Long-term clinical outcomes following 3- and 4-level anterior cervical discectomy and fusion

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OBJECTIVE The purpose of this study was to report the long-term clinical outcomes following 3- and 4-level anterior cervical discectomy and fusion (ACDF).

METHODS A retrospective review of all adult neurosurgical patients undergoing elective ACDF for degenerative disease at a single institution between 1996 and 2013 was performed. Patients who underwent first-time 3- or 4-level ACDF were included; patients with previous cervical spine surgery, those undergoing anterior/posterior approaches, and those with corpectomy were excluded. Outcome measures included perioperative complication rates, fusion rates, need for revision surgery, Nurick Scores, Odom's criteria, symptom resolution, neck visual analog scale (VAS) pain score, and persistent narcotics usage.

RESULTS Seventy-one patients who underwent 3-level ACDF and 26 patients who underwent 4-level ACDF were identified and followed for an average of 7.6 ± 4.2 years. There was 1 case (3.9%) of deep wound infection in the 4-level group and 1 case in the 3-level group (1.4%; $p = 0.454$). Postoperatively, 31% of patients in the 4-level group complained of dysphagia, compared with 12.7% in the 3-level group ($p = 0.038$). The fusion rate was 84.6% after 4-level ACDF and 94.4% after 3-level ACDF ($p = 0.122$). At last follow-up, a significantly higher proportion of patients in the 4-level group continued to have axial neck pain (53.8%) than in the 3-level group (31%; $p = 0.039$); the daily oral morphine equivalent dose was significantly higher in the 4-level group (143 ± 97 mg/day) than in the 3-level group (25 ± 10 mg/day; $p = 0.030$). Outcomes based on Odom's criteria were also different between cohorts ($p = 0.044$), with a significantly lower proportion of patients in the 4-level ACDF group experiencing an excellent/good outcome.

CONCLUSIONS In this study, patients who underwent 4-level ACDF had significantly higher rates of dysphagia, postoperative neck pain, and postoperative narcotic usage when compared with patients who underwent 3-level ACDF. Pseudarthrosis and deep wound infection rates were also higher in the 4-level group, although this did not reach statistical significance. Additionally, a smaller proportion of patients achieved a good/excellent outcome in the 4-level group than in the 3-level group. These findings suggest a significant increase of perioperative morbidity and worsened outcomes for patients who undergo 4- versus 3-level ACDF.

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KEY WORDS ACDF; anterior cervical discectomy and fusion; 3-level; 4-level; cervical spine; fusion; outcomes

FIRST introduced by Smith, Robinson, and Cloward in 1958,^{6,27} anterior cervical discectomy and fusion (ACDF) is currently one of the most commonly performed procedures in the cervical spine.^{17,19} Usually reserved for patients with myelopathy and/or intractable radiculopathy secondary to age-related degeneration,

ACDF most commonly addresses 1- or 2-level disease.⁴ Three-level and 4-level ACDF procedures, however, are less common and there are limited data regarding their clinical outcomes, particularly for 4-level ACDF.^{2,15,16} Furthermore, there is concern for higher rates of complications and pseudarthrosis with multilevel anterior cervical

ABBREVIATIONS ACDF = anterior cervical discectomy and fusion; ASD = adjacent-segment disease.

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fusion procedures.²⁹ The purpose of this study is to report surgical and long-term clinical outcomes of 3- and 4-level ACDF for patients with cervical spondylosis.

Methods

Study Sample

Following institutional review board approval, a retrospective review of clinical and operative notes was performed to identify all neurosurgical patients undergoing an ACDF at a single academic institution between 1996 and 2013. Inclusion criteria were patients older than 18 years undergoing 3- or 4-level ACDF for treatment of cervical spondylosis with myelopathy and/or radiculopathy (n = 166). Exclusion criteria were 1) patients with a history of previous cervical spine surgery (n = 19), 2) patients with neck pain only (n = 10), and 3) patients with less than 12 months of follow-up (n = 40). Patients undergoing ACDF following trauma, tumor resection, or primary spinal infections, patients undergoing corpectomy with cage reconstruction, and patients undergoing combined (anterior-posterior) approaches were not included in this study.

Covariates

Patient data such as age, sex, comorbidities, presenting symptoms, neck visual analog scale (VAS) pain score, and Nurick scores were collected from clinical notes. Intraoperative data, including discectomy levels, type of bone graft, and estimated blood loss, were gathered from operative notes.

Outcomes included perioperative complications, fusion rates, need for revision surgery due to pseudarthrosis or adjacent-segment disease (ASD), symptoms at last follow-up, Nurick score, pain score, narcotic usage, and Odom's criteria. Odom's criteria defines outcomes as excellent if all preoperative symptoms and abnormal findings are improved; good if there is minimal persistence of symptoms and abnormal findings are improved; fair if there is relief of some symptoms and other symptoms are slightly improved; and poor if symptoms and signs are unchanged or worse.¹⁸ Bony fusion was assessed on follow-up visits (3, 6, and 12 months in most cases) via a combination of conventional radiographs and CT scans. Outcome variables were obtained from clinic notes at last available follow-up for each patient.

Statistical Analysis

Patient variables are presented as the mean $\pm$ standard deviation where applicable. Binary outcomes were compared using chi-square tests and continuous variables using unpaired 2-tailed t-tests with unequal variances. Statistical analyses were performed using Stata/SE 12 (StataCorp.) and GraphPad Prism 6 (GraphPad Software Inc.). A p value < 0.05 was defined as statistically significant.

Results

Demographics

A total of 97 patients met our inclusion criteria, with 71 undergoing 3-level ACDF and 26 undergoing 4-level ACDF (Table 1). Patients who underwent 4-level ACDF

were significantly older than those in the 3-level group (57 vs 52 years; $p = 0.020$). There were no significant differences in terms of patient sex or comorbidities. When examining presenting symptoms, a significantly higher proportion of patients presented with myelopathy in the 4-level group (61.6%) compared with those in the 3-level group (36.6%; $p = 0.028$). However, the severity of myelopathy was not different between groups based on the Nurick score ($p = 0.119$). The proportion of patients in whom iliac crest autograft was used did not differ between groups, and the intraoperative estimated blood loss was not significantly different between groups (Table 2).

While the C4–5 and C5–6 levels were instrumented in almost 100% of patients in both groups, a significantly higher proportion of patients in the 4-level ACDF group required instrumentation at C3–4 (92.3%) compared with patients in the 3-level group (18.3%, $p < 0.001$). Likewise, a significantly higher proportion of patients in the 4-level group (100%) required instrumentation at C6–7 compared with the 3-level group (81.7%, $p = 0.019$). There were no instrumentations at C2–3 in the present study.

Comparison of Perioperative and Long-Term Outcomes

In the perioperative period, 10 patients (38.5%) in the 4-level group experienced at least one complication, compared with 10 patients (14.1%) in the 3-level group ($p = 0.009$). The most common adverse events were dysphagia and vertebral artery injury, both of which were significantly higher in the 4-level cohort (Table 3). Major complications occurred in 3 patients in the 4-level cohort (2 vertebral artery injuries and 1 deep wound infection), compared with only 1 patient in the 3-level group (1 deep wound infection); this major complication rate was signifi-

TABLE 1. Demographics of all patients undergoing 3- and 4-level ACDF*

Parameter	3-Level ACDF	4-Level ACDF	p Value
No. of patients	71	26	
Mean age (yrs)	52.3 $\pm$ 9.7	57.2 $\pm$ 8.8	0.020
Male sex	37 (52.1)	13 (50.0)	0.854
Comorbidities			
Diabetes mellitus	7 (9.9)	3 (11.5)	0.810
Obesity	4 (5.6)	1 (3.9)	0.724
Hypertension	17 (23.9)	6 (23.1)	0.929
Smoking history	13 (18.3)	3 (11.5)	0.426
Presenting symptoms			
Neck pain	54 (76.1)	20 (76.9)	0.929
Radiculopathy	48 (67.6)	15 (57.7)	0.365
Myelopathy	26 (36.6)	16 (61.6)	0.028
Weakness	22 (31.0)	10 (38.5)	0.488
Sensory deficit	13 (18.3)	7 (26.9)	0.353
Bladder dysfunction	3 (4.2)	1 (3.9)	0.934
Mean preop Nurick grade	0.7 $\pm$ 1.0	1.1 $\pm$ 1.3	0.119
Mean preop pain	6.6 $\pm$ 4.0	5.4 $\pm$ 4.2	0.449

* Values are presented as the number of patients (%) unless indicated otherwise. Mean values are reported as the mean $\pm$ SD. Boldface type indicates statistical significance.

TABLE 2. Intraoperative characteristics of all patients undergoing 3- and 4-level ACDF*

Parameter	3-Level ACDF	4-Level ACDF	p Value
No. of patients	71	26	
Treated levels			
C2–3	0 (0.0)	0 (0.0)	
C3–4	13 (18.3)	24 (92.3)	<0.001
C4–5	69 (97.2)	26 (100.0)	0.387
C5–6	71 (100.0)	26 (100.0)	
C6–7	58 (81.7)	26 (100.0)	0.019
C7–T1	2 (2.8)	2 (7.7)	0.285
Iliac crest autograft	8 (11.3)	3 (11.5)	0.970
Allograft	63 (88.7)	23 (88.5)	0.970
Mean estimated blood loss (ml)	82 ± 95	214 ± 245	0.208

* Values are presented as the number of patients (%) unless indicated otherwise. Mean values are reported as the mean ± SD. Boldface type indicates statistical significance.

cantly different between groups ($p = 0.026$). Of the 17 patients with postoperative dysphagia, spontaneous resolution was observed in 14 cases (82.4%); 2 patients required temporary percutaneous endoscopic gastrostomy tube placement (1 in each treatment group) and 1 patient had permanent dysphagia (in the 3-level group).

One patient suffered a vertebral artery injury during surgery due to an aberrant medial location, and bleeding was controlled with absorbable gelatin powder and microfibrillar collagen hemostat balls. She later developed a thrombus within the artery during her hospital stay and was placed temporarily on a regimen of anticoagulants; no permanent neurological deficits occurred. The second patient developed acute difficulty with gait and coordination 2 days after surgery, and emergent CT and brain MRI/MR angiography revealed findings compatible with acute infarction involving most of the right cerebellar hemisphere with multiple small infarcts involving the left cerebellar hemisphere. A CT angiogram revealed left vertebral artery dissection. The patient was started on heparin and bridged to warfarin; upon discharge the patient had minimal dysmetria bilaterally and was walking with a walker.

The overall pseudarthrosis rate was 8.3% ($n = 8$) after index surgery. The rate in the 4-level group was 15.4% ($n = 4$), and 5.6% ($n = 4$) in the 3-level group ($p = 0.122$) (Fig. 1). The total reoperation rates were 19.2% and 21.1% in the 4- and 3-level groups, respectively ($p = 0.838$). Although the proportion of patients who developed ASD requiring reoperation was lower in the 4-level group (3.9%) compared with the 3-level group (15.6%), this was not significantly different ($p = 0.123$). Furthermore, there were 5 patients (7%) in the 3-level group with radiographic ASD that did not require reoperation. Of 8 patients who underwent reoperation for pseudarthrosis, neck pain was present in 5 patients (62.5%), radiculopathy in 5 (62.5%), and swallowing difficulty due to screw pullout in 1 case (12.5%). Likewise, of 12 patients who underwent reoperation for ASD, 9 patients (75%) complained of neck pain, 4 patients of radiculopathy (33.3%), and 3 patients of progressive myelopathy

TABLE 3. Outcomes of all patients undergoing 3- and 4-level ACDF*

Parameter	3-Level ACDF	4-Level ACDF	p Value
No. of patients	71	26	
Periop complications			
Vertebral artery injury	0 (0.0)	2 (7.7)	0.018
Transient C-5 palsy	0 (0.0)	1 (3.9)	0.097
Deep wound infection	1 (1.4)	1 (3.9)	0.454
Laryngeal nerve palsy	0 (0.0)	1 (3.9)	0.097
Dysphagia	9 (12.7)	8 (30.8)	0.038
Mean length of stay (days)	2.5 ± 2.5	3.5 ± 2.8	0.134
Need for revision surgery	15 (21.1)	5 (19.2)	0.838
Pseudarthrosis	4 (5.6)	4 (15.4)	0.122
ASD	11 (15.6)	1 (3.9)	0.123
Symptoms at last FU			
Neck pain	22 (31.0)	14 (53.8)	0.039
Radiculopathy	3 (4.2)	2 (7.7)	0.494
Myelopathy	11 (15.5)	7 (26.9)	0.200
Weakness	3 (4.2)	5 (19.2)	0.017
Sensory deficit	1 (1.4)	1 (3.9)	0.454
Bladder dysfunction	0 (0.0)	0 (0.0)	
Mean Nurick score at last FU	0.4 ± 0.8	0.7 ± 1.4	0.258
Pain score at last FU	3.1 ± 3.4	3.9 ± 3.8	0.517
Odom's criteria			0.044
Excellent	39 (54.9)	6 (23.1)	
Good	10 (14.1)	9 (34.6)	
Fair	14 (19.7)	5 (19.2)	
Poor	8 (11.3)	6 (23.1)	
Mean FU time (yrs)	7.6 ± 4.2	7.6 ± 4.2	0.939

FU = follow-up.

* Values are presented as the number of patients (%) unless indicated otherwise. Mean values are reported as the mean ± SD. Boldface type indicates statistical significance.

(25%). Kaplan-Meier survivorship analysis showed that reoperation-free survival was not different between groups ($p = 0.912$, log-rank test) (Fig. 2). Patients were followed for an average time of 7.6 years (range 1–22 years).

At last follow-up, a significantly greater proportion of patients in the 4-level group reported axial neck pain and weakness when compared with the 3-level group (Table 3). When examining specific symptoms, it was found that 38 of 74 patients (51.4%) improved postoperatively in terms of neck pain; 58 of 63 patients (92.1%) experienced improvement in radiculopathy, and 24 of 42 patients (57.1%) experienced improvement in myelopathy. Weakness improved in 75% of patients, 90% had sensory improvement, and 100% of patients who had preoperative bladder symptoms improved postoperatively. It is important to note, however, that the improvement was partial and not always complete in all modalities noted above. Of the 4 patients with preoperative bladder symptoms, 3 presented with mild urinary urgency/frequency and 1 with mild urinary retention; they all improved postoperatively.

FIG. 1. A 54-year-old woman presented with neck pain and intractable upper-extremity radiculopathy. After nonsurgical treatment failed, the patient underwent a C3–7 ACDF. However, she was a smoker and developed pseudarthrosis at C5–6 and C6–7, seen as “halo signs” around the bottom screws in this postoperative CT image (left). The patient then underwent a posterior approach consisting of a C3–T1 fusion with left C5–6 and C6–7 laminoforaminotomies, as seen on this postoperative radiograph (right).

Preoperatively, 23 patients (41.1%) required narcotics to treat their pain (46.7% in the 4-level group and 39% in the 3-level group, $p = 0.607$), which decreased to 18 patients (32.7%) postoperatively (40% of patients in the 4-level group vs 30% in the 3-level group [$p = 0.481$]). The average pain score at last follow-up was not different between the groups ($p = 0.517$). However, the daily oral morphine equivalent dose was significantly higher in the 4-level group (143 ± 97 mg/day) than in the 3-level group (25 ± 10 mg/day; $p = 0.030$). According to Odom’s criteria, the proportion of patients experiencing an excellent, good, fair, or poor outcome was significantly different between groups ($p = 0.044$) (Fig. 3). A subset analysis of patients who underwent fusion at the C3–4 level revealed a higher rate of complications (40.5% vs 8.3%, $p < 0.001$) and postoperative neck pain (54.1% vs 30.0%, $p = 0.018$) compared with patients who did not.

Discussion

Three-level and 4-level ACDFs are less common procedures, even in high-volume spine centers. In a study of 888 patients undergoing ACDF at a tertiary care institution, 81% of patients underwent 1- or 2-level ACDF, 137 patients (15.4%) underwent 3-level ACDF, and only 29 patients (3.3%) underwent 4-level ACDF.⁴ To date, however, the morbidity rates and risk of pseudarthrosis after 3- or 4-level ACDF remain controversial.^{2,15}

In a prospective study by Bolesta et al. of 15 patients undergoing 3- or 4-level ACDF with a unicortical anterior plate (Cervical Spine Locking Plate, Synthes) and iliac crest autograft, the nonunion rate in at least 1 level was 53%.² All patients in that series were nonsmokers or former smokers. Of the 8 patients with pseudarthrosis, 3 required revision surgery, and the authors of the study

FIG. 2. Kaplan-Meier curve showing reoperation-free survival for both groups. Figure is available in color online only.

concluded that they “no longer recommend this particular construct and are currently investigating concomitant anterior and posterior arthrodesis in this challenging group of patients.”² Contrary to these findings, a recent study of 48 patients by Jack et al. undergoing 4-level ACDF found a fusion rate of greater than 80%, and no patients required reoperation for pseudarthrosis.¹² The fusion rate in our study was 91.8%, similar to the rate found by Jack et al. Nevertheless, this fusion rate remains lower than the rate for single-level ACDF, which ranges from 96% to 100%.^{11,13,26}

In the present study, the risk of ASD requiring reoperation was higher in the 3-level group (15.6%) than in the 4-level group (3.9%), but this was not statistically significant ($p = 0.123$). Although ASD is a well-known sequela of cervical fusion, opinions vary regarding etiology: natural disease progression versus postoperative biomechanical alterations of the spine.^{3,21,28,30} Additionally, there are conflicting data on whether the rate of ASD is higher in single versus multilevel fusion. In a biomechanical study, Prasarn et al. found that adjacent-segment motion at the levels above and below a fusion was significantly higher after a 2-level fusion than after a 1-level fusion.²¹ In a clinical study, however, Bydon et al. demonstrated that the rates of ASD requiring reoperation were not significantly different in patients undergoing 1-, 2-, or ≥ 3 -level ACDF ($p = 0.910$).⁴

Complication rates were significantly different between groups. There were 10 patients (38.5%) who experienced at least 1 perioperative complication in the 4-level group, compared with 10 patients (14.1%) in the 3-level group ($p = 0.009$). The main differences in complications included rates of vertebral artery injury and postoperative dysphagia. Vertebral artery injury occurs in 0.3%–8% of cervical spine procedures,²⁵ and in the present study it occurred in 2 patients in the 4-level ACDF cohort. Although rare, potential sequelae include thrombosis, embolism, cerebral ischemia, late-onset hemorrhage, death, and others.²⁰ Risk factors include technical errors and unrecognized vertebral artery anomalies.⁷ In the present study, 1 case involved an aberrant medial vertebral artery, and in the second case, a vertebral artery dissection was recognized postoperatively.

Likewise, dysphagia was also more common in the

FIG. 3. Outcomes for all patients according to Odom's criteria at last follow-up ($p = 0.044$). Figure is available in color online only.

4-level group than in the 3-level group (30.8% vs 12.7%, $p = 0.038$). Although it resolved spontaneously in 82.4% of all cases, 2 patients (11.8%) required temporary percutaneous endoscopic gastrostomy tube placement, and 1 patient (5.6%) sustained permanent dysphagia. Dysphagia is one of the most common findings after anterior cervical spinal procedures, and its incidence varies greatly (1%–79%).¹ Risk factors include a greater number of operated levels^{8,14,23,24} (which may explain the increased risk in 4- vs 3-level ACDF), female sex,^{8,24} increased operative time,^{9,14} operations above C-4,⁵ and others.¹ Although the majority of cases are mild and transient, dysphagia may persist 6–24 months postoperatively in about 5%–7% of cases.¹ Management includes behavioral changes (postural, sensory input enhancements, diet modifications, and swallowing maneuvers); a temporary feeding tube may be needed if aspiration risk is high and/or nutritional needs are not met.^{1,7} Functional outcomes based on symptom resolution were significantly different between cohorts, with a significantly higher proportion of patients complaining of axial neck pain in the 4-level group (53.8% vs 31%; $p = 0.039$). Additionally, 30% of patients in the 3-level group reported narcotic use to treat their neck pain and 40% reported this in the 4-level group. This suggests that although 3- and 4-level ACDF relieves most symptoms of myeloradiculopathy (based on the decrease in Nurick scores), it may not be successful at relieving neck pain. Although the proportion of patients with neck pain was higher in the 4-level group, the average pain scores were not different between groups, which could be attributed to the significantly higher dose of narcotics consumed by the 4-level group.

A significantly higher proportion of patients experienced an excellent/good outcome in the 3-level group compared with the 4-level group based on Odom's criteria. Overall, 45 patients (46.4%) had improvement in their preoperative symptoms, 23 patients (23.7%) had minimal persistence of symptoms, 15 patients (15.5%) experienced relief/slight improvement of a few preoperative symptoms, and 14 patients (14.4%) had unchanged or worsening of symptoms. Neck pain was the symptom that either persist-

ed or slightly improved in the majority of patients. Seven patients developed worse axial neck pain after ACDF, suggesting that biomechanical alterations of multilevel instrumentations may be one of the causes of postoperative neck pain. However, whether this is the ultimate mechanism for new postoperative axial neck pain development or whether it is due to disease progression is unclear and warrants further investigation.

There may be several possible explanations for the worse outcomes observed in patients who underwent 4-level ACDF compared with 3-level ACDF. While the higher rates of postoperative neck pain may be attributed to longer constructs and secondary biomechanical alterations, it might also be possible that this was due to worse baseline degeneration and not necessarily the procedure itself. On the other hand, the inclusion of the C3–4 level in 92.3% of patients in the 4-level group versus only 18.3% in the 3-level group warrants special attention. For example, although no differences have been found between the specific instrumented levels and risk of dysphagia in some studies,²² others have suggested that involvement of higher levels adds to the risk of this finding.¹⁰ In the present study, we found that complications (including dysphagia) and postoperative neck pain rates were significantly higher in patients who underwent instrumentation at C3–4 compared with patients who did not, suggesting that inclusion of C3–4 may be an important contributor for worse outcomes. Ultimately, differences in results (higher rates of complications and postoperative neck pain) for patients who underwent 4- versus 3-level ACDF are most likely multifactorial—a combination of more extensive baseline degeneration, biomechanical alterations secondary to fusion of 4 cervical spine segments, and inclusion of higher levels such as C3–4.

Limitations

This study has several limitations. Given the retrospective nature of this study, patient-reported outcomes such as the Neck Disability Index could not be assessed, and specific complications such as dysphagia were assessed

based on the attending surgeon's clinical assessments and not on other more objective measures such as swallowing evaluations and/or direct laryngoscopy. Additionally, there is also risk of information bias as with all retrospective studies based on chart/note reviews. Given that pseudarthrosis was assessed by radiographic means (CT and/or radiography) in standard follow-up visits or symptomatic patients, it may be possible that a certain percentage of patients with asymptomatic pseudarthrosis were missed. Global sagittal balance and other radiographic measures were not available for review in all patients, and these may have contributed to overall outcomes and revision rates. Prospective studies are the most desired for these types of clinical questions, and future research into long-term outcomes of ACDF (including multilevel instrumentation) such as reoperation rates, patient-reported outcomes, and complications, among others, are encouraged. Nevertheless, this study is one of the largest series to date on 3- and 4-level ACDF, and provides one of the longest available follow-up times.

Conclusions

In this study, a significantly greater proportion of patients who underwent 4-level ACDF continued to have axial neck pain at last follow-up compared with patients who underwent 3-level ACDF. Patients in the 4-level group also required a significantly higher dosage of narcotics to treat this pain. Additionally, the rates of dysphagia and vertebral artery injury were also significantly higher in patients who underwent 4-level ACDF. These findings suggest an increase of perioperative morbidity and worsened outcomes for patients who undergo 4- versus 3-level ACDF; future prospective cohort studies are needed to substantiate the present findings.

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