Washington University School of Medicine
Digital Commons@Becker

Open Access Publications

2018

The effect of aging on cervical parameters in a normative North American population

Justin Iorio

Virginie Lafage

Renaud Lafage

Jensen K. Henry

Dan Stein

See next page for additional authors

Follow this and additional works at: https://digitalcommons.wustl.edu/open_access_pubs

Authors

Justin Iorio, Virginie Lafage, Renaud Lafage, Jensen K. Henry, Dan Stein, Lawrence G. Lenke, Munish Gupta, Michael P. Kelly, Brenda Sides, and Han Jo Kim

The Effect of Aging on Cervical Parameters in a Normative North American Population

Justin Iorio, MD[1], Virginie Lafage, PhD[1], Renaud Lafage, MS[1],
Jensen K. Henry, MD[1], Dan Stein, BS[1], Lawrence G. Lenke, MD[2],
Munish Gupta[3], Michael P. Kelly, MD[3], Brenda Sides[3],
and Han Jo Kim MD[1]

Abstract

Study Design: Retrospective cohort study.

Objectives: To investigate age-based changes in cervical alignment parameters in an asymptomatic population.

Methods: Retrospective review of a prospective study of 118 asymptomatic subjects who underwent biplanar imaging with 3-dimensional capabilities. Demographic and health-related quality of life data was collected prior to imaging. Patients were stratified into 5 age groups: <35 years, 35-44 years, 45-54 years, 55-64 years, and ≥65 years. Radiographic measurements of the cervical spine and spinopelvic parameters were compared between age groups. The normal distribution of parameters was assessed followed by analysis of variance for comparison of variance between age groups.

Results: C2-C7 lordosis, C0-C7 lordosis, and T1 slope demonstrated significant increases with age. C0-C7 lordosis was significantly less in subjects <35 years compared with ≥55 years. Significant differences in T1 slope were identified in patients <35 versus ≥65, 35-44 versus ≥65, and 45-54 versus ≥65 years. T1 slope demonstrated a positive correlation with age. Horizontal gaze parameters did not change linearly with age and mean averages of all age groups were within 10° of one another. Cervical kyphosis was present in approximately half of subjects who were <55 compared with approximately 10% of subjects ≥55 years. Differences in pelvic tilt, pelvic incidence-lumbar lordosis, and C7-S1 sagittal vertical axis were identified with age.

Conclusions: C0-C7 lordosis, C2-C7 lordosis, and T1 slope demonstrate age-based changes while other cervical and horizontal gaze parameters remain relatively constant with age.

Keywords

cervical alignment, age-based alignment, horizontal gaze, asymptomatic population

Introduction

The number of cervical spine surgeries performed in the United States has increased over the past several decades.[1] One of the goals of surgical correction is restoration of normal anatomic alignment; however, age-based normative values for cervical parameters have not been well defined. Prior studies have reported radiographic parameters in asymptomatic subjects, but these studies dichotomized groups into <30 versus >60 years old,[2] but failed to provide a comprehensive analysis of cervical parameters, including overall (C0-C7) lordosis, horizontal gaze parameters, and cervical sagittal vertical axis,[2-4] and did not obtain baseline health-related quality of life (HRQOL) measurements.[2,3,5-7] Additionally, studies have been limited by the inclusion of mixed populations of

asymptomatic and surgical patients,[5,7] focused on occipitocervical, rather than cervical, relationships[8] and reporting of patients from other countries,[2,6,8] which may differ from a North American population based on variability of spinal parameters between races.[9,10]

[1] Hospital for Special Surgery, New York, NY, USA
[2] Columbia University Medical Center, New York, NY, USA
[3] Washington University, St Louis, MO, USA

Corresponding Author:
Han Jo Kim, Spine Care Institute, Hospital for Special Surgery, 523 East 72nd Street, 2nd Floor, New York, NY 10021, USA.
Email: hanjokimmd@gmail.com

Furthermore, cervical alignment correlates with HRQOL scores, as demonstrated by Tang et al,[5] and Villavicencio et al[11] who reported more favorable clinical outcomes in patients with cervical sagittal vertical axis (SVA) less than 40 mm and greater cervical lordosis after cervical spine surgery. Recent studies have described age-based changes among spinopelvic parameters[12] as well as reciprocal changes in cervical sagittal alignment secondary to spinopelvic parameters.[13] Consequently, it is likely that cervical parameters change with age. Therefore, identifying age-adjusted normative cervical parameters will provide radiographic guidelines for the assessment and management of cervical spine patients. Additionally, the inclusion of thoracic and spinopelvic parameters on full-length standing radiographs will provide additional insight into the relationships between spinal segments.

The purpose of this study was to investigate cervical alignment parameters in North American subjects without symptomatic spinal pathology. Our primary hypothesis was that sagittal cervical radiographic parameters vary with age. A secondary hypothesis is that the changes in spinopelvic parameters will parallel those of previous studies,[12] and will demonstrate relationships with the cervical spine. The identification of age-adjusted cervical parameters may provide benchmarks for both nonsurgical and surgical treatment.

Methods

This study is a single-center retrospective review of a prospective database of 118 asymptomatic adult subjects who underwent biplanar imaging with 3-dimensional capabilities (EOS Imaging, Paris, France) between October 2014 and October 2015 to determine age-adjusted alignment parameters of the cervical spine. Institutional review board approval was obtained for the study. Patients aged 18 to 79 years were included if they did not have a history of back or neck pain and if they passed the exclusion criteria. Exclusion criteria were the following: coronal deformities (Cobb angle >10°); a history of previous spine surgery; history of hip or knee arthroplasty or any other realignment surgery of the lower extremities; complaints of back pain or neck pain that resulted in missed work, affected activities of daily living, participation in recreational activities, or required narcotic pain medication; degenerative or pathologic condition of the spine that necessitated physician intervention; nonambulatory patients; history of neuromuscular disorders, inflammatory arthritis, or congenital anomalies; and pregnancy. Solicitation of volunteers was performed via advertising and providing a gift card with a value of $25. Demographic data (age and body mass index [BMI]) and HRQOL data (Oswestry Disability Index [ODI] and Neck Disability Index [NDI] scores) were collected prior to imaging. Patients were divided into the following age groups: <35 years, 35-44 years, 45-54 years, 55-64 years, and >65 years.

Radiographic Analysis

Measurements of cervical, thoracic, and spinopelvic parameters were collected on sagittal EOS imaging via validated and dedicated software (Spineview, ENSAM Laboratory of Biomechanics, Paris, France).[14] Measurements were obtained by demarcating the margins of the superior and inferior endplates. Spinal parameters were generated using Matlab software (Matlab 2015b, MathWorks, Natick, MA). Standing, full-body EOS images were obtained with the patient standing in a relaxed position of comfort with their fingers resting on their clavicles and without any specific recommendation regarding horizontal gaze. Radiographic measurements were performed by one assessor followed by subsequent verification by a second assessor.

The cervical parameters included in this study were C0-C2 (angle between base of skull and inferior endplate of C2), C2-C7 (angle between inferior endplate of C2 and inferior endplate of C7), and C0-C7 lordosis (angle between foramen magnum and inferior endplate of C7); C2-C7 sagittal vertical axis (SVA; distance between a plumb line drawn from the midbody of C2 and the posterosuperior corner of C7); apex of cervical lordosis; T1 slope minus cervical lordosis (TS-CL); chin brow vertical angle (CBVA; angle subtended by a line tangential to the chin and supraorbital ridge, and a vertical reference line); slope of line of sight (SLS; angle between the horizontal and a line from the infraorbital rim and through the inner ear); McGregor slope (McGS; the angle subtended by a line extending from the hard palate and opisthion and a horizontal reference line); and the contribution of the upper cervical angle to total cervical lordosis (UpperC%), defined as C0-C2 divided by C0-C7 (Figure 1a and b).

Measurements of the thoracic spine included the T1 pelvic angle (TPA; angle subtended by a line drawn from the centroid of T1 to the femoral head axis and a line from the midpoint of the S1 endplate to the femoral head axis), T1 slope (T1 S; angle between a horizontal reference line and the superior endplate of T1), T4-12 kyphosis, and location of the apex of kyphosis. Spinopelvic measurements were performed as in previous studies[15] and included sacral slope (SS), pelvic tilt (PT), pelvic incidence (PI), pelvic incidence–lumbar lordosis (PI-LL) mismatch, L1-S1 lumbar lordosis (LL), C7-S1 SVA, and location of the apex of lumbar lordosis.

Statistical Analysis

The following data was collected for each of the 5 age groups: mean, range, standard deviation (SD), standard error (SE), and 95% confidence interval (CI). Statistical analyses were performed using SPSS 20.0 (IBM Corp, Armonk, NY). The normal distribution of parameters was assessed followed by analysis of variance for comparison of variance between age groups. Post hoc analysis were then completed to determine if the differences between specific age groups were statistically significant, as defined by $P \leq .05$. Pearson's correlations were calculated to examine the relationship between age and
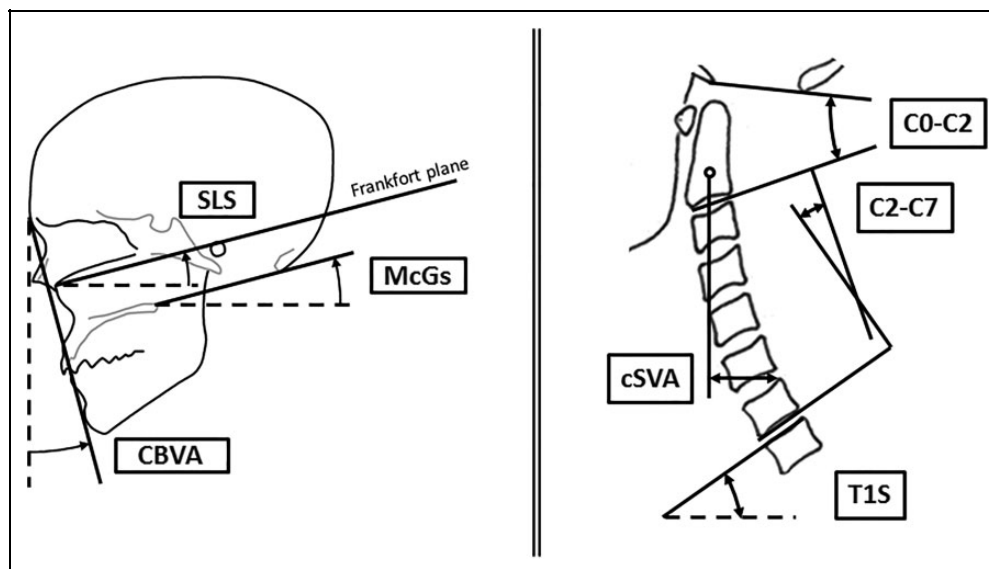
Figure 1. Illustrative explanation of horizontal gaze (a) and sagittal cervical parameters (b). SLS, slope of line of sight; McGs, McGregor slope; CBVA, chin brow vertical angle; C0-C2, occiput-C2 angle; C2-C7, C2-C7 angle; cSVA, cervical sagittal vertical axis; T1 S, T1 slope.

Table 1. Stratification of Groups Based on Age (N = 118).

	n	Percent	ODI	NDI
Gender				
Male	37	31.4		
Female	81	68.6		
Age group, years				
<35	30	25.4	0.9 ± 3.0	3.2 ± 3.1
35-44	18	15.3	3.0 ± 7.2	4.6 ± 5.3
45-54	17	14.4	1.1 ± 3.4	3.9 ± 4.2
55-64	21	17.8	1.3 ± 4.0	3.0 ± 3.4
≥65	32	27.1	2.1 ± 5.7	3.0 ± 5.9
Total	118	100		

Abbreviations: NDI, Neck disability Index; ODI, Oswestry Disability index.

cervical parameters. Correlation coefficients (r) were interpreted as follows: 0.00-0.29 no correlation, 0.30-0.49 weak correlation, 0.50-0.69 moderate correlation, 0.70-0.89 strong correlation, and 0.90-1.00 very strong correlation.

Results

Patient Population

A total of 118 subjects were enrolled (Table 1). The average age of the cohort was 50.5 ± 16.9 years and the average BMI measured 28 kg/m². A total of 31.4% of patients were male. The mean NDI and ODI scores were 3.39 ± 4.5 and 1.64 ± 4.80, respectively. There were no statistically significant differences between groups with regard to NDI ($P = .749$) and ODI ($P = .583$) scores.

Cervical Parameters

The values of cervical parameters are shown in Tables 2 and 3. C2-C7, C0-C7, and T1 S demonstrated significant increases with age. C0-C7 lordosis was not significantly different among patients <55 years. However, patients <35 years had less lordosis than those aged 55 to 64 ($P < .001$) and ≥65 ($P < .001$) years. C2-C7 lordosis was significantly greater in patients ≥65 years than in those <45 years ($P ≤ .03$). Patients <35 years were also found to be significantly less lordotic than patients aged 55 to 64 years ($P = .001$). Significant differences in T1 S were identified in patients <35 versus ≥65 years ($P < .001$), 35-44 versus ≥65 years ($P = .005$), and 45-54 versus ≥ 65 years ($P = .009$). T1 S demonstrated a moderate, positive correlation with age ($r = 0.446$, $P < .001$) as shown in Table 2. McGS, SLS, and CBVA did not change linearly with age despite statistical significance, and mean averages of all age groups were within 10° of one another. C0-C2 lordosis and ratio of upper cervical to total cervical angle (UpperC%) were not significantly different among groups. Cervical kyphosis was present in approximately half of subjects in the <35, 35- to 44-, and 45- to 54-year age groups (56.7%, 50.0%, and 47.1%, respectively) compared with 9.5% of subjects between 55 and 64 years and 12.5% of those ≥65 years. Younger patients had a significantly higher rate of cervical kyphosis compared with older patients ($P = .005$). T1S-CL and cSVA were not significantly different between groups and failed to show a relationship with age. The mean apex of cervical lordosis was located at C5 in all groups.

Thoracic Parameters

T1 pelvic angle was similar among all age groups and failed to correlate with age (mean, 2.9° ± 1.0°). The difference in thoracic kyphosis from T4-12 was not statistically significant among groups. Mean kyphosis measured between 37° and 45° in all cohorts and the overall average thoracic kyphosis for

Table 2. Cervical Sagittal Radiographic Parameters.

Age (Years)	C0-C2 (deg)	C2-C7 (deg)	C0-C7 (deg)	T1S-CL (deg)	T1 S (deg)	cSVA (mm)
<35	19.1 ± 9.7	−2.2 ± 13.8	17.0 ± 12.7	24.2 ± 10.1	22.0 ± 8.1	28.4 ± 16.7
35-44	23.3 ± 7.9	1.6 ± 7.8	24.8 ± 6.8	21.8 ± 8.0	23.4 ± 5.6	23.4 ± 14.1
45-54	21.6 ± 9.3	3.6 ± 11.1	25.2 ± 10.2	19.9 ± 8.8	23.5 ± 7.4	26.2 ± 26.2
55-64	19.7 ± 7.7	10.7 ± 9.9	30.6 ± 9.1	17.6 ± 8.9	28.4 ± 6.9	22.7 ± 15.6
≥65	21.0 ± 7.6	11.8 ± 12.1	32.7 ± 11.0	20.6 ± 10.3	32.5 ± 11.5	30.1 ± 15.3
P	.526	<.001*	<.001*	.170	<.001*	.381

Abbreviations: CL, cervical lordosis; cSvA, cSVA, cervical sagittal vertical axis; T1 S, T1 slope.
*Statistically significant.

Table 3. Horizontal Gaze Radiographic Parameters.

Age (Years)	CBVA (deg)	SLS (deg)	McGS (deg)
<35	6.0 ± 7.1	5.4 ± 7.8	7.8 ± 8.1
35-44	−1.8 ± 6.8	−2.7 ± 5.6	0.8 ± 4.9
45-54	0.7 ± 9.6	−1.6 ± 9.3	1.6 ± 7.3
55-64	1.3 ± 8.7	−1.7 ± 9.0	0.9 ± 9.5
≥65	1.7 ± 1.7	0.1 ± 7.7	2.2 ± 7.9
P	.033*	.004*	.007*

Abbreviations: CBVA, chin brow vertical angle; McGS, McGregor slope; SLS, slope of line of sight.
*Statistically significant.

the entire group was 41.5°. The mean apex of thoracic kyphosis was located at T7 in all groups.

Spinopelvic Parameters

Significant between-group differences were identified for PT, PI-LL mismatch, and C7-S1 SVA (Table 4). Specifically, PT was found to be significantly greater in subjects aged 55-64 years ($P = .036$) and ≥65 years ($P < .001$) compared with those <35 years. PI-LL mismatch was found to differ significantly between subjects ≥65 compared with those <35 years ($P = .001$); C7-S1 SVA was not significantly different in patients <65 years, but significant differences were observed in subjects <35 ($P < .001$), 35-44 ($P = .010$), 45-54 ($P = .001$), and 55-64 ($P = .004$) compared with patients ≥65 years. Pelvic incidence, sacral slope, lumbar lordosis did not vary with age. The average apex of lumbar lordosis was located at L3 in all groups.

Discussion

Previous studies have not comprehensively analyzed changes in cervical alignment with increasing age in an asymptomatic North American population. In our study, we found significant increases in C2-C7 and C0-C7 lordosis with age, without a reciprocal change in C0-C2 angle. Additionally, at least 50% of patients <45 years are kyphotic from C0-C7. T1 S, which represents the angle of T1 to a horizontal reference line, is also significantly greater in older than in younger patients. Horizontal gaze parameters (CBVA, SLS, McGS) did not demonstrate a meaningful correlation with age. PT, PI-LL, and C7-S1 SVA

are significantly different between certain age groups, which is in agreement with prior research.[12]

C2-C7, C0-C7, and T1 S angles significantly increase with age in an asymptomatic North American cohort. Specifically, differences in C0-C7 and C2-C7 angles are present in patients <35 compared with those ≥55 years. A mean difference in C0-C7 lordosis of approximately 15° was found between patients <35 and ≥55 years; a similar difference was observed for C2-C7 lordosis. C0-C2 and the contribution of the upper cervical angle to total cervical lordosis (UpperC%) did not change with age, suggesting that the increase in C0-C7 lordosis is driven by an increase in C2-C7 angle without any change in C0-C2. C0-C2 lordosis may not have changed significantly because the majority of flexion-extension occurs at the occiput-C1 articulation. An increase in C0-C2 lordosis with age would theoretically reduce the amount of extension reserve, thereby negatively affecting the ability to navigate a 3-dimensional environment. Horizontal gaze parameters did not vary linearly with age and meaningful trends were not observed between groups. Mean values for McGS, CBVA, and SLS were within a 10° range between all age groups, reflecting a relatively constant position over time. The unchanged position of the head (and therefore the eyes) likely reflects a requirement of humans to visualize a constant degree of environment; changing these parameters would result in either a more downward or upward gaze, which would not be advantageous.

T1 S is significantly greater in patents ≥65 compared with patients <55 years old, which likely represents a response to increasing C2-C7 SVA and PI-LL mismatch (or decreasing lumbar lordosis) in the setting of fixed thoracic kyphosis. These changes in alignment would drive an increase in T1 S and thus greater cervical lordosis as a compensatory measure. C2-C7 SVA, a measure of cervical offset, did not increase in age as has been found with C7-S1 SVA in our study as well as previous research.[12] Rather, C2-C7 became more lordotic possibly to compensate for increasing C7-S1 SVA, PI-LL mismatch, and T1 S. Failure to increase cervical lordosis with age would result in an impairment of horizontal gaze in addition to greater cervical offset and presumably worsening HRQOL as C2-C7 SVA increases beyond 40 mm.[5] In our study, significant changes in thoracic kyphosis were not observed despite alterations in cervical and spinopelvic parameters; it appears that the cervical and lumbar spine may change with age because they are less rigid than the thoracic region.

Table 4. Spinopelvic Parameters.

Age (Years)	SS (deg)	PT (deg)	PI (deg)	PI-LL (deg)	L1-S1 (deg)	C7-S1 SVA (mm)	T4-12 Kyphosis (deg)
<35	39.1 ± 8.3	9.3 ± 6.7	48.4 ± 10.9	12.6 ± 11.5	61.0 ± 13.2	−35.5 ± 34.4	37.8 ± 11.7
35-44	39.8 ± 8.4	13.9 ± 7.5	53.7 ± 10.5	5 ± 11.8	58.7 ± 12.4	−11.4 ± 32.0	39.2 ± 11.9
45-54	37.2 ± 7.7	13.5 ± 6.0	50.8 ± 8.5	6.5 ± 9.2	57.4 ± 10.7	−21.5 ± 27.2	38.2 ± 10.4
55-64	39.1 ± 8.7	15.3 ± 8.2	54.4 ± 14.7	7.2 ± 12.4	61.6 ± 11.6	−12.6 ± 34.1	45.3 ± 11.9
≥65	35.9 ± 9.9	17.3 ± 6.9	53.3 ± 11.3	12.5 ± 2.2	53.8 ± 14.4	27.2 ± 51.3	45.3 ± 14.5
P	.493	.001*	.312	.003*	.151	<.001*	.057

Abbreviations: LL, lumbar lordosis; PI, pelvic incidence; PT, pelvic tilt; SS, sacral slope; SVA, sagittal vertical axis.
*Statistically significant.

Increasing sagittal offset has been shown to negatively affect SF-36 (Short Form–36 health survey) and NDI scores in patients who underwent posterior cervical fusion[5] and other studies have shown worse HRQOL scores with abnormal cervical alignment.[16,17] However, age-related normative cervical parameters in a North American population have not been established. Hardacker et al[4] reported on overall cervical lordosis in asymptomatic subjects but failed to include a comprehensive analysis of other cervical parameters and did not stratify subjects by age. Park et al[2] compared cervical parameters in asymptomatic subjects who were less than 30 years of age and those who were at least 60 years, thus excluding patients between 30 and 60 years. In our study, we stratified patients into 5 age groups ranging from <35 to >65 years, and therefore included adult subjects of all ages. Additionally, radiographs in our study were obtained with biplanar imaging with 3-dimensional capabilities, which is in contrast to previous studies that used standard radiography.[2-4] Computer-assisted radiographic measurement, as used in our study, has been shown to have less standard measurement error than manual measurement for the determination of Cobb angles.[18]

In our study, we found that patients aged >55 years had, on average, approximately 15 more degrees of C0-C7 lordosis than those <35 years. However, C0-C2 was not found to be different between groups; consequently, the C2-C7 segment became significantly more lordotic with age as shown by the greater C2-C7 lordosis in patients >55 compared with those <35 years. These findings are in agreement with Park et al,[2] who reported no difference in C0-C2 angle with age but did find greater C2-C7 lordosis in subjects >60 compared with those <30 years. Although we found a similar trend of greater lordosis in older subjects, the average alignment in the <35 age group measured −2.2° with an average difference of 12.9° and 14° from patients in the 55-64 and ≥65 age groups, respectively. This is greater than the 4.7° difference between younger and older subjects reported by Park et al.[2] Yukawa et al[3] studied 1230 asymptomatic Japanese subjects and similarly concluded that C2-C7 lordosis increased with age. Their results stratified age groups by decade and direct comparisons are not possible. However, subjects in their third and fourth decades exhibited greater C2-C7 lordosis than patients <35 years in our study (mean, 8.4° vs −2.2°) and those in their seventh and eighth decades were more lordotic than patients in our study who were ≥65 years (mean, 18.7° vs 11.8°). The differences

between the studies may reflect variations in C2-C7 lordosis between Japanese and North American populations. Le Huec et al[8] found that C2-C7 lordosis averaged 4.8° in 106 asymptomatic volunteers and had a moderate, positive correlation with C7 slope ($r = 0.516$, $P < .001$). In our study, we measured T1 S rather than C7 slope, but also found that T1 S increased with C2-C7 lordosis. That T1 S changes with age has not been reported.

Cervical parameters were not stratified by age in the study by Le Huec et al,[8] though 33.96% of patients presented with cervical kyphosis. In our study, the overall rate of cervical kyphosis was 33.9%, which is identical to that of Le Huec et al.[8] As expected, cervical kyphosis occurred more commonly in younger patients (≥50% of patients <45 years) than in older patients (≤12.5% of patients ≥55 years). The kyphotic cervical alignments may be secondary to subjects' postures during EOS imaging rather than fixed kyphosis as seen in advanced degenerative conditions. Thus, kyphosis or straightening of the cervical spine in younger patients likely represents a flexible reversal of cervical lordosis rather than true kyphosis. In contrast, Been et al[19] found that total cervical lordosis, defined as the angle between the foramen magnum and inferior endplate of C7, did not vary between subjects <20 years of age compared with those between 20 and 50 years old. Additionally, kyphosis was only observed in less than 10% of all subjects.

This study is a radiographic assessment of asymptomatic patients and therefore has limited applicability to patients undergoing complex spinal realignment or other fusion procedures for symptomatic, degenerative conditions. Likewise, we cannot conclude that patients with symptomatic spinal pathology, such as cervical radiculopathy or stenosis, demonstrate similar radiographic parameters compared with the asymptomatic population in this study. However, our results provide a benchmark of several radiographic parameters that may assist in the evaluation of patients. An additional shortcoming is the limited sample size in our study and future research is aimed at analyzing larger cohorts. Another limitation includes the inability to determine the relationship between gender and cervical parameters. We acknowledge that gender may affect cervical alignment; the aim of our study was to focus on the effect of age. A retrospective study of the effect of gender on cervical lordosis did not find any difference in total cervical lordosis, but males were found to have greater C3-C7 lordosis and

females demonstrated more lordosis from the foramen magnum to C3.[19] Interrater reliability for the radiographic measurements was not reported in this study. However, the reliability of computer-assisted sagittal plane radiographs has been previously published.[20] Finally, asymptomatic subjects were enrolled but we did not control for pelvic incidence. It is possible that patients with a low PI have less cervical lordosis than patients with a high incidence, for example.

Cervical alignment correlates with HRQOL after cervical spine surgery, but a comprehensive analysis of cervical and horizontal gaze parameters has not been described. In our study, we identified several cervical and horizontal gaze parameters that remain relatively constant with age and established parameters that change with age. The evaluation of cervical parameters in patients with cervical spine disease and performing age-based comparisons of these results to an asymptomatic population may benefit future research and surgical plans.

Declaration of Conflicting Interests

Funding

References

1. Wang MC, Chan L, Maiman DJ, Kreuter W, Deyo RA. Complications and mortality associated with cervical spine surgery for degenerative disease in the United States. *Spine (Phila Pa 1976)*. 2007;32:342-347.

2. Park MS, Moon SH, Lee HM, et al. The effect of age on cervical sagittal alignment: normative data on 100 asymptomatic subjects. *Spine (Phila Pa 1976)*. 2013;38:E458-E463.

3. Yukawa Y, Kato F, Suda K, Yamagata M, Ueta T. Age-related changes in osseous anatomy, alignment, and range of motion of the cervical spine. Part I: radiographic data from over 1,200 asymptomatic subjects. *Eur Spine J*. 2012;21:1492-1498.

4. Hardacker JW, Shuford RF, Capicotto PN, Pryor PW. Radiographic standing cervical segmental alignment in adult volunteers without neck symptoms. *Spine (Phila Pa 1976)*. 1997;22:1472-1480.

5. Tang JA, Scheer JK, Smith JS, et al. The impact of standing regional cervical sagittal alignment on outcomes in posterior cervical fusion surgery. *Neurosurgery*. 2012;71:662-669.

6. Guo Q, Ni B, Yang J, et al. Relation between alignments of upper and subaxial cervical spine: a radiological study. *Arch Orthop Trauma Surg*. 2011;131:857-862.

7. Nunez-Pereira S, Hitzl W, Bullmann V, Meier O, Koller H. Sagittal balance of the cervical spine: an analysis of occipitocervical and spinopelvic interdependence, with C-7 slope as a marker of cervical and spinopelvic alignment. *J Neurosurg Spine*. 2015;23:16-23.

8. Le Huec JC, Demezon H, Aunoble S. Sagittal parameters of global cervical balance using EOS imaging: normative values from a prospective cohort of asymptomatic volunteers. *Eur Spine J*. 2015;24:63-71.

9. Lonner BS, Auerbach JD, Sponseller P, Rajadhyaksha AD, Newton PO. Variations in pelvic and other sagittal spinal parameters as a function of race in adolescent idiopathic scoliosis. *Spine (Phila Pa 1976)*. 2010;35:E374-E377.

10. Yong Q, Zhen L, Zezhang Z, et al. Comparison of sagittal spinopelvic alignment in Chinese adolescents with and without idiopathic thoracic scoliosis. *Spine (Phila Pa 1976)*. 2012;37:E714-E720.

11. Villavicencio AT, Babuska JM, Ashton A, et al. Prospective, randomized, double-blind clinical study evaluating the correlation of clinical outcomes and cervical sagittal alignment. *Neurosurgery*. 2011;68:1309-1316.

12. Lafage R, Schwab F, Challier V, et al. Defining spino-pelvic alignment thresholds: should operative goals in adult spinal deformity surgery account for age? *Spine (Phila Pa 1976)*. 2016;41:62-68.

13. Blondel B, Schwab F, Ames C, JC L, Smith J, Demakakos J. The crucial role of cervical aligment in regulating sagittal spino-pelvic alignment in human standing posture. Paper presented at: The 19th International Meeting on Advanced Spine Techniques; July 18-21, 2012; Istanbul, Turkey.

14. Champain S, Benchikh K, Nogier A, Mazel C, Guise JD, Skalli W. Validation of new clinical quantitative analysis software applicable in spine orthopaedic studies. *Eur Spine J*. 2006;15:982-991.

15. Schwab FJ, Blondel B, Bess S, et al. Radiographical spinopelvic parameters and disability in the setting of adult spinal deformity: a prospective multicenter analysis. *Spine (Phila Pa 1976)*. 2013;38:E803-E812.

16. Lafage R, Challier V, Liabaud B, et al. Natural head posture in the setting of sagittal spinal deformity: validation of chin-brow vertical angle, slope of line of sight, and McGregor's slope with health-related quality of life. *Neurosurgery*. 2016;79:108-115.

17. Youn MS, Shin JK, Goh TS, Kang SS, Jeon WK, Lee JS. Relationship between cervical sagittal alignment and health-related

quality of life in adolescent idiopathic scoliosis. *Eur Spine J.* 2016;25:3114-3119.

18. Sardjono TA, Wilkinson MH, Veldhuizen AG, van Ooijen PM, Purnama KE, Verkerke GJ. Automatic Cobb angle determination from radiographic images. *Spine (Phila Pa 1976).* 2013;38:E1256-E1262.

19. Been E, Shefi S, Soudack M. Cervical lordosis: the effect of age and gender. *Spine J.* 2017;17:880-888.

20. Rajnics P, Pomero V, Templier A, Lavaste F, Illes T. Computer-assisted assessment of spinal sagittal plane radiographs. *J Spinal Disord.* 2001;14:135-142.