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A single-center retrospective analysis of 3- or 4-level anterior cervical discectomy and fusion: surgical outcomes in 66 patients

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OBJECTIVE Anterior cervical discectomy and fusion (ACDF) is a safe and effective intervention to treat cervical spine pathology. Although these were originally performed as single-level procedures, multilevel ACDF has been performed for patients with extensive degenerative disc disease. To date, there is a paucity of data regarding outcomes related to ACDFs of 3 or more levels. The purpose of this study was to compare surgical outcomes of 3- and 4-level ACDF procedures.

METHODS The authors performed a retrospective chart review of patients who underwent 3- and 4-level ACDF at the University of Virginia Health System between January 2010 and December 2017. In patients meeting the inclusion/exclusion criteria, demographics, fusion rates, time to fusion, and reoperation rates were evaluated. Fusion was determined by < 1 mm of change in interspinous distance between individual fused vertebrae on lateral flexion/extension radiographs and lack of radiolucency between the grafts and vertebral bodies. Any procedure requiring a surgical revision was considered a failure.

RESULTS Sixty-six patients (47 with 3-level and 19 with 4-level ACDFs) met the inclusion/exclusion criteria of having at least one lateral flexion/extension radiograph series ≥ 12 months after surgery. Seventy percent of 3-level patients and 68% of 4-level patients had ≥ 24 months of follow-up. Ninety-four percent of 3-level patients and 100% of 4-level patients achieved radiographic fusion for at least 1 surgical level. Eighty-eight percent and 82% of 3- and 4-level patients achieved fusion at C3–4; 85% and 89% of 3- and 4-level patients achieved fusion at C4–5; 68% and 89% of 3- and 4-level patients achieved fusion at C5–6; 44% and 42% of 3- and 4-level patients achieved fusion at C6–7; and no patients achieved fusion at C7–T1. Time to fusion was not significantly different between levels. Revision was required in 6.4% of patients with 3-level and in 16% of patients with 4-level ACDF. The mean time to revision was 46.2 and 45.4 months for 3- and 4-level ACDF, respectively. The most common reason for revision was worsening of initial symptoms.

CONCLUSIONS The authors' experience with long-segment anterior cervical fusions shows their fusion rates exceeding most of the reported fusion rates for similar procedures in the literature, with rates similar to those reported for short-segment ACDFs. Three-level and 4-level ACDF procedures are viable options for cervical spine pathology, and the authors' analysis demonstrates an equivalent rate of fusion and time to fusion between 3- and 4-level surgeries.

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KEYWORDS ACDF; fusion; 3 levels; 4 levels; anterior cervical discectomy and fusion; time to fusion

The anterior cervical discectomy and fusion (ACDF) procedure is a common surgical approach for treating cervical spine pathology due to its safety and efficacy.[1,2] Although it was originally performed as a single-level procedure, it has become increasingly used in multilevel spine disease.[3,4] The procedure has a well-studied history of significantly improving symptoms of radiculopathy and myelopathy, improving health-related quality of life, and having low associated morbidity and mortality.[5–9] The success of the ACDF procedure largely depends on formation of arthrodesis.

The ACDF procedure is most commonly used for 1- or 2-level cervical disc disease;[10] however, in many instances degenerative cervical spine pathology may affect 3 or more

ABBREVIATIONS ACDF = anterior cervical discectomy and fusion; PSIF = posterior spinal instrumentation and fusion.

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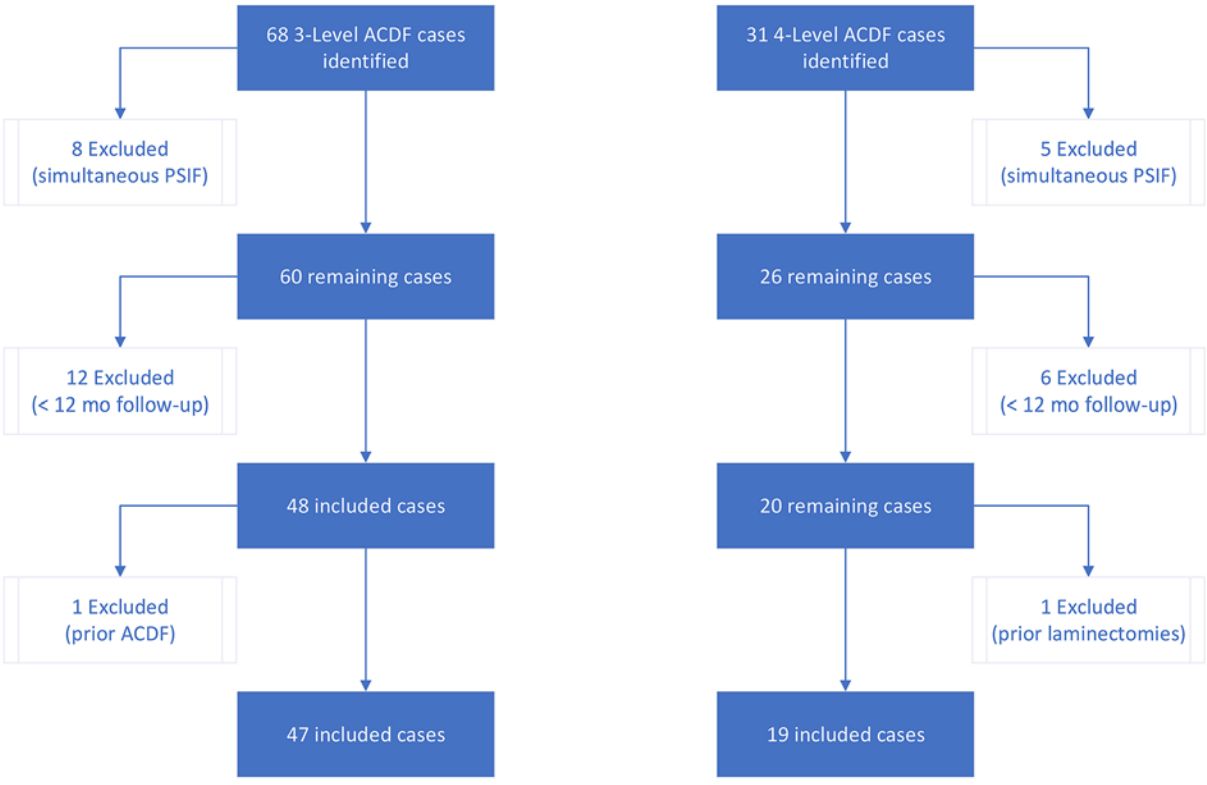

FIG. 1. Inclusion/exclusion criteria of 3- and 4-level ACDF cases. Figure is available in color online only.

levels. As such, "long-segment" ACDF procedures involving 3 or more levels are becoming more common. Previous literature differs on the fusion rates of long-segment ACDF, with a wide range of reported fusion rates between 42% and 92%.[4,10–18] The greater surface area required for fusion, the increased number of mobile segments, and increased motion arm across the fusion construct may negatively impact fusion rates.[19] As such, the utility of 3- and 4-level ACDF is often debated, with many surgeons citing a low rate of reported fusions. The purpose of this study was to evaluate the fusion rates and report long-term surgical outcomes of 3- and 4-level ACDF procedures for our cohort of patients.

Methods

Study Sample

Following institutional review board approval and after obtaining informed consent, we performed a retrospective review of all ACDF procedures involving 3 or more contiguous levels performed at the University of Virginia Health System between January 2010 and December 2017 by the neurosurgery service. We identified 99 total cases, of which 66 met the inclusion/exclusion criteria (Fig. 1).

Covariates

We gathered patient demographics including age, sex, BMI, smoking status, and osteoporosis status from our electronic medical record for each case. We also gathered intraoperative data including discectomy levels, type of bone graft, estimated blood loss, surgical duration, and nights spent in the hospital. Patients who smoked before the procedure but had documentation of cessation before surgery or patients who had documentation of normal preoperative serum nicotine and cotinine were considered to be former smokers in our analysis. We considered any case requiring a posterior fusion or anterior revision as a failure. Our primary outcome was fusion success.

The individual lateral flexion/extension radiographs or cervical CT scans of each follow-up for each included patient were reviewed. Radiographs were universally magnified to 150% and the interspinous distance between adjacent surgical levels was measured. An identifiable landmark present on the both flexion and extension films was identified and used to measure the distance. Additionally, patients' radiographs had to demonstrate evidence of good flexion/extension effort, which was defined by > 4 mm of motion between the skull and C1 or between C1 and C2 on flexion/extension. To be considered fused, a vertebral level had to have ≤ 1 mm of interspinous distance motion on sagittal flexion/extension radiographs and be free of any lucencies between the vertebral endplate and allograft. We considered time to fusion as the earliest instance of a vertebral level meeting these criteria. In instances in which the patient underwent a cervical CT scan, a vertebral level had to be free of any lucencies between the vertebral endplate and allograft at each sagittal cross-section where the graft could be seen. An example measurement with annotation may be found in Fig. 2.

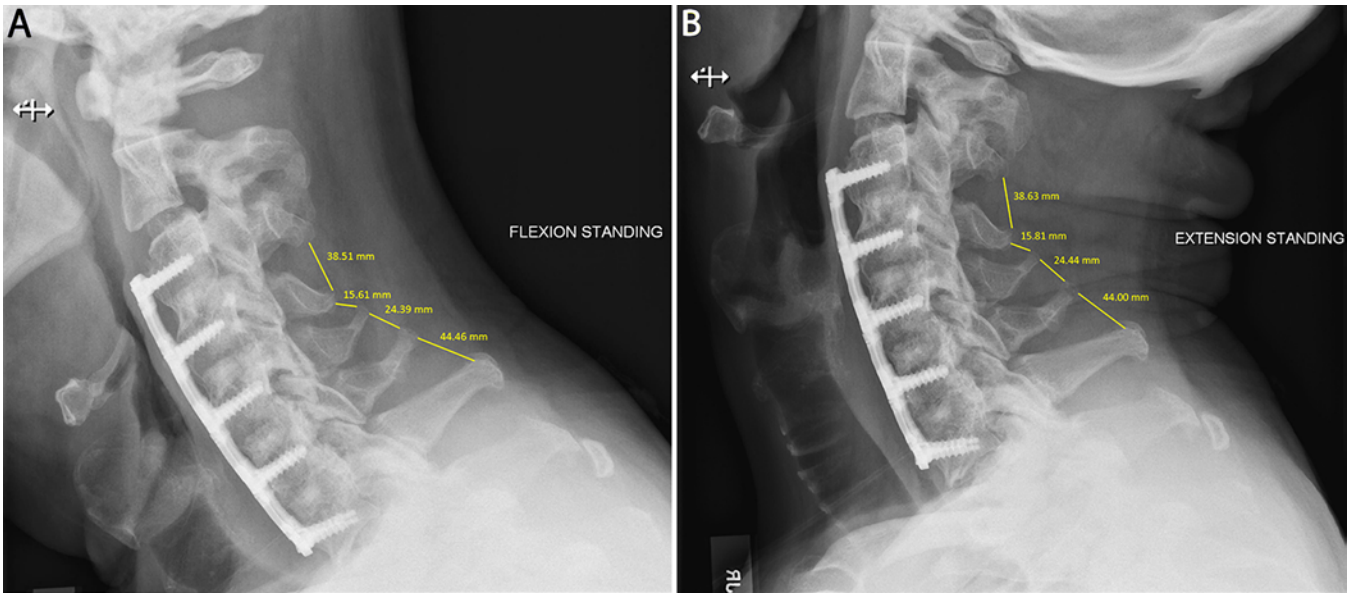

FIG. 2. Representative radiographic outcomes and measurement technique after a 4-level ACDF operation. **A:** Lateral radiograph of the postoperative cervical spine during flexion. **B:** Lateral radiograph of the postoperative cervical spine during extension. Figure is available in color online only.

Surgical Technique

Patients were positioned supine on the operating table. The neck was appropriately extended using a combination of a shoulder bump and in some cases head halter traction with 5–10 pounds. Shoulders were taped down to provide appropriate visualization on lateral fluoroscopy. Neuromonitoring was used per surgeon preference. A standard Smith-Robinson approach with a left-sided transverse or oblique incision was made at the appropriate level, as described by other studies.[20,21] Caspar pins were used to aid in distraction, and the discectomy, decompression, and placement of allografts were completed under the microscope to aid in visualization. All fusions were completed using prefabricated cortico-cancellous allograft constructs. An appropriate 3- to 4-level cervical plate was placed with screws. A drain was left postoperatively when needed, and the patient was admitted to an appropriate inpatient unit based on their level of medical comorbidities. Patients received a hard cervical collar postoperatively for all cervical fusion procedures. Collars were worn for a 6-week duration.

Statistical Analysis

Patient demographics are presented as the mean (SD) and range where applicable. We compared the binary outcomes using Fisher's tests. After assessing for normal distribution using the D'Agostino-Pearson omnibus K^2 method, we compared continuous variables with unpaired 2-tailed t-tests with Welch's correction or Mann-Whitney tests depending on normalcy. We used both Mantel-Cox and Gehan-Breslow-Wilcoxon tests to compare time to fusion between groups. We used GraphPad Prism 8.3.0 (GraphPad Software Inc.) for graph generation and statistical analysis. We used Microsoft Visio v2002 to generate the inclusion/exclusion criteria flowchart. Figures were edited with Adobe Illustrator CC 20 24.1.1 and Photoshop CC 20 21.1.1 (Adobe Inc.). We considered a p value < 0.05 to be statistically significant.

Results

Sixty-six patients met our inclusion/exclusion criteria; 47 and 19 underwent 3- and 4-level ACDF procedures, respectively. The baseline demographic values for the patient population in our study were not significantly different across the two groups with respect to age, sex, smoking history, or history of osteoporosis; patients undergoing 4-level fusions had significantly lower BMI values (Table 1).

There were significant differences in perioperative variables between those undergoing 3-level versus 4-level ACDF procedures. Notably, patients undergoing 4-level operations were significantly more likely to require fixation at C3–4, have longer operation times, and have an increased estimated blood loss during the operation (Table 2).

With regard to postoperative outcomes, there was no

TABLE 1. Demographics of 66 patients who underwent ACDF

Characteristic	3-Level Op	4-Level Op	p Value
No. of patients	47	19	
Age (yrs), range	57, 35–83	56, 6–76	0.6414
% male	36	42	0.7806
BMI, range	31, 20–46	26, 18–42	**0.0113**
Smoking history	47 (40) [13]	32 (42) [26]	0.3264
% osteoporotic	13	0	0.1793

Age and BMI are presented as the mean with ranges; smoking history is presented as % nonsmoker (% former smoker) [% current smoker]. Boldface type indicates statistical significance.

TABLE 2. Perioperative variables in 66 patients who underwent ACDF

Variable	3-Level Op	4-Level Op	p Value
Total no. of patients	47	19	
C3–4	8 (17%)	17 (89%)	**<0.0001**
C4–5	46 (98%)	19 (100%)	>0.9999
C5–6	47 (100%)	19 (100%)	
C6–7	39 (83%)	19 (100%)	0.0960
C7–T1	1 (2.1%)	2 (11%)	0.1968
Op time, mins	275 (43.8) [179–369]	330 (73.3) [245–504]	**0.0069**
EBL, mL	80.5 (40.9) [20.0–200]	135 (107) [25.0–500]	**0.0184**
Postop LOS, nights	3.3 (2.4) [1–12]	4.2 (2.8) [2–12]	0.0874

EBL = estimated blood loss; LOS = length of hospital stay.
Operative time, estimated blood loss, and postoperative hospital stay are presented as the mean (SD) [range]. Boldface type indicates statistical significance.

difference in the proportion of patients who had at least 24 months of follow-up, nor were there differences in number of follow-ups, length of follow-up after surgery, frequency of revision surgeries, or time to revision surgery (Table 3). The proportion of patients who achieved fusion was also comparable between groups at each surgical level (Fig. 3, Table 4). The median time to fusion was not significantly different either between the two groups or between comparable levels within each group. There were 3 patients who did not achieve fusion at any level in the 3-level ACDF cohort; 1 of these 3 required a revision posterior spinal instrumentation and fusion (PSIF). All 3 of these patients had < 24 months of follow-up. All patients achieved fusion at least at 1 level in the 4-level ACDF cohort.

Of the 6 total patients who had worsening pain or neurological symptoms after the ACDF procedure, 5 underwent secondary posterior fusions to further stabilize the region. The sole patient who elected for an anterior approach underwent an extension of their initial ACDF with a removal and replacement of their initial anterior plate. One patient's symptoms were determined to be due to a screw fracture. Three patients had evidence of adjacent segment disease. Three patients identified a fall that was temporally correlative to the start of their symptoms, including radiculopathies, neck pain, myelopathy, and, in one case, motor weakness. All 6 patients report satisfactory outcomes thus far after their revisions; the time since their surgeries ranges from 18 to 90 months.

TABLE 3. Postoperative follow-up in 66 patients who underwent ACDF

Postop Data	3-Level Op	4-Level Op	p Value
Total no. of patients	47	19	
Time to 1st FU, mos	5.0 (1.7) [2.7–9.5]	7.0 (13) [1.6–61]	0.1120
No. of FU visits	3.6 (1.2) [2–7]	4.2 (2.3) [2–12]	0.5158
Max FU length, mos	31 (17) [12–72]	40 (27) [12–90]	0.1883
No. w/ 24 mos of FU	33 (70%)	13 (68%)	>0.9999
Req revision	3 (6.4%)	3 (16%)	0.3435
Time to revision, mos	46.2 [15.1–69.8]	45.4 [15.1–85.5]	

FU = follow-up; max = maximum; req = required.
Time to first follow-up, no. of follow-up visits, and maximum follow-up length are presented as the mean (SD) [range]. Time to revision is presented as the mean [range]. Sagittal flexion/extension films or cervical CT imaging were used to assess patients at follow-up.

Discussion

ACDF procedures have been well established to improve both radicular and myelopathic symptoms in appropriately selected patients. As with any spinal fusion procedure, a concern for increased rates of pseudarthrosis accompanies larger fusion constructs. To our knowledge, 10 papers addressing the fusion rates of 3- and 4-level ACDF procedures have been published.[4,10–18] The authors of these 10 papers report a wide range of fusion rates and success, from approximately 40% to nearly 100%. Although there are many factors that may lead to these discrepancies, two variables alone probably account for most of the discrepancy: fusion criteria and follow-up time.

Many authors use different methodologies for determining fusion/nonfusion/pseudarthrosis, and many report different ways of approximating the same goal. Articles that focus more heavily on fusion rather than pseudarthrosis have a higher percentage of reported success. Conversely, articles that report pseudarthrosis have a lower percentage of reported success. Despite the vast differences in published radiographic success, the number of patients requiring revisions or reporting unsatisfactory symptomatic relief remains more consistent. Another recent review of clinical outcomes of 4-level ACDFs demonstrated a low rate of revision cervical surgery for any reason (8% at a mean of 19 months of follow-up), and neurological status consistently improved despite a 31% rate of radiographic nonunion.[20]

After reviewing the different methods for determining fusion, we believe a cutoff of 1 mm of interspinous motion on sagittal flexion/extension films with absence of lucency at the graft–endplate convergence to be the most robust strategy to determine fusion—aside from cervical CT and microscopic, intraoperative verification. An analysis of this technique and others was recently published by Oshina et al.[15]

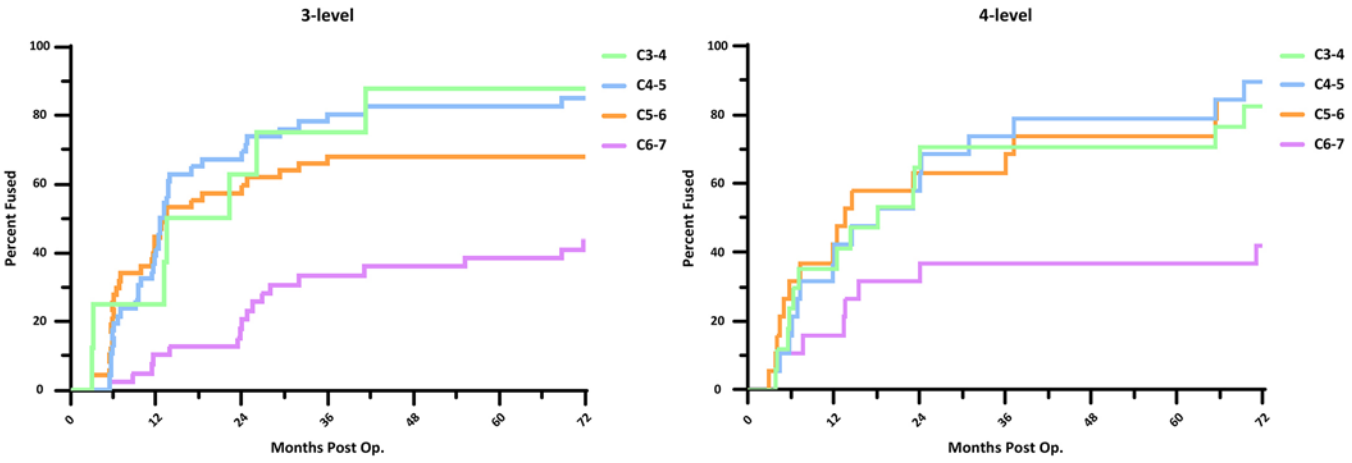

FIG. 3. Time to fusion for patients undergoing long-segment ACDF procedures. Figure is available in color online only.

In addition to fusion determination methodology, we believe follow-up time is another critical variable accounting for large differences in reported fusion rates. Supporting this idea, a recent meta-analysis of the literature surrounding interpreting postsurgical radiographs to determine fusion suggested that papers that reported longer follow-up also reported higher fusion times.[22] These authors' findings suggested waiting a minimum of 24 months before making definitive conclusions regarding pseudarthrosis. Our results mirror this opinion. With a median time to fusion of 10–14 months, roughly 50% of the fused levels would occur after a 12-month follow-up. If we stopped following these patients at 12 months our results for this study would be quite different (Fig. 3). It would be perhaps interesting to again review the patients whose outcomes were published in articles with cutoffs at 12 months after up to 24 months of radiographic and clinical follow-up to determine if the reported rates change significantly.

After reviewing our data, which demonstrated significantly lower rates of fusion for C6–7 and C7–T1, we believe that the fusion criteria published by Oshina et al.[15] needs to have two caveats if it is to be applied to patients with 3- and 4-level ACDF.

TABLE 4. Postoperative outcomes in 66 patients who underwent ACDF

Outcome	3-Level Op	4-Level Op	p Value
Total no. of patients	47	19	
Fusion level			
C3–4	7/8 (87.5%)	14/17 (82.4%)	>0.9999
C4–5	39/46 (84.8%)	17/19 (89.5%)	>0.4992
C5–6	32/47 (68.1%)	17/19 (89.5%)	0.1187
C6–7	17/39 (43.6%)	8/19 (42.1%)	>0.9999
C7–T1	0/1 (0%)	0/2 (0%)	
Time to fusion, mos			
C3–4	13.5 [3.1–41]	12.5 [3.9–69]	0.7309
C4–5	12.3 [5.5–69]	14.4 [3.9–69]	0.4992
C5–6	10.0 [3.0–36]	12.3 [3.0–69]	0.7553
C6–7	24.7 [5.5–72]	13.5 [3.9–71]	0.0858

Time to fusion is expressed as the mean [range].

First, when measuring the C6–7 and C7–T1 levels, we believe a 2-mm cutoff provides a more anatomically homogeneous approach. This caveat is still in line with the methods previously proposed, but accounts for the spinous processes of C6, C7, and T1 being approximately twice as long as C3–5.[23] As such, the same degree of movement that results in up to 1 mm of interspinous motion on flexion/extension for C3–5 would lead to 2 mm of motion if the point of measurement is twice as far—like that seen in C6–T1. To maintain consistency and avoid confusion, we used a 1-mm cutoff throughout this paper for all levels, which at least partially lowers our rates of fusion for C6–7.

That is not to say this one change would result in fusion rates for C6–7 being comparable to C3–5. We believe the amount of motion that occurs at C6–7 during flexion and extension accounts for the vast majority of the difference in fusion rates for this level compared to the others. In-depth biomechanical studies of the cervical spine have consistently found that the C6–7 vertebral level is the first to move when performing flexion and extension, and the amount of motion it goes through during flexion and extension is much greater than other cervical vertebrae.[24] As such, we expect the increased movement of this level to delay if not outright prevent its fusion.

The second caveat is a slight change to the determination of "good effort" on flexion/extension films. Previous articles reported a method of determining if a patient put in good effort by measuring the interspinous motion on flexion/extension of superjacent levels.[15,25] Briefly, these authors posited that a patient needed to have ≥ 4 mm of interspinous motion at the level directly cranial to the surgically fused region; however, their patients primarily underwent 1- and 2-level ACDFs. In our patients we noticed many did not have adequate superjacent motion, but they were showing satisfactory movement between the skull and C1 and between C1 and C2. We posited that the extensive fusion length interfered with the patient's ability to adequately flex and extend the superjacent level despite having no surgical fusion or hardware affecting this level. An example of this may be seen in Fig. 2. As such, we

believe the superjacent interspinous motion measurement to be a useful marker of good effort, but in patients with 3- and 4-level ACDF, one must also look at levels even more cranial to assess if a good effort was made by the patient.

We believe this work provides novel insight into what we think is the most important facet of determining the fusion rates for these long-segment ACDF procedures: time to fusion. Although many articles have reported fusion rates with appreciable sample sizes, most determined fusion at 12 months rather than waiting for additional time. Although the 12-month window is appropriate in most cases, particularly with the more common 1- or 2-level ACDF procedures, our data suggest that longer segments may require longer time to fuse. In the case of C6–7 fusion, the median time to fusion in patients with 3-level ACDF was 24 months. Furthermore, this is the first publication to our knowledge that demonstrates similar time to fusion between 3- and 4-level ACDF procedures.

Our results indicate that we had excellent fusion rates at C3–5 levels, closely mirroring that of 1- and 2-level fusions. One meta-analysis including 1- and 2-level ACDF procedures reported pseudarthrosis rates of 3.1% at 12 months and 2.3% at 24 months, with an overall single-level ACDF pseudarthrosis rate of 3.7% over all studies.[22] Fusion rates will naturally vary between studies based on the strictness of the fusion criteria. Despite using strict criteria of < 1 mm of interspinous motion on sagittal flexion/extension films, we reported fusion rates on the higher end of previously published data from studies using standard ACDF operative techniques and allograft spacers. Many patient factors may also play a role, including the use of the hard cervical collar as well as refraining from using any nicotine products. Three of 47 (6.4%) 3-level ACDFs and 3 of 19 (16%) 4-level ACDFs required revision or extension procedures, which was not significantly different between groups.

There are intrinsic limitations in this paper because it is a retrospective review of surgical outcomes that relies on physician evaluation of flexion/extension radiographs as well as patients relaying symptoms back to physicians in terms of radiculopathy, myelopathy, and other concerns. It would be beneficial to continue following these patients for further data regarding long-term fusion rates and revision rates for these procedures. A more effective way of assessing fusion would use CT radiography rather than plain film. Although some patients did undergo CT imaging of the cervical spine, the vast majority of our patients were managed with single-view films alone. Our assessment of fusion, like most interpretations in the literature, relies more heavily on subjective interpretation of what is fused and what is not. However, our revision rates remain quite low. This suggests that in spite of the fact that surgeons may differ in their interpretation of fusion, the patients whose symptoms are satisfactorily treated with these operations are well managed.

Conclusions

Historically, fusion rates for 3- and 4-level ACDF procedures have been reported to range from 42% to 92%.[4,10–18] Our retrospective review of these long-segment anterior cervical fusions showed our fusion rates to be more in line with the higher end of these reported values and comparable to the reported fusion rates for short-segment ACDFs. Furthermore, we differentiated the fusion rates and time to fusion for the individual levels. This will provide more descriptive expectations for both surgeons and patients preoperatively with respect to which levels are likely to fuse and how long it will take for this fusion to occur. Three- and 4-level ACDF procedures are viable options for cervical spine pathology, and our analysis demonstrates an equivalent rate of good clinical and radiographic outcomes between cohorts. Further evaluation of longer clinical and radiographic follow-up of up to 24 months may result in a more accurate interpretation of surgical success.

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Disclosures

Dr. C. Shaffrey has direct stock ownership in NuVasive; is a consultant for NuVasive, Medtronic, and SI Bone; and receives royalties from NuVasive, Medtronic, and Zimmer. Dr. Smith is a consultant for Zimmer Biomet, NuVasive, Stryker, Cerapedics, Astura, and Carlsmed; receives royalties from Zimmer Biomet and NuVasive; receives support of non–study-related clinical or research effort that he oversees from DePuy Synthes/ISSG and AO Spine; receives fellowship funding from NREF and AO Spine; and holds stock in Alphatec. Dr. Yen is a consultant for NuVasive.

Author Contributions

Conception and design: Buchholz, McClure. Acquisition of data: McClure, Desai, Shabo. Analysis and interpretation of data: Buchholz, McClure, Desai, Buell. Drafting the article: McClure, Desai, Shabo. Critically revising the article: Buchholz, McClure, Shabo, Buell, Yen, Smith, CI Shaffrey, ME Shaffrey. Reviewed submitted version of manuscript: Buchholz, McClure, Desai, Buell, Yen, Smith, CI Shaffrey, ME Shaffrey. Statistical analysis: McClure, Buell. Administrative/technical/material support: Buchholz, Buell, Yen. Study supervision: Buchholz, Buell.

Supplemental Information

Previous Presentations

Portions of this work were presented in poster form at the Medical Student Research Symposium, UVA Medical School, Charlottesville, VA, in November 2019. Portions of this work were presented in e-poster form at the AANS 2020 Online E-Poster Symposium, Boston, MA, in June 2020.

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