeneration. No high-quality randomized controlled trials or high-quality cohort comparisons directly compared structural allograft versus PEEK interbody devices in ACDF. Future research is needed to assess the outcomes of various modified PEEK devices and bone graft substitutes and extenders.

Authors' Note

This study used publicly available information and thus was not subject to review from our institutional review board.

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ORCID iD

Amit Jain, MD  <https://orcid.org/0000-0002-9983-3365>

Majd Marrache, MD  <https://orcid.org/0000-0001-5768-3541>

Zorica Buser, PhD  <https://orcid.org/0000-0002-5680-0643>

S. Tim Yoon, MD  <https://orcid.org/0000-0003-0497-1130>

Supplemental Material

The supplemental material is available in the online version of the article.

References

- Cherry C. Anterior cervical discectomy and fusion for cervical disc disease. *AORN J*. 2002;76:996-1004,1007-1012.
- Riew KD, Ecker E, Dettori JR. Anterior cervical discectomy and fusion for the management of axial neck pain in the absence of radiculopathy or myelopathy. *Evid Based Spine Care J*. 2010;1:45-50.
- Hosoi K, Tonomura H, Takatori R, et al. Usefulness of anterior cervical fusion using titanium interbody cage for treatment of cervical degenerative disease with preoperative segmental kyphosis. *Medicine (Baltimore)*. 2017;96:e7749.
- Liu J, Xiong X, Long X, et al. A new source of structural autograft for ACDF surgery: cervical laminae. *Int J Clin Exp Med*. 2015;8:9100-9106.
- Cloward RB. The anterior approach for removal of ruptured cervical disks. *J Neurosurg*. 1958;15:602-617.
- Kim SY, Park KS, Jung SS, et al. An early comparative analysis of the use of autograft versus allograft in anterior cervical discectomy and fusion. *Korean J Spine*. 2012;9:142-146.
- Yoon ST, Konopka JA, Wang JC, et al. ACDF graft selection by surgeons: survey of AOSpine members. *Global Spine J*. 2017;7:410-416.
- Lemcke J, Al-Zain F, Meier U, Suess O. Polyetheretherketone (PEEK) spacers for anterior cervical fusion: A retrospective comparative effectiveness clinical trial. *Open Orthop J*. 2011;5:348-353.
- Suess O, Schomaker M, Cabraja M, Danne M, Kombos T, Hanna M. Empty polyetheretherketone (PEEK) cages in anterior cervical discectomy and fusion (ACDF) show slow radiographic fusion that reduces clinical improvement: results from the prospective multicenter "PIERCE-PEEK" study. *Patient Saf Surg*. 2017;11:12.
- Panayotov IV, Orti V, Cuisinier F, Yachouh J. Polyetheretherketone (PEEK) for medical applications. *J Mater Sci Mater Med*. 2016;27:118.
- Torstrick FB, Lin ASP, Potter D, et al. Porous PEEK improves the bone-implant interface compared to plasma-sprayed titanium coating on PEEK. *Biomaterials*. 2018;185:106-116.
- 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;60:211-219.
- Yi J, Lee GW, Nam WD, et al. A prospective randomized clinical trial comparing bone union rate following anterior cervical discectomy and fusion using a polyetheretherketone cage: hydroxyapatite/B-tricalcium phosphate mixture versus hydroxyapatite/demineralized bone matrix mixture. *Asian Spine J*. 2015;9:30-38.
- 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.
- Samartzis D, Shen FH, Goldberg EJ, An HS. Is autograft the gold standard in achieving radiographic fusion in one-level anterior cervical discectomy and fusion with rigid anterior plate fixation? *Spine (Phila Pa 1976)*. 2005;30:1756-1761.
- Virk SS, Elder JB, Sandhu HS, Khan SN. The cost effectiveness of polyetheretherketone (PEEK) cages for anterior cervical discectomy and fusion. *J Spinal Disord Tech*. 2015;28:E482-E492.
- Oryan A, Alidadi S, Moshiri A, Maffulli N. Bone regenerative medicine: classic options, novel strategies, and future directions. *J Orthop Surg Res*. 2014;9:18.
- 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)*. 2007;32:2980-2984.
- Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6:e1000097.
- Centre for Evidence-Based Medicine. OCEBM levels of evidence. <https://www.cebm.net/2016/05/ocebml-levels-of-evidence/>. Accessed July 17; 2019
- Hisey MS, Bae HW, Davis RJ, et al. Prospective, randomized comparison of cervical total disk replacement versus anterior cervical fusion: results at 48 months follow-up. *J Spinal Disord Tech*. 2015;28:E237-E243.
- Gornet MF, Lanman TH, Burkus JK, et al. Cervical disc arthroplasty with the Prestige LP disc versus anterior cervical discectomy and fusion, at 2 levels: results of a prospective, multicenter randomized controlled clinical trial at 24 months. *J Neurosurg Spine*. 2017;26:653-667.
- Campbell MJ, Carreon LY, Traynelis V, Anderson PA. Use of cervical collar after single-level anterior cervical fusion with plate: is it necessary? *Spine (Phila Pa 1976)*. 2009;34:43-48.
- Feiz-Erfan I, Harrigan M, Sonntag VK, Harrington TR. Effect of autologous platelet gel on early and late graft fusion in anterior cervical spine surgery. *J Neurosurg Spine*. 2007;7:496-502.
- Mummaneni PV, Burkus JK, Haid RW, Traynelis VC, Zdeblick TA. Clinical and radiographic analysis of cervical disc arthroplasty compared with allograft fusion: a randomized controlled clinical trial. *J Neurosurg Spine*. 2007;6:198-209.
- Coric D, Nunley PD, Guyer RD, et al. Prospective, randomized, multicenter study of cervical arthroplasty: 269 patients from the Kineflex/C artificial disc investigational device exemption study with a minimum 2-year follow-up. *J Neurosurg Spine*. 2011;15:348-358.
- Feng SW, Chang MC, Chou PH, Lin HH, Wang ST, Liu CL. Implantation of an empty polyetheretherketone cage in anterior cervical discectomy and fusion: a prospective randomised controlled study with 2 years follow-up. *Eur Spine J*. 2018;27:1358-1364.
- 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;41:463-469.
- Niu CC, Liao JC, Chen WJ, Chen LH. Outcomes of interbody fusion cages used in 1 and 2-levels anterior cervical discectomy and fusion: titanium cages versus polyetheretherketone (PEEK) cages. *J Spinal Disord Tech*. 2010;23:310-316.

30. Suchomel P, Barsa P, Buchvald P, Svobodnik A, Vanickova E. Autologous versus allogenic bone grafts in instrumented anterior cervical discectomy and fusion: a prospective study with respect to bone union pattern. *Eur Spine J.* 2004;13:510-515.
31. Schlosser MJ, Schwarz JP, Awad JN, et al. Anterior cervical discectomy and fusion with allograft and anterior plating: a report on 219 patients/469 levels with a minimum of 2-year follow-up. *Neurosurg Q.* 2006;16:183-186.
32. El-Tantawy A. Is it possible to eliminate the plate-related problems and still achieve satisfactory outcome after multilevel anterior cervical discectomy? *Eur J Orthop Surg Traumatol.* 2015; 25(suppl 1):S135-S145.
33. Dufour T, Huppert J, Louis C, et al. Radiological analysis of 37 segments in cervical spine implanted with a peek stand-alone device, with at least one year follow-up. *Br J Neurosurg.* 2010; 24:633-640.
34. 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.
35. Kotsias A, Mularski S, Kuhn B, Hanna M, Suess O. Does partial coating with titanium improve the radiographic fusion rate of empty PEEK cages in cervical spine surgery? A comparative analysis of clinical data. *Patient Saf Surg.* 2017;11:13.
36. Sethi N, Devney J, Steiner HL, Riew KD. Diagnosing cervical fusion: a comprehensive literature review. *Asian Spine J.* 2008;2: 127-143.
37. Oshina M, Oshima Y, Tanaka S, Riew KD. Radiological fusion criteria of postoperative anterior cervical discectomy and fusion: a systematic review. *Global Spine J.* 2018;8:739-750.
38. Zadegan SA, Abedi A, Jazayeri SB, et al. Bone morphogenetic proteins in anterior cervical fusion: a systematic review and meta-analysis. *World Neurosurg.* 2017;104:752-787.
39. Oliver JD, Goncalves S, Kerezoudis P, et al. Comparison of outcomes for anterior cervical discectomy and fusion with and without anterior plate fixation: a systematic review and meta-analysis. *Spine (Phila Pa 1976).* 2018;43:E413-E422.
40. Tuchman A, Brodke DS, Youssef JA, et al. Autograft versus allograft for cervical spinal fusion: a systematic review. *Global Spine J.* 2017;7:59-70.
41. Nayak NR, Coats JM, Abdullah KG, Stein SC, Malhotra NR. Tracking patient-reported outcomes in spinal disorders. *Surg Neurol Int.* 2015;6:S490-S499.
42. Fischer CR, Cassilly R, Cantor W, Edusei E, Hammouri Q, Errico T. A systematic review of comparative studies on bone graft alternatives for common spine fusion procedures. *Eur Spine J.* 2013;22:1423-1435.
43. Walsh WR, Bertollo N, Christou C, Schaffner D, Mobbs RJ. Plasma-sprayed titanium coating to polyetheretherketone improves the bone-implant interface. *Spine J.* 2015;15:1041-1049.
44. Torstrick FB, Safranski DL, Burkus JK, et al. Getting PEEK to stick to bone: the development of porous PEEK for interbody fusion devices. *Tech Orthop.* 2017;32:158-166.
45. Mobbs RJ, Rao P, Chandran NK. Anterior cervical discectomy and fusion: analysis of surgical outcome with and without plating. *J Clin Neurosci.* 2007;14:639-642.
46. Yson SC, Sembrano JN, Santos ER. Comparison of allograft and polyetheretherketone (PEEK) cage subsidence rates in anterior cervical discectomy and fusion (ACDF). *J Clin Neurosci.* 2017;38:118-121.
47. 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.
48. Brown MD, Malinin TI, Davis PB. A roentgenographic evaluation of frozen allografts versus autografts in anterior cervical spine fusions. *Clin Orthop Relat Res.* 1976;119:231-236.