Adjacent Segment Disease After Anterior Cervical Discectomy and Fusion in a Large Series

**BACKGROUND:** Adjacent segment disease (ASD) development is known to occur after anterior cervical discectomy and fusion (ACDF).

**OBJECTIVE:** To study the relationship between index ACDF levels and the location of ASD development (above/below), as well as the effect of fusion length on ASD development.

**METHODS:** We report 888 patients who underwent ACDF for cervical spondylosis over a twenty-year period at a single institution. Of these patients, 108 had re-do surgery due to symptomatic ASD. Patients were followed for an average of 92.4 ± 52.6 months after the index ACDF.

**RESULTS:** In agreement with previous ACDF case series, we found the highest rates of cervical spinal degenerative disease requiring surgery at C5/C6, followed by C6/C7. Interestingly, neither the inherent location of index ACDF nor the length of instrumented arthrodesis appeared to correlate with the propensity to develop ASD. However, patients were more likely to develop ASD above the index level of fusion. This was true even for patients undergoing a second revision surgery due to recurrent ASD. Importantly, our data are consistent with existing in vitro biomechanical data in cadaveric spines.

**CONCLUSION:** We describe in detail the location and length of arthrodesis for index ACDFs, as well as first and second revision fusion surgeries in one of the largest Western cohorts in the literature. Our findings support the theory that iatrogenically introduced stress and instability at adjacent spinal segments contribute to the pathogenesis of ASD.

**KEY WORDS:** Adjacent level disease, Adjacent segment disease, Anterior cervical discectomy and fusion, Cervical, Fusion

In Hilibrand et al’s seminal study, 374 patients underwent ACDF; of these, there was an annualized incidence of 2.9% per year for developing ASD. Hilibrand et al estimated that more than a quarter of all patients would develop radiographic degeneration of spinal elements adjacent to the index surgery, and two-thirds of those would go on to require additional surgery.\(^\text{19,20}\) Indeed, the advent of total disc arthroplasty is predicated upon the assumption that restoring normal spinal kinematics would alleviate further spinal degeneration and development of ASD.\(^\text{3,15,21-35}\) Nonetheless, despite a number of studies looking at the effectiveness of total disc arthroplasty, to date there exists no Level I evidence that restoration of spinal biomechanics using disc replacements prevents or even abrogates the incidence of ASD.
development, highlighting the need for a better understanding of this pathophysiologic process. A review of the literature reveals few studies that specifically analyze the location and spinal construct lengths in patients who develop ASD.

In this original study, we present a single-institution series of patients who underwent ACDF, and report an incidence of 108 patients who required repeat cervical fusion due to symptomatic ASD after an initial ACDF. We compare the location and fusion construct lengths of patients undergoing index ACDF surgery, and patients requiring 1 or 2 revision surgeries due to onset of symptomatic ASD.

PATIENTS AND METHODS

Patients

In conducting the study, we retrospectively reviewed clinical notes, operative narratives, and radiology reports for all neurosurgical patients undergoing ACDF at our institution over a 20-year period. Our inclusion criteria were patients who had undergone ACDF exclusively for symptomatic cervical spondylosis and who subsequently also developed symptomatic ASD, defined as radiographic evidence of immediate above or below ASD as well as associated clinical symptoms in patients with a history of ACDF at least 6 months prior. Patients undergoing ACDF for neoplastic, infectious, or traumatic etiologies were excluded. In addition, patients receiving combined circumferential surgeries were excluded. Patients who underwent revision surgery due to wound infection, dehiscence, instrumentation failure or pseudoarthrosis were also excluded from this study.

Utilizing the aforementioned criteria, we identified 888 patients who underwent ACDF exclusively for symptomatic cervical spondylosis. Notably, 124 patients (13.9%) had a previous ACDF done at an outside institution. We identified 108 patients from the total cohort who underwent revision surgery for ASD at our institution.

Given that this is a retrospective study, we invariably lost some patients who moved away from the region or sought the services of other surgeons. When possible, we attempted to mitigate this factor through telephone calls to the patients to inquire about their functional status and surgical history since our last follow-up. Patients who had follow-up times of less than 6 months were not included in this study.

Variables and Statistical Methods

Our main outcome variables were the location and fused levels of the index ACDF, as well as levels involved during revision fusion surgeries. These variables were ascertained via operative notes. In order to account for fewer patients in the ASD cohort (108 patients) compared to the non-ASD cohort (780 patients), data are presented both as raw data and percentages. Distributions of vertebral levels were analyzed during index ACDF as well as during ASD revision surgeries. ASD development was noted for each affected spinal level, as well as sub-categorized as above or below the index ACDF surgery. Similarly, each vertebral level was re-evaluated for ASD re-development after first revision fusion surgery, and compared to ASD vertebral involvement after initial ACDF. The distributions of affected spinal levels were compared via Kaplan-Meier analyses and log-rank tests (cumulative distributions). Statistical tests were analyzed using GraphPad Prism 6.0. Statistical significance was defined as $P < .05$. Descriptive statistical results are presented as mean ± standard deviations when applicable.

RESULTS

A total of 888 patients underwent ACDF for degenerative spinal disease over the past 20 years at our institution. Of these, 401 (45.1%) were men and 487 (54.9%) women. Mean age at surgery was 50.8 ± 10.8 years. Mean follow-up time was 92.4 ± 52.6 months (Figure 1). The vast majority of patients underwent ACDF at the C5/C6 spinal level (Figure 2A). This was followed by the C6/C7, C4/C5, and C3/C4 levels in descending order of frequency. A total of 822 patients (92.6%) were fused with constrained plates and screws. Bone autograft was utilized in 163 cases (18.4%) and bone allograft (VG2 and MTF bone spacers, DePuy, Johnson & Johnson, Raynham, Massachusetts) was utilized in 725 (81.6%) cases. Specifically, of the 780 patients who only received index ACDF surgery, the most common fused levels were C5/C6 in 565 (40.13%) occasions and C6/C7 in 423 (30.04%) cases. For patients who eventually developed ASD, the most common fused levels were also C5/C6 in 75 (40.1%) cases and C6/C7 in 54 (28.88%) cases (Figure 2B).

Of the 780 patients who only received index ACDF surgery, the majority of cases (325; 41.61%) involved a 1-level fusion, followed by a 2-level fusion in 311 (39.82%) cases (Figure 3A). For the 108 patients who developed ASD, most (51; 47.22%) also involved single-level fusions (Figure 3B). We analyzed the development of ASD over time as a function of levels fused via Kaplan-Meier analysis, but found no statistical significance between the 2 via log-rank analysis, $P = .91$ (Figure 4). Of the total 888 patients, 108 (12.2%) developed symptomatic ASD requiring revision surgery during an average follow-up time of 92.4 ± 52.6 months after the index ACDF. As patients were lost to follow-up over time, this may underestimate the true rate of ASD development. We attempted to correct for this via Kaplan-Meier analysis. Thus, accounting for time and censored patients, the rate of ASD development was 31.0% at 10 years (Figure 1).
For the 108 patients who developed ASD, we sought to determine the location of their ASD relative to their initial surgery (Figure 5A). The most common levels fused were C5/C6 in 75 cases and C6/C7 in 54 cases. The symptomatic ASD that developed afflicated more commonly the C4/C5 levels in 35 cases and C3/C4 in 29 cases. Patients who developed ASD at the C1/C2 levels were treated with posterior fusions. Notably, 4 patients developed ASD at the C1/C2 level when only 1 patient had an index fusion at C2/C3. This occurred because the other 3 patients in fact developed 2-level ASD, which in these cases involved C1/C2. We sought to determine whether the location of index ACDF correlated with ASD development over time via Kaplan Meier analysis. Log-rank tests showed similar rates of ASD development over all surgical cohorts, \( P = .09 \) (Figure 6).

We also analyzed whether ASD developed at levels above or below relative to the original index ACDF (Figure 5B). 7 and 6 ASD spinal levels occurred above and below the index C3/C4 level, respectively. At C4/C5, 27 and 19 spinal levels developed ASD above and below the index ACDF site, respectively. 50 spinal levels developed ASD above C5/C6, whereas 27 developed below. 45 levels acquired ASD above the index C6/C7 ACDF level, in contrast to 4 spinal levels below C6/C7. Thus, the majority of ASD developed above the index level of ACDF.

For the 108 patients who developed adjacent segment disease after index ACDF, 27 patients developed re-occurrence of adjacent segment disease and required a second revision fusion surgery. Of the 81 who did not require a second revision surgery, most (29 patients; 37.18%) had a 3-level fusion (Figure 7A). Amongst the 27 patients who required a second revision surgery for re-development of adjacent segment disease, 12 (44.44%) had been fused at 2 levels (Figure 7B). We analyzed potential differences in ASD development location between patients who developed reoccurrence of ASD after first revision fusion surgery and those who did not...
Amongst the 81 patients who did not develop recurrence of ASD, most cases involved single or multi-level spinal fusions at C4/C5 and C5/C6 (Figure 8A, B). For the 27 patients who did develop ASD following 1 revision fusion surgery after index ACDF, most (24 cases; 32%) were located at the C5/C6 level. Interestingly, ASD redevelopment was again more likely to occur cephalad to the first revision fusion surgery levels (Figure 8C).

**DISCUSSION**

Anterior cervical discectomy and fusion is a commonly applied procedure for cervical spondylosis. However, arthrodesis of the cervical spine segments during ACDF irreversibly destroys the intervertebral disks, resulting in alterations to the physiological biomechanics of the spine. A number of biomechanical studies have shown that loss of mobility at a given spinal level increases the range of motion and intradiscal pressure experienced at both cephalad and caudal adjacent spinal segments. These studies have been correlated with clinical series documenting the development of degenerative changes in adjacent spinal levels following ACDF.

*Key Results*

Given that different intervertebral discs of the cervical spine experience different physiological ranges of motion and intradiscal pressures, we wondered if the level of index ACDF surgery influenced the potential development of ASD. Our data suggest that the specific spinal level is a predictor of likelihood of degenerative spinal disease development, but is not directly related to ASD. Thus, patients were at highest risk of degenerative cervical spinal disease requiring surgery at C5/C6, followed by C6/C7, C4/C5, and the C3/C4 spinal levels. This was true for all patients undergoing ACDF—regardless of whether they eventually developed ASD (Figure 2). This suggests that while the development of degenerative spinal disease is location-dependent, the advent of ASD is not directly due to the level of the index fusion itself.

As longer fusion constructs exhibit higher forces and more torque, we sought to analyze whether the length of instrumented arthrodesis correlated with ASD development (Figure 3). The majority of our patients either had 1- or 2-level index ACDFs. There was no statistical difference between the rate of ASD development in patients undergoing 1 level index ACDF vs 2 or 3+ ACDF via log-rank test, \( P = .91 \). Thus, our data suggest that the number of vertebral levels fused is not an immediate factor related to ASD development in vivo. We also compared the rate of ASD development over time as a function of the location of the index ACDF surgery (Figure 4). There was no statistical difference between the cohorts, \( P = .91 \).
index ACDF surgery. There was no statistical association between index ACDF fusion location and ASD development as assessed via log-rank test, \( P = .09 \).

We sought to determine the location of ASD development relative to the index ACDF (Figure 5A). Interestingly, for all levels of the cervical spine, patients were more likely to develop ASD above the index fusion level. While this was most pronounced for C6/C7, this trend held true at all cervical spinal levels (Figure 5B). Upon subsequent analysis of patients who underwent 2 revision surgeries for recurrence of ASD after 1 revision fusion surgery, this trend still remained true.

**Interpretation and Generalizability**

Our data are commensurate with existing biomechanical data. In Eck et al’s biomechanical analysis of vertebral levels adjacent to C5/C6 simulated ACDF via instrumented fusion in cadaveric cervical spines revealed increased intradiscal pressures and ranges of motion at both superior and inferior adjacent levels during both flexion and extension. However, closer analysis of the data reveals that the C4/C5 spinal level had higher intradiscal pressures relative to the C6/C7 level during flexion (C4/C5 intradiscal pressure increased by 73.2% vs 45.3% at C6/C7 during flexion). During extension, the C4/C5 range of motion increased 32.5%, more than 145% times the range of motion experienced by the C6/C7 level. Thus, both in flexion and extension, vertebral levels superior to the index ACDF experience higher intra-discal pressures and increased range of motion. These results are further corroborated by Park et al’s findings in cadaveric spines experiencing 2-level fusions from C5-C7. When intradiscal pressure changes were compared between pre- and post-ACDF cervical spines, only flexion produced statistically significant increased intradiscal pressures and range of motion anterior to the fused levels at C4/C5. Our study provides critical corroboration of these in vitro biomechanical findings, and highlights in vivo the increased risks of developing ASD anterior to the index ACDF compared to below the level of arthrodesis. Importantly, this increased risk held true even after 1 revision fusion surgery for ASD. Thus, for patients who are considering a second revision fusion surgery for recurrent ASD, this heightened risk must be kept in mind.

**Limitations**

As with all retrospective clinical studies, certain biases may play a confounding role. Because this study takes place over a long period of time, certain patients may have been lost eventually to follow-up. However, we were able to identify specific ASD rates based on follow-up times. Moreover, we tried to follow-up each patient via phone calls as well as clinic notes, and so were able to contact a subset of patients who moved away from the immediate area. With this method, we were able to...
achieve an average 92.4-month follow-up time. Thus, this study represents one of the largest Western cohorts of ASD after ACDF and provides one of the longest follow-up periods for these patients. Notably, we found a total of 108 patients (12.2%) who required revision surgery for ASD, which is relatively similar to Hilibrand et al.’s prediction of 16% of patients requiring revision surgery for ASD after ACDF. Prospective, randomized studies would help to not only clarify the contribution of index ACDF location to the development of ASD, but also broaden our understanding of ACDF as part of the treatment of degenerative spinal disease.

CONCLUSION

ACDF is the preferred surgical procedure for symptomatic degenerative cervical spinal disease and cervical spondylosis. However, ASD is a common effect of this procedure and remains a poorly understood and highly morbid condition. In this manuscript, we describe in detail the location and length of arthrodesis for index ACDFs, as well as first and second revision fusion surgeries in one of the largest Western cohorts in the literature. In agreement with previous ACDF case series, we found the highest rates of cervical spinal degenerative disease requiring surgery at C5/C6, followed by C6/C7. Interestingly, neither the inherent location of index ACDF nor the length of instrumented arthrodesis affected the propensity to develop ASD. However, patients were statistically more likely to develop ASD above—compared to below—the index level of fusion. This was true even for patients undergoing a second revision surgery due to recurrent ASD. Importantly, our data are consistent with existing in vitro biomechanical data in cadaveric spines. These findings support the theory that iatrogenically introduced stress and instability at adjacent spinal segments—as opposed to endogenous degeneration of existing vertebral levels—contribute predominantly to the pathogenesis of ASD.

Disclosures

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REFERENCES


COMMENT

The authors describe 888 patients who had an index operation and followed up over a period of 20 years (an average follow-up of 92.4 ± 52.6 months), and found that 108 patients required a second operation. 27 of those 108 patients required a third operation and second revision. Adjacent segment disease after an anterior cervical discectomy and fusion certainly exists, but is still unclear if this is secondary to the natural history of the degenerative cervical spine, or whether it is secondary to increased stress causing the iatrogenic instability or degenerative disease at the adjacent spinal segments. The authors have documented nicely that approximately 12 percent of patients that had an anterior cervical discectomy and fusion will require repeat operation over a period of 20 years. These findings are valuable to spine surgeons advising patients and their families of their chances of needing repeat surgery after the index operation.

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CME QUESTIONS:

1. What is the approximate annualized incidence of adjacent segment disease (ASD) after anterior cervical discectomy and fusion (ACDF)?
   A. 1%
   B. 2%
   C. 3%
   D. 4%
   E. 5%

2. What is the most significant factor that contributes to the development of adjacent segment disease after anterior cervical discectomy and fusion?
   A. Location of the index fused level
   B. Length of the instrumented arthrodesis
   C. Alteration of biomechanics above the index fusion level
   D. Alteration of biomechanics below the index fusion level

3. What is the effect of cervical arthroplasty on adjacent segment disease (ASD) relative to anterior cervical fixation and fusion?
   A. Reduction in short term ASD incidence but no change in incidence on long-term follow-up.
   B. Increase in short term ASD incidence but no change in incidence on long-term follow-up.
   C. No change in short term ASD incidence but reduction in incidence on long-term follow-up.
   D. No change in short term ASD incidence but increase in incidence on long-term follow-up.
   E. No impact on the incidence of ASD