



Variation of cervical sagittal alignment parameters according to gender, pelvic incidence and age

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Abstract

Purpose The aim was to describe radiographic cervical sagittal alignment variations according to age, gender and pelvic incidence (PI) and to investigate relationships with thoracic alignment.

Methods A total of 2599 individuals (5–93 years) without spinal deformity were studied. Cranial cervical parameters were: McGregor slope, occipita-C2 angle, McGregor-C2 lordosis and C1–C2 lordosis. Caudal cervical parameters were: C2–C7, cranial arch and caudal arch lordosis and C7- and T1-slope. A Bayesian inference compared parameter distributions. Correlations with spinopelvic and global alignment parameters were investigated.

Results Among cranial cervical parameters, variations of McGregor slope were non-significant. McGregor-C2 lordosis and C1–C2 lordosis were smaller in males and increased significantly during growth, whereas the occipito-C2 angle decreased ($Pr > 0.95$). The occipito-C2 angle was larger and McGregor-C2 lordosis was smaller in low PI ($Pr > 0.95$). Among caudal cervical parameters, C2–C7 lordosis and C7- and T1-slope were larger in males and increased after 50 years ($Pr > 0.95$). Lordosis changes were non-significant in the cranial arch, whereas values increased in the caudal arch after 35 years ($Pr > 0.95$). Caudal parameter differences were non-significant between PI groups. Strong correlations existed between C2–C7, caudal arch lordosis, C7-slope, T1-slope and thoracic kyphosis. The sagittal vertical axis C2 correlated with caudal arch lordosis and T1-slope ($\rho > 0.5$; $Pr > 0.95$).

Conclusion Cervical alignment parameters vary according to age, gender and PI. In the cranial cervical spine, changes occur mainly during growth. In the caudal cervical spine, lordosis increases in the caudal arch, which is related to thoracic kyphosis increase with age. The caudal cervical arch acts as a compensatory segment by progressive extension, allowing horizontal gaze.

Keywords Sagittal alignment · Cervical spine · Radiographic parameters · Age · Gender · Pelvic incidence

Introduction

The cervical spine represents a mobile segment between the head and trunk. Its sagittal alignment involves cognitive, neurosensory and motor control to maintain horizontal gaze during standing, walking and daily activities. In clinical practice, radiographic parameters are used when analyzing

cervical alignment, which represents a single momentum in static position. Radiographic alignment is considered when planning multiple-level subaxial or occipitocervical fusion [1, 2]. Cervical alignment is further considered in adolescent idiopathic scoliosis, where a relationship between thoracic hypokyphosis and decreased cervical lordosis exists [3–6]. In adult spinal deformity, cervical deformity might occur if the ability to maintain compensatory lordosis decreases. This results in anterior C2-plumbline migration and deterioration of health-related quality of life [7]. Although cervical and thoracolumbar relationships were described in deformed

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spine, there is a lack of normative values that could be used when treating spinal deformities.

Normal cervical and thoracic alignment is linked: Cervical lordosis correlates with T1-slope and thoracic kyphosis in children and adults [8–11]. The amount of cervical lordosis increases with age [12, 13]. In the thoracolumbar segment, an age-related thoracic kyphosis increase, lumbar lordosis decrease and spinopelvic adaptive phenomena were described [14, 15]. The physiologic amount of lumbar lordosis and thoracic kyphosis and the shape of thoracolumbar curvatures are related to the spinopelvic configuration [16].

It remains unclear how cervical alignment varies according to gender, age and spinopelvic alignment types. The amount of pelvic incidence influences thoracolumbar lordosis and kyphosis distribution, which might influence cervical alignment. We hypothesize that normal variations exist in individuals without spinal deformity.

The purpose of this cross-sectional study was to describe cervical parameters across age groups from the growth period to the elderly and to analyze differences by gender and pelvic incidence.

Materials and methods

Institutional review board approval (FC/2019-91) was obtained. Sagittal full spine radiographs (EOS Imaging, Paris, France) performed in 16 pediatric and adult spine centers were prospectively collected in a national registry from September 2019 to March 2020 and analyzed retrospectively. Clinical charts were screened, and radiographs of patients with limb length discrepancy less than 2 cm, spondylolysis, common low back or radicular leg pain were used. If several radiographs were available, the most recent image was selected. One radiograph was analyzed per patient. Exclusion criteria were: spinal deformity such as scoliosis, Scheuermann's kyphosis or spondylolisthesis more than grade 1, spinal or pelvic fractures, tumors, infection and neuromuscular disorders, previous spine surgery other than microdiscectomy and severe degenerative changes or osteoporosis leading to thoracolumbar deformity. Intervertebral disc degeneration, facet joint osteoarthritis and degenerative spondylolisthesis without thoracolumbar malalignment did not represent exclusion criteria since these radiographic changes commonly occur during aging.

In each center, a trained operator reconstructed radiographic landmarks between the cranial auditory meatus and femoral heads using KEOPS software (SMAIO, Lyon, France) (Fig. 1). Five senior spine surgeons then checked each reconstruction to minimize inter-rater errors. This method is reliable and superior to manual measurements [17]. Spinopelvic parameters were assessed: pelvic incidence (PI), pelvic tilt (PT) and sacral slope (SS), thoracic kyphosis

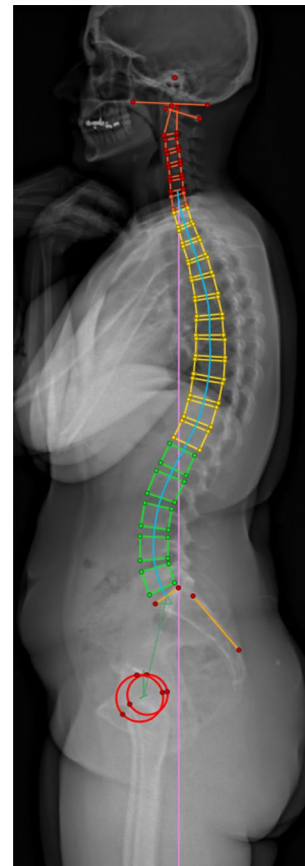


Fig. 1 KEOPS software reconstruction of each vertebra from C1 to the sacrum, cranial auditory meatus, McGregor line and femoral heads on lateral full spine EOS radiograph

(TK) between cranial T1 and caudal T12 endplates and lumbar lordosis (LL) between cranial L1 and S1 endplates. TK and LL were expressed as positive values. Among global alignment parameters, sagittal vertical axis (SVA) of C7 and C2 measured the distances between vertebral plumb lines and the posterior corner of S1 [18]. The odontoid-hip axis (OD-HA) determined the angle between the vertical axis originating from the midpoint between femoral heads and the axis joining the odontoid tip [19].

Cervical parameters were divided into cranial (C0–C2) and caudal (C3–C7) measurements. Among cranial parameters, McGregor slope represented the angle between the horizontal axis and McGregor line: the tangent to the caudal occiput joining the hard palate. Positive values reflected head flexion and negative values extension. The occipito-C2 angle was measured between McGregor line and the posterior odontoid cortical margin. McGregor-C2 lordosis was determined between McGregor line and C2 endplate. C1–C2 lordosis was measured between the anterior–posterior atlas axis and C2 endplate (Fig. 2). Among caudal parameters, C2–C7 lordosis was measured between caudal

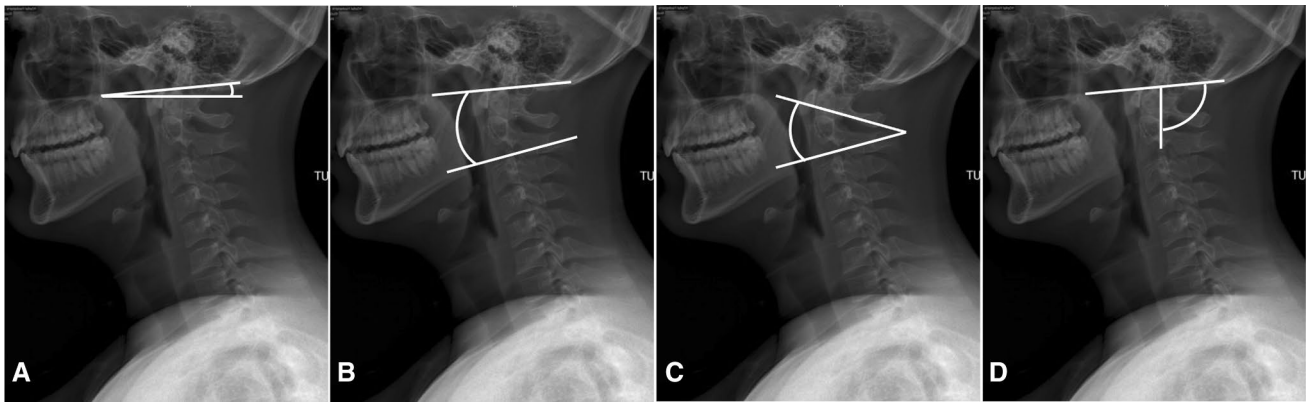


Fig. 2 Cranial cervical parameters: McGregor slope (A), occipito-C2 angle (B), McGregor-C2 lordosis (C) and C1–C2 lordosis (D)

C2 and C7 endplates. Cervical lordosis was then divided into a cranial arch between C2 and cervical apex (inflexion point in sigmoid alignment types) and into a caudal arch between cervical apex and cervicothoracic inflexion point. Segmental cervical lordosis was expressed as positive value and kyphosis as negative value. C7-slope and T1-slope were determined as angles between cranial endplates and the horizontal axis (Fig. 3). The cervical morphology was analyzed by counting the number of vertebrae included from C1 to cervicothoracic inflexion point. Cervical alignment patterns were described: global lordosis, global kyphosis, sigmoid shape with proximal kyphosis and distal lordosis, sigmoid shape with proximal lordosis and distal kyphosis (Fig. 4).

Statistical evaluation was performed with R software, version 3.5.3 (R Foundation for Statistical Computing, Vienna, Austria). A Bayesian inference using Markov chain Monte Carlo techniques with low informative priors was used. To infer the mean of indices and correlation coefficients between two indices, point estimates corresponded to the median of posterior distributions and credibility intervals to their 2.5 and 97.5 percentiles. Cervical alignment parameters

were compared by gender, age groups and PI. Ages were grouped by 5-year spans in children and adolescents, as growth-related changes might occur, and by 15-year spans in adults. The thresholds for PI were determined according to first and third quartiles: low PI $< 45^\circ$, medium PI 45° – 60° and high PI $> 60^\circ$. Significance tests were based on the probability of superiority for the difference between 2 means and for correlation coefficients (strong if $\rho < -0.5$ or $\rho > 0.5$). For PI the medium group and for ages the group 20–34 years were considered as references. The significance level was set at a 0.95 probability of superiority.

Results

A total of 2599 individuals, 1488 females and 1111 males, were included. The ages ranged from 5 to 93 years. The distribution by age was: 5–9 years $n = 94$, 10–14 years $n = 516$, 15–19 years $n = 448$, 20–34 years $n = 224$, 35–49 years $n = 424$, 50–64 years $n = 449$, 65–79 years $n = 340$ and > 80 years $n = 104$. The distribution by PI was: low PI

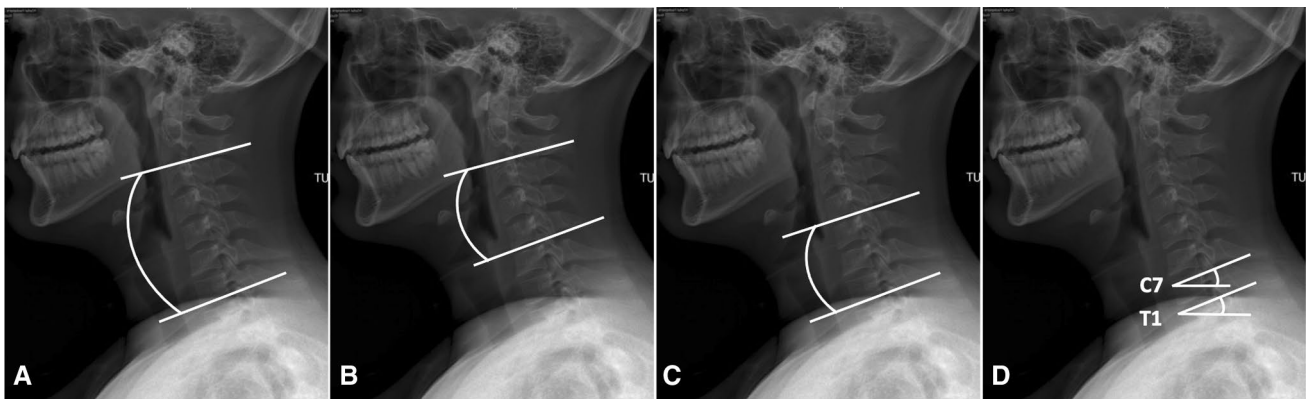


Fig. 3 Caudal cervical parameters: C2–C7 lordosis (A), cranial arch lordosis (B), caudal arch lordosis (C), C7- and T1-slope (D)

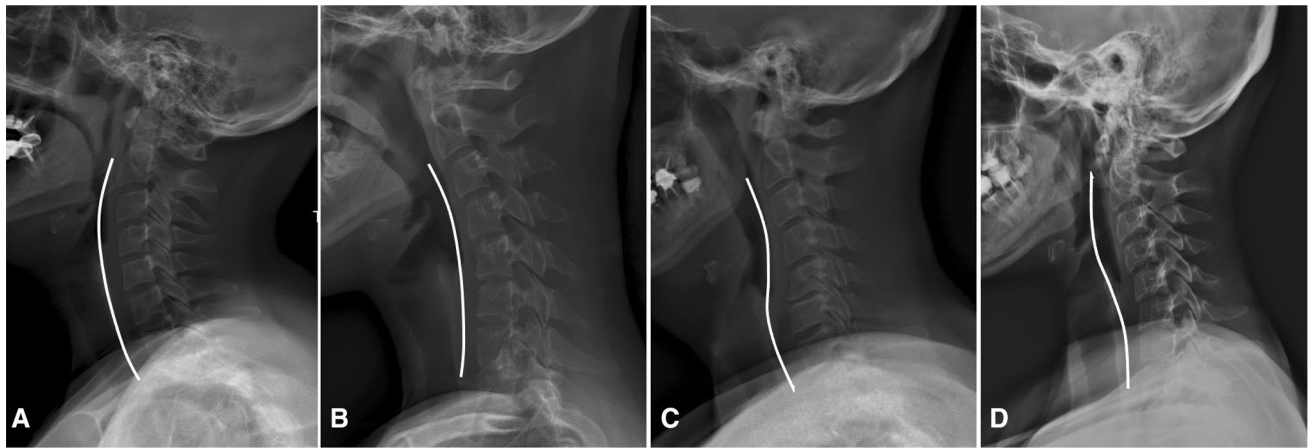


Fig. 4 Morphologic variations of cervical alignment patterns: global lordosis (A), global kyphosis (B), sigmoid shape with proximal kyphosis and distal lordosis (C), sigmoid shape with proximal lordosis and distal kyphosis (D)

$n = 972$, medium PI $n = 1123$ and high PI $n = 504$. Table 1 gives an overview of SVA-C7, SVA-C2, OD-HA, TK, LL, PI, PT and SS per gender, PI and age groups.

Cranial cervical parameters

Table 2 demonstrates the distribution of cranial cervical parameters by gender, PI and age. Variations of McGregor slope were small without significant differences between gender and age groups. Individuals with low PI had larger values ($Pr = 0.9606$). The occipito-C2 angle was similar in males and females. This parameter was significantly higher in low PI ($Pr > 0.9999$) and in adolescents from 10 to 19 years compared to young adults aged 20–34 years ($Pr > 0.95$). A progressive decrease was observed with

age. McGregor-C2 lordosis was significantly smaller in males ($Pr > 0.9999$) and in low PI ($Pr = 0.9732$). A progressive increase with age was observed. Values were significantly smaller in individuals younger than 15 years ($Pr > 0.95$). C1–C2 lordosis was significantly smaller in males ($Pr > 0.9999$). This parameter was similar in PI groups. C1–C2 lordosis increased during growth with significantly smaller values in children younger than 10 years ($Pr > 0.9999$), and it then kept constant in adults (Fig. 5).

Caudal cervical parameters

Table 3 displays caudal cervical parameters by gender, PI and age. Differences of C2–C7 lordosis were non-significant between males and females. Individuals with low PI

Table 1 Overview of distribution of global alignment and spinopelvic parameters per gender pelvic incidence and age groups: mean \pm SD

Groups	SVA-C7 (mm)	SVA-C2 (mm)	OH-HA (°)	Thoracic kyphosis (°)	Lumbar lordosis (°)	Pelvic incidence (°)	Pelvic tilt (°)	Sacral slope (°)
Female	11.7 \pm 35.2	26.7 \pm 35.2	0.7 \pm 3.0	42.5 \pm 14.0	55.9 \pm 12.3	50.2 \pm 12.6	12.6 \pm 10.0	37.6 \pm 8.9
Male	24.2 \pm 36.1	41.1 \pm 36.1	-0.4 \pm 3.2	44.6 \pm 13.4	52.2 \pm 12.6	48.8 \pm 11.5	12.5 \pm 8.9	36.2 \pm 8.8
Low PI	7.8 \pm 31.6	22.3 \pm 36.0	0.3 \pm 2.9	40.7 \pm 13.0	48.3 \pm 11.6	37.5 \pm 5.6	5.9 \pm 7.7	31.5 \pm 7.5
Medium PI	19.4 \pm 35.4	37.4 \pm 41.8	0.2 \pm 3.2	44.7 \pm 14.0	55.2 \pm 11.1	51.9 \pm 4.2	14.1 \pm 7.3	37.8 \pm 6.9
High PI	29.2 \pm 41.0	49.3 \pm 50.0	0.3 \pm 3.5	45.7 \pm 14.1	64.3 \pm 10.7	67.9 \pm 6.3	21.9 \pm 7.8	45.9 \pm 7.6
5–9 years	15.7 \pm 34.6	26.1 \pm 38.0	-0.5 \pm 3.1	37.5 \pm 12.1	50.8 \pm 11.2	39.9 \pm 8.7	3.5 \pm 7.7	3.5 \pm 7.7
10–14 years	8.8 \pm 29.6	23.5 \pm 31.9	0.1 \pm 2.8	38.0 \pm 12.2	54.1 \pm 11.5	44.0 \pm 10.6	6.0 \pm 8.1	6.0 \pm 8.1
15–19 years	5.8 \pm 26.4	21.5 \pm 29.5	0.6 \pm 2.2	40.3 \pm 12.4	55.3 \pm 11.7	45.5 \pm 12.0	8.2 \pm 8.1	8.2 \pm 8.1
20–34 years	-0.2 \pm 33.7	16.5 \pm 36.3	1.5 \pm 2.8	43.3 \pm 12.0	58.2 \pm 12.0	50.1 \pm 11.3	11.8 \pm 7.0	11.8 \pm 7.0
35–49 years	12.3 \pm 33.3	27.8 \pm 37.9	1.2 \pm 2.8	43.5 \pm 11.9	55.8 \pm 12.8	52.7 \pm 12.5	15.0 \pm 8.2	15.0 \pm 8.2
50–64 years	22.6 \pm 32.7	39.0 \pm 40.1	0.5 \pm 3.3	45.7 \pm 13.4	53.6 \pm 13.2	53.1 \pm 10.8	16.7 \pm 7.5	16.7 \pm 7.5
65–79 years	40.6 \pm 37.7	63.4 \pm 47.0	-1.1 \pm 3.7	51.5 \pm 14.9	52.1 \pm 13.5	55.4 \pm 10.5	20.2 \pm 7.7	20.2 \pm 7.7
> 80 years	61.8 \pm 31.4	94.2 \pm 64.5	-3.1 \pm 4.2	52.7 \pm 17.6	50.7 \pm 14.5	55.6 \pm 11.7	20.6 \pm 8.6	20.6 \pm 8.6

PI pelvic incidence, SVA sagittal vertical axis, OD-HA odontoid-hip axis

Table 2 Distribution of cranial cervical parameters (mean ± SD) and prediction of significant difference (Pr > 0.95) between median of posterior distributions and credibility intervals (95% CI)

Parameter	Variable	Mean ± SD	Median	95% CI	Pr(<i>d</i> > 0)
McGregor slope (°)	Female	- 0.5 ± 13.7	- 0.5	[- 1.2; 0.1]	Reference
	Male	- 0.1 ± 11.6	- 0.1	[- 0.9; 0.7]	0.8016
	Low PI	0.3 ± 10.7	0.3	[- 0.6; 1.1]	0.9606
	Medium PI	- 0.7 ± 12.8	- 0.7	[- 1.5; 0.0]	Reference
	High PI	- 0.6 ± 16.1	- 0.6	[- 1.7; 0.5]	0.5803
	5–9 years	- 0.6 ± 10.1	- 0.6	[- 3.1; 1.9]	0.2133
	10–14 years	2.1 ± 9.1	2.1	[1.0; 3.2]	0.9258
	15–19 years	1.5 ± 12.0	1.5	[0.3; 2.7]	0.8013
	20–34 years	0.7 ± 14.2	0.6	[- 1.0; 2.3]	Reference
	35–49 years	- 0.4 ± 11.7	- 0.4	[- 1.6; 0.8]	0.1603
	50–64 years	- 2.7 ± 16.6	- 2.7	[- 3.9; - 1.5]	0.0003
	65–79 years	- 3.5 ± 9.5	- 3.5	[- 4.9; - 2.2]	0.0001
	> 80 years	- 0.9 ± 20.6	- 0.8	[- 3.3; 1.6]	0.1659
	Occipito-C2 angle (°)	Female	91.6 ± 14.5	91.6	[90.8; 92.4]
Male		92.4 ± 15.4	92.4	[91.6; 93.3]	0.9191
Low PI		94.1 ± 14.2	94.1	[93.1; 95.0]	> 0.9999
Medium PI		90.9 ± 15.2	90.9	[90.0; 91.8]	Reference
High PI		90.3 ± 15.1	90.3	[89.0; 91.6]	0.2097
5–9 years		94.8 ± 16.2	94.8	[92.0; 97.7]	0.8015
10–14 years		95.7 ± 13.0	95.7	[94.4; 96.9]	0.9780
15–19 years		95.4 ± 14.1	95.5	[94.5; 97.2]	0.9847
20–34 years		93.5 ± 14.4	93.4	[91.5; 95.2]	Reference
35–49 years		91.5 ± 14.7	91.5	[90.1; 92.9]	0.3569
50–64 years		88.0 ± 14.6	88.0	[86.7; 89.4]	< 6.7 × 10 ⁻⁵
65–79 years		88.1 ± 15.6	88.1	[86.6; 89.7]	< 6.7 × 10 ⁻⁵
> 80 years		82.8 ± 15.2	83.0	[80.2; 85.8]	< 6.7 × 10 ⁻⁵
McGregor-C2 lordosis (°)		Female	18.5 ± 10.1	18.5	[18.0; 19.0]
	Male	16.6 ± 9.7	16.6	[16.3; 17.2]	> 0.9999
	Low PI	17.0 ± 10.0	17.0	[16.4; 17.7]	0.9732
	Medium PI	17.9 ± 9.8	17.9	[17.3; 18.5]	Reference
	High PI	18.7 ± 10.1	18.7	[17.8; 19.5]	0.0718
	5–9 years	13.6 ± 10.3	13.6	[17.4; 32.4]	0.9995
	10–14 years	15.7 ± 9.4	15.7	[20.3; 27.2]	0.9890
	15–19 years	17.1 ± 10.3	17.1	[18.6; 26.1]	0.6804
	20–34 years	17.4 ± 8.3	17.4	[19.1; 27.6]	Reference
	35–49 years	17.8 ± 9.6	17.8	[20.0; 27.7]	0.3569
	50–64 years	19.1 ± 9.4	19.1	[32.5; 39.9]	0.0209
	65–79 years	19.6 ± 10.7	19.6	[54.8; 63.3]	0.0049
	> 80 years	22.4 ± 12.0	22.4	[75.5; 90.2]	< 6.7 × 10 ⁻⁵

Table 2 (continued)

Parameter	Variable	Mean \pm SD	Median	95% CI	Pr($d > 0$)
C1–C2 lordosis ($^{\circ}$)	Female	30.3 \pm 8.4	30.3	[29.1; 30.8]	Reference
	Male	28.4 \pm 8.4	28.4	[27.9; 28.9]	> 0.9999
	Low PI	29.3 \pm 8.6	29.3	[28.7; 29.8]	0.8409
	Medium PI	29.6 \pm 8.2	29.6	[29.1; 30.1]	Reference
	High PI	29.7 \pm 8.8	29.7	[29.0; 30.5]	0.4191
	5–9 years	25.1 \pm 9.7	25.1	[23.4; 26.8]	> 0.9999
	10–14 years	29.0 \pm 8.4	29.0	[28.2; 29.7]	0.9132
	15–19 years	30.6 \pm 8.9	30.6	[29.8; 31.4]	0.1405
	20–34 years	29.9 \pm 8.1	29.9	[28.8; 31.0]	Reference
	35–49 years	29.2 \pm 7.8	29.2	[28.4; 30.0]	0.8380
	50–64 years	29.8 \pm 8.1	29.8	[28.0; 30.6]	0.5287
	65–79 years	29.5 \pm 8.7	29.5	[28.5; 30.4]	0.7266
	> 80 years	30.6 \pm 8.5	30.6	[28.9; 32.2]	0.2499

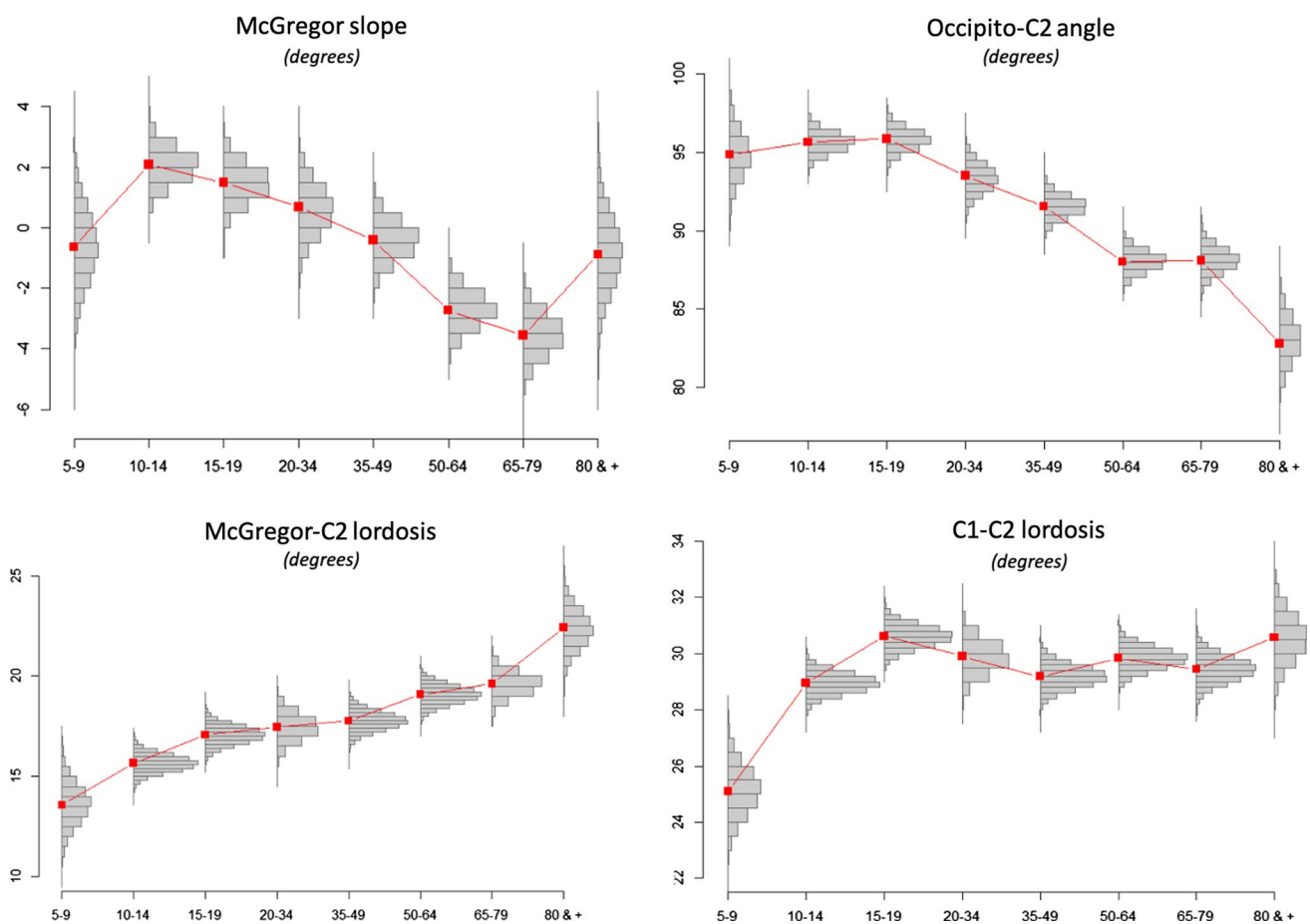
PI pelvic incidence

Fig. 5 Distribution of cranial cervical parameters per age group. Red squares indicate median values

Table 3 Distribution of caudal cervical parameters (mean \pm SD) and prediction of significant difference ($Pr > 0.95$) between median of posterior distributions and credibility intervals (95% CI)

Parameter	Variable	Mean \pm SD	Median	95% CI	Pr($d > 0$)
C2–C7 lordosis ($^{\circ}$)	Female	29.1 \pm 13.7	29.1	[28.3; 29.9]	Reference
	Male	31.7 \pm 11.6	31.7	[30.8; 32.7]	$< 6.7 \times 10^{-5}$
	Low PI	28.7 \pm 15.4	28.7	[27.6; 29.7]	> 0.9999
	Medium PI	31.3 \pm 16.8	31.3	[30.4; 32.3]	Reference
	High PI	30.7 \pm 15.6	30.7	[29.3; 32.1]	0.2097
	5–9 years	28.9 \pm 16.1	28.9	[25.8; 31.9]	0.0571
	10–14 years	25.8 \pm 15.5	25.8	[24.4; 27.1]	0.5359
	15–19 years	29.2 \pm 15.4	29.2	[27.8; 30.6]	0.0031
	20–34 years	25.4 \pm 15.1	25.9	[23.9; 27.8]	Reference
	35–49 years	28.4 \pm 15.0	28.4	[26.9; 29.9]	0.0203
	50–64 years	32.3 \pm 15.9	32.3	[30.8; 33.7]	$< 6.7 \times 10^{-5}$
	65–79 years	38.3 \pm 15.5	38.2	[36.5; 39.8]	$< 6.7 \times 10^{-5}$
	> 80 years	40.3 \pm 16.3	40.0	[37.0; 43.0]	$< 6.7 \times 10^{-5}$
Cranial arch lordosis ($^{\circ}$)	Female	7.2 \pm 14.9	7.2	[6.5; 8.0]	Reference
	Male	5.9 \pm 13.3	5.9	[5.1; 6.8]	0.9901
	Low PI	7.7 \pm 12.6	7.7	[6.8; 8.6]	0.0050
	Medium PI	6.1 \pm 15.2	6.1	[5.3; 6.9]	Reference
	High PI	5.9 \pm 14.8	5.9	[4.6; 7.1]	0.6189
	5–9 years	8.6 \pm 10.5	8.5	[5.7; 11.3]	0.0109
	10–14 years	6.7 \pm 12.1	6.7	[5.4; 7.9]	0.0343
	15–19 years	10.0 \pm 13.0	9.9	[8.6; 11.3]	$< 6.7 \times 10^{-5}$
	20–34 years	4.5 \pm 12.3	4.6	[2.8; 6.4]	Reference
	35–49 years	5.1 \pm 13.7	5.1	[3.7; 6.4]	0.3581
	50–64 years	6.8 \pm 16.8	6.8	[5.4; 8.1]	0.0307
	65–79 years	5.7 \pm 17.3	5.7	[4.2; 7.2]	0.1870
	> 80 years	4.6 \pm 13.2	4.6	[1.9; 7.3]	0.5121
Caudal arch lordosis ($^{\circ}$)	Female	23.1 \pm 10.1	23.1	[22.6; 23.6]	Reference
	Male	26.8 \pm 10.2	26.8	[26.2; 27.4]	> 0.9999
	Low PI	22.9 \pm 9.1	22.9	[22.3; 23.6]	0.9732
	Medium PI	25.5 \pm 10.7	25.5	[24.9; 26.1]	Reference
	High PI	26.2 \pm 11.3	26.2	[25.3; 27.1]	0.0718
	5–9 years	21.8 \pm 9.8	21.8	[19.9; 23.6]	0.2440
	10–14 years	20.8 \pm 8.8	20.8	[20.0; 21.6]	0.0095
	15–19 years	20.8 \pm 8.4	20.8	[19.9; 21.6]	0.0085
	20–34 years	22.5 \pm 10.3	22.6	[21.4; 23.8]	Reference
	35–49 years	24.0 \pm 8.6	24.0	[23.1; 24.9]	0.9693
	50–64 years	27.0 \pm 8.8	27.0	[26.1; 27.8]	> 0.9999
	65–79 years	32.5 \pm 9.8	32.4	[31.5; 33.5]	> 0.9999
	> 80 years	35.6 \pm 14.9	35.5	[33.7; 37.3]	> 0.9999

Table 3 (continued)

Parameter	Variable	Mean \pm SD	Median	95% CI	Pr($d > 0$)
C7-slope ($^{\circ}$)	Female	19.6 \pm 11.1	19.6	[19.1; 20.2]	Reference
	Male	23.8 \pm 11.0	23.8	[23.1; 24.4]	> 0.9999
	Low PI	19.3 \pm 10.1	19.3	[18.6; 20.0]	< 6.7×10^{-5}
	Medium PI	22.6 \pm 11.7	22.6	[21.9; 23.2]	Reference
	High PI	23.0 \pm 11.7	23.0	[22.0; 23.9]	0.7289
	5–9 years	20.3 \pm 11.1	20.3	[18.3; 22.4]	0.9106
	10–14 years	17.5 \pm 10.0	17.5	[16.7; 18.4]	0.0864
	15–19 years	17.3 \pm 9.1	17.3	[16.4; 18.3]	0.0540
	20–34 years	18.5 \pm 9.8	18.6	[17.3; 20.0]	Reference
	35–49 years	20.6 \pm 9.1	20.6	[19.6; 21.6]	0.9885
	50–64 years	23.2 \pm 11.1	23.2	[22.2; 24.1]	> 0.9999
	65–79 years	29.9 \pm 11.0	29.8	[28.7; 30.4]	> 0.9999
	> 80 years	33.7 \pm 12.7	33.6	[31.6; 35.6]	> 0.9999
	T1-slope ($^{\circ}$)	Female	23.2 \pm 11.3	23.2	[22.6; 23.8]
Male		27.7 \pm 11.0	27.7	[27.0; 28.3]	> 0.9999
Low PI		23.0 \pm 10.4	23.0	[22.3; 23.8]	< 6.7×10^{-5}
Medium PI		26.5 \pm 11.8	26.5	[25.8; 27.1]	Reference
High PI		26.1 \pm 11.8	26.1	[25.1; 27.1]	0.2914
5–9 years		22.3 \pm 10.6	22.3	[20.2; 24.3]	0.4159
10–14 years		20.1 \pm 9.8	20.1	[20.0; 21.7]	0.0195
15–19 years		21.2 \pm 9.5	21.2	[20.2; 22.1]	0.0502
20–34 years		22.4 \pm 10.1	22.5	[21.2; 23.9]	Reference
35–49 years		24.2 \pm 9.6	24.2	[23.2; 25.2]	0.9714
50–64 years		27.4 \pm 10.4	27.4	[26.5; 28.4]	> 0.9999
65–79 years		33.9 \pm 11.4	33.8	[32.7; 35.0]	> 0.9999
> 80 years		37.2 \pm 13.7	37.1	[35.1; 39.1]	> 0.9999

PI pelvic incidence

had significantly smaller C2–C7 lordosis ($Pr > 0.9999$). A progressive increase was observed after 50 years. Cranial arch lordosis was significantly smaller in males ($Pr = 0.9901$). Differences between PI groups were non-significant. This parameter kept constant during adulthood. Caudal arch lordosis was significantly larger in males ($Pr > 0.9999$). Differences between PI groups were non-significant. This parameter increased progressively during adulthood. When compared to young adults, there was a significant difference in the age group between 35 and 49 years ($Pr = 0.9693$) and after 50 years ($Pr > 0.9999$). Similar observations were made for C7- and T1-slope. Both parameters were significantly larger in males ($Pr > 0.9999$). Differences between PI groups were non-significant. A significant increase with aging was observed for both parameters in the group 35–49 years ($Pr > 0.95$) and after 50 years ($Pr > 0.9999$) (Fig. 6).

Cervical morphology

Cervicothoracic inflexion levels were at C6 in 526 (20.2%), C7 in 978 (37.6%), T1 in 768 (29.6%), T2 in 256 (9.9%) and T3 in 71 (2.7%) individuals. Variations in number of vertebrae from C1 to the cervicothoracic inflexion were small (Table 4). The cervical segment included more vertebrae in low PI ($Pr > 0.9999$) and in the group 10–14 years ($Pr = 0.9813$). The distribution by cervical alignment patterns (Fig. 4) was: global lordosis $n = 1323$ (50.9%), global kyphosis $n = 34$ (1.3%), sigmoid shape with proximal kyphosis and distal lordosis $n = 894$ (34.4%) and sigmoid shape with proximal lordosis and distal kyphosis $n = 348$ (13.4%).

Correlation between cervical, global and spinopelvic alignment

Table 5 displays correlation coefficients ρ between cervical and global alignment parameters. SVA-C2

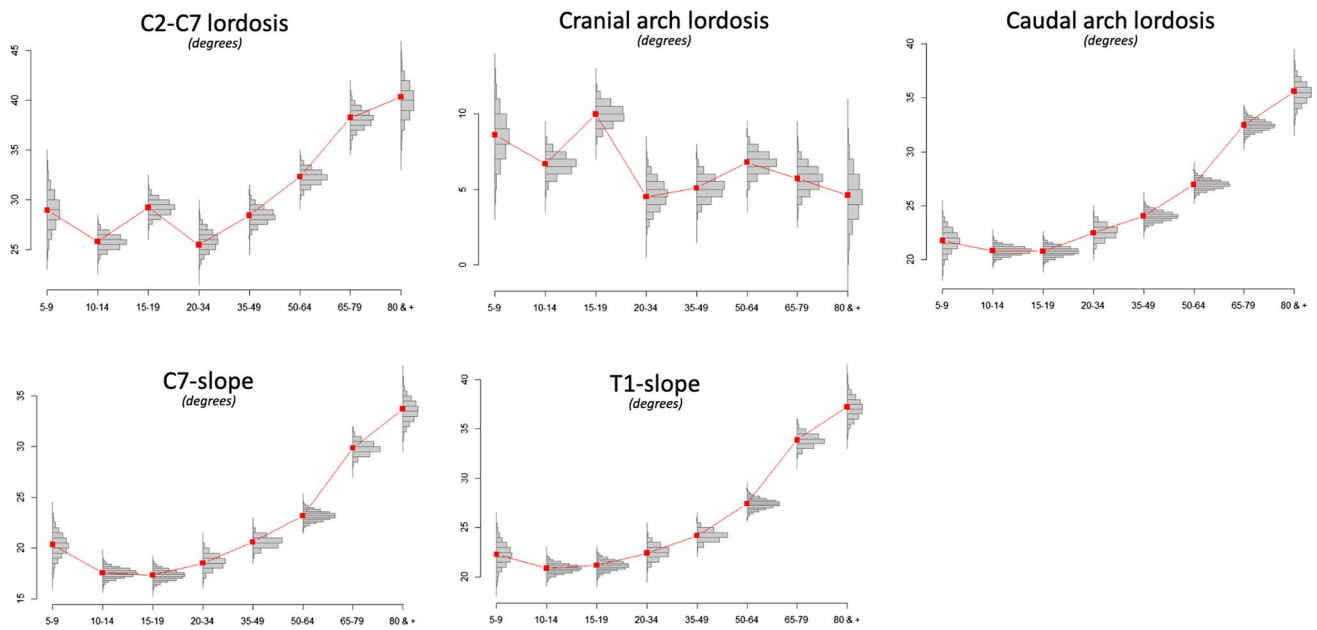


Fig. 6 Distribution of caudal cervical parameters per age group. Red squares indicate median values

Table 4 Distribution of number of cervical vertebrae from C1 to the cervicothoracic inflexion point (mean ± SD) and prediction of significant difference ($Pr > 0.95$) between median of posterior distributions and credibility intervals (95% CI)

Parameter	Variable	Mean ± SD	Median	95% CI	Pr($d > 0$)
Number of cervical vertebrae	Female	7.5 ± 1.1	7.5	[7.4; 7.5]	Reference
	Male	7.2 ± 1.1	7.2	[7.2; 7.3]	$< 6.7 \times 10^{-5}$
	Low PI	7.5 ± 1.1	7.5	[7.4; 7.6]	> 0.9999
	Medium PI	7.3 ± 1.0	7.3	[7.2; 7.4]	Reference
	High PI	7.3 ± 1.2	7.3	[7.2; 7.4]	0.2914
	5–9 years	7.3 ± 1.0	7.3	[7.0; 7.5]	0.2546
	10–14 years	7.5 ± 0.9	7.5	[7.4; 7.6]	0.9813
	15–19 years	7.4 ± 1.0	7.4	[7.3; 7.5]	0.7785
	20–34 years	7.3 ± 1.1	7.3	[7.2; 7.5]	Reference
	35–49 years	7.4 ± 1.1	7.4	[7.3; 7.5]	0.6385
	50–64 years	7.3 ± 1.2	7.3	[7.2; 7.4]	0.2190
	65–79 years	7.2 ± 1.1	7.2	[7.0; 7.3]	0.0224
	> 80 years	7.2 ± 1.3	7.2	[7.0; 7.4]	0.1801

PI pelvic incidence

correlated significantly with caudal arch lordosis ($\rho = 0.5526$; $Pr = 0.9997$) and non-significantly with T1-slope ($\rho = 0.5217$; $Pr = 0.9337$) and C7-slope ($\rho = 0.5001$; $Pr = 0.5026$). No correlation was observed for SVA-C7 and OD-HA. Table 6 demonstrates correlation coefficients between cervical and spinopelvic parameters. TK correlated significantly with C2–C7 lordosis ($\rho = 0.5359$; $Pr = 0.9943$), caudal arch lordosis ($\rho = 0.7267$; $Pr > 0.9999$), C7-slope ($\rho = 0.7073$; $Pr > 0.9999$) and T1-slope ($\rho = 0.8491$; $Pr > 0.9999$). There was no correlation between cervical parameters and LL, PI, PT or SS.

Discussion

Analyzing cervical alignment in spinal deformity has gained interest [3–7]. Cervical malalignment represents a consequence of thoracolumbar deformity as interactions with the mobile cervical segment exist [11, 20]. Although age-related changes of cervical parameters have been reported on the one hand [11–13] and spinopelvic and global alignment parameters on the other hand [14, 15], there is a lack of knowledge about the interaction of both. PI- and age-related alignment targets have been defined in adult spinal deformity [21], seeking for optimal thoracolumbar alignment, thus

Table 5 Correlation between cervical and global alignment parameters: correlation coefficients ρ strong if $\rho < -0.5$ or $\rho > 0.5$ and prediction of significance only if $\text{Pr} > 0.95$ indicated below each coefficient

Parameters	SVA-C7	SVA-C2	OD-HA
McGregor slope	-0.0529 < 6.7×10^{-5}	-0.0003 < 6.7×10^{-5}	-0.0455 < 6.7×10^{-5}
Occipito-C2 angle	0.0592 < 6.7×10^{-5}	-0.1489 < 6.7×10^{-5}	0.2479 < 6.7×10^{-5}
McGregor-C2 lordosis	0.0186 < 6.7×10^{-5}	0.1306 < 6.7×10^{-5}	0.1216 < 6.7×10^{-5}
C1-C2 lordosis	0.0342 < 6.7×10^{-5}	0.0488 < 6.7×10^{-5}	0.0548 < 6.7×10^{-5}
C2-C7 lordosis	0.2978 < 6.7×10^{-5}	0.2730 < 6.7×10^{-5}	0.2120 < 6.7×10^{-5}
Cranial arch lordosis	0.0045 < 6.7×10^{-5}	0.0914 < 6.7×10^{-5}	0.1171 < 6.7×10^{-5}
Caudal arch lordosis	0.4916 0.2816	0.5526 0.9997	0.4961 0.3936
C7-slope	0.4132 < 6.7×10^{-5}	0.5001 0.5026	-0.4498 0.0006
T1-slope	0.4587 0.0032	0.5217 0.9337	-0.4667 0.0128

SVA sagittal vertical axis, OD-HA odontoid-hip axis

limiting the risk of secondary cervical decompensation [7]. Therefore, the present study aimed to provide a comprehensive description of cranial and caudal cervical alignment

according to gender, PI and age, to provide a repository of reference parameters when treating spinal deformity.

Cranial parameters are mainly influenced by head position, which is often analyzed by the chin-brow vertical angle. Moses et al. [22] demonstrated a correlation with McGregor slope. Le Huec et al. [9] reported a mean value of 1.59° (range -18° to 16°) in adults. Abelin-Genevois et al. [8] reported a mean McGregor-C2 lordosis of 15.2° in children and 18.3° in adolescents, with larger values in girls. In asymptomatic adults, mean values range from 12.7° to 22.4° [9, 23–26]. Our results are in line with these findings. Gender-specific differences exist for McGregor-C2 lordosis, and a progressive increase with age was observed. McGregor slope and occipito-C2 angle decreased with age, describing a progressive head extension. Significant differences existed between pediatric and young adult populations, which might be explained by a lower muscle tone of cervicothoracic erector spinae and trapezius muscles in children and adolescents. The amount of PI influenced the occipitocervical orientation, especially in low PI, which is associated lower TK and LL. Positive McGregor slope values indicated a flexed head position, which resulted in larger occipito-C2 angles and smaller McGregor-C2 lordosis. C1-C2 lordosis accounts for the main part of cervical lordosis. Mean values range from 26.0° to 30.3° in children and adolescents [8] and 20.8° – 31.9° in adults [9, 12, 24–28]. Our findings fit within these ranges. C1-C2 lordosis increased during growth, whereas values kept stable during

Table 6 Correlation between cervical and spinopelvic parameters: correlation coefficients ρ strong if $\rho < -0.5$ or $\rho > 0.5$, and prediction of significance only if $\text{Pr} > 0.95$ indicated below each coefficient

Parameters	Thoracic kyphosis	Lumbar lordosis	Pelvic incidence	Pelvic tilt	Sacral slope
McGregor slope	-0.0853 < 6.7×10^{-5}	0.0171 < 6.7×10^{-5}	-0.0248 < 6.7×10^{-5}	-0.0620 < 6.7×10^{-5}	0.0326 < 6.7×10^{-5}
Occipito-C2 angle	-0.0578 < 6.7×10^{-5}	0.0259 < 6.7×10^{-5}	-0.1017 < 6.7×10^{-5}	-0.1255 < 6.7×10^{-5}	-0.0036 < 6.7×10^{-5}
McGregor-C2 lordosis	0.0420 < 6.7×10^{-5}	0.0115 < 6.7×10^{-5}	0.0698 < 6.7×10^{-5}	0.1029 < 6.7×10^{-5}	-0.0149 < 6.7×10^{-5}
C1-C2 lordosis	0.0265 < 6.7×10^{-5}	-0.0242 < 6.7×10^{-5}	0.0413 < 6.7×10^{-5}	0.0355 < 6.7×10^{-5}	0.0181 < 6.7×10^{-5}
C2-C7 lordosis	0.5359 0.9943	0.0175 < 6.7×10^{-5}	0.0534 < 6.7×10^{-5}	0.1478 < 6.7×10^{-5}	0.0854 < 6.7×10^{-5}
Cranial arch lordosis	0.0091 < 6.7×10^{-5}	0.0220 < 6.7×10^{-5}	0.0646 < 6.7×10^{-5}	0.0430 < 6.7×10^{-5}	-0.0423 < 6.7×10^{-5}
Caudal arch lordosis	0.7267 > 0.9999	0.0047 < 6.7×10^{-5}	0.1293 0.3936	0.2558 < 6.7×10^{-5}	0.0970 < 6.7×10^{-5}
C7-slope	0.7073 > 0.9999	0.0010 < 6.7×10^{-5}	0.1439 0.0006	0.2307 < 6.7×10^{-5}	-0.0502 < 6.7×10^{-5}
T1-slope	0.8491 > 0.9999	0.0223 < 6.7×10^{-5}	0.1233 0.0128	0.2465 < 6.7×10^{-5}	-0.0951 < 6.7×10^{-5}

adulthood. Gender-specific differences existed with smaller values in males.

The literature indicates a large variability of C2–C7 lordosis, due to varying measurement methods, different alignment patterns and age-related changes. In children and adolescents, mean values of 6.5° and 0.7° were reported [8]. In adults, means range from 4.9° to 40.0° [9–13, 20, 22–28]. In our study, values were higher in the pediatric population, but similar in adults. Scheer et al. [11] described a C2–C7 lordosis increase from 9.4° at 20–34 years to 22.2° over 60 years. Hardacker et al. [12] demonstrated an increase from 37° at 20–30 years to 47° at 61–70 years. Iyer et al. [13] showed an increase from 4.5° at 21–30 years to 15.7° over 71 years. Our results showed that this lordosis increase mainly occurred in the caudal arch, whereas the cranial arch kept stable. Caudal arch lordosis increased with age in parallel to C7-slope, T1-slope and TK. An age-related TK increase was described by Iyer et al. [14] and Hu et al. [15]. This suggests that progressive caudal cervical hyperextension compensating increasing proximal TK to maintain horizontal gaze. This phenomenon was more prominent in males and individuals with high PI. C7-slope and T1-slope represent similar parameters. Mean C7-slope values were 21.3° and 17.4° in children and adolescents [8] and 19.64° in adults [9]. Iyer et al. [13] described a T1-slope increase from 21.7° at 21–30 years to 35.3° over 71 years. Chen et al. [28] demonstrated an increase from 23.0° under 21 years to 28.7° at 41–60 years, like our findings.

Correlation analyses confirmed a strong relationship between C2–C7 lordosis, C7-slope, T1-slope and TK in pediatric and adult populations [8–11, 13, 20, 24]. Núñez-Pereira et al. [24] found a weak ($r = -0.3$) but significant correlation between C7-slope and SS. Lee et al. [10] and Scheer et al. [11] investigated correlation chains between cervical, thoracolumbar and spinopelvic parameters. Correlations exist between cervical and thoracic parameters around the cervicothoracic junction, between TK and LL and between LL and spinopelvic parameters. A direct correlation between cervical parameters, LL and spinopelvic parameters was not evidenced. Among global alignment parameters, Iyer et al. [13] demonstrated weak but significant correlations for SVA-C2–C7 with T1-slope ($r = 0.306$) and C2–C7 lordosis ($r = 0.221$). In our study, only SVA-C2 correlated with caudal arch lordosis and T1-slope. Global alignment results showed that SVA-C2 and TK increased with age. This indicates a relationship between progressive anterior C2-plumbline migration, TK changes and compensatory hyperextension of the caudal cervical arch. This phenomenon might influence cervical morphology and the level of cervicothoracic inflexion point which varied from C6 to T3. In our population, 50.9% presented an evenly distributed cervical lordosis. Kyphotic alignment represented only 1.3%. This pattern is more common in patients with scoliosis and

thoracic hypokyphosis [3–6]. Yu et al. [4] and Charles et al. [5] described sigmoid shapes in scoliosis, which represented compensation phenomena of thoracic malalignment. Sigmoid patterns were also found in our asymptomatic population. Proximal kyphosis and distal lordosis represented 34.4%, possibly related to degenerative changes, adaptive C2–plumbline translation and caudal arch increase with age. Proximal lordosis and distal kyphosis represented 13.4%, where TK extended into the caudal cervical spine.

This cross-sectional study has limitations as the evolution of alignment parameters cannot be assessed over a lifetime. Quality-of-life scores and muscle strength were not assessed, although these clinical factors might influence radiographic alignment. Moderate intervertebral disc degeneration and osteoarthritis represent an inevitable age-related phenomenon. Severe changes leading to deformity were excluded. The influence of degenerative changes was not specifically analyzed.

Conclusion

Cervical alignment parameters vary according to age, gender and PI. In the cranial cervical segment, the main changes occur during growth. In the caudal cervical segment, lordosis increases mainly in the lower arch during adulthood, which is strongly related to thoracic kyphosis increase with age. The caudal cervical arch acts as a compensatory segment.

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Authors' contribution Yann Philippe Charles designed and coordinated the study, collected and analyzed data and wrote the manuscript. Benjamin Blondel, Solène Prost, Sébastien Pesenti, Brice Iharrebordé, Eloïse Bauduin and Féthi Laouissat designed the study, collected and analyzed data and approved the manuscript. Erik André Sauleau designed the study, analyzed data and approved the manuscript. Guillaume Riouallon, Stéphane Wolff, Vincent Challier, Ibrahim Obeid, Louis Boissière, Emmanuelle Ferrero, Federico Solla, Jean-Charles Le Huec, Stéphane Bourret, Joe Faddoul, Georges Naïm Abi Lahoud, Vincent Fièrè, Michiel Vande Kerckhove, Matthieu Campana, Jonathan Lebhar, Hadrien Giorgi and Aymeric Faure collected and analyzed data and approved the manuscript.

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Declarations

Conflict of interest Yann Philippe Charles is consultant for Stryker, Clariance, Philips and Ceraver; he received royalties and grants unrelated to this study from Stryker and Clariance. Brice Iharrebordé is consultant for Zimmer Biomet, Medtronic and Implanet. Féthi Laouissat is consultant for Spineart and SMAIO. Guillaume Riouallon is

consultant for Medtronic, Stryker and NewClip; he received royalties from Euros. Vincent Challier is shareholder of Follow Health SA and consultant for Clariance. Ibrahim Obeid is consultant for Medtronic and DePuy Synthes; he received grants from DePuy Synthes unrelated to this study and royalties from Clariance, Alphatec and Spineart. Louis Boissière is consultant for Neo and Euros; he received grants from DePuy Synthes unrelated to this study. Federico Solla received funding to attend meetings from Medicea, Medtronic and Euros. Jean-Charles Le Huec is consultant for Medtronic and BD Bard; he received royalties and grants unrelated to this study from Medtronic. Vincent Fièrè is consultant for Clariance; he received royalties Medicea and Clariance. Aymeric Faure is consultant for OSD. Benjamin Blondel is associate editor for OTSR Elsevier-Masson and consultant for Medicea, Medtronic, Implanet, Vexim Stryker and M. Solène Prost, Sébastien Pesenti, Eloïse Bauduin, Stéphane Wolff, Emmanuelle Ferrero, Stéphane Bourret, Joe Faddoul, Georges Naïm Abi Lahoud, Michiel Vande Kerckhove, Matthieu Campana, Jonathan Lebhar, Hadrien Giorgi and Erik André Sauleau have no conflict of interest.

Ethics approval Institutional review board approval (FC/2019-91) was obtained. The study was declared at ClinicalTrials.gov ID: NCT04467775.

Consent to participate Informed consent was obtained from study participants.

Consent for publication Informed consent for publication of results was obtained from study participants.

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