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CLINICAL ARTICLE

The morphology of cervical deformities: a two-step cluster analysis to identify cervical deformity patterns

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OBJECTIVE Cervical deformity (CD) is difficult to define due to the high variability in normal cervical alignment based on postural- and thoracolumbar-driven changes to cervical alignment. The purpose of this study was to identify whether patterns of sagittal deformity could be established based on neutral and dynamic alignment, as shown on radiographs.

METHODS This study is a retrospective review of a prospective, multicenter database of CD patients who underwent surgery from 2013 to 2015. Their radiographs were reviewed by 12 individuals using a consensus-based method to identify severe sagittal CD. Radiographic parameters correlating with health-related quality of life were introduced in a two-step cluster analysis (a combination of hierarchical cluster and k-means cluster) to identify patterns of sagittal deformity. A comparison of lateral and lateral extension radiographs between clusters was performed using an ANOVA in a post hoc analysis.

RESULTS Overall, 75 patients were identified as having severe CD due to sagittal malalignment, and they formed the basis of this study. Their mean age was 64 years, their body mass index was 29 kg/m^2, and 66% were female. There were significant correlations between focal alignment/flexibility of maximum kyphosis, cervical lordosis, and thoracic slope minus cervical lordosis (TS-CL) flexibility ($r = 0.27$, 0.31, and -0.36, respectively). Cluster analysis revealed 3 distinct groups based on alignment and flexibility. Group 1 (a pattern involving a flat neck with lack of compensation) had a large TS-CL mismatch despite flexibility in cervical lordosis; group 2 (a pattern involving focal deformity) had focal kyphosis between 2 adjacent levels but no large regional cervical kyphosis under the setting of a low T1 slope (T1S); and group 3 (a pattern involving a cervicothoracic deformity) had a very large T1S with a compensatory hyperlordosis of the cervical spine.

CONCLUSIONS Three distinct patterns of CD were identified in this cohort: flat neck, focal deformity, and cervicothoracic deformity. One key element to understanding the difference between these groups was the alignment seen on extension radiographs. This information is a first step in developing a classification system that can guide the surgical treatment for CD and the choice of fusion level.

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KEYWORDS cervical deformity; cluster analysis; extension alignment; focal deformity; cervicothoracic deformity; flat neck

ABBREVIATIONS CD = cervical deformity; cSVA= cervical sagittal vertical axis; HRQOL = health-related quality of life; mJOA = modified Japanese Orthopaedic Association; NDI = Neck Disability Index; NRS = numeric rating scale; TS-CL = thoracic slope minus cervical lordosis; T1S = T1 slope.

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Cervical deformity (CD) represents a significant disability for patients and a challenge for surgeons to treat.[7,19,23,25] The disability largely stems from a loss of balance, maintenance of horizontal gaze, or the ability of patients to maintain alignment of their head over their pelvis.[1,13] When CD begins to alter aspects of spinal alignment such as horizontal gaze, patients must expend energy to keep their head over their trunk, resulting in significant detrimental effects to quality of life, rivaling other debilitating conditions such as blindness and cancer.[5,11,14]

While there have been well-established parameters governing how overall sagittal alignment relates to patient outcomes in cases of thoracolumbar spinal deformity, such correlations between sagittal alignment and CD are not as clear.[9,20] Previous research has shown that changes in cervical lordosis impact outcomes related to thoracolumbar scoliosis and surgery for cervical myelopathy.[16,17] To date, the potential relationship between cervical sagittal alignment and outcomes for CD patients has not been well defined.

One of the first steps in better understanding how cervical sagittal alignment impacts clinical outcomes in CD is to classify the various types of sagittal alignment deformity involved in CD. A previous classification by Ames et al. provided a common language for CD. This classification, however, was defined a priori, based only on surgeon experience, and was not linked to health-related quality of life (HRQOL) measurements.[3] In addition, this classification was largely based on a previous thoracolumbar classification of ASD.[21] We ultimately aim to create a new, data-driven classification for CD. The first steps in this process will be to understand the various patient presentations for CD.

We hypothesized that there are subgroups of severe CD that behave differently based on different patterns of sagittal alignment. These subgroups would largely be based on dynamic radiographs that measure patients' ability to correct their cervical sagittal alignment. We used a consensus approach to accurately define a cohort of patients and subsequently performed a two-step cluster analysis to objectively define subgroups of severe CD. The goal of this study was to better define CD in groups that might behave uniquely in the context of both surgical and nonsurgical treatment of CD.

Methods

Study Sample

We performed a retrospective review of a prospective multicenter database. This database represents a longitudinal collection of clinical information and radiographs from a large prospective series from centers caring for patients with spinal pathology. This study was approved by the institutional review board across the 13 medical centers that recruited patients for our study prior to study initiation. The inclusion period was between 2013 and 2015. The inclusion criteria for the prospective database were age > 18 years and the presence of at least one of the radiographic parameters shown in Table 1. Of note, all these angles are based on previously described literature.[2]

TABLE 1. Radiographic parameters for the prospective database retrospectively queried

Radiographic Parameter	Inclusion Criterion
Cervical Cobb angle (°)*	>10
Cervical kyphosis (°)	>10
cSVA (cm)	>4
Chin-brow vertical angle (°)	>25

* Also known as anteroposterior cervical scoliosis.

Data Collection

We first collected basic demographic data on our cohort of patients. This included age, sex, and body mass index. Outcome measurement scores, such as the modified Japanese Orthopaedic Association (mJOA) scale, Neck Disability Index (NDI), EQ-5D, and visual analog scale and numeric rating scale (NRS) for back and neck pain, were collected for all patients.

We evaluated radiographs from each patient. Radiographic analysis was conducted at a single center using a validated and dedicated software for spinal alignment analysis.[4,12] These included full-length standing spine radiographs with anteroposterior and lateral views, cervical anteroposterior and lateral radiographs, and flexion/extension cervical radiographs. There were several radiographic parameters included within this study. These were spinopelvic parameters, including pelvic incidence, pelvic tilt, pelvic incidence minus lumbar lordosis, sagittal vertical axis, and T1 pelvic angle, that were measured on 36-inch long-cassette films. Cervical parameters were also analyzed using the radiographs. Regional cervical parameters included C2–7 Cobb angle, cervical sagittal vertical axis (cSVA), T1 and C2 slope, and thoracic slope minus cervical lordosis (TS-CL). Local cervical parameters included maximum focal kyphosis between 2 adjacent segments and the number of kyphotic levels that had an angle greater than 5°. The flexibility of each measurement refers to the absolute change in a measurement between the lateral radiograph and the extension radiograph, as it represents the flexibility available for lordotic/posterior correction. The radiographic parameters used in this study are shown in Fig. 1.

Panel Review

A panel of 12 experts in CD surgery reviewed the complete set of preoperative radiographs (36-inch whole-spine, free-standing, coronal and sagittal radiographs and coronal, lateral neutral, flexion/extension cervical radiographs). Each case was discussed and classified as either severe CD or nonsevere CD if at least 10 of 12 (approximately 80%) experts agreed. Cases in which consensus was not reached were classified as "undefined." In the cases of severe CD, experts were also asked to further separate patients into those with a sagittal, coronal, or combined sagittal and coronal deformity, as well as to indicate the location of the main deformity (e.g., driver of deformity).

Statistical Analysis

Linear Regression and Cluster Analysis

A cluster analysis was performed on individuals with

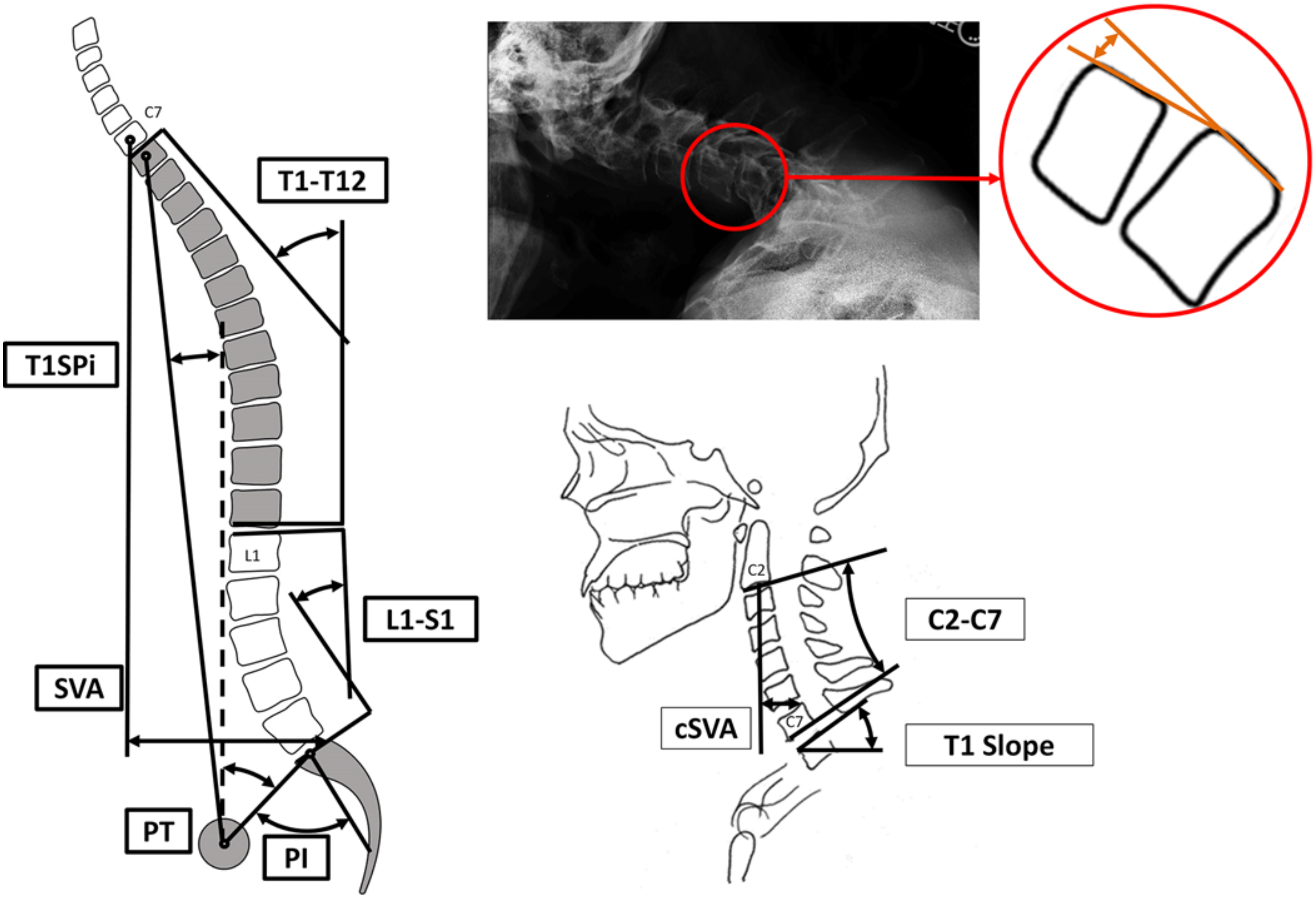


FIG. 1. The relevant angles measured in our study are delineated. The *red circle* with angle measurement represents focal kyphosis at a single segment. PI = pelvic incidence; PT = pelvic tilt; SVA = sagittal vertical alignment; T1SPi = T1 spinopelvic inclination. Figure is available in color online only.

severe CD to categorize the patients based on sagittal deformity. An association between alignment and patient-reported outcomes was found for regional and focal cervical parameters. This was repeated for all flexion, extension, and neutral radiographs. This was done using a linear regression analysis and identifying a Pearson correlation coefficient.

We then performed a two-step cluster analysis using a combination of hierarchical cluster and k-means cluster analysis. The parameters used for cluster analysis were lateral alignment and all parameters that correlated significantly to patient-reported outcomes (i.e., those from the linear regression analysis outlined above).

Comparison Between Groups

A comparison was then performed between the groups created after our cluster analysis. We compared cervical neutral sagittal alignment and neutral to extension alignment. A post hoc analysis was then performed using a Bonferroni correction factor. A comparison was also done based on the main driver of deformity between the two groups. This referred to whether deformity was driven by the cervical versus the cervicothoracic spine. Finally, a comparison was done regarding patient-reported outcomes between groups.

Results

Cohort Description

There were 146 patients who met our inclusion criteria. Of these patients, 83 (56.8%) were determined to have severe CD by our expert panel, 51 patients (34.9%) were found to have nonsevere CD, and 12 patients (8.2%) remained unclassified due to a lack of consensus by the expert panel. Of the patients with severe CD, 8 patients (9.6%) were found to have a coronal deformity and 75 (90.4%) were determined to have a sagittal deformity. The patients with sagittal deformity were retained for further analysis.

The patients with a sagittal-plane deformity had a mean age of 63.4 ± 8.8 years, 66% were women, and the mean body mass index was 29.2 ± 7.8 kg/m^2. The mean preoperative alignment in this cohort is outlined in Table 2. We also took note of the change in cervical parameters between neutral and extension radiographs. These are outlined in Table 3.

Correlations

The results of our linear regression analysis between cervical radiographic parameters and patient-reported outcome scores are outlined in Table 4. In this table, only

TABLE 2. Preoperative radiographic cervical alignment of patients with severe CD

Radiographic Parameter	Measurement
T1S (°)	36.8 ± 20.4
C2–7 (°)	−9.4 ± 25.9
TS-CL (°)	46.1 ± 19.8
cSVA (mm)	48.8 ± 18.1
Max kyphosis (°)	−13.8 ± 9.7

TABLE 4. Results of linear regression analysis of cervical radiographic parameters and patient-reported outcomes

Radiographic Parameter	Clinical Outcome Measure	Correlation Coefficient
Max focal kyphosis	mJOA	0.27
C2–7 flexibility	NRS neck	0.31
TS-CL flexibility	NRS neck	−0.36
Max kyphotic flexibility	NRS neck	0.27

statistically significant results were included. The rest of the correlations were nonsignificant. When referring to the flexibility of measurements, we are referring to the change seen between the neutral lateral cervical radiograph and the extension lateral cervical radiograph.

Two-Step Cluster Analysis

A cluster analysis was then performed with the variables deemed to be significant correlates to patient-reported outcome scores and lateral alignment. We found 3 distinct groups with a silhouette measure of 0.3. This demonstrates fair cohesion and separation between cohorts. Group 1 refers to the "flat neck" group with 30 patients (46.2%). Group 2 refers to the "focal deformity" cohort with 20 patients (30.8%). Finally, group 3 refers to the "cervicothoracic deformity" cohort with 15 patients (23.1%). These groups are summarized and illustrative cases are shown in Fig. 2. There were 10 patients who were unclassified due to at least one missing radiographic parameter. The top 3 most important parameters based on the cluster analysis were as follows: 1) lateral neutral cSVA, 2) change in TS-CL between lateral neutral radiograph and lateral extension radiograph, and 3) neutral T1 slope (T1S).

Comparison Between Groups

To better differentiate the 3 groups from our cluster analysis, we performed an ANOVA and post hoc analysis. The results are summarized in Table 5. We found that there was a smaller cSVA in the focal deformity cohort (group 2). There was a larger cervical lordosis found in patients with cervicothoracic deformity (group 3). There was also larger TS-CL in patients with a flat neck. We did not note any statistically significant differences in patient-reported outcomes (NDI, mJOA, NRS neck, or NRS back scores) between groups.

TABLE 3. The difference in measurements between neutral lateral and extension lateral cervical radiographs

Parameter	Measurement*
T1S (°)	4.4 ± 8.0
C2–7 (°)	−9.1 ± 11.4
TS-CL (°)	14.0 ± 13.4
cSVA (mm)	9.5 ± 10.1
Max kyphosis (°)	−3.2 ± 7.4

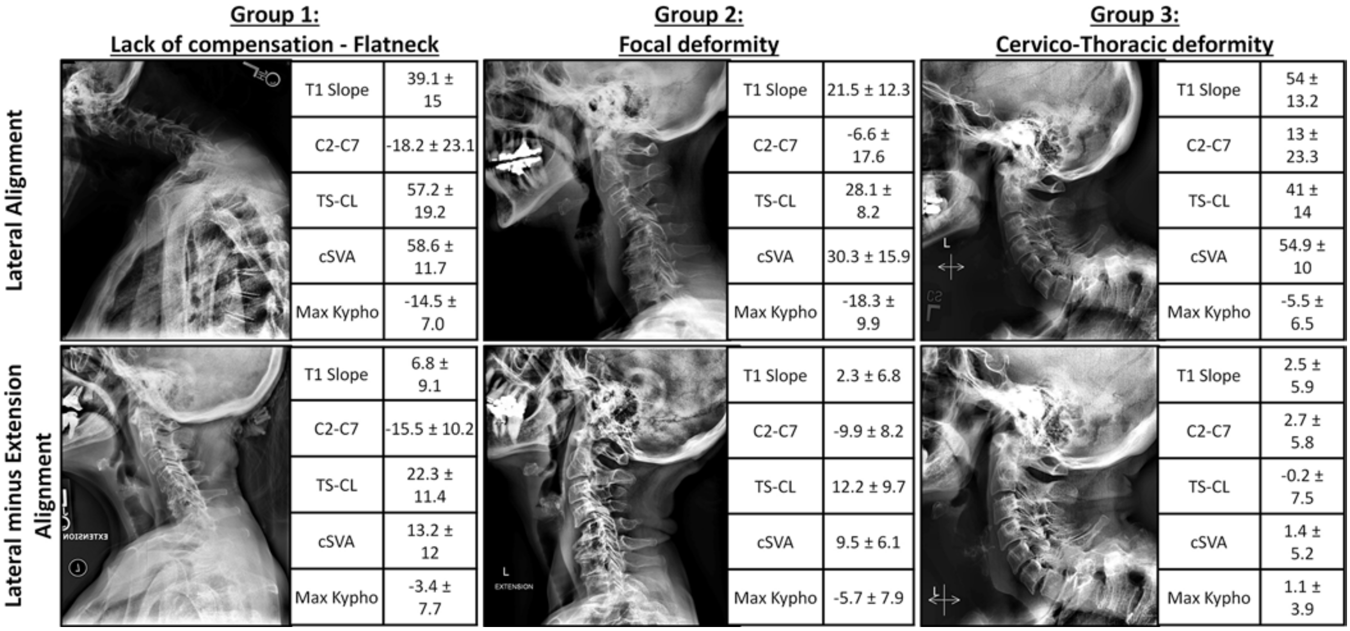
* The measurements reflect the difference between measurements on neutral lateral radiographs and extension lateral cervical radiographs.

The final step of our analysis was to determine the main driver of CD. In the flat-neck cohort, 80% had a cervicothoracic driver. In the focal deformity subgroup, 99.3% of patients had a cervical driver of deformity. Finally, in the cervicothoracic cohort, 55% of patients had a cervical driver and 45% had a cervicothoracic driver of deformity. These differences in proportion to cervical and cervicothoracic drivers of deformities were statistically significant between groups ($p < 0.001$).

Discussion

We were able to perform a two-step cluster analysis of patients with severe CD to better understand the nature of sagittal deformity in severe CD. We found that distinct clinical entities exist based on specific findings on dynamic and static radiographs. Specifically, in our group 1 cervical flat-neck group, these patients had a large cervical mismatch (TS-CL) despite having some ability to compensate for their deformity. In group 2 (focal deformity), the patients had a large focal kyphosis between 2 adjacent vertebrae without a necessarily large regional cervical kyphosis. Global alignment of the cervical spine for these patients with focal deformity, however, was not compromised due to large compensation in T1S (< 22°). In group 3, there were patients who had a cervicothoracic deformity. For this third group, there was a cervical mismatch due an extremely large T1S (> 50°). These patients had hyperlordosis of the cervical spine as a compensatory mechanism that was not able to compensate enough to meet the T1S and resulted in CD.

Our first subgroup of patients with a flat-neck deformity may require specific surgical interventions for correction and special pre- and postoperative interventions for optimal outcomes. Patients with extreme flat neck can also be categorized as having a "chin-on-chest" deformity or those patients with poor muscle health who are unable to maintain horizontal gaze. Given that the deformity is more likely passively correctable, the use of preoperative traction might be avoided for these patients.[24] Flat-neck patients might also benefit from longer-length cervicothoracic constructs that extend into the cervical spine and distally past the cervicothoracic junction, given their flexible CD.[8] In patients without prior spine surgery, this may entail a CD operation that extends distally from the cervical spine to the upper thoracic spine. In patients with prior fusions or thoracolumbar reconstructions, revision surgery would likely need to extend proximally past the cervicothoracic junction into the upper cervical spine. As



Group 1: Lateral Alignment	
T1 Slope	39.1 ± 15
C2-C7	-18.2 ± 23.1
TS-CL	57.2 ± 19.2
cSVA	58.6 ± 11.7
Max Kypho	-14.5 ± 7.0

Group 2: Lateral Alignment	
T1 Slope	21.5 ± 12.3
C2-C7	-6.6 ± 17.6
TS-CL	28.1 ± 8.2
cSVA	30.3 ± 15.9
Max Kypho	-18.3 ± 9.9

Group 3: Lateral Alignment	
T1 Slope	54 ± 13.2
C2-C7	13 ± 23.3
TS-CL	41 ± 14
cSVA	54.9 ± 10
Max Kypho	-5.5 ± 6.5

Group 1: Lateral minus Extension Alignment	
T1 Slope	6.8 ± 9.1
C2-C7	-15.5 ± 10.2
TS-CL	22.3 ± 11.4
cSVA	13.2 ± 12
Max Kypho	-3.4 ± 7.7

Group 2: Lateral minus Extension Alignment	
T1 Slope	2.3 ± 6.8
C2-C7	-9.9 ± 8.2
TS-CL	12.2 ± 9.7
cSVA	9.5 ± 6.1
Max Kypho	-5.7 ± 7.9

Group 3: Lateral minus Extension Alignment	
T1 Slope	2.5 ± 5.9
C2-C7	2.7 ± 5.8
TS-CL	-0.2 ± 7.5
cSVA	1.4 ± 5.2
Max Kypho	1.1 ± 3.9

FIG. 2. The 3 groups of sagittal cervical alignment based on our two-step cluster analysis. An example case is shown for each subcategory of severe CD. T1S, C2–7, TS-CL, and maximum kyphosis (Max Kypho) are measured in degrees, and cSVA is measured in millimeters.

with many issues in spinal surgery, and adult spinal deformity in particular, approaches for correction of a patient's deformity remain controversial.[22]

Patients in the focal deformity group, in contrast, might require focal correction. These patients likely do not have a large global CD, and addressing the specific levels with malalignment may provide significant correction. This might allow for constructs that stay within the cervical spine.

Finally, in the cervicothoracic deformity cohort, there is a longer, more sweeping deformity with the individual having minimal ability to fully compensate alignment with extension, largely due to the high T1S. This cohort of patients would likely require further study to answer a multitude of clinical questions.[15] These include which level should be used as the upper instrumented vertebra or the lower instrumented vertebra in the setting of a thoracolumbar fusion or whether this cohort of patients is more at risk of proximal junctional kyphosis, in addition to adequately characterizing the location of the deformity driver that is resulting in the high T1S. For example, if the high T1S is driven by a large proximal junctional kyphosis in the lower thoracic spine, adequate correction of the lower thoracic kyphosis may, in some cases, result in a normalization of the T1S without necessitating a fusion that extends into the cervical spine. We hope that classify-

TABLE 5. Comparison of neutral and reserve of extension between groups using an ANOVA

Radiographic Parameter	Group 1 (n = 30)	Group 2 (n = 20)	Group 3 (n = 15)	p Value	G1 vs G2	G1 vs G3	G2 vs G3
Lateral							
T1S (°)	39.1 ± 15.0	21.5 ± 12.3	54.0 ± 13.2	<0.001	<0.001	0.003	<0.001
C2–7 (°)	−18.2 ± 23.1	−6.6 ± 17.6	13.0 ± 23.3	<0.001	0.207	<0.001	0.030
TS-CL (°)	57.2 ± 19.2	28.1 ± 8.2	41.0 ± 14.0	<0.001	<0.001	0.005	0.052
cSVA (mm)	58.6 ± 11.7	30.3 ± 15.9	54.9 ± 10.0	<0.001	<0.001	1.000	<0.001
Max kyphosis (°)	−14.5 ± 7.0	−18.3 ± 9.9	−5.5 ± 6.5	<0.001	0.306	0.002	<0.001
Flex/ext							
T1S (°)	6.8 ± 9.1	2.3 ± 6.8	2.5 ± 5.9	0.084	0.150	0.267	1.000
C2–7 (°)	−15.5 ± 10.2	−9.9 ± 8.2	2.7 ± 5.8	<0.001	0.090	<0.001	<0.001
TS-CL (°)	22.3 ± 11.4	12.2 ± 9.7	−0.2 ± 7.5	<0.001	0.003	<0.001	0.002
cSVA (mm)	13.2 ± 12.0	9.5 ± 6.1	1.4 ± 5.2	0.001	0.511	<0.001	0.036
Max kyphosis (°)	−3.4 ± 7.7	−5.7 ± 7.9	1.1 ± 3.9	0.022	0.786	0.141	0.019

Flex/ext = flexion/extension; G = group.

ing this cohort of patients as a separate clinical entity of CD might facilitate more specific study on these types of surgical/clinical questions.

Our findings underscore once again the importance of dynamic radiographs in evaluating patients with CD. As has been stated previously, "balance is not static but dynamic," and our understanding of the primary driver of deformity is incomplete without thorough evaluation of a patient's ability to compensate for their deformity, as evidenced on flexion and extension radiographs.[6,18] This reserve of extension, as measured by flexion/extension radiographs, is vital for preoperative planning. It signals whether an osteotomy or a front-back construct might be necessary. These radiographs also help demonstrate the driver of the cervicothoracic deformity itself and areas within the cervical spine that require focused correction of deformity.

It was surprising for our group to find that HRQOL scores were not significantly correlated to overall cervical sagittal alignment measured on neutral radiographs. Tang et al. did show a correlation with sagittal alignment and HRQOL scores, but these were in postoperative patients.[10,25] We believe that in native cervical spines without surgery, there might be a greater role for an analysis of extension radiographs to determine patients' ability to restore their sagittal alignment. Further investigations may be necessary to determine how well patients are able to compensate for residual deformity after cervical spinal fusion.

There are several important limitations to this study. It is a retrospective review of a database of patients preselected by clinicians/researchers for enrollment into studies. It is also a relatively small sample size of patients with severe CD (75 patients). We also did not test/retest our expert panel to ensure consistent classification of our patient population. There was no way for us to standardize flexion/extension radiograph protocols for all patients in the study across a myriad of study sites, and we did not include supine imaging, which might have shown flexibility not captured in flexion/extension radiographs. Nonetheless, this a relatively large cohort based on a review of the current literature on a subset of patients with CD.

Conclusions

We have classified severe CD based on 3 categories of sagittal alignment. In order to correct deformity, we believe this classification will help surgeons better understand the driving forces behind a patient's CD. Our analysis highlights the importance of whether patients are able to properly compensate for their deformity with extension, as measured on extension radiographs. Further investigation is required to determine a classification of CD that can guide surgical treatment.

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Disclosures

Dr. Passias reports being a paid presenter or speaker for AlloSource, the Cervical Scoliosis Research Society, Globus Medical, Medicrea, SpineWave, and Zimmer Biomet. Dr. Ames reports he is an employee of the University of California, San Francisco; he is a consultant for DePuy Synthes, Medtronic, Stryker, Medicrea, K2M, and Zimmer Biomet; he receives royalties from Stryker, Zimmer Biomet, DePuy Synthes, NuVasive, Next Orthosurgical, K2M, and Medicrea; he does research for Titan Spine, DePuy Synthes, and the International Spine Study Group (ISSG); he is on the editorial board of *Operative Neurosurgery*; he has received grant funding from the Scoliosis Research Society; he is on the executive committee of ISSG; and he is the director of Global Spine Analytics. Dr. Shaffrey reports he owns stock in NuVasive; he is a consultant for Medtronic, NuVasive, SI-Bone, and Siemens; and he holds patents with Medtronic, NuVasive, Zimmer Biomet, and SI-Bone. Dr. Mundis reports being a consultant for NuVasive, K2M, Viseon, and SeaSpine; and he owns stock in NuVasive and Viseon. Dr. Gutpa reports being a consultant for Medtronic and DePuy Synthes; he owns stock in J&J and P&G; he receives royalties from Innomed; he has received funds for travel expenses from Medicrea; and his institution receives grant funding for a fellowship from AOSpine and OMeGA. Dr. Klineberg reports being a consultant for DePuy Synthes, Stryker, and Medicrea; and he has received fellowship grant funding and honoraria from AOSpine. Dr. Smith reports being a consultant for Zimmer Biomet, NuVasive, Stryker, AlloSource, and Cerapedics; he received clinical or research support for the present study from DePuy Synthes and ISSG, which also provided funding for non–study-related clinical or research efforts that he oversees; he has received fellowship support from NREF and AOSpine; he receives royalties from Zimmer Biomet and NuVasive; and he owns stock in Alphatec. Dr. Burton reports receiving clinical or research support for the present study from DePuy Synthes; he is a consultant for Bioventus; he has received funding of non–study-related clinical or research efforts that he oversees from Pfizer; and he holds a patent with DePuy Synthes. Dr. Schwab reports being a consultant for Globus Medical, Zimmer Biomet, K2M, and MSD; he has received funding for non–study-related clinical or research efforts that he oversees from DePuy Synthes, K2M, NuVasive, Medtronic, AlloSource, Orthofix, and SI-Bone through ISSG; and he has paid speaking/teaching arrangements with Globus Medical, Zimmer Biomet, K2M, and MSD. Dr. V. LaFage reports she has received funding for non–study-related clinical or research efforts that she oversees from DePuy Synthes, K2M, NuVasive, Medtronic, AlloSource, Orthofix, and SI-Bone through ISSG; she is a consultant for Globus Medical; and she has paid teaching/speaking arrangements with DePuy Synthes. Mr. R. LaFage reports owning stock in Nemaris.

Author Contributions

Conception and design: R Lafage, Kim. Acquisition of data: Elysee. Analysis and interpretation of data: R Lafage, Elysee. Drafting the article: R Lafage, Kim, Virk. Critically revising the article: R Lafage, Kim, Virk, Passias, Ames, Shaffrey, Mundis, Protopsaltis, Gupta, Klineberg, Smith, Burton, Schwab, V Lafage. Reviewed submitted version of manuscript: R Lafage, Kim, Virk, Passias, Ames, Shaffrey, Mundis, Protopsaltis, Gupta, Klineberg, Smith, Burton, Schwab, V Lafage. Approved the final version of the manuscript on behalf of all authors: R Lafage. Statistical analysis: R Lafage. Study supervision: V Lafage.

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