Original Article

Redefining cervical spine deformity classification through novel cutoffs: An assessment of the relationship between radiographic parameters and functional neurological outcomes

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ABSTRACT

Purpose: The aim is to investigate the relationship between cervical parameters and the modified Japanese Orthopedic Association scale (mJOA).

Materials and Methods: Surgical adult cervical deformity (CD) patients were included in this retrospective analysis. After determining data followed a parametric distribution through the Shapiro–Wilk Normality (P = 0.15, P > 0.05), Pearson correlations were run for radiographic parameters and mJOA. For significant correlations, logistic regressions were performed to determine a threshold of radiographic measures for which the correlation with mJOA scores was most significant. mJOA score of 14 and <12 reported cut-off values for moderate (M) and severe (S) disability. New modifiers were compared to an existing classification using Spearman's rho and logistic regression analyses to predict outcomes up to 2 years.

Results: A total of 123 CD patients were included (60.5 years, 65%F, 29.1 kg/m^2). For significant baseline factors from Pearson correlations, the following thresholds were predicted: MGS (M:-12 to-9° and 0°–19°, P = 0.020; S: >19° and <−12°, χ^2 = 4.291, P = 0.036), TS-CL (M: 26°to 45°, P = 0.201; S: >45°, χ^2 = 7.8, P = 0.005), CL (M:-21° to 3°, χ^2 = 8.947, P = 0.004; S: <−21°, χ^2 = 9.3, P = 0.009), C2-T3 (M: −35° to −25°, χ^2 = 5.485, P = 0.046; S: <−35°, χ^2 = 4.1, P = 0.041), C2 Slope (M: 33° to 49°, P = 0.122; S: >49°, χ^2 = 5.7, P = 0.008), and Frailty (Mild: 0.18–0.27, P = 0.129; Severe: >0.27, P = 0.002). Compared to existing Ames- International Spine Study Group classification, the novel thresholds demonstrated significant predictive value for reoperation and mortality up to 2 years.

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Conclusions: Collectively, these radiographic values can be utilized in refining existing classifications and developing collective understanding of severity and surgical targets in corrective surgery for adult CD.

Keywords: Adult cervical deformity, cervical spine, thresholds of severity

INTRODUCTION

Cervical deformity (CD) is associated with debilitating disability, neurologic compromise, major neck pain, and severe malalignment.[1,2] To effectively treat CD, evaluate patient outcomes, and execute studies surrounding cervical spine deformity, a standardized classification system of deformity severity must exist.[3] Ames and the International Spine Study Group (ISSG) developed a novel CD classification including five modifiers.[4] It encompasses sagittal, regional, and global alignment, but is inherently based upon a modified Delphi approach, expert surgeon opinion, and available literature. The parameters in the Ames-ISSG classification include moderate and severe cutoffs for TS-CL (the mismatch between T1 slope and cervical lordosis), C2-C7 sagittal vertical axis (SVA), horizontal gaze (through chin-to-brow vertical angle [CBVA]), myelopathy severity (through the modified Japanese Orthopedic Association scale [mJOA]), and the SRS-Schwab Classification for adult spinal deformity.

Currently, the established classification system for adult spinal deformity, developed by the Scoliosis Research Society and Schwab *et al*., has been extensively validated and found to correlate with patient-reported outcomes (Health-Related Quality of Life [HRQLs]).[5-7] This has yet to be successfully completed for the Ames-ISSG CD classification. Bakouny and colleagues investigated the relationship between this novel CD categorization method and HRQLs.[8] Their results suggested that the modifiers of CBVA and TS-CL were not specific to individuals with CD and can occur in asymptomatic patients; furthermore, the radiographic parameter cutoffs were unrelated to patient-reported outcomes.

Patient-reported outcomes, including myelopathy severity, in the cervical region and their relationship to cervical malalignment is an emerging topic.[9,10] A recent study by Smith and colleagues was the first to find the correlation between C2-C7 SVA and myelopathy severity.[11] An increase in cervical malalignment, namely progressive cervical kyphosis, has been shown to ultimately lead to cord tension and intramedullary pressure, resulting in great neurologic disability.[12-17] This neurologic functional status can be measured in patients with potential degenerative cervical myelopathy through an investigator-administered tool, mJOA.

This study hypothesized that pegging deformity to a patient-reported outcome may more accurately represent CD severity grades and predict poor postoperative outcomes. We investigated the relationship between cervical parameters and baseline frailty with the myelopathy measure mJOA. Specifically, we aimed to redefine moderate and severe CD cutoffs of cervical radiographic parameters in conjunction with patient-reported myelopathy severity.

MATERIALS AND METHODS

Study design and ethics

We retrospectively analyzed a prospective, multicenter ISSG database of CD patients enrolled from 2013 to 2018 at 13 participating centers around the United States. Institutional Review Board approval was required protocol by each site and informed patient consent was obtained. The ISSG database inclusion criteria were patients >18 years with radiographic evidence of CD. This was defined by the presence of at least one of the following: cervical kyphosis (C2-C7 Cobb angle >10°), cervical scoliosis (C2-C7 coronal Cobb angle >10°), C2-C7 SVA (cSVA) >40 mm or CBVA >25°. Patients with spinal deformity of neuromuscular etiology, presence of active infection, or malignancy were excluded from the database. The study inclusion criteria required the relevant radiographic data and mJOA scores at baseline.

Data collection, radiographic, and health-related quality of life assessment

Baseline patient demographic and clinical data assessed patient age, gender, body mass index (BMI), and Charlson Comorbidity Index (CCI), and frailty as defined by Miller *et al*. Preoperative full-length free-standing lateral spine radiographs were analyzed with SpineView® (ENSAM, Laboratory of Biomechanics, Paris, France) software according to the literature.[18-20] Radiographic parameters assessed included C2-C7 lordosis (CL: angle between the C2 inferior endplate and the C7 inferior endplate), pelvic tilt (PT: the angle between the vertical and the line through the sacral midpoint to the center of the two femoral heads), T1 slope (angle between the horizontal line and the T1 superior endplate), cervical SVA (cSVA: C2 plumbline offset from the posterosuperior corner of C7), T1 slope minus CL (TS-CL: mismatch between T1 slope and cervical curvature), C2-T3 angle, C2 Slope, McGregor's slope [MGS: angle between the line from the

posterosuperior aspect of the hard palate to the caudal portion of the opisthion and the horizontal, Figure 1], and CBVA. The health-related quality of life questionnaire utilized in this study was the modified Japanese Orthopedic Association scale (mJOA) administered by each of the participating centers.

Statistics

Demographic, clinical, and surgical data were assessed with descriptive analyses. Frequency analysis evaluated categorical variables with Chi-square test determining the significant variance of expected versus observed values. Statistical analyses were performed to determine correlations between HRQLs and possible modifiers. The statistical method was the same as previously published literature by Tang *et al*.[9,21] Data were analyzed for following a parametric distribution using the Shapiro Wilk Normality test ($P > 0.05$, the distribution of the sample is not significantly different from a normal distribution), defined as a W statistic that tests whether a random sample, $x_1, x_2, \ldots, x_n$ comes from (specifically) a normal distribution. Small values of W are evidence of departure from normality and percentage points for the W statistic:

$$W = \frac{(\Sigma_{i=1}^{n} a_i x_{(i)})^2}{\Sigma_{i=1}^{n} (x_i - \overline{x})^2}$$

Where the $x_{(i)}$ are the ordered sample values ($x_{(1)}$ is the smallest) and the a_i are constants generated from the means, variances, and covariances of the order statistics of a sample of size n from a normal distribution.[22] Then, Pearson correlation coefficients were calculated for all combinations of radiographic measures and HRQLs. For significant correlations, linear regression and a binary logistic regression model were performed to determine a possible threshold of radiographic measures for which the correlation with mJOA scores was most significant. The logistic regression model assigned values as binary variables greater or less than a predicted threshold value. Predicted threshold values were made at various increments for all radiographic variables and frailty. The rough threshold for each "modifier" was the value that demonstrated the lowest *P* value. The degree of myelopathy severity was evaluated by categorizing mJOA scores into groups: 18 (None), 17–15 (Mild), 14–12 (Moderate), 12 (Severe).[23] mJOA score published cutoffs of 14 for moderate and <12 for severe myelopathy disability were used to find the new modifiers. Spearman's rho assessed the strength of association between existing CD classification and the novel proposed. An area-under-the-curve (c-statistic) was run between the existing and newly-proposed classifications. Predictive values of the modifiers were compared with binary logistic models, with each modifier as the sole predictor of each outcome. Three outcomes were assessed: Reoperation, Major complication, Mortaility up to 2 years. Statistical analysis was performed using SPSS software (version 21.0 IBM, Armonk, NY, USA). All analyses were two-sided and the level of significance was set to $P < 0.05$.

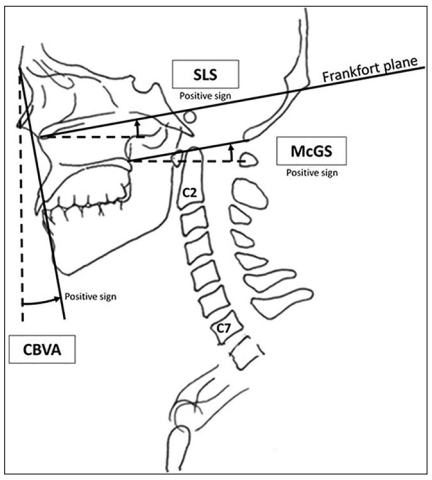

Figure 1: Visual representation of McGregor's Slope (MGS), or the angle between the line from the posterosuperior aspect of the hard palate to the caudal portion of the opisthion and the horizontal

RESULTS

Overall cohort patient characteristics

One-hundred and twenty-three CD patients met inclusion criteria. Mean patient age was 60.5 ± 10.1 years, mean BMI of 29.1 ± 8.2 kg/m^2, with 65% of the cohort being female. The average CCI score was 0.90, while the frailty score was 0.31 ± 0.13. These CD patients underwent majorly posterior surgeries (50.4%), while 32.5% had combined approaches and 17.1% anterior. The average levels fused was 8.05 (posterior: 8.93, anterior: 3.36). The mean total operative time was 534.3 min, with an estimated blood loss of 890.6 ccs. The average baseline mJOA score was 13.54 ± 2.8 (mean moderate myelopathy severity). Table 1

Table 1: Preoperative cervical radiographic measurements and frailty averages for the cohort

	Average baseline
McGregor's slope (°)	4.89±15.5
T1 slope (°)	33.1±18.3
C2-C7 lordosis (°)	−6.27±22.1
TS-CL (°)	39.3±21
C2-T3 angle (°)	−17.7±22.8
C2 slope (°)	39±21.8
cSVA (mm)	39.5±18.3
CBVA (°)	4.12±7.8
PT (°)	20.1±10.8
Frailty	0.31±0.13

cSVA – Cervical sagittal vertical axis, CBVA – Chin-to-brow vertical angle, PT – Pelvic tilt, TS-CL – T1 slope and cervical lordosis

Table 2: Pearson's *r* values and their associated *P* values between baseline modified Japanese Orthopaedic Association scores, as well as between each of the radiographic parameters assessed

HRQL	Correlation (pearson's *r*)	*P*
Baseline mJOA scores		
McGregor's slope	−0.236	**0.015**
T1 slope	0.006	0.945
C2-C7 lordosis	0.225	**0.012**
TS-CL	−0.246	**0.006**
C2-T3 angle	0.180	**0.046**
C2 slope	−0.234	**0.009**
cSVA	−0.033	0.714
CBVA	−0.055	0.841
PT	0.004	0.966
Frailty	0.517	**<0.001**
*Significant pairs of radiographic parameters		
McGregor's slope		
T1 slope	0.403	**<0.001**
C2-C7 lordosis	−0.399	**<0.001**
TS-CL	0.809	**<0.001**
C2-T3 angle	−0.589	**<0.001**
C2 slope	0.828	**<0.001**
cSVA	0.551	**<0.001**
CBVA	0.839	**<0.001**
PT	0.004	0.966
T1 slope		
C2-C7 lordosis	0.648	**<0.001**
TS-CL	0.371	**<0.001**
C2-T3 angle	−0.007	0.940
C2 slope	0.402	**<0.001**
cSVA	0.648	**<0.001**
CBVA	−0.124	0.648
PT	0.146	0.108
C2-C7 lordosis		
TS-CL	−0.642	**<0.001**
C2-T3 angle	0.721	**<0.001**
C2 slope	−0.597	**<0.001**
cSVA	−0.054	0.553
CBVA	−0.341	0.196
PT	0.078	0.391
TS-CL		
C2-T3 angle	−0.766	**<0.001**
C2 slope	0.980	**<0.001**
cSVA	0.622	**<0.001**
CBVA	0.347	0.188
PT	0.045	0.623
C2-T3 angle		
C2 slope	−0.782	**<0.001**
cSVA	−0.475	**<0.001**
CBVA	−0.488	0.082
PT	0.033	0.714
C2 Slope		
cSVA	0.686	**<0.001**
CBVA	0.441	0.087
PT	0.031	0.729
cSVA		
CBVA	0.306	0.250
PT	0.113	0.214
CBVA		
PT	−0.173	0.521

Bolded values represent significant correlation ($P<0.05$). cSVA – Cervical sagittal vertical axis, CBVA – Chin-to-brow vertical angle, PT – Pelvic tilt, TS-CL – T1 slope and cervical lordosis, HRQL – Health related quality of life, mJOA – Modified Japanese Orthopaedic Association

summarizes the preoperative values of radiographic measurements and frailty for the cohort.

Correlations between possible cervical deformity modifiers and modified Japanese Orthopedic Association scores

Comparisons by way of Pearson correlations between potential CD modifiers and baseline mJOA scores demonstrated significant correlation between mJOA and McGregor's Slope (−0.236, $P = 0.015$), TS-CL (−0.246, $P = 0.006$), CL (0.225, $P = 0.012$), C2-T3 (0.180, $P = 0.046$), C2 Slope (−0.234, $P = 0.009$), and frailty (0.517, $P < 0.001$). The radiographic parameters of T1 slope, cSVA, CBVA, and PT did not have significant correlation with mJOA scores.

Correlations between the radiographic parameters were examined. Significant correlation was found between McGregor's slope, C2-C7 lordosis, TS-CL, C2-T3 Angle, C2 Slope, cSVA, and CBVA. McGregor's Slope was the sole parameter that significantly correlated with CBVA ($r = 0.839$, $P < 0.001$), while none correlated with the global pelvic tilt measurement. All Pearson's r values and their associated *P* values between the radiographic parameters assessed in this study can be found in Table 2.

Predicted thresholds with logistic regression analyses

For those potential modifiers that demonstrated a significant correlation with baseline mJOA scores, logistic regression models predicted values for moderate and severe myelopathy scores, and significance was determined with linear regression analyses. These assigned values as binary variables greater or less than a predicted threshold value, and were tested at varying increments and modifier estimate was chosen at which the statistical power was the most significant (*P*-value closest to 0).[21] With an mJOA cut-off value of 14 (corresponding to moderate neurologic disability), the logistic regression model predicted a range of McGregor's Slope measurements of −12° to −9° and from 0° to 19° ($\chi^2 = 5.522$, $P = 0.020$). The published cutoff of <12 for severe myelopathy predicted McGregor's Slope values of >19° and <−12° ($\chi^2 = 4.291$, $P = 0.036$). Predicted threshold range for TS-CL parameter for

the mJOA 14 cut-off was 26° to 45°, while <12 mJOA regression model predicted >45° for severe (χ^2 = 7.8, P = 0.005). Regression analysis of CL found significant threshold from −21°–3° for mJOA 14 (χ^2 = 8.947, P = 0.004) and <−21° for < 12 (χ^2 = 9.3, P = 0.009). C2-T3 angle thresholds were most significant for moderate myelopathy (mJOA 14) from −35–−25° (χ^2 = 5.485, P = 0.046) and <−35° for mJOA <12 (χ^2 = 5.485, P = 0.046). C2 slope moderate cut-off values were 33° to 49° (χ^2 = 2.355, P = 0.120), with severe (mJOA < 12) >49° (χ^2 = 6.881, P = 0.008). Finally, frailty score cutoffs were found by similar regression models where moderate mJOA was a range from 0.18–0.27 (χ^2 = 2.399, P = 0.142), and severe mJOA score had the most significant threshold for >0.27 (χ^2 = 13.362, P = 0.001). The cutoffs established from the moderate and severe mJOA scores categorized patients into low, moderate and high deformity groups for each modifier (Patient-reported [PR] modifiers), which can be seen in Figure 2. Average mJOA scores by severity group are shown in Figure 3.

Comparison with established ames cervical deformity classification

TS-CL and horizontal (CBVA/MGS) are the two modifiers in common between the Ames CD classification and the proposed cutoffs for moderate and severe deformity in this study. Spearman's Rho between the Ames TS-CL and PR TS-CL modifiers was determined to be 0.417 (P < 0.001) with an AUC of 0.845. Meanwhile, Ames CBVA and PR MGS had a Spearman's Rho value of 0.518 (P < 0.001) with an AUC of 0.887.

Binary logistic regression models analyzed each modifier from the Ames classification and the PR modifiers for their predictive value of reoperation, major complications, and mortality. The cSVA modifier was the sole parameter which demonstrated significant predictive ability of the Ames classification, that of which being reoperation (odds ratio [OR]: 3.818 [1.280–11.387], P = 0.016). Ames TS-CL and CBVA did not have significant predictive value for any of the three outcomes.

PR MGS did not exhibit significant predictive ability for reoperation, major complication, or mortality. PR TS-CL revealed significant predictive ability for reoperation (OR: 2.151 [1.024–4.517], P = 0.043), and a trend (P < 0.100) for mortality (OR: 2.332 [0.864–6.293], P = 0.095). PR CL modifier trended as predictive for mortality (OR: 0.469 [0.193–1.139], P = 0.094). The logistic regression models for PR C2-T3 modifier significantly predicted the outcome of reoperation (OR: 0.435 [0.246–0.769], P = 0.004) and trended for mortality (OR: 0.536 [0.266–1.081], P = 0.082). PR C2 Slope modifier significantly predicted reoperation (OR: 1.960 [1.102–3.483], P = 0.022) and mortality (OR: 2.043 [0.979–4.263], P = 0.050).

Case example

Figure 4 shows the baseline lateral cervical radiograph of a 67-year-old female who underwent CD corrective surgery. She underwent reoperation due to neurologic complications. According to the proposed PR modifier, the patient presented with severe TS-CL (62.3°), CL (−32.3°), C2-T3 (−49.9°), and C2 slope (67.1°) modifiers, while was categorized with moderate baseline PR modifier deformity for MGS (10.6°) and presented as PR low frailty (0.13) at baseline.

DISCUSSION

The proposed Ames CD classification system encompasses novel cutoffs for five modifiers defining low, (0) moderate (1) and severe (2) deformity (4). This method stands as an initial attempt to classify a disease which utilized a modified Delphi approach and expert opinion similar to the process in defining thoracolumbar spine deformity and will need subsequent refinement before academic and surgical consensus on a final form.[5,21] Namely, radiographic cutoffs for such a debilitating disease should have a strong association with patient-reported outcomes.

We aimed to reveal the relationship between cervical parameters and frailty with the neurologic function/myelopathy health-related life questionnaire, mJOA. This was accomplished

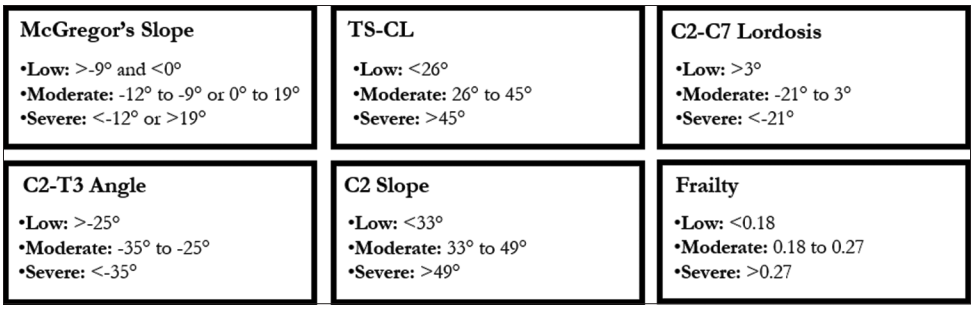

Figure 2: The proposed cut-offs for McGregor's Slope, T1 slope minus cervical lordosis (TS-CL), C2-C7 lordosis, C2-T3 angle, C2 slope, and frailty categorized into low, moderate, and severe deformity based off of modified Japanese Orthopedic Association scale scores

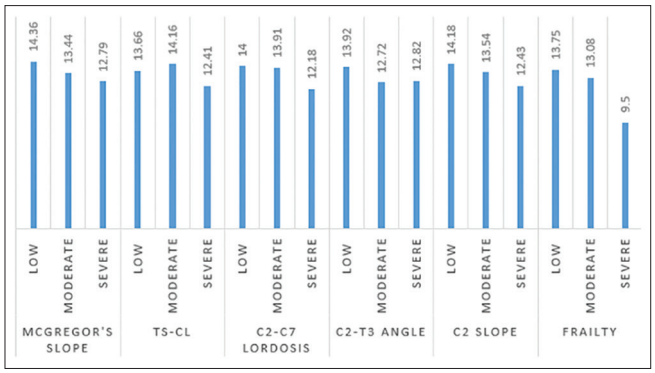

Figure 3: The average modified Japanese Orthopedic Association scale scores for patients included in each proposed modifier severity group

Figure 4: The baseline lateral cervical radiograph of a 67 year-old female who underwent cervical deformity corrective surgery. She underwent a reoperation due to neurologic complications. According to the proposed PR modifier, the patient presented with severe TS-CL (62.3°), CL (–32.3°), C2-T3 (–49.9°), and C2 slope (67.1°) modifiers, while was categorized with moderate baseline Patient-reported modifier deformity for McGregor's Slope (10.6°) and presented as Patient-reported low frailty (0.13) at baseline

by presenting novel cut-off values for moderate and severe disability by mJOA score of 14 and <12, respectively, for potential modifiers that were found to initially correlate with myelopathy severity. Pearson's correlation with baseline mJOA scores demonstrated significance with McGregor's Slope, TS-CL, CL, C2-T3 angle, C2 Slope, and frailty.

The inability to look straight ahead or lie down flat on a bed and an overall restriction on daily living as the result of CD calls for the measure of horizontal gaze as a modifier of CD classification.[24] Although the Ames classification chose CBVA as their measure of horizontal gaze, MGS was assessed in our cohort as it initially correlated with our baseline HRQL. In a study by Lafage *et al*., the slope of McGregor's line correlates strongly to CBVA, concluding that the two parameters can be used as surrogate measures.[25] Through the use of regression models, cutoffs for CD disability of McGregor's Slope were predicted: (0) −9° to 0° (1) −12° to −9° or 0° to 19° and (2) <−12° or >19°.

Cervical kyphosis is the most common aspect of CD and has been identified as a parameter with substantial clinical impact. It was important to involve the radiographic measure for cervical lordosis as a modifier as the Ames-ISSG classification did.[4] In patients with reported myelopathy, abnormal cervical lordosis may lead to less postoperative neurologic improvement.[26] Significant correlation was found between CL and baseline mJOA scores as well as with all additional modifiers analyzed in this study. Logistic regression cutoffs for CL predicted: (0) >3° (1) −21° to 3° (2) <−21°, consistent with the relationship between increased cervical kyphosis and patient-reported disability.

TS-CL also demonstrated correlation with mJOA and all modifiers explored. Larger T1S places pressure on CL to increase to achieve the balance of the head over the thoracic inlet. In addition to their proportional association, TS-CL has also shown clinical relevancy in recent studies.[27] Due to its importance in cervical alignment and association with mJOA scores, the regression models determined cutoffs: (0) <26° (1) 26° to 45° (2) >45°. Though these novel thresholds are much higher than the Ames-ISSG of >20° for severe CD and the cutoff proposed by Hyun and colleagues of >25° (established with Neck Disability Index scores), our values were chosen based on the greatest statistical power with myelopathy severity.

The C2-T3 angle presents as an adequate measure of cervical malalignment and myelopathy severity.[28,29] It differs from the well-studied C2-C7 cervical lordosis as it incorporates the cervicothoracic junction morphology, anatomy which may considerably influence CD.[30,31] Using C2-T3 angle as a modifier we can represent the connection between the regional components of the spine, including cervical lordosis, thoracic kyphosis, and lumbar lordosis.[32] The thresholds found for the C2-T3 angle are: (0) >−25° (1) −35 to − 25° (2) <−35°.

The last radiographic measure significantly correlating with mJOA, was the C2 slope. Protopsaltis *et al*. proposed C2 slope as a singular CD parameter and is essentially a mathematical approximation of TS-CL.[33,34] Due to its unique nature of marking overall cervical sagittal alignment, linking the occipitocervical and cervico-thoracic spine, C2 slope was assessed as to its own modifier for CD. Its thresholds included: (0) <33° (1) 33° to 49° (2) >49°.

The frailty score was included as a modifier in the classification of CD. Frailty has consistently been characterized in the literature as a strong predictor of adverse outcomes

following spine surgery and has become an important aspect of preoperative risk stratification.[35] It embodies patient baseline disability and is shown in the literature to impact cervical radiographic alignment with severity.[36] Through regression analyses with mJOA scores, frailty CD cutoffs included: (0) <0.18 (1) 0.18–0.27 (2) >0.27.

Compared to the Ames-ISSG CD classification system, most modifiers in the newly developed PR modifiers demonstrated predictability for reoperation or mortality with the increase in severity. This preliminary analysis of modifier impact on outcomes in conjunction with the inherent HRQL relationship presents that the new proposed PR modifiers may be a strong potential refinement to existing CD classification.

Cervical deformities represent one of the more challenging and uncertain areas of spinal surgery. Ames and colleagues attempted to provide a unified language. Despite representing progress, this was not based on clinical correlations and was found to have weak-to-moderate correlation with baseline disability and functional outcomes. Often, patients have associated spinal cord dysfunction as a result of direct compression or tension on the cord due to deformity. To further our common language of cervical deformities for research and clinical realignment goals with clinical meaning, we have based our realignment goals in this series with myelopathy scores. Correlation with neurological improvement is paramount when developing and applying CD classification schemes.

Limitations include the retrospective nature of this study and the small number of patients. While the multicenter methodology used for database construction increases generalizability, the data analyzed for the purposes of this study may be skewed toward more complex cases. Another limitation lies in the heterogeneous nature of the patient population in regard to the small sample size with cervical procedure and complexity. The study was limited to the data supplied from the multiple centers included, so information regarding the amount or length of spinal cord compression is lacking. Future studies should investigate the proposed thresholds for moderate and severe disability on a prospective trial with a larger, homogenous population of patients undergoing CD corrective surgery, as well as how improvement/decline in the modifiers influences postoperative outcomes.

CONCLUSIONS

Novel thresholds for moderate and severe disability were established for McGregor's Slope, TS-CL, CL, C2-T3 angle, C2 Slope, and frailty in CD patients. Each modifier correlated with moderate or severe neurologic myelopathy by way of mJOA score. These cut-off values can be utilized in further developing our collective understanding of severity grades for cervical deformities based on patient-reported outcomes rooted in myelopathy severity.

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Conflicts of interest

There are no conflicts of interest.

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