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Three-Level Anterior Cervical Discectomy and Fusion With or Without an Investigational Posterior Stabilization System Assessed Through 24 Months

A Multicenter Randomized Controlled Trial

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Study Design. Prospective randomized controlled trial.

Objective. This trial was designed to understand safety and effectiveness outcomes in subjects with three-level cervical degenerative disc disease treated with anterior cervical discectomy and fusion (ACDF) alone or supplemented with a posterior cervical fusion (PCF) performed using an investigational posterior cervical stabilization system (PCSS).

Background. ACDF remains the most common surgical treatment for cervical disc disease. Long-segment (3+ disc levels) procedures are associated with increased risk of complications including symptomatic nonunion. Supplementing ACDF with PCF to form a circumferential cervical fusion (CCF) improves biomechanical stability but increases the surgical burden for the patient.

Materials and Methods. This multicenter study compared outcomes in participants with three-level symptomatic cervical disc degeneration treated with either ACDF or CCF. The CCF procedure incorporated PCF with PCSS. The primary endpoint was 12-month fusion success, defined by bridging bone across the interbody and range of motion $< 2°$ across all treated disc levels. The 24-month secondary endpoint was a composite of fusion success, neck disability index (NDI) improvement, neurological status success, and freedom from surgical revision.

Results. This protocol-defined interim analysis included 202 participants with 12-month outcomes and 116 participants with 24-month outcomes. Twelve-month fusion success was higher for CCF (61/100, 61%) compared with ACDF (17/102, 17%) ($P < 0.001$). The 24-month secondary endpoint was also improved with CCF compared with ACDF [51% (30/59) vs. 23% (13/57); $P = 0.002$]. Revision rates were lower for CCF (1/59, 2%) compared with ACDF (13/57, 23%) ($P < 0.001$), with 11 of 13 ACDF revisions addressing symptomatic nonunion. Adding supplemental PCF with PCSS did not increase the rates of adverse events (ACDF = 65%, CCF = 46%, $P = 0.005$).

Conclusions. This study represents the first randomized controlled trial assessing treatment of three-level cervical disc disease. Long-segment ACDF demonstrated low fusion rates and high rates of revision. Adding supplemental PCF with PCSS improved fusion without increasing the risk of surgical complications.

Key Words: cervical spine, degenerative disease, fusion, anterior cervical discectomy and fusion, circumferential cervical fusion,

Received for publication March 6, 2025; accepted April 29, 2025.

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The device(s)/drug(s) is/are FDA-approved or approved by the corresponding national agency for this indication. This study was an FDA approved IDE Trial sponsored by Providence Medical Technology (Pleasanton, CA, USA).

K.B.S., J.H., D.W., A.L., R.S., P.N., G.T., and M.S. received institutional support for research activities. B.M. has a financial interest in the Sponsor. J.B. and A.S. received consulting fees to support research activities. M.J. and E.S. are employed by the Sponsor.

The authors report no conflicts of interest.

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Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, www.spinejournal.com.

DOI: 10.1097/BRS.0000000000005387

posterior cervical fusion, pseudarthrosis, nonunion, randomized controlled trial, multilevel

(*Spine* 2025;50:1161–1170)

Anterior cervical discectomy and fusion (ACDF) remains the mainstay surgical procedure for treating cervical radiculopathy and myelopathy, accounting for about 85% of the ~180,000 cervical fusion procedures performed annually in the United States.[1,2] Patients typically report substantial symptom amelioration, and follow-up imaging consistently demonstrates radiographic evidence of solid arthrodesis for cases requiring a one-level or two-level ACDF.[3,4] However, for degenerative changes requiring long-segment neural decompression (3+ level), anterior column stabilization alone may be insufficient to handle the increased biomechanical stresses across the fusion construct.[5–7] Consequently, long-segment ACDF is associated with markedly higher rates of nonunion, adverse events, and revision surgeries than one-level and two-level ACDF procedures.[8–13]

In the absence of a solid arthrodesis, many patients experience a relapse in symptoms.[14] To maximize the likelihood of a successful fusion, long-segment ACDF can be augmented with posterior cervical fusion (PCF) to form a circumferential cervical fusion (CCF). The attempt at improving fusion with CCF must be balanced against risks from added surgical burden from the supplemental procedure, particularly for high-risk patients. The posterior cervical stabilization system (PCSS) is an investigational device used as part of PCF, developed to provide supplemental fixation while preserving soft tissue attachments of the dorsal spine. A description of this technique has been previously published in detail by Summerside *et al.*[15] Laratta *et al.*[16] published a review summarizing outcomes of a predicate device to PCSS where they reported that available evidence suggested the device as a viable approach for performing PCF, but that the quality of evidence was lacking. The purpose of this prospective randomized controlled IDE trial was to understand clinical and radiographic outcomes through 24 months in patients treated for three-level cervical degenerative disease and to evaluate the potential improvements in fusion status when performing CCF using the investigational PCSS device.

MATERIALS AND METHODS

Trial Design

This was a randomized controlled trial conducted at 19 clinical sites across 13 states within the United States. The study protocol was designed by the trial sponsor after conferring with the US Food and Drug Administration (FDA). Outcomes and definitions of success for primary and secondary endpoints were influenced by previous FDA regulated studies involving the cervical spine.[17–19] The study protocol was approved by the FDA in March 2020 and conducted as an investigational device exemption (IDE) trial [IDE G190235]. Research activities described in this manuscript were reviewed, approved, and overseen by WCG IRB (Study ID# 20193399). The primary objective was to evaluate the safety and effectiveness of CCF with PCSS *versus* ACDF, in patients with three-level cervical degenerative disc disease. This study was approved by the institutional review board at each participating site and participants provided written informed consent before any study-related procedures. The trial was prospectively registered at ClinicalTrials.gov (NCT04229017).

Participants

Eligible participants included adults aged 18 to 80 years with symptomatic cervical degenerative disc disease at three contiguous levels (C3–C6 or C4–C7). All participants had degenerative changes confirmed radiographically with clinical diagnosis of radiculopathy, myelopathy, or myeloradiculopathy of the cervical spine with pain. Key exclusion criteria included prior cervical spine surgery at the operative site, active infection, malignancy, or systemic disease affecting bone quality. A complete listing of eligibility criteria is provided in the Supplemental Material, Supplemental Digital Content 1, http://links.lww.com/BRS/C699.

Interventions and Randomization

This trial compared ACDF with CCF in participants with three-level disease. ACDF was performed using a modified Smith-Robinson approach. Interbody material was limited to manufactured structural allograft augmented with locally harvested morselized autograft and demineralized allograft bone matrix (limited to DePuy Synthes, Seaspine Evo3, or Medtronic Grafton). The surgeon was free to select their preferred anterior plate with a semiconstrained design (rigid plate with two variable angle screws placed using a unicortical technique at each level). A complete list of manufacturers for allograft interbody spacers and anterior plates is provided in the Supplemental Material, Supplemental Digital Content 1, http://links.lww.com/BRS/C699. Participants assigned to CCF received supplemental PCF including the PCSS device (Fig. 1).

Randomization was stratified by age (under 65 yr and 65 yr of age or older) and smoking history. Assignment was known to investigators and their clinical teams at the time of randomization, but was blinded to participants until after surgery.

Outcomes

The primary endpoint was fusion success at month 12, defined as evidence of bridging trabecular bone adjacent to the graft across interbody endplates (using 1 mm slice CT) and <2° segmental angular range of motion (rROM, using dynamic flexion/extension radiograph] for all visible levels treated. Radiographic outcomes were determined from an independent third-party core imaging lab (Medical Metrics Inc., Houston, TX).

The secondary endpoint was composite safety success at 24 months. A participant was considered a success if all the following criteria were met:

(1) Fusion success, defined the same as for the primary endpoint.

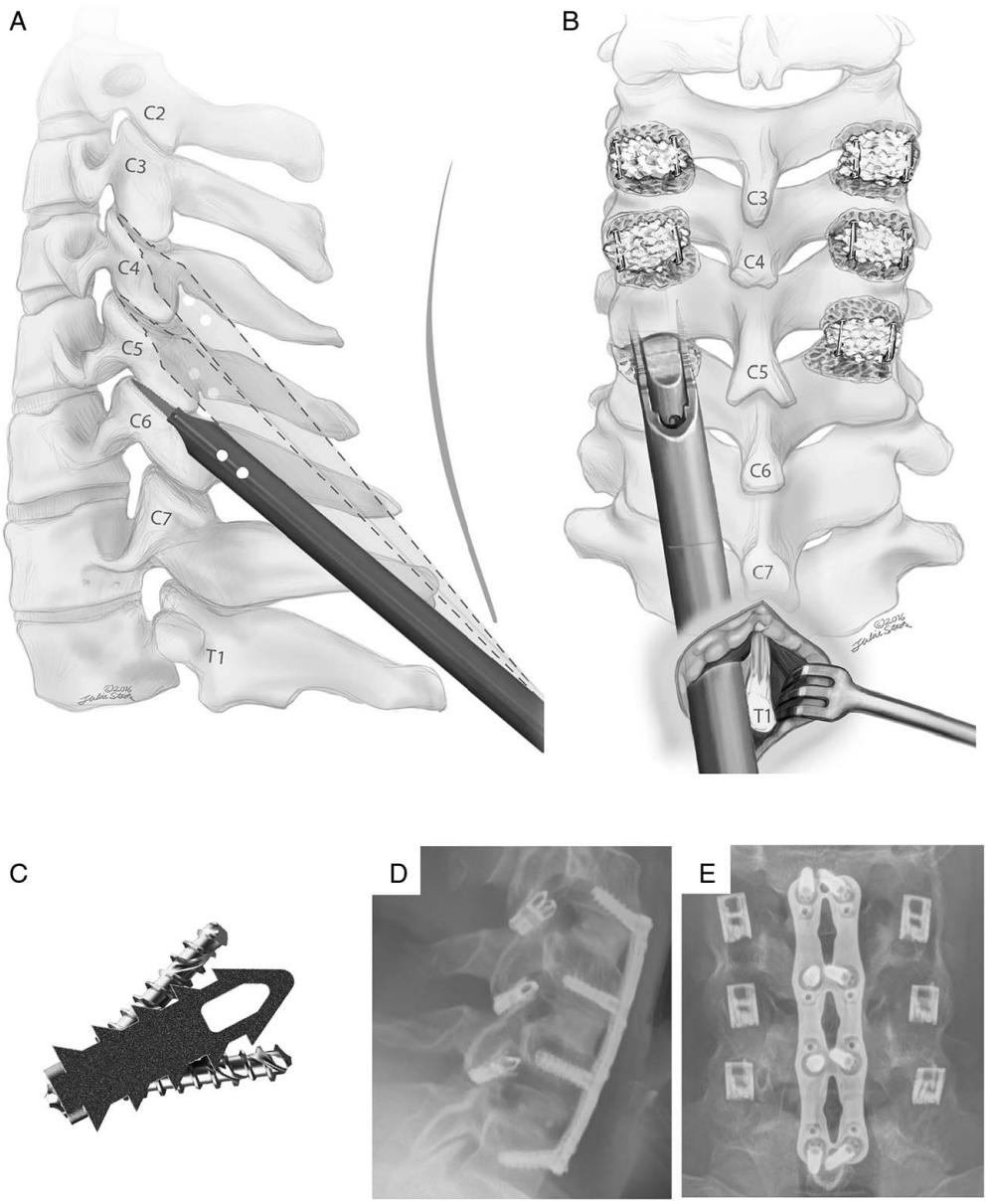

Figure 1. A and B, A longitudinal incision as small as 2 cm is made at the lowest level. At the surgeon's discretion, a single incision can be made midsagittal (shown) or bilateral incisions off sagittal inferior to the lowest level. Under the aid of fluoroscopy, a guide tube is then anchored into the joint which allows access for a series of decorticators that prepare the joint and lateral mass for fusion. C, The joint is then stabilized with the investigational device, a nonsegmental construct comprised of a cage packed with demineralized bone matrix allograft and two integral fixation screws. D and E, Lateral and anteroposterior radiographs of CCF subject taken at 12-month visit. A and B have been reproduced with permission from a prior publication.[20]

(2) Neck disability index (NDI) success, defined as improvement in NDI of $\geq$15/50 points if baseline score of $\geq$30/50 or a $\geq$50% improvement if a baseline NDI score of <30/50 (score of 0 is no pain and 50 is maximum pain).
(3) Neurological success, defined as maintenance or improvement of neurological status.
(4) Freedom from surgical reinterventions at all index levels.

Neurological success was adjudicated by an independently managed clinical events committee (CEC) comprised of three spine surgeons. Relationship of all reported adverse events was also adjudicated by the CEC.

Exploratory endpoints included incidence of related adverse events and incidence of adjacent segment degeneration (radiographic) or disease (clinical). Cranial and caudal adjacent segments were assessed for signs of radiographic adjacent segment degeneration (ASD). Presence of radiographic ASD was summarized for subjects with complete imaging at month 24 who did not require

subsequent revision surgery at any index levels. Scoring for ASD was adjudicated at month 24 by the same laboratory determining fusion outcomes. A post hoc assessment of C2–C7 Cobb angle (CapeStart, Cambridge, MA) was measured and compared between baseline and 24 months post-treatment. The presence of ASD and the change in Cobb angle were summarized from all subjects with complete 24-month imaging who did not require subsequent revision surgery at any index levels.

Length of stay was reported as nights in hospital. Operative durations were reported for each anterior and posterior procedure as time between first incision to last closure of each procedure. Total procedure time was reported for CCF subjects and represented the time from the first ACDF incision to last PCF closure. For subjects in the ACDF arm, total procedure time and ACDF procedure times were represented by the same measurement.

This report summarizes outcomes assessed during the protocol-defined interim analysis (IA) and is based on study data collected through December 29, 2023. Enrollment was completed before IA with a total 227 participants being treated. At the time of IA, a total 202 participants contributed to 12-month outcomes of which 116 of those participants additionally contributed to the final 24-month composite safety endpoint.

Statistical Methods

The primary hypothesis tested whether 12-month fusion success was superior for CCF compared with ACDF. The secondary endpoint was composite safety success measured at 24 months. An interim analysis for the secondary endpoint was planned when ~100 participants completed 24-month follow-up. Secondary endpoint success was determined based on a test of noninferiority for CCF against ACDF with a noninferiority margin of 15% at the IA. To account for this analysis, 0.5% of the total one-sided type 1 error allowance of 2.5% was allocated to the IA, with the remaining 2% reserved for the final analysis. The secondary endpoint, 24-month composite safety success, was estimated as 26% and 36% for ACDF and CCF, respectively.[21] If 180 participants complete 24-month assessments, the study will have 80% power to show noninferiority of CCF to ACDF for the 24-month composite safety endpoint with a 10% noninferiority margin.

Because study success required demonstration of success for both the primary and secondary endpoint, no type 1 error adjustment for multiplicity was required. The analysis population contained all subjects who underwent surgery before December 29, 2022. Participants were analyzed by randomization assignment except for adverse events. Responder rates for the primary and secondary outcome variables as well as all subcomponents of each outcome were compared between groups using χ^2 tests or the Fisher exact tests, as appropriate.

RESULTS

From March 18, 2020 to August 15, 2023, 306 prospective participants were screened at 19 clinical sites with 227 meeting eligibility criteria and receiving treatment (114 CCF, 113 ACDF). Of the 227 treated participants, 202 participants (100 CCF, 102 ACDF) were included in the interim 12-month primary endpoint analysis, with 116 (59 CCF, 57 ACDF) additionally included in the 24-month secondary endpoint analysis (Fig. 2). Baseline characteristics were similar between arms and are described in Table 1.

Results of the 12-month primary endpoint analysis are provided in Table 2. Eight CCF participants and 11 ACDF participants that had missing 12-month imaging were imputed as protocol-defined failures in the intent-to-treat primary endpoint analysis. The fusion success rate for participants treated with CCF (61/100, 61%) was significantly higher than for ACDF participants (17/102, 17%) ($P < 0.001$). The 44% difference in fusion rates demonstrated superiority of CCF over ACDF (95% CI: 32.3–56.3). Outcomes were unaffected when comparing only those with complete imaging in each arm. In the CCF arm, 61/92 participants (66.3%) achieved success, which was significantly higher than the 17/91 (18.7%) in the ACDF arm ($P < 0.001$). A breakdown of the number of levels and relative location of nonunion is provided in Table 3. There were no associations between participant background characteristics and treatment effect for the primary endpoint (Supplemental Material, Supplemental Digital Content 1, http://links.lww.com/BRS/C699).

The 24-month secondary endpoint was achieved in 30/59 (50.8%) CCF and 13/57 (22.8%) ACDF participants, representing a statistically significant difference in success rates of 28-percentage points (95% CI: 11.3–44.8, $P = 0.002$). When comparing only those with completed 24-month visits, the outcomes remained unchanged. In the CCF arm 30/56 (53.6%) were successful, which was significantly higher than the 12/51(23.5%) participants in the ACDF arm ($P = 0.001$). There were no associations between participant background characteristics and treatment effect for the secondary endpoint (Supplemental Material, Supplemental Digital Content 1, http://links.lww.com/BRS/C699).

Fusion success remained significantly higher at 24 months for CCF participants (44/59, 75%) compared with ACDF participants (19/57, 33%) ($P < 0.001$). In addition to fusion success, the proportion of participants requiring surgical revision was significantly lower for CCF participants (1/59, 2%) compared with ACDF participants (13/57, 23%) ($P < 0.001$). Eleven of the 13 ACDF participants who underwent surgical revision did so for treatment of nonunion, as indicated by significant movement on flexion/extension radiographs at the index levels, which correlated with re-emerged symptoms not improved with conservative treatments. The remaining two components of the secondary composite endpoint, neck pain, and neurological status, were not significantly different between treatment groups (Fig. 3). Successful improvement in NDI was achieved in 39/56 (69.6%) of CCF and 30/52 (57.7%) of ACDF participants ($P = 0.196$). Maintenance or improvement of neurological status was observed in 53/57 (93.0%) of CCF and 49/51 (96.1%) of ACDF partici-

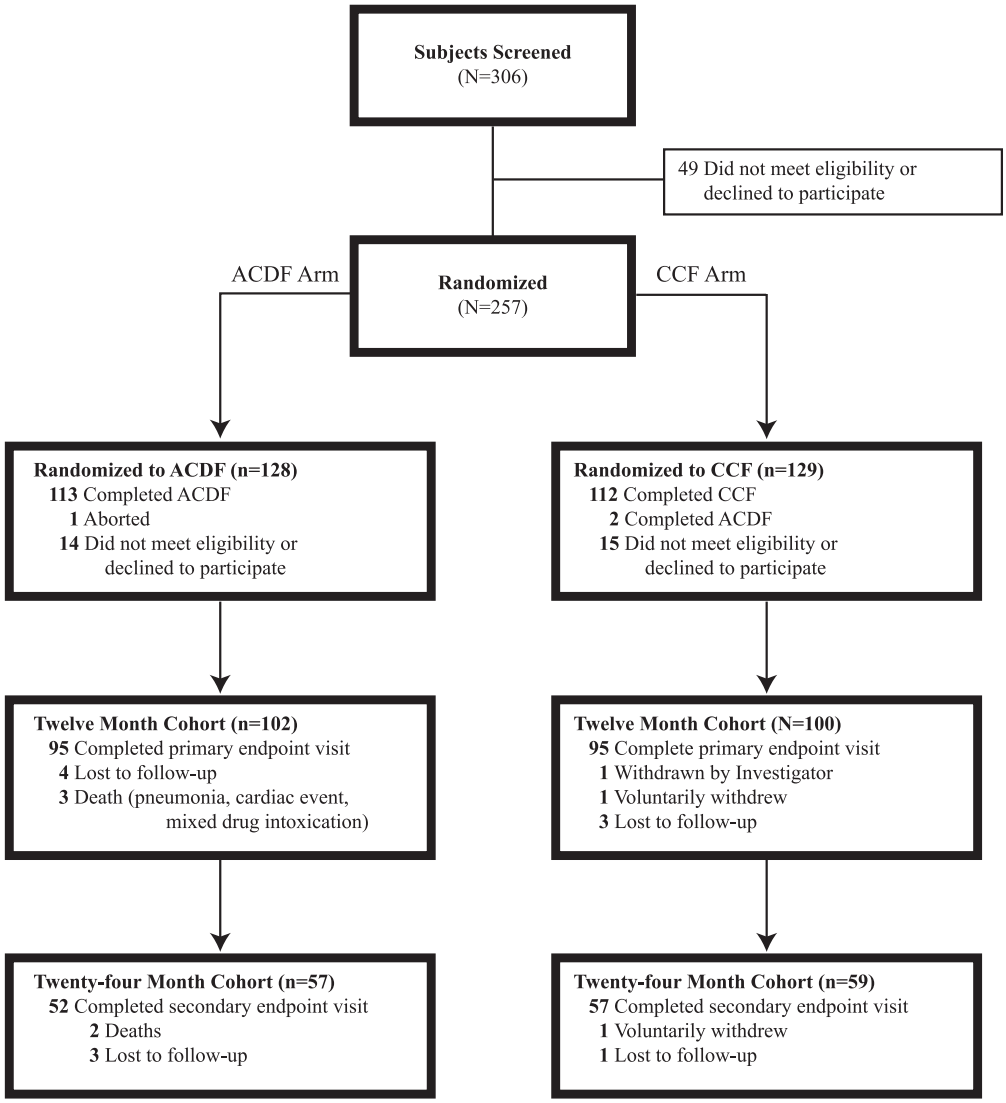

Figure 2. CONSORT diagram.

pants ($P = 0.682$). Of the subjects requiring revision for nonunion, prerevision NDI was an average of 20.9/50 (± 10.6) and all had a maintained or improved neurological status when compared with baseline.

A summary of radiographic ASD severity is provided in Table 4. Evidence of severe, moderate, or minimal degeneration at the most severe segment was similarly identified in both arms (CCF = 46.3%, ACDF = 59.5%, $P = 0.198$). There were three instances of symptomatic ASD in the ACDF group (2.9%) and four instances in the CCF group (4%) when assessed through 12 months. Of the subjects followed through 24 months, there was one additional instance of symptomatic ASD in the CCF arms and two additional instances in the ACDF arm. There were no differences in pre-operative C2–C7 Cobb angle measurements between arms [median degrees (IQR); CCF = 6.0 (4.7, 12.7), ACDF = 7.6 (2.4, 11.1); $P = 0.26$]. When assessed at 24 months, subjects treated with ACDF showed an average increase in lordosis by $1.5 \pm 8.5°$ compared with an increase of $1.6 \pm 7.3°$ in the CCF group ($P = 0.95$).

Treatment with PCSS increased total estimated blood loss by a median 10 mL (CCF = 60 mL, ACDF = 50 mL, $P = 0.010$) and added an average 98 minutes to the total procedure time (CCF = 227 min, ACDF = 129 min, $P < 0.001$). This includes the time between procedures for the CCF group. The PCF procedure itself required an additional 47 minutes. There was no difference between arms for manufacturer of anterior plate used (Supplemental Material, Supplemental Digital Content 1, http://links.lww.com/BRS/C699, $P = 0.375$) nor anterior screw dimension (mean length, mm: ACDF = 14.4 ± 1.31, CCF = 14.4 ± 1.19, $P = 0.701$; mean diameter, mm: ACDF = 4.01 ± 0.22, CCF = 4.02 ± 0.20, $P = 0.721$). There was also no difference between arms for allograft manufacturer (Supplemental Material, Supplemental Digital

TABLE 1. Baseline Background Characteristics by Treatment

Characteristic	CCF (N = 114), n (%)	ACDF (N = 113), n (%)	*P*
Age, mean (SD) (yr)	58 (9.2)	59 (9.9)	0.634
Female sex	70 (61.4)	60 (53.1)	0.206
Race			0.574
American Indian or Alaskan Native	4 (3.5)	1 (0.9)	
Asian	0	2 (1.8)	
Black or African American	10 (8.8)	13 (11.5)	
Native Hawaiian/ Pacific Islander	1 (0.9)	1 (0.9)	
White	97 (85.1)	93 (82.3)	
Other	2 (1.8)	2 (1.8)	
Declined to respond	0	1 (0.9)	
Ethnicity			0.860
Hispanic or Latino	3 (2.6)	4 (3.5)	
Not Hispanic or Latino	110 (96.5)	108 (95.6)	
Declined to respond	1 (0.9)	1 (0.9)	
Body mass index, mean (SD) (kg/m^2)	31 (6.0)	31 (5.5)	0.458
Current smoker	19 (16.7)	17 (15.0)	0.738
Diabetes	15 (13.2)	17 (15.0)	0.683
Rheumatoid arthritis	3 (2.6)	3 (2.7)	0.991

Content 1, http://links.lww.com/BRS/C699, $P = 0.228$), profile (lordotic: ACDF = 97.6% with mean angle of $6.5 \pm 0.62°$, CCF = 98.2% with mean angle of $6.5 \pm 0.68°$, $P_{\%} = 0.513$, $P_{angle} = 0.355$), or height (mean height, mm: ACDF = 7.1 ± 1.2, CCF = 7.2 ± 1.2, $P = 0.597$). Length of stay was similar between arms (CCF = 1 night, ACDF = 1 night, $P = 0.293$). The treatment-related adverse event rate through 12 months was significantly lower for CCF participants (45/99, 46%) than for ACDF participants (67/103, 65%) ($P = 0.005$). A complete listing of related adverse events is provided in the Supplemental Material, Supplemental Digital Content 1, http://links.lww.com/BRS/C699.

DISCUSSION

In this randomized controlled trial evaluating three-level cervical fusion for treatment of degenerative disease, 67% of participants treated with ACDF had radiographic evidence of nonunion at one or more levels when assessed at 24 months, with 23% requiring surgical reintervention. Adding PCF reduced radiographic nonunion rates to 25%, with 2% of participants requiring surgical reintervention without increasing hospital length of stay or the incidence of postoperative complications.

Long-segment cervical fusion is considered more challenging with respect to achieving a solid arthrodesis, although estimates of fusion success vary widely in the literature.[5,9] Since commencing the IDE trial, retrospective studies have been published that indicate a significant decrease in fusion for 3+ level treatment when compared with shorter segment treatment. Nichols *et al.*[10] reported radiographic outcomes on three-level ACDF patients at 18 to 24 months post-treatment and found that only 11% of subjects achieved complete fusion, with the caudal level most likely to fail. Wewel and colleagues found that 42% of subjects treated with three-level ACDF had nonunion at one or more levels with a quarter of nonunion patients requiring subsequent revision surgery. There are at least three interactions to consider that may have contributed to lower-than-expected success in the current cohort. First, using a core image laboratory with a dual success criterion (bone bridging and ROM) can greatly increase sensitivity to detecting nonunion over more common definitions such as using a single-image modality[22] or using investigators to determine radiographic outcomes.[23] Second, the eligibility criteria for this study enrolled participants with comorbidities that would commonly exclude them from RCTs. Some of these included low bone density (DEXA *T*-score up to -2.5), history of tobacco use, and high BMI, which may have contributed to worse outcomes. The average age of participants in this study was roughly a decade older than in previously reported IDEs investigating two-level disease.[24] Lastly, after discussions with the FDA during the initial trial design, it was decided that all ACDFs were to be performed using structural allograft interbody spacers. There are sources of variability unique to structural allograft when compared with PEEK or titanium. These include differences in harvesting and manufacturing processes as well as differences in bone mineral density, both which may impact the biomechanical characteristics of each implant. While each surgeon may have a preference for interbody material, there is no strong consensus on how alternative materials would have definitively impacted arthrodesis. For example, Goldberg *et al.*[25] per-

TABLE 2. Fusion Rates at 12 and 24 Months by Treatment

Modified intent to treat (missing = failure)	Month 12 visit: CCF (N = 100), n (%)	Month 12 visit: ACDF (N = 102), n (%)	Month 12 visit: *P*	Month 24 visit: CCF (N = 59), n (%)	Month 24 visit: ACDF (N = 57), n (%)	Month 24 visit: *P*
Composite fusion: success	61 (61.0)	17 (16.7)	< 0.001	44 (74.6)	19 (33.3)	< 0.001
Bridging bone (CT) at all levels and no revision*	63 (63.0)	22 (21.6)	< 0.001	47 (79.7)	19 (33.3)	< 0.001
ROM < 2° (dynamic X-ray) at all levels and no revision*	74 (74.0)	46 (45.1)	< 0.001	49 (83.1)	23 (40.4)	< 0.001

Participants with missing images were imputed as failures for that visit.
No revisions contributed to failures for CCF at either month 12 or month 24.
*There were two revisions contributing to ACDF failures at month 12 and 13 revisions at month 24.

TABLE 3. Breakdown of 12-Month Nonunion Rates by Treatment*

	CCF (N = 92), n (%)	ACDF (N = 91), n (%)	*P*
All levels fused	61 (66.3)	18 (19.8)	< 0.001
One level not fused	21 (22.8)	42 (46.2)	
Two levels not fused	9 (9.8)	18 (19.8)	
No levels fused	1 (1.1)	13 (14.3)	
Cranial level not fused	12 (13)	36 (39.6)	
Middle level not fused	6 (6.6)	19 (21.1)	
Caudal level not fused	24 (26.7)	62 (70.5)	

*Values do not include participants with missing images or that required revision before the month 12 visit.

formed a systematic review of 34 eligible studies to compare fusion outcomes of titanium, PEEK, and structural allograft interbody spacers and found no evidence that one material outperformed the others. Titanium had an average fusion rate of 87.3% (range = 84%–100%), PEEK had an average of 92.8% (62%–100%), and structural allograft had an average of 94.7% (82%–100%).

In addition, a radiographic failure should not immediately be assumed to indicate a clinical failure for either treatment paradigm. The low rate of radiographic success observed in the ACDF group did not reflect how many participants rated their symptom relief. When followed through 24 months, most ACDF participants maintained a clinically relevant improvement over baseline according to NDI. While complete fusion at 24 months is correlated with better chance of sustained symptom relief,[26] there are cases where a stable nonunion develops. Radiographic fusion alone may not best predict clinical outcomes; however, instances of gross mobility at one or more levels should not be ignored when considering a patient's long-term prognosis.

Observed revision rates in the current study complement rates previously reported for three-level ACDF,[8,13,27,28] with one study by Laratta *et al.*[13] reporting revision rates exceeding 35% when assessed through 24 months. The most common indication for revision was to address symptoms related to nonunion (11/13, 85%). Revision for nonunion was performed at the discretion of the surgeon investigator after discussing all treatment options with the subject. In all cases, surgical revision was performed only after conservative treatments for reemergent symptoms were unsuccessful and evidence of gross mobility at the index levels was confirmed radiographically. It is important to acknowledge that all participating surgeons were proficient in performing posterior fusion with PCSS used in this trial, with some regularly implementing the technique to revise symptomatic nonunion.[29,30] As a result, the reported rates of revision for nonunion may be elevated when compared with rates where the revision is performed with a repeat ACDF or conventional open posterior approach.

Our results confirm previous research showing improved radiographic outcomes for CCF over ACDF to treat multilevel disease.[9,31–33] When considering supplemental posterior fusion, a surgeon must weigh the benefits of improving fusion rates with the collateral risks of additional surgery. Posterior fusion with a conventional screw and rod approach introduces a large open incision and extensive muscle dissection that leads to longer procedures, increased blood loss, and prolonged hospital

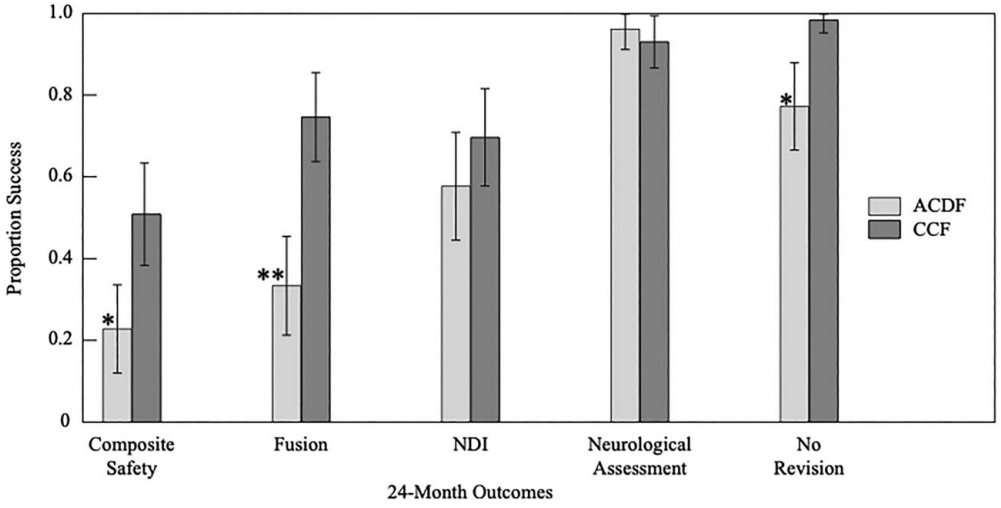

Figure 3. Frequency distributions of success rates by treatment for the 24-month secondary safety composite endpoint and contributing components. Error bars represent 95% CIs. *$P < 0.01$; **$P < 0.001$.

TABLE 4. Incidence and Severity of Radiographic Adjacent Segment Degeneration by Treatment at 24-Month Visit*

	CCF (N = 54), n (%)	ACDF (N = 42), n (%)
Most severe adjacent segment disease		
Severe	4 (7.4)	6 (14.3)
Moderate	9 (16.7)	5 (11.9)
Minimal	12 (22.2)	14 (33.3)
Doubtful	18 (33.3)	14 (33.3)
None	11 (20.4)	3 (7.1)
Severe, moderate, or minimal†	25 (46.3)	25 (59.5)

*Values do not include participants with missing images or that required revision before the month 24 visit.
†$P = 0.198$ between CCF and ACDF groups.

stays.[34] These shortcomings collectively increase the likelihood of complications including sepsis, wound infection, need for blood transfusion, and pneumonia.[35,36] One previous case study performed by Kramer *et al.*[37] summarized outcomes in patients treated with CCF using a facet cage to treat degenerative disease at two or more levels. They reported a total average estimated blood loss of 70 mL and stayed an average one night in hospital. There were no instances of adverse intraoperative events, reoperations, or readmissions. Posterior fusion with PCSS incurred an additional 10 mL of blood loss with the entire CCF procedure requiring an additional 98 minutes to complete when compared with ACDF alone. Length of stay was indistinguishable between the groups and the added surgical burden in the CCF group did not produce greater rates of postoperative complications.

Spinal fusion represents the largest aggregate expense to payers across all surgical procedures.[38] Including posterior fusion with PCSS to an index ACDF increases cost and requires greater time and resources from both surgeon and hospital. However, results from the current study suggest that including this additional up-front cost significantly reduces the need for subsequent unplanned surgical revisions. Compared with primary procedures, revisions are often more complex and less likely to succeed, resulting in a larger cost per quality-of-life improvement.[39–41] Future efforts need to consider not only surgical revisions, but all planned and unplanned postoperative care between ACDF and CCF to better understand the relative value of these approaches on health care economics.

When placing instrumentation into the cervical spine, a surgeon needs to be diligent to maintain, or restore sagittal lordosis, as this clinical outcome may directly impact patient-reported outcomes.[42] When assessed at 24 months post-treatment, both arms showed similarly marginal improvements in lordosis, suggesting that the addition of posterior instrumentation had no observable impact on alignment. These findings support a previous cadaveric study by Havey *et al.*[43] who reported that that the addition of posterior instrumentation, combined with an integrated anterior screw and cage construct, resulted in no change in segmental lordosis when compared with the intact condition.

As an industry-sponsored IDE trial (funded by Providence Medical Technology, Pleasanton, CA) there is concern that favorable outcomes may be biased toward the investigational arm. To mitigate these potential biases, the responsibility of adjudicating outcomes contributing to primary and secondary endpoint success was assigned to independent parties with no investment in study outcomes. Radiographic results were determined using validated protocols from an independent core imaging laboratory[44] and all safety and neurological outcomes were adjudicated by an independently managed clinical events committee of three board certified experts in orthopedic or neurosurgery. Another limitation is that the current findings are based on a protocol-defined interim analysis triggered when ~100 patients reached the 24-month evaluation interval. An increase in participants followed through study completion will allow for more confident understanding of how differences in radiographic outcomes between groups may explain variability in clinical and patient-reported outcomes such as NDI, particularly for those with asymptomatic nonunion. There are several risk factors beyond long-segment disease that can influence the risk of nonunion. Through stratification, smoking status and age were balanced between arms. Other risk factors such as systemic infection/disease or osteoporosis were listed as contraindications for treatment with the PCSS and were not eligible to be studied in the current design. Future research should focus on how other well-documented risk factors for nonunion are impacted when including PCSS as part of a CCF procedure. The selection of anterior plate technology can vary between manufacturers and models. The current study attempted to minimize that source of variability through limiting the features of the plates allowed. All subjects were treated with a semiconstrained anterior plate and screw construct. All plates were made of ridged metal that allowed for two variable angle screws per level placed using a unicortical technique. The types of plate/screw constructs and the dimensions of the screws were represented equally between arms suggesting that any impact of anterior plating options did not confound the comparisons between the ACDF and CCF arms. It is unclear what effect using a fixed or dynamic plate would have on the overall success rates reported in this study. Lastly, the study did not include a PCF only cohort with treatment using a conventional lateral mass screws and rods approach. As such, it is difficult to directly compare how outcomes from this treatment plan would compare to the two approaches studied in the trial.

The radiographic evidence and rates of revision in the ACDF group suggest that the risk of developing nonunion following three-level treatment may be greater than what is currently understood. There has been a growing body of evidence supporting the use of PCF with PCSS to supplement ACDF for patients with symptomatic disc degeneration.[29,30,45] The results of the current randomized clinical trial extend these findings.

➢ Key Points

- ❑ Subjects with cervical degenerative disc disease at three levels were randomized to receive surgical treatment with ACDF alone or supplemented with posterior fusion including an investigational stabilization device.
- ❑ Through 24 months, 33% of ACDF subjects achieved complete arthrodesis and 23% required revision, primarily for symptomatic nonunion.
- ❑ Including supplemental posterior fixation improved both arthrodesis rates (75% of subjects) and reduced revision rates (2% of subjects) without increasing the risk of complications from an additional procedure.
- ❑ Treating long-segment cervical disease (3+ disc levels) with ACDF is associated with a significant risk of one or more levels requiring future surgical reintervention.

References

1. Salzmann SN, Derman PB, Lampe LP, et al. Cervical spinal fusion: 16-year trends in epidemiology, indications, and in-hospital outcomes by surgical approach. *World Neurosurg*. 2018;113:e280–e295.
2. Neifert SN, Martini ML, Yuk F, et al. Predicting trends in cervical spinal surgery in the United States from 2020 to 2040. *World Neurosurg*. 2020;141:e175–e181.
3. Buttermann GR. Anterior cervical discectomy and fusion outcomes over 10 years: a prospective study. *Spine*. 2018;43:207–214.
4. Fehlings MG, Wilson JR, Kopjar B, et al. Efficacy and safety of surgical decompression in patients with cervical spondylotic myelopathy: results of the AOSpine North America prospective multicenter study. *J Bone Joint Surg Am*. 2013;95:1651–1658.
5. Zuckerman SL, Devin CJ. Pseudarthrosis of the cervical spine. *Clin Spine Surg*. 2022;35:97–106.
6. Eck JC, Humphreys SC, Lim T-H, et al. Biomechanical study on the effect of cervical spine fusion on adjacent-level intradiscal pressure and segmental motion. *Spine*. 2002;27:2431–2434.
7. Wang B, Liu H, Wang H, Zhou D. Segmental instability in cervical spondylotic myelopathy with severe disc degeneration. *Spine*. 2006; 31:1327–1331.
8. Wewel JT, Kasliwal MK, Adogwa O, Deutsch H, O'Toole JE, Traynelis VC. Fusion rate following three- and four-level ACDF using allograft and segmental instrumentation: a radiographic study. *J Clin Neurosci*. 2019;62:142–146.
9. Leven D, Cho SK. Pseudarthrosis of the cervical spine: risk factors, diagnosis and management. *Asian Spine J*. 2016;10:776–786.
10. Nichols NM, Jamieson A, Wang M, Chou D, Mummaneni PV, Tan LA. Characterizing the fusion order and level-specific rates of arthrodesis in 3-level anterior cervical discectomy and fusion: a radiographic study. *J Clin Neurosci*. 2020;81:328–333.
11. Bolesta MJ, Rechtine GR, Chrin AM. Three- and four-level anterior cervical discectomy and fusion with plate fixation: a prospective study. *Spine*. 2000;25:2040–2044; discussion 2045.
12. Epstein NE. A review of complication rates for anterior cervical diskectomy and fusion (ACDF). *Surg Neurol Int*. 2019;10:100.
13. Laratta JL, Reddy HP, Bratcher KR, McGraw KE, Carreon LY, Owens RK. Outcomes and revision rates following multilevel anterior cervical discectomy and fusion. *J Spine Surg*. 2018;4:496–500.
14. Vender JR, Rekito AJ, Harrison SJ, McDonnell DE. The evolution of posterior cervical and occipitocervical fusion and instrumentation. *Neurosurg Focus*. 2004;16:E9.
15. Summerside E, Heller J, Glenn J, McCormack B, Menchetti PPM. Tissue sparing posterior fixation as a treatment option for degenerative disc disease. In: Menchetti PPM, editor. *Cervical Spine: Minimally Invasive and OPEN SURGERY*. Cham: Springer International Publishing; 2022:231–245.
16. Laratta JL, Gupta K, Smith WD. Tissue-sparing posterior cervical fusion with interfacet cages: a systematic review of the literature. *Global Spine J*. 2020;10:230–236.
17. Hisey MS, Bae HW, Davis R, et al. Multi-center, prospective, randomized, controlled investigational device exemption clinical trial comparing Mobi-C Cervical Artificial Disc to anterior discectomy and fusion in the treatment of symptomatic degenerative disc disease in the cervical spine. *Int J Spine Surg*. 2014;8:7.
18. Burkus JK, Traynelis VC, Haid RW, Mummaneni PV. Clinical and radiographic analysis of an artificial cervical disc: 7-year follow-up from the Prestige prospective randomized controlled clinical trial (Clinical article). *J Neurosurg Spine*. 2014;21:516–528.
19. Coric D, Guyer RD, Nunley PD, et al. Prospective, randomized multicenter study of cervical arthroplasty versus anterior cervical discectomy and fusion: 5-year results with a metal-on-metal artificial disc. *J Neurosurg Spine*. 2018;28:252–261.
20. McCormack BM, Dhawan R. Novel instrumentation and technique for tissue sparing posterior cervical fusion. *J Clin Neurosci*. 2016;34: 299–302.
21. McClure JJ, Desai BD, Shabo LM, et al. A single-center retrospective analysis of 3- or 4-level anterior cervical discectomy and fusion: surgical outcomes in 66 patients. *J Neurosurg Spine*. 2020;34:45–51.
22. 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*. 2011;36:463–468.
23. Skolasky RL, Maggard AM, Hilibrand AS, et al. Agreement between surgeons and an independent panel with respect to surgical site fusion after single-level anterior cervical spine surgery: a prospective, multicenter study. *Spine*. 2006;31:E503–E506.
24. Davis RJ, Nunley PD, Kim KD, et al. Two-level total disc replacement with Mobi-C cervical artificial disc versus anterior discectomy and fusion: a prospective, randomized, controlled multicenter clinical trial with 4-year follow-up results. *J Neurosurg Spine*. 2015;22:15–25.
25. Goldberg JL, Meaden RM, Hussain I, et al. Titanium versus polyetheretherketone versus structural allograft in anterior cervical discectomy and fusion: a systematic review. *Brain Spine*. 2022;2:100923.
26. Lee D-H, Park S, Seok SY, et al. Fate of pseudarthrosis detected 2 years after anterior cervical discectomy and fusion: results of a minimum 5-year follow-up. *Spine J*. 2023;23:1790–1798.
27. Joo PY, Zhu JR, Kammien AJ, Gouzoulis MJ, Arnold PM, Grauer JN. Clinical outcomes following one-, two-, three-, and four-level anterior cervical discectomy and fusion: a national database study. *Spine J*. 2022;22:542–548.
28. Wang JC, McDonough PW, Kanim LE, Endow KK, Delamarter RB. Increased fusion rates with cervical plating for three-level anterior cervical discectomy and fusion. *Spine*. 2001;26:643–646; discussion 646.
29. Haglund MM, McCormack BM, Williams DM, Lemons AC, Summerside EM. Long-term outcomes in patients treated with tissue-sparing posterior cervical fusion to revise a 1-level pseudarthrosis following ACDF. *J Clin Neurosci*. 2023;119:85–92.
30. Lemons AC, Haglund MM, McCormack BM, Williams DM, Bohr AD, Summerside EM. Perioperative and safety outcomes following tissue-sparing posterior cervical fusion to revise a pseudarthrosis: a multicenter retrospective review of 150 cases. *J Craniovertebr Junction Spine*. 2024;15:216–223.
31. Joaquim AF, Lee NJ, Riew KD. Circumferential operations of the cervical spine. *Neurospine*. 2021;18:55–66.
32. König SA, Spetzger U. Surgical management of cervical spondylotic myelopathy - indications for anterior, posterior or combined procedures for decompression and stabilisation. *Acta Neurochir (Wien)*. 2014;156:253–258; discussion 258.

33. Konya D, Ozgen S, Gercek A, Pamir MN. Outcomes for combined anterior and posterior surgical approaches for patients with multisegmental cervical spondylotic myelopathy. *J Clin Neurosci*. 2009;16:404–409.
34. Carreon L, Glassman SD, Campbell MJ. Treatment of anterior cervical pseudoarthrosis: posterior fusion versus anterior revision. *Spine J*. 2006;6:154–156.
35. Yue JK, Upadhyayula PS, Deng H, Sing DC, Ciacci JD. Risk factors for 30-day outcomes in elective anterior versus posterior cervical fusion: a matched cohort analysis. *J Craniovertebr Junction Spine*. 2017;8:222–230.
36. Zaki O, Jain N, Yu EM, Khan SN. 30- and 90-day unplanned readmission rates, causes, and risk factors after cervical fusion: a single-institution analysis. *Spine*. 2019;44:762–769.
37. Kramer S, Albana MF, Ferraro JB, Shah RV. Minimally invasive posterior cervical fusion with facet cages to augment high-risk anterior cervical arthrodesis: a case series. *Global Spine J*. 2020;10(suppl):56S–60S.
38. Overview of Operating Room Procedures During Inpatient Stays in US Hospitals, 2018 #281. Accessed May 28, 2024. https://hcup-us.ahrq.gov/reports/statbriefs/sb281-Operating-Room-Procedures-During-Hospitalization-2018.jsp
39. Pennington Z, Mehta VA, Lubelski D, et al. Quality of life and cost implications of pseudarthrosis after anterior cervical discectomy and fusion and its subsequent revision surgery. *World Neurosurg*. 2020;133:e592–e599.
40. Arima H, Hasegawa T, Yamato Y, et al. Cost-effectiveness of corrective fusion surgeries for adult spinal deformities: does unexpected revision surgery affect cost-effectiveness? *Spine Surg Relat Res*. 2024;8:306–314.
41. Bonano J, Cummins DD, Burch S, et al. Economic impact of revision operations for adjacent segment disease of the subaxial cervical spine. *J Am Acad Orthop Surg Glob Res Rev*. 2022;6:e22.00058.
42. Gadia A, Shah K, Nene A. Cervical kyphosis. *Asian Spine J*. 2019;13:163–172.
43. Havey RM, Blank KR, Khayatzadeh S, Muriuki MG, Pappu S, Patwardhan AG. Effectiveness of cervical zero profile integrated cage with and without supplemental posterior Interfacet stabilization. *Clin Biomech (Bristol, Avon)*. 2020;78:105078.
44. Reitman CA, Hipp JA, Nguyen L, Esses SI. Changes in segmental intervertebral motion adjacent to cervical arthrodesis: a prospective study. *Spine*. 2004;29:E221–E226.
45. Pinto V, Pereira L, Reinas R, Kitumba D, Alves OL. Minimally invasive posterior cervical fusion: a handsome option. *Acta Neurochir Suppl*. 2023;135:351–356.