Postoperative Delayed Cervical Palsies: Understanding the Etiology

Ryan F. Planchard1  Patrick R. Maloney1  Grant W. Mallory1  Ross C. Puffer1  Robert J. Spinner1  Ahmad Nassr2  Jeremy L. Fogelson1  William E. Krauss1  Michelle J. Clarke1

1 Department of Neurosurgery, Mayo Clinic, Rochester, Minnesota, United States
2 Department of Orthopedic Surgery, Mayo Clinic, Rochester, Minnesota, United States

Address for correspondence Michelle J. Clarke, MD, Department of Neurosurgery, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, United States (e-mail: clarke.michelle@mayo.edu).

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Study Design  Retrospective study.
Objective  This study reviews 1,768 consecutive cervical decompressions with or without instrumented fusion to identify patient-specific and procedural risk factors significantly correlated with the development of delayed cervical palsy (DCP).
Methods  Baseline demographic and procedural information was collected from the electronic medical record. Particular attention was devoted to reviewing each chart for recognized risk factors of postsurgical inflammatory neuropathy: autoimmune disease, blood transfusions, diabetes, and smoking.
Results  Of 1,669 patients, 56 (3.4%) developed a DCP. Although 71% of the palsies involved C5, 55% of palsies were multimyotomal and 18% were bilateral. Significant risk factors on univariate analysis included age ($p = 0.0061$, odds ratio [OR] = 1.07, 95% confidence interval [CI] 1.008 to 1.050), posterior instrumented fusion ($p < 0.0001$, OR = 3.30, 95% CI 1.920 to 5.653), prone versus semisitting/sitting position ($p = 0.0036$, OR = 3.58, 95% CI 1.451 to 11.881), number of operative levels ($p < 0.0001$, OR = 1.42, 95% CI 1.247 to 1.605), intraoperative transfusions ($p = 0.0231$, OR = 2.57, 95% CI 1.152 to 5.132), and nonspecific autoimmune disease ($p = 0.0107$, OR = 3.83, 95% CI 1.418 to 8.730). On multivariate analysis, number of operative levels ($p = 0.0036$, OR = 1.27, 95% CI 1.075 to 1.496) and nonspecific autoimmune disease ($p = 0.0416$, OR 2.95, 95% CI 1.047 to 7.092) remained significant.
Conclusions  Although this study partially supports a mechanical etiology in the pathogenesis of a DCP, we also describe a notable correlation with autoimmune risk factors. Bilateral and multimyotomal involvement provides additional support that some DCPs may result from an inflammatory response and thus an underlying multifactorial etiology for this complication.

Introduction

Delayed cervical palsy (DCP) is a recognized complication of cervical spine surgery. Although unilateral C5 paresis of the deltoid and/or biceps brachia muscles in the absence of myelopathic symptoms is the most common presentation, DCPs can also manifest bilaterally involving different and/or multiple cervical myotomes.1 Varying degrees of sensory loss and pain often accompany weakness; however, neither is a

Abstract

Keywords  ► postoperative C5 palsy
► cervical spine
► etiology
► autoimmune
► inflammatory neuropathy

myelopathic symptoms is the most common presentation, DCPs can also manifest bilaterally involving different and/or multiple cervical myotomes.1 Varying degrees of sensory loss and pain often accompany weakness; however, neither is a
requirement for diagnosis. The reported incidence ranges from 0 to 30%, depending on the study population and procedure type, with overall mean incidence 5% via metanalysis. DCPs most commonly present within the first 3 days following surgery but have been reported up to 2 months after surgery. Fortunately, the majority resolve within 6 months, though residual deficits may persist in up to 20%.

Despite identification of the predisposing factors and plausible theories, the true etiology remains unknown. The majority of the proposed theories can be categorized as either mechanical or vascular and include nerve root traction due to postoperative cord shift or change in alignment, spinal cord ischemia, and reperfusion injury. Excessive root traction is the most commonly cited mechanical etiology, supported by differences in preoperative foraminal width, laminectomy trough width, preexisting rotation of the spinal cord, and postlaminectomy cord drift posteriorly in patients who developed C5 palsies compared with controls. Root traction is also supported by a decreased incidence of DCPs following prophylactic foraminotomies. Autoimmune and inflammatory etiologies such as idiopathic brachial neuritis (Parsong-Turner syndrome) and postsurgical inflammatory neuropathy (PSIN) have less frequently been cited but have certainly been described after cervical decompression and fusion. Other variables that have been associated with an increased incidence of DCPs include male gender and the underlying pathology (ossification of the posterior longitudinal ligament > cervical spondylomyelopathy). The heterogeneity of previously established risk factors and lack of an all-encompassing theory indicate that the etiology may be multifactorial. Additionally, most previous studies focused on Asian cohorts developing DCPs following laminoplasty, specifically confined to the C5 level. Thus, the incidence in patients undergoing either laminectomy alone or cervical decompression with instrumented fusion in North American populations is not well established, as is the frequency of involvement of other cervical levels.

The present study evaluated the overall incidence of DCPs in all cervical myotomes following cervical decompression with and without instrumented fusion for degenerative disease of the cervical spine. The presence of previously established risk factors for PSIN outlined by Staff et al was also assessed relative to internal controls.

Materials and Methods

Selection Criteria

All aspects of this study were approved by the Institutional Review Board and in adherence with ethical standards. We retrospectively reviewed 1,768 consecutive, current procedural terminology (CPT)-coded cervical decompressions with and without instrumented fusion at Mayo Clinic Rochester between January 2008 and December 2013 for postoperative weakness within 6 weeks of the operative date. DCPs were defined as either unilateral or bilateral, new onset or worsened motor function confined to one or more cervical myotomes. Both the operative note and the immediate postoperative exam record were carefully evaluated for weakness or pain consistent with iatrogenic injury. Patients who experienced weakness directly attributable to intraoperative injury or upper extremity pain or sensory symptoms without accompanying weakness were excluded. We also excluded all tumor and trauma cases following review of all the pertinent preoperative documentation to specifically evaluate the incidence of DCPs in patients treated for degenerative disease.

Baseline Characteristics and Assessment of Risk Factors

The electronic medical record of every patient was reviewed for baseline data including age, gender, and length of follow-up. DCPs were further characterized by myotomal involvement, either unilateral or bilateral, and worse/end motor grade. Finally, the presence of suggested risk factors for PSIN were recorded as outlined by Staff et al (intraoperative transfusions, history of diabetes, comorbid cancer, concomitant history of infection, and history of smoking). Several categorical variables were further analyzed in more specific subcategories including transfusion (intraoperative versus postoperative prior to discharge), comorbid cancer (active—metastatic disease or active tumor burden; remote—no evidence of disease), concomitant history of infection (active—current use of antibiotics or chronic infection; remote—acute infection within three months), and smoking (active—smoking within 3 months of operative date; remote—any other history). A history of autoimmune disease was also recorded as positive if the patient had a documented history of 1 or more of the 81 autoimmune diseases as reported in a recent comprehensive review by Hayter and Cook (Appendix A). Seronegative spondyloarthropathies (ankylosing spondylitis, reactive arthritis, and psoriatic arthritis) are notable diseases of the spine with a potential autoimmune origin excluded by Hayter and Cook and thus were evaluated as a separate variable. The history of autoimmune disease was further classified into one of four categories: diabetes mellitus type 1, inflammatory bowel disease (Crohn disease, ulcerative colitis), rheumatoid arthritis, and other. Underlying ossification of the posterior longitudinal ligament was not specifically evaluated given its low incidence among our study cohort, a finding consistent with epidemiologic studies completed in North America. Additional analysis was performed on operative differences including approach (anterior, posterior, or both) and use of instrumentation. The intraoperative somatosensory and motor evoked potentials were reviewed when available only in patients who developed a DCP. CPT coding and chart review were used in tandem to classify procedures. When both CPT coding and reviewer classification were concordant, procedures were classified into one of several nonexclusive categories: anterior fusion, anterior disectomy and fusion, arthroplasty, corpectomy, laminotomy, laminectomy without fusion, laminoplasty, osteotomy, posterior fusion, and revision. Cases were included in multiple categories if applicable. Procedure categories including more than 100 cases were analyzed as a categorical variable for the entire cohort, as well as examined separately for procedure specific risk factors. Postoperative
We found significant associations between the incidence of DCP with age (positive DCP: 62.2 versus negative DCP: 57.1, \( p = 0.0061 \)), intraoperative transfusion (positive DCP: 16.1% versus negative DCP: 6.9%, \( p = 0.0231 \)), and history of other autoimmune disease (positive DCP: 10.7% versus negative DCP: 3.0%, \( p = 0.0107 \)). Significant procedural factors included posterior fusion (positive DCP: 48.2% versus negative DCP: 22.0%, \( p < 0.0001 \)), sitting (positive DCP: 7.0% versus negative DCP: 21.2%, \( p = 0.0037 \)), and number of levels (positive DCP mean: 3.52 versus negative DCP: 2.26, \( p < 0.0001 \)). Table 3 summarizes the significant variables identified on univariate and multivariate analysis as well as provides a calculated odds ratio for each associated risk factor. On multivariate analysis, the number of operative levels (\( p = 0.0053 \), odds ratio [OR] = 1.27, 95% confidence interval [CI] 1.075 to 1.496) and nonspecific autoimmune disease (\( p = 0.0416 \), OR 2.95, 95% CI 1.047 to 7.092) remained significant.

Table 4 summarizes the risk factors for specific procedure categories with a sufficient number of cases for analysis. The risk factors identified for the entire cohort were not significant for anterior diskectomy and fusion or corpectomy. Anterior fusions (number of levels, intraoperative transfusion), posterior fusions (number of levels), foraminotomies (age, sitting, number of levels, other autoimmune disease), laminectomies without fusion (author autoimmune disease), and all nonfusion procedures (sitting, other autoimmune disease) had at least one significantly correlated risk factor.

Foraminotomies were performed in 677 cases and a DCP occurred in 24 individuals (3.5%) and at one of the roots expressly decompressed in 18 cases (2.7%). Comparing those not undergoing a foraminotomy to those who did, there was no significant difference in the rate of a DCP. Chi-square analysis was done both including cases occurring at a root not decompressed with a foraminotomy (Fisher exact test \( p = 0.78 \)) and excluding cases where a DCP occurred at a root not decompressed with a foraminotomy (Fisher exact test \( p = 0.56 \)).

Intraoperative monitoring of somatosensory and motor evoked potentials were reviewable for 13 individuals. Only one patient exhibited any abnormality during the procedure, but the motor evoked potential instability was not consistent

### Table 1 Characteristics of delayed cervical palsies

| Characteristic | Value |
|----------------|-------|
| Temporal profile |       |
| Median days to onset of symptoms ± SD, \( n \) (range) | 1 (0–14) |
| Median days to maximal neurologic deficit, \( n \) ± SD (range) | 2 ± 6.8 (0–38) |
| Myotomal involvement |       |
| Nerve root, \( n \) (% of patients with delayed cervical palsies) |   |
| C5 | 40 (71.4%) |
| C6 | 12 (21.4%) |
| C7 | 20 (35.7%) |
| C8 | 13 (23.2%) |
| T1 | 3 (5.6%) |

Abbreviation: SD, standard deviation.
| Positive delayed cervical palsy | Negative delayed cervical palsy | Combined | Likelihood ratio test p value |
|---------------------------------|---------------------------------|----------|-----------------------------|
| Number of patients              | 56 (3.4%)                       | 1,613    | 1,669                       |
| Male/female, n (% male)         | 37/19 (66.1%)                   | 999/614  | 1,036/633 (62.1%)           | 0.5275 |
| Age ± SD                        | 62.2 ± 11.8                     | 57.1 ± 13.7 | 57.3 ± 13.7 | 0.0061* |
| Procedure                       |                                 |          |                             |
| Anterior fusion                 | 13 (2.6%)                       | 483      | 496 (29.7%)                 | 0.2676 |
| With diskectomy                 | 3 (1.7%)                        | 171      | 174 (10.4%)                 | 0.1689 |
| Posterior fusion                | 27 (7.1%)                       | 355      | 382 (22.8%)                 | <0.0001* |
| Corpectomy                      | 5 (4.9%)                        | 97       | 102 (6.1%)                  | 0.3992 |
| Foraminotomity                  | 24 (3.5%)                       | 653      | 677 (40.6%)                 | 0.7228 |
| Laminectomy (without fusion)    | 7 (2.6%)                        | 265      | 272 (16.3%)                 | 0.4184 |
| Sitting                          | 4 (1.1%)                        | 348      | 352 (21.1%)                 | 0.0036* |
| Approach                        |                                 |          |                             |
| Anterior                        | 10 (2.0%)                       | 482      | 492 (29.5%)                 | 0.0554 |
| Posterior                       | 42 (3.7%)                       | 1083     | 1125 (67.4%)                |        |
| Both                            | 4 (7.7%)                        | 48       | 52 (3.1%)                   |        |
| Number of operative levels      |                                 |          |                             |
| 1                               | 9 (1.2%)                        | 721      | 730 (43.7%)                 |        |
| 2                               | 11 (2.9%)                       | 363      | 374 (22.4%)                 |        |
| 3                               | 12 (5.0%)                       | 230      | 242 (14.5%)                 |        |
| 4                               | 11 (6.9%)                       | 148      | 159 (9.5%)                  |        |
| 5                               | 2 (3.0%)                        | 64       | 66 (4.0%)                   |        |
| 6                               | 3 (9.4%)                        | 29       | 32 (1.9%)                   |        |
| 7+                              | 8 (12.1%)                       | 58       | 66 (4.0%)                   |        |
| Previous cervical spine surgery | 12 (5.0%)                       | 226      | 238 (14.3%)                 | 0.1404 |
| Transfusion                     | 10 (6.2%)                       | 151      | 161 (9.6%)                  | 0.0543 |
| Intraoperative                  | 9 (7.4%)                        | 112      | 121 (7.2%)                  | 0.0231* |
| Postoperative                   | 4 (5.7%)                        | 66       | 70 (4.2%)                   | 0.3054 |
| Cancer                          | 9 (4.3%)                        | 199      | 208 (12.5%)                 | 0.4225 |
| Active                          | 0 (0%)                          | 47       | 47 (2.8%)                   | 0.0712 |
| Remote                          | 9 (5.6%)                        | 152      | 161 (9.6%)                  | 0.1255 |
| History of smoking              | 22 (3.3%)                       | 635      | 657 (39.4%)                 | 0.9902 |
| Active                          | 8 (2.8%)                        | 275      | 283 (17.0%)                 | 0.5799 |
| Remote                          | 14 (3.7%)                       | 360      | 374 (22.4%)                 | 0.6404 |
| Infection                       | 1 (2.2%)                        | 45       | 46 (2.8%)                   | 0.6307 |
| Active                          | 1 (4.0%)                        | 24       | 25 (1.5%)                   | 0.8609 |
| Remote                          | 0 (0%)                          | 21       | 21 (1.3%)                   | 0.2297 |
| Diabetes mellitus               | 10 (4.1%)                       | 236      | 246 (14.7%)                 | 0.5142 |
| Type I                          | 0 (0%)                          | 23       | 23 (1.4%)                   | 0.2086 |
| Type II                         | 10 (8.5%)                       | 213      | 223 (13.4%)                 | 0.3342 |
| Seronegative spondylotic arthropathies | 0 (0%)                       | 14       | 14 (0.8%)                   | 0.3273 |
| History of autoimmune disease   | 7 (5.1%)                        | 130      | 137 (8.2%)                  | 0.2648 |
| Rheumatoid arthritis            | 1 (2.3%)                        | 42       | 43 (2.6%)                   | 0.6884 |
| Inflammatory bowel disease      | 0 (0%)                          | 20       | 20 (1.2%)                   | 0.2412 |
| Diabetes mellitus (type I)      | 0 (0%)                          | 23       | 23 (1.4%)                   | 0.2086 |
| Other                           | 6 (10.9%)                       | 49       | 55 (3.3%)                   | 0.0107* |

Abbreviation: SD, standard deviation.

*p < 0.05.
with the myotome affected postoperatively. EMG results were available for 17 patients (30%) postoperatively (Table 5). The incidence of bilateral (24%) and multilevel level (88%) involvement was increased when compared with clinician evaluation consistent with the DCP. Additionally, 5 (29%) were consistent with a brachial plexopathy and less indicative of a process occurring at the nerve root.

The median neurologic follow-up for our cohort is 15.6 months (range 0.1 to 65.84 months). Unfortunately, there has been no recovery of motor function in 4 (7.1%) patients. However, for those with documented improvement, the first increases in motor grade were observed a median of 22.5 days postoperatively (range, 1 to 424). At last follow-up, the majority of individuals had regained normal (n = 27, 48.2%) or near normal (n = 12, 21.4%) strength.

### Discussion

Postoperative DCP is a known complication of cervical spine surgery with a reported incidence around 5% based on a recent meta-analysis. In the current study, we demonstrated that DCP occurred in 3.4% of our cohort, and the majority of these cases involved the C5 myotome. Just greater than half of cases included multiple myotomes, and 18% were bilateral. Although abnormal transcranial electrical stimulation-induced evoked potentials are highly sensitive and specific for radiculopathy that manifests immediately upon waking from anesthesia, DCP injury does not exhibit any signs of a potentially injurious event. Although nerve root irritation remains a possible consideration, our limited intraoperative monitoring results support the suggestion that these palsies

### Table 3
Univariate logistic regression and multivariate logistic regression for significant risk factors for entire cohort

| Variable                           | Univariate analysis |         | Multivariate analysis |         |
|------------------------------------|---------------------|---------|-----------------------|---------|
|                                    | OR                  | 95% CI  | p Value               | OR      | 95% CI  | p Value               |
| Age (per year)                     | 1.07                | 1.008–1.050 | 0.0061*               | 1.01    | 0.993–1.037 | 0.1815               |
| History of other autoimmune disease | 3.83                | 1.418–8.730 | 0.0107*               | 2.95    | 1.047–7.092 | 0.0416*               |
| Intraoperative transfusion         | 2.57                | 1.152–5.132 | 0.0231*               | 0.85    | 0.346–1.890 | 0.6966               |
| Number of levels (per level)       | 1.42                | 1.247–1.605 | <0.0001*              | 1.27    | 1.075–1.496 | 0.0053*               |
| Posterior fusion                   | 3.30                | 1.920–5.653 | <0.0001*              | 1.54    | 0.781–3.020 | 0.2133               |
| Sitting                            | 0.28                | 0.084–0.689 | 0.0036*               | 0.42    | 0.123–1.103 | 0.0816               |

Abbreviations: CI, confidence interval; OR, odds ratio.

### Table 4
Significant risk factors for specific procedure categories

| Procedure Category                  | Anterior fusion | Anterior diskectomy and fusion | Posterior fusion | Corpectomy | Foraminotomy | Laminctomy without fusion | Nonfusion (all) | Entire cohort |
|-------------------------------------|-----------------|--------------------------------|------------------|------------|--------------|--------------------------|----------------|--------------|
| n                                   | 496             | 174                            | 582              | 102        | 677          | 272                      | 827            | 1,669*       |
| DCP incidence (%)                   | 2.6             | 1.7                            | 7.1              | 4.9        | 3.5          | 2.5                      | 2.4            | 3.4%         |
| Risk factors (p values)             |                 |                                |                  |            |              |                          |                |              |
| Age                                 | 0.2421          | 0.7626                         | 0.1474           | 0.3994     | 0.0228*      | 0.4378                   | 0.2002         | 0.0061*      |
| Sitting                             | –               | –                              | –                | –          | 0.0009*      | 0.5206                   | 0.0308*        | 0.0036*      |
| Number of levels                    | 0.0082*         | 0.1290                         | 0.0188*          | 0.2089     | 0.0002*      | 0.4975                   | 0.0501         | <0.0001*     |
| Intraoperative transfusion          | 0.0204*         | 0.7075                         | 0.9700           | 0.1772     | 0.1128       | 0.2975                   | 0.1514         | 0.0231*      |
| Autoimmune other                    | 0.4860          | 0.6449                         | 0.4289           | 0.5218     | 0.0038*      | 0.0184*                  | 0.0018*        | 0.0107*      |

Abbreviation: DCP, delayed cervical palsy.

*p < 0.05.

Several cases are included in more than one procedure category.

### Table 5
Postoperative electromyography characteristics in patients developing delayed cervical palsies

| Characteristic                        | n (%)          |
|---------------------------------------|----------------|
| EMG within 6 mo                       | 17 (30.4%)     |
| Bilateral involvement                 | 17 (23.5%)     |
| Multilevel                            | 15 (88.2%)     |
| Pattern consistent with brachial plexopathy | 5 (29.4%)     |

Abbreviation: EMG, electromyogram.
were not likely the result of intraoperative trauma or positioning. At final follow-up, 7% had stable or worsening weakness. The rate of improvement reported in our cohort is slightly better than the 80% noted in the literature, though likely attributable to variability in follow-up and the definition of improvement.

Some authors have suggested prophylactic foraminotomies may lead to decreased rates of DCP, particularly after laminoplasty. Although we were unable to determine whether a foraminotomy was prophylactic from a retrospective review of operative reports, the rate of DCP at nerve roots decompressed with foraminotomies was not statistically different from those not operated upon. In fact, there was a slight trend toward an increased prevalence of DCP when a foraminotomy was performed. Although the protective effect of prophylactic foraminotomies would be better studied prospectively, this difference may suggest that the benefit of foraminotomy noted following laminoplasty in Asian cohorts may not be applicable to North American populations undergoing laminectomy and fusion.

Interestingly, none of the risk factors for PSIN as suggested by Staff et al were correlated with the development of a DCP; however, nonspecific autoimmune disease remained statistically significant on multivariate analysis (\(p = 0.0416\)). This finding, in addition to the clinical presence of bilateral (18%) and multilevel (55%) involvement and involvement of roots that were not at the operative levels (9%), suggests that autoimmune reactions or nonmechanical factors potentially play a role. Further consideration of the EMG results suggest that the reported incidences of bilaterality and multilevel involvement may be underestimated. However, the higher rates of bilateral and multimyotomal palsies observed in this subpopulation may be the result of more significant or prolonged disease requiring nerve conduction studies for further evaluation. The present study also identified increased age to be significantly correlated with the development of a DCP, which is consistent with a large series by Nassr et al, which reports an association with age and C5 palsy after corpectomy and laminoplasty.

We also describe several procedural risk factors that are correlated with an increased rate of DCPs on univariate analysis including posterior fusions (\(p < 0.0001\)), prone versus sitting (0.0036), and number of operative levels (\(p < 0.0001\)). Recently, the development of DCPs was reported by Yamanaka et al to be higher in patients undergoing instrumented fusion after cervical laminoplasty, a finding that was replicated in this study. Although the difference in cases selected for anterior and sitting approaches may explain this finding, another potential explanation is that the anterior approach and the sitting/semisitting position could offer some anatomical advantage or minimizes manipulation of the nerve roots. Other studies have suggested that the correction of cervical lordosis that is targeted following laminectomy and fusion can close the foramen and exacerbate the compression of the C5 root in cases of preexisting foraminal stenosis. It may be possible to evaluate potential differences in positioning with an anatomic study, but a complete understanding of this finding may prove elusive.

The number of operative levels was extremely significant on univariate analysis (\(p < 0.0001\)) and the only mechanical variable that remained significant on multivariate analysis (0.0053). This result suggests that the extent of the operation is the primary risk factor for this complication, and supports the theory that mechanical factors significantly contribute to the development of this complication.

Specifying risk factors by procedure categories further elucidates evidence regarding the etiology of risk factors. The prevalence of DCP across procedure categories in the present study is similar to values reported previously and suggests that the highest prevalence of DCP is observed during posterior fusion. Again, the number of operative levels appears as the dominant risk factor for both anterior and posterior fusions, which may be the result of increased traction on the nerve roots from changes in alignment/cord position and higher rates of transfusion. There is also evidence from Odate et al suggesting that one can reduce the incidence of DCPs in anterior cervical decompression and fusion cases by restricting the decompression to 15 mm and avoiding asymmetric decompressions. Interestingly, sitting was correlated with a lower incidence for all nonfusion cases. Due to the limited applicability of the sitting position for anterior and instrumented cases, there was a valid concern that sitting may be a proxy variable for posterior noninstrumented cases; however, the result of this study validates that sitting may be protective for this complication. The most interesting outcome of this section is the strong correlations of nonspecific autoimmune disease and age with foraminotomies. The development of a DCP seems to correlate with those undergoing direct manipulation of the nerve root in those with preexisting autoimmune disease. Although it is purely conjecture, manipulation of the nerve roots may expose immune-privileged antigens, which could further propagate an autoimmune response in an individual with heightened immunity. The bilateral and multiple myotomal presentation as well as EMG findings supporting plexopathy in some patients lend further support to this hypothesis. Further evaluation in larger cohorts may be appropriately powered to more specifically evaluate this general result.

Although there is significant evidence for a multifactorial etiology, this study identifies the number of operative levels as the most specific etiologic factor. Age and history of nonspecific autoimmune disease are identified as risk factors for this complication, which could be useful when selecting patients for surgery and counseling them as to the risks of the procedure. From a surgical perspective, the association of extent of surgery with development of DCP may lead the surgeon to be more conservative with the decompression to decrease the risk of this complication; however, this risk must be weighed against the risk of inadequate decompression resulting in continued symptoms postoperatively. Additionally, the positioning concerns may lead to specific planning considerations to minimize risk. Finally, this study is important because it represents a Western cohort of patients undergoing cervical decompression with or without fusion. Many previous studies have focused on Asian cohorts undergoing laminoplasty operations, with only C5 myotomes.
This study is limited by its retrospective design, study population, methodology, and inclusion criteria. Although verifying procedure specifics with both CPT codes and independent chart review increases our confidence in the data set, each method has its own inherent limitations that do not disappear when they are combined. The chosen study cohort also may prevent the broad applicability of this study’s results, as nearly all of the cases were originally indicated for the treatment of degenerative spine disease. This cohort is only a segment of the larger cervical spine surgery population, and the current study does not sufficiently evaluate the potentially important variable of the original underlying pathology. Additionally, in an attempt to identify all atypical DCPs, it was necessary to use rather loose exclusion criteria. Neurologic deterioration resulting from a myelopathy or exacerbation of the original pathology could present similarly to a multifactorial DCP. Each misclassification of other similar pathologies weakens the results and conclusions of the present study. There has also been increasing evidence that radiographic measurements including anteroposterior diameter, foramina diameter, and/or cord–lamina angle can be predictive of DCPs. These and other radiographic measurements should continue to be evaluated in similar cohorts to identify predictive factors that could be easily applied to clinical practice.23

**Conclusion**

The incidence of DCP is higher in patients undergoing more extensive procedures. Although a mechanical etiology is partially supported as a cause for DCP, notable correlations with autoimmune risk factors as well as bilateral and multifactorial involvement does support the hypothesis that some DCPs may result from an autoimmune response. The present series suggests that the etiology of DCPs is multifactorial.

**Disclosures**

Ryan F. Planchard, none
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### Appendix A: Complete list of the 81 autoimmune diseases, by selected epidemiologic and genetic characteristics

| Disorder (system) | Tissue autoantibody | Molecular target | Pathogenic molecular target | Females (%) | Prevalence (per 10^5) | Location |
|-------------------|---------------------|------------------|----------------------------|-------------|----------------------|----------|
| Autoimmune disseminated encephalomyelitis | Anti-myelin | MOG | Probable | 43 | 0.4<sup>a</sup> | World |
| Autoimmune inner ear disease | Anti-cochlear |  |  | 65 | <0.1 | World |
| Batten disease/neuronal ceroid lipofuscinoses | Anti-GAD | GAD65 | Probable | 40 | 0.8 | Norway |
| Chronic inflammatory demyelinating polyneuropathy | Anti-myelin | Myelin associated glycoprotein | Probable | 30 | 1.3 | World |
| Encephalitis lethargica<sup>b</sup> | Anti-streptolysin-O |  |  |  | <0.1 | World |
|  | Anti-basal ganglia |  |  |  |  |  |
| Guillain–Barré syndrome | Anti-ganglioside GM1 | PMP22 | Possible | 43 | 1.3<sup>a</sup> | World |
|  | Anti-PMP22 |  |  |  |  |  |
| Hashimoto encephalopathy | Anti-thyroid microsomal antibodies | TPO | Possible | 90 | 0.7 | Italy |
|  | Anti-TPO |  |  |  |  |  |
| Isaacs syndrome/acquired neuromyotonia<sup>a</sup> | Anti-VGKC | VGKC | Probable |  | <0.1 | World |
|  | Anti-AChR |  |  |  |  |  |
| Miller Fisher syndrome<sup>c</sup> | Anti-GQ1b |  |  | 43 | <0.1 | World |
|  | Anti-GM1 |  |  |  |  |  |
|  | Anti-GD1a |  |  |  |  |  |
| Morvan syndrome | Anti-VGKC | VGKC | Probable | 70 | <0.1 | World |
|  | Anti-neuronal AChR |  |  |  |  |  |
| Multiple sclerosis<sup>b</sup> | Anti-MOG | Multiple<sup>d</sup> | Probable | 64 | 58.3 | World |
|  | Anti-proteolipid protein |  |  |  |  |  |
| Myasthenia gravis | Anti-AChR | AChR | Likely | 73 | 5.1 | USA |
|  | MuSK |  |  |  |  |  |
| Narcolepsy | Anti-TRIB2 | TRIB2 | Probable | 39 | 30.6 | USA |
| Pediatric autoimmune neuropsychiatric disorders associated with Streptococcal infections (PANDAS)<sup>b</sup> | Anti-neuronal |  |  | 40 | <0.1 | World |
|  | Anti-GlcNAc |  |  |  |  |  |
|  | Anti-DNase B |  |  |  |  |  |
| Disorder (system) | Tissue autoantibody | Molecular target | Pathogenic molecular target | Females (%) | Prevalence (per 10^5) | Location |
|------------------|--------------------|------------------|-----------------------------|-------------|----------------------|----------|
| Rasmussen encephalitis | Anti-NMDA-type GluR | NMDA-type GluR | Probable | <0.1 | World |
| Stiff-person syndrome | Anti-GAD | GAD2 | Probable | >50 | <0.1 | World |
| | Anti-amphiphysin | | | | | |
| Vogt–Koyanagi–Harada syndrome | Anti-Ku-Mel-1 | KUMEL1 | Probable | 65 | <0.1 | World |
| Addison disease | Anti-21-hydroxylase | CYP21A2 | Probable | 63 | 14 | World |
| | Anti-17 α-hydroxylase | | | | | |
| | Anti-P450scc | | | | | |
| Autoimmune hypoparathyroidism | Anti-CaSR | Calcium sensing receptor | Probable | 55 | <0.1 | World |
| Autoimmune hypophysitis | Anti-pituitary cytosolic protein | | | 90 | <0.1 | World |
| Autoimmune oophoritis | Anti-OA | | | 100 | <0.1 | World |
| | Anti-21OH | | | | | |
| Autoimmune orchitis | Anti-NASP | Nuclear autoanti-genic sperm protein | Possible | 0 | <0.1 | World |
| Autoimmune polyglandular syndrome I (APECED, autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy syndrome) | Multiple | | | 57 | 0.9 | World |
| Autoimmune polyglandular syndrome II | Anti-21-hydroxylase | | | 75 | 1.7 | USA |
| | Anti-17 α-hydroxylase | | | | | |
| Autoimmune polyglandular syndrome III | Multiple | | | 83 | <0.1 | World |
| Diabetes mellitus, type 1 | Anti-GAD | Insulin/GAD65 | Probable | 45 | 480 | World |
| | Anti-insulin | | | | | |
| | Anti-ICA512 | | | | | |
| | Anti-HA-2β | | | | | |
| Graves disease | TS Ig | TSHR | Likely | 88 | 629 | Denmark |
| | Anti-TBII | | | | | |

(Continued)
| Disorder (system)                                | Tissue autoantibody                  | Molecular target              | Pathogenic molecular target | Females (%) | Prevalence (per 10^5) | Location |
|------------------------------------------------|-------------------------------------|--------------------------------|-----------------------------|-------------|-----------------------|----------|
| Hashimoto autoimmune thyroiditis               | Anti-TPO                            | Thyroperoxidase               | Probable                    | 95          | 791.7^h               | USA      |
|                                                | Anti-TG                             |                                |                             |             |                       |          |
| Immunodysregulation, polyendocrinopathy, enteropathy, X-linked |                      |                                |                             | 0           | <0.1                  | World    |
| Autoimmune hepatitis type 1                    | Anti-smooth muscle antibody         | Asioglycoprotein receptor     | Possible                    | 78          | 16.9                  | Norway   |
|                                                | ANA                                 |                                |                             |             |                       |          |
|                                                | Anti-actin                          |                                |                             |             |                       |          |
| Autoimmune hepatitis type 2                    | Anti-LKM-1                          | CYP2D6                         | Possible                    | 89          | 3                     | World    |
|                                                | Anti-P-450 IID6                     |                                |                             |             |                       |          |
| Autoimmune pancreatitis                        | Anti-lactoferrin                    | Lactoferrin                    | Unlikely                    | 33          | 0.7                   | World    |
| Celiac disease                                 | Anti-TG2                            | Tissue transglutaminase        | Probable                    | 57          | 750                   | USA      |
|                                                | Anti-gliadin                        |                                |                             |             |                       |          |
| Crohn diseaseb                                 | ASCA                                |                                |                             | 41          | 25                    | World    |
| Pernicious anemia/atrophic gastritis           | Anti-H/K                            | H/K ATP-ase                    | Likely                      | 67          | 150.9                 | USA      |
| Primary biliary cirrhosis                       | Anti-mitochondrial antibodies       | Multiple^1                     | Probable                    | 89          | 14.6                  | World    |
| Primary sclerosing cholangitis                 | pANCA                               |                                |                             | 33          | 8                     | USA      |
| Ulcerative colitisb                            | pANCA                               |                                |                             | 65          | 30                    | World    |
| Acquired hemophilia A                          | Anti-FVIII                          | Factor VIII                    | Likely                      | 50          | 0.8                   | Wales    |
| Antiphospholipid syndrome                      | Anti-cardiolipin                    | Beta2-GPI                      | Probable                    | 74          | 21.5                  | World    |
|                                                | Lupus anticoagulant                 |                                |                             |             |                       |          |
|                                                | Anti-b2GPI                          |                                |                             |             |                       |          |
| Autoimmune hemolytic anemia                    | Anti-erythrocyte I/i                | Erythrocyte I/i                | Probable                    | 64          | 1.6                   | Norway   |
| Autoimmune lymphoproliferative syndrome        | Anti-erythrocyte                    |                                |                             | 50          | <0.1                  | World    |
|                                                | Anti-neutrophil                     |                                |                             |             |                       |          |
| Disorder (system) | Tissue autoantibody | Molecular target | Pathogenic molecular target | Females (%) | Prevalence (per 10^5) | Location |
|------------------|---------------------|------------------|----------------------------|-------------|-----------------------|----------|
| Autoimmune neutropenia | Anti-NA1 | B2 Integrin | Possible | 54 | 1b | Scotland |
|  | Anti-NA2 |  |  |  |  |  |
| Evans syndrome | Anti-platelet |  |  |  |  |  |
|  | Anti-erythrocyte |  |  |  |  |  |
| Felty syndrome | Anti-G-CSF | G-CSF | Possible | 75 | 1.7 | USA |
| Immune thrombocytopenic purpura | Anti-GpIb/IIa | Glycoprotein IIb/IIIa | Probable | 70 | 72 | Denmark |
|  | Anti-ADAMTS13 |  |  |  |  |  |
|  | Anti-glycoprotein lb-IX |  |  |  |  |  |
| Polymyositis/dermatomyositis | Anti-Jo1 | Multiple | Probable | 67 | 5.1 | USA |
|  | Anti-Mi-2 |  |  |  |  |  |
|  | Anti-CADM140 |  |  |  |  |  |
| Relapsing polychondritis | Anti-collagen II | Collagen II | Probable | 66 | 0.4a | USA |
|  | Anti-collagen IV |  |  |  |  |  |
|  | Anti-collagen IX |  |  |  |  |  |
| Rheumatoid arthritis | Rheumatoid factor | Fibrinogen, βα | Probable | 75 | 860b | USA |
|  | Anti-CCP |  |  |  |  |  |
|  | Anti-collagen II |  |  |  |  |  |
| Still diseaseb | ANA |  |  |  |  | World |
|  | Anti-endothelial cell antibodies |  |  |  |  |  |
| Erythema elevatum diutinumb | IgA ANCA |  |  |  |  | World |
| Kawasaki diseaseb |  |  |  |  |  | USA |
| Microscopic polyangiitis | pANCA | Myeloperoxidase | Probable | 50 | 2 | World |
| Polyarteritis nodosaab | Anti-endothelial cell antibodies |  |  |  |  | World |
| Rheumatic fever | Anti-streptolysin O | Cardiac myosin | Likely | 50 | 250 | World |
|  | Anti-DNase B |  |  |  |  |  |
| Takayasu arteritisb |  |  |  |  |  | USA |
| Temporal arteritisb |  |  |  |  |  | USA |
| Disorder (system) | Tissue autoantibody | Molecular target | Pathogenic molecular target | Females (%) | Prevalence (per 10^5) | Location |
|------------------|---------------------|------------------|-----------------------------|-------------|----------------------|----------|
| Wegener's granulomatosis | cANCA | Proteinase 3 | Probable | 43 | 3 | World |
| Alopecia areata | Anti-hair follicle antibodies | Trichohyalin | Possible | 50 | 150 | World |
| Bullous pemphigoid | Anti-BP180 | Bullous pemphigoid associated glycoprotein 1 | Likely | 50 | 1 | World |
| Cicatricial pemphigoid | Anti-BP230 | Laminin-332 | Likely | 75 | 0.1 | World |
| Dermatitis herpetiformis | Anti-TGase3 | Transglutaminase | Probable | 36 | 11.2 | USA |
| Discoid lupus erythematosus | | | | 66 | 7.3 | World |
| Epidermolysis bullosa acquisita | Anti-type VII collagen | Type VII collagen | Likely | 58 | 0.2^a | France |
| Linear morphea | Anti-P80 Collin | P80 Collin | Probable | 75 | 1 | World |
| Pemphigus foliaceus | Anti-Desmoglein I | Desmoglein I | Probable | 50 | 0.1^a | World |
| Pemphigus vulgaris | Anti-Desmoglein III | Desmoglein III | Probable | 60 | 0.5^a | World |
| Vitiligo | Anti-MCHR1 | SOX10 | Possible | 52 | 400.2 | World |
| | Anti-SOX-10 | | | | | |
| Behçet disease^b | Anti-oral mucous membrane | | | 50 | 1.2 | World |
| Churg–Strauss syndrome^b | cANCA | | | 43 | 0.2 | World |
| Cogan syndrome^b | | | | 60 | <0.1 | World |
| Calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia (CREST) syndrome | Anti-centromere | | | 82 | 5.6 | USA |
| | Anti-fibrillarin | | | | | |
| Essential mixed cryoglobulinemia^b | Anti-IgG | | | 75 | 1 | USA |
| | AECA | | | | | |
| Mixed connective tissue disease | Anti-U1ribonucleoprotein | SNRNP70 | | 80 | 2.7 | Japan |
| Polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes (POEMS) syndrome^b | Anti-MAG | | | 70 | <0.1 | World |
| | Anti-GM1 | | | | | |
### Appendix A (Continued)

| Disorder (system)                        | Tissue autoantibody | Molecular target | Pathogenic molecular target | Females (%) | Prevalence (per 10^5) | Location |
|------------------------------------------|---------------------|------------------|-----------------------------|-------------|-----------------------|----------|
| Scleroderma                              | Multiple^k          | Multiple^l        | Possible                    | 92          | 24                    | World    |
| Sjögren syndrome                         | ANA                 | Multiple^m        | Possible                    | 94          | 14.4                  | USA      |
| Systemic lupus erythematosus             | Multiple^n          | Multiple^o        | Possible                    | 88          | 32                    | World    |
| HLA-B27-associated acute anterior uveitis| Anti-S-antigen      | S-antigen         | Possible                    | 34          | 8.7^a                 | World    |
| Sympathetic ophthalmia                   | Anti-basement       | α3(IV)NC1 collagen| Likely                     | 25          | 0.5                   | World    |

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^aIncidence data (no prevalence studies identified).

^bAutoimmune etiology is not well established.

^cGenerally regarded as a subset of Guillain-Barré syndrome.

^dProteolipid protein, myelin oligodendrocyte glycoprotein, myelin basic protein, neurofilament light polypeptide.

^eAnti-candidal enolase, anti-pituitary, anti-calcium sensing receptor protein, anti-aromatic L-amino acid decarboxylase, anti-tyrosine hydroxylase.

^fAnti-t21-hydroxylase, anti-17 α-hydroxylase, anti-thyroperoxidase.

^gWorld prevalence is difficult as disease displays latitude dependence.

^hPopulation limited to adults (over 18 years).

^iSeventy-four kilodalton E2, keratin, sp100, actin.

^jHistidyl tRNA, aminoacyl tRNA synthetase, DNA-dependent nucleosome-stimulated ATPase, EXOSC10 protein, chromodomain-helicase-DNA-binding protein 4.

^kAnti-ScI70, anti-PM/ScI, anti-RNA polymerase III, anti-centromere.

^lTopoisomerase I, Ro, La, Ku, fibrillarin.

^mRo, La, golgin.

^nAnti-dsDNA, Anti-U1A, Anti-U2B, Anti-PCNA, Anti-Smith, Anti-SSA, Anti-SSB.

^oU2 snRNP B, cardiolipin, fibronectin, Ro, La, histone H2A H2B, vimentin.