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ORIGINAL RESEARCH

Sex differences in craniofacial parameters of children and adolescents: a comparative study with the maturation of cervical vertebrae using a cephalometric method

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Abstract

This study aimed to investigate sex differences in craniomaxillofacial parameters in children and adolescents. Lateral cephalograms were obtained from 340 subjects (141 male, 199 female) aged 6 to 18 years, and their craniofacial characteristics and cervical vertebral maturity were assessed using the quantitative cervical vertebral maturity (QCVM) method. Age-based stratified analyses on craniofacial parameters and further comparison in QCVM III subjects were performed. Among all analyses, male subjects had significantly greater value than females in sex-different parameters except for facial convexity. The overall group had 17 sex-different parameters (ramus height, anterior facial height (AFH), posterior facial height (PFH), upper anterior facial height (UAFH), lower anterior facial height (LAFH), anterior cranial base length, posterior cranial base length, facial convexity, upper lip length, upper lip thickness, lower lip thickness, soft tissue chin thickness, nasion of soft tissue-subnasale (N'-Sn), subnasale-menton of soft tissue (Sn-Me'), subnasale-stomion inferius (Sn-Sto)). The $<$12 years old group showed 6 significant sex differences (AFH, LAFH, lower lip protrusion, lower lip thickness, N'-Sn, Sn-Me'). While the $\geq$12 years old group occurred two more parameters (mandibular body length, AFH/PFH) than the overall group. 12 cephalometric parameters had significant sex differences among QCMV III patients. After age adjustment, the number of sex-different parameters only increased in soft tissue. Craniofacial characteristics and cervical vertebrae maturation of the youngsters exhibited significant sex differences. Though females reached an earlier cervical vertebral maturation, they still had smaller craniofacial linear features. Sex differences should be taken into account in developing reference standards for cephalometric measurements and treatment planning in the clinic.

Keywords

Cephalometric; Craniofacial; Sex; Orthodontics

1. Introduction

Craniomaxillofacial growth and development is a complex and ongoing process that is affected by a variety of factors, including genetics, environment, hormones and altered biological clocks [1–4]. It has a crucial impact on the establishment of normal occlusion and a harmonious system of oral function, as well as on facial aesthetics. Special craniomaxillofacial morphology can cause physical and psychological suffering, prompting patients to seek help from orthodontic treatment, or even orthognathic surgery [5]. There have been studies conducted on the relationship between craniomaxillofacial features and obstructive sleep apnea, and a previous study from our group confirmed that craniofacial morphology is associated with temporomandibular joint disorders [6, 7]. With detailed identification of soft and hard tissues using sophisticated technology, orthodontists can gain a complete picture of the patient's current condition and potential problems.

Exploring the craniomaxillofacial characteristics of diverse populations can make the treatment more targeted, which contributes to achieving the best outcomes. And researches into sex differences is undoubtedly an integral part of the whole field, but not enough attention has been paid. As is common knowledge, individuals of different sexes have distinctive craniofacial features. Craniomaxillofacial differences between males and females have often been reported to be related to occlusion types [8, 9]. Sex-different craniofacial parameters in adults have been examined and reported by Avci *et al.* [10]. However, recent research in this area scarcely focused on children and adolescents, the group with the greatest orthodontic demands. Meanwhile, the values of the corresponding craniomaxillofacial characteristics need to be updated and supplemented.

Given the large individual differences in the timing of growth acceleration in childhood and adolescence, it is also necessary to combine skeletal age to accurately assess the developmental stage of the individual, excluding influences attributed to sex differences in growth and development. The hand-wrist maturation method which assesses skeletal maturation by hand-wrist radiograph, is a traditional and extensively used approach for determining the degree of craniofacial development and is regarded as the gold standard [11, 12]. However, the cervical vertebral maturation method is increasingly recommended as an alternative, considering it eliminates the need for an additional radiograph exposing the subject to the lowest possible level of radiation [13, 14]. In 2008, Chen *et al.* [15] proposed a pioneering method of quantitative cervical vertebral maturation (QCVM), which is a simple and reliable new standard for cervical vertebral maturation staging. It avoids the problems of high subjectivity and large interobserver error in the qualitative method. In this study, we employed the QCVM method to evaluate the stage of craniofacial development of the subjects and to observe the differences in craniofacial morphology between the sexes at the same stage of development.

Therefore, the present study aimed to analyze the sex differences in craniofacial features among children and adolescents. The null hypothesis was that there would be no sex difference in craniofacial parameters of children and adolescents.

2. Materials and methods

2.1 Subjects

A total of 340 lateral cephalograms were collected from patients visiting the orthodontic department of our hospital between 01 January 2022 and 31 August 2022.

The inclusion criteria were (i) possession of a qualified cephalogram showing the fourth cervical vertebra at the first visit to our hospital; (ii) age between 6 and 18 years old. The exclusion criteria were (i) a history of orthodontic or orthognathic treatment; (ii) a history of plastic surgery or other craniofacial surgery; (iii) the presence of head and neck tumors and trauma; (iv) the presence of congenital and acquired malformations of the craniofacial and spine; (v) diagnosis of systemic diseases.

The study sample was divided into two age subgroups at the cutoff value of 12 years old when the permanent dentition is almost complete and the craniofacial growth is rapid. The number of subjects for the <12 years old group and the ≥12 years old group was 123 (F: 73 (59.35%); M: 50 (40.65%)) and 217 (F: 126 (58.06%); M: 91 (41.94%)), respectively. The population of the two subgroups was slightly female-dominant. The subjects were also categorized using the QCVM method.

2.2 Cephalometric analysis

The lateral cephalograms were performed at the Department of Medical Imaging, West China Hospital of Stomatology, Sichuan University by the same radiologist. Patients were instructed to hold the natural head position with their teeth in an intercuspal position and not to swallow during the filming. Uceph software (Version 1103, Yacent, Chengdu, Sichuan, China) was used for cephalometric analysis.

There was a total of 46 craniofacial parameters applied in this research, including 7 morphologic characteristic parameters of the cervical vertebra and 38 craniofacial parameters (21 hard tissue and 17 soft tissue) (Fig. 1). The definition of cervical vertebra parameters and craniofacial parameters with both hard and soft tissue was presented in Table 1 [5, 15].

The cephalogram tracing was performed by two researchers blinded to additional information about the patients. To evaluate the inter-observer reliability, 30 lateral cranial radiographs were selected randomly and measured by two researchers simultaneously. To test the intra-observer reliability, each researcher randomly selected 30 lateral radiographs for the first measurement and repeated measurements one month later [7]. Both intraclass correlation coefficient were >0.75, showing high reliability.

2.3 QCVM method

The QCVM system, established by Chen *et al.* [15], is an extremely accurate and convenient method that simply adds the 2nd to 4th cervical vertebrae landmarks to the conventional craniofacial cephalogram to obtain the values of the 4 cervical vertebra parameters which have been demonstrated in Table 1 (@2, PH3, AH3, H4 and W4). After cephalometric analysis, we substituted data into the following equation: cervical vertebral maturation stage (CVMS) = $-4.13 + 3.57 \times \text{H4/W4} + 4.07 \times \text{AH3/PH3} + 0.03 \times @2$ to estimate the maturation of the cervical vertebra. According to the CVMS value, QCVM was divided into 4 stages: in QCVM I: CVMS <1.7404; in QCVM II, 1.7404 < CVMS < 2.623; in QCVM III, 2.623 < CVMS < 3.5199; and in QCVM IV, CVMS >3.5199. QCVM I corresponds to Fishman skeletal maturity indicators (SMI) 1–3 (accelerating velocity period), QCVM II corresponds to SMI 4–7 (high velocity period), QCVM III corresponds to SMI 8 and 9 (decelerating velocity period) and QCVM IV corresponds to SMI 10 and 11 (completing velocity period).

2.4 Statistical analysis

Data management and analysis were performed using SPSS 26.0 software (IBM, Armonk, NY, USA). All descriptive statistics were presented as mean ± standard deviation (minimum–maximum). The Shapiro-Wilk test was used to analyze the normality of age and all parameters. Nonnormally distributed data between the female and male groups were analyzed by the Mann-Whitney U test, and normally distributed parameters data were analyzed by independent samples *t*-test. The differences in age distribution and QCVM stages between the groups were analyzed by Chi-squared test. Separate stratified analyses were conducted based on age (<12 years *vs.* ≥12 years). In addition, we specifically chose patients of QCVM III to show the differences in craniomaxillofacial morphology between male and female subjects at the same developmental maturity, as it had the highest number of patients among all QCVM stages. Age adjustment employed the multiple linear regression analysis. The values were considered statistically significant at $p < 0.05$.

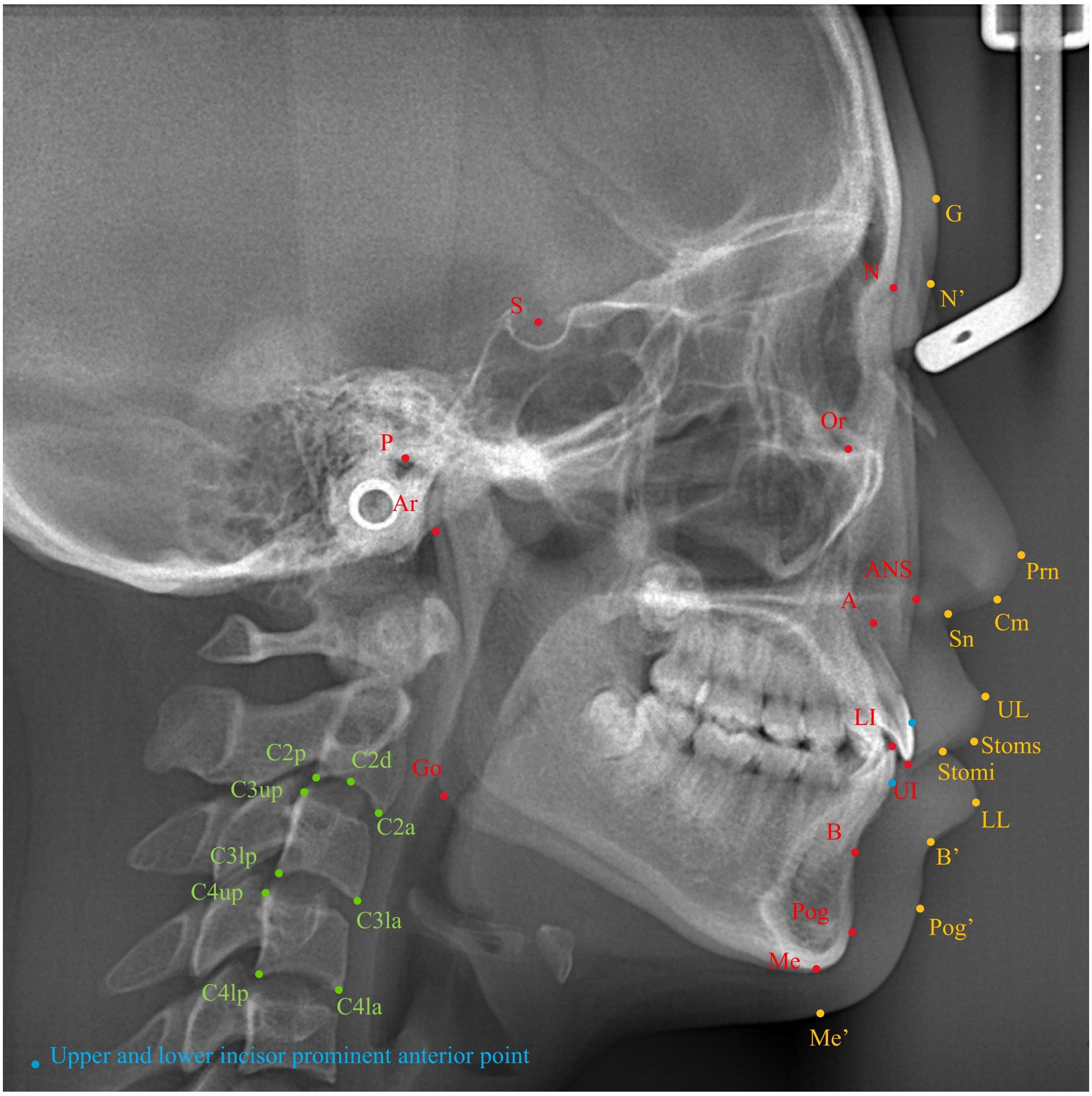

FIGURE 1. Hard tissue and soft tissue landmarks and measuring points used in the quantitative cervical vertebral maturation analysis on lateral cephalogram. Red and blue dots show hard tissue landmarks on lateral cephalogram; yellow dots show soft tissue landmarks; green dots show measuring points used in the quantitative cervical vertebral maturation analysis. N: nasion; S: sella; P: porion; Or: orbitale; Ar: articulare; ANS: anterior nasal spine; A: subspinale; UI: upper incisor; LI: lower incisor; B: supramental; Pog: pogonion; Me: menton; Go: gonion; G: glabella; N': nasion of soft tissue; Prn: pronasale; Cm: columella; Sn: subnasale; UL: upper lip; Stoms: stomion superius; Stomi: stomion inferius; LL: lower lip; B': soft tissue B point; Pog': pogonion of soft tissue; Me': menton of soft tissue. C2d: the most superior point of the lower border of the bodies of C2; C2a, C2p, C3la, C3lp, C4la and C4lp: the most posterior and most anterior points on the lower border of the bodies of C2, C3 and C4, respectively; C3up and C4up: the most superior points of the posterior bodies of C3 and C4.

3. Results

3.1 Descriptive characteristics

There was no significant sex difference in sample age or between subgroups (Table 2).

3.2 Overall sex comparison in different QCVM stages

Significant sex differences were demonstrated in each cervical vertebrae maturation stage ($p < 0.001$). For both subgroups, females were more concentrated in a later cervical vertebrae maturation stage, while males were more concentrated in an earlier stage (Table 3 and Fig. 2). In adolescents, who were in active cervical vertebrae maturation development, the girl population centered in QCVM III/IV (QCVM III: 53 (42.06%); QCVM IV: 58 (46.03%)), whereas boys concentrated in QCVM II/III (QCVM II: 37 (40.66%); QCVM III: 30 (32.97%)).

3.3 Correlations

Correlations among all the craniofacial parameters and QCVM stages were shown in Fig. 3.

TABLE 1. Measuring parameters in the cephalometric analysis.

	Definition
Cervical vertebra parameters	
@2 (°)	Antero-superior angle of C2d-C2p connection to C2p-C2a connection.
PH3 (mm)	Vertical distance of C3up to the connection of C3lp and C3la.
AH3 (mm)	Vertical distance of C3ua to the connection of C3lp and C3la.
AH3/PH3	Ratio of AH3 to PH3.
H4 (mm)	Vertical distance of C4um to the connection of C4lp and C4la.
W4 (mm)	Vertical distance of C4am to the connection of C4up and C4lp.
H4/W4	Ratio of H4 to W4.
Craniofacial parameters	
Hard tissue	
SNA (°)	Angle between the SN plane and the nasion-A point line.
SNB (°)	Angle between the SN plane and the nasion-B point line.
ANB (°)	Angle between the nasion-A point line and the nasion-B point line.
Wits appraisal (mm)	The distance between vertical lines from A point and B point to the occlusal plane.
FMA (°)	Frankfurt-mandibular plane, formed by the mandibular plane and the FH angle.
Saddle angle (°)	Angle formed by the SN plane and the S-Ar line.
Articular angle (°)	Angle formed by the S-Ar line and the Ar-Go line.
Gonial angle (°)	Angle formed by the Ar-Go line and the mandibular plane.
Interincisal angle (°)	Angle formed the long axis of the upper incisor and low incisor.
Ramus height (mm)	Ar-Go, the distance between articulare and gonion.
Mandibular body length (mm)	Go-Me, the distance between gonion and menton.
Anterior cranial base length (mm)	S-N, the distance between sella and nasion.
Posterior cranial base length (mm)	S-Ar, the distance between sella and articulare.
Anterior facial height (mm)	N-Me, the distance between nasion and menton.
Posterior facial height (mm)	S-Go, the distance between sella and gonion.
Lower anterior facial height (mm)	ANS-Me, the vertical distance between the anterior nasal spine and the menton.
Upper anterior facial height (mm)	ANS-N, the vertical distance between the anterior nasal spine and the nasion.
Overjet (mm)	The horizontal distance between the upper and lower incisal edge with reference to the occlusal plane.
Overbite (mm)	The vertical overlap between the upper and lower incisal edge.
AFH/PFH	N-Me/S-Go, ratio of anterior facial height to posterior facial height.
UAFH/LAFH	ANS-N/ANS-Me, ratio of upper anterior facial height to lower anterior facial height.
Soft tissue	
Facial convexity (°)	G-Sn-Pog’, Angle formed by the G-Sn line and the Sn-Pog line.
Soft tissue profile (°)	N’-Sn-Pog’, Angle formed by the N’-Sn line and the Sn-Pog’ line.
Soft tissue convexity (°)	N’-Prn- Pog’, Angle formed by the N’-Prn line and the Prn- Pog’ line.
Nasolabial angle (°)	Cm-Sn-UL, Angle formed by the Cm-Sn line and the Sn-UL line.
Nasal prominence (°)	Prn-N’-Sn, Angle formed by the Prn-N’ line and the N’-Sn line.
Upper lip length (mm)	stoms-Sn, the distance between stomion superius and subnasale.
Lower lip length (mm)	stomi-B’, the distance between stomion inferius and soft tissue B point.
Lower lip to E plane (mm)	horizontal distance between LL and esthetic plane (Prn-Pog).
Upper lip to E plane (mm)	horizontal distance between UL and esthetic plane (Prn-Pog).

TABLE 1. Continued.

	Definition
Upper lip protrusion (mm)	horizontal distance between UL and Sn-Pog’.
Lower lip protrusion (mm)	horizontal distance between LL and Sn-Pog’.
Lower lip thickness (mm)	LL to lower incisor prominent anterior point.
Upper lip thickness (mm)	UL to upper incisor prominent anterior point.
Soft tissue chin thickness (mm)	Pog-Pog’, the distance between pogonion and pogonion of soft tissue.
N’-Sn (mm)	The distance between nasion of soft tissue.
Sn-Me’ (mm)	The distance between subnasale and menton of soft tissue.
Sn-Sto (mm)	The distance between subnasale and stomion inferius.

C: cervical vertebrae; C2d: the most superior point of the lower border of the bodies of C2; C2a, C2p, C3la, C3lp, C4la and C4lp: the most posterior and most anterior points on the lower border of the bodies of C2, C3 and C4, respectively; C3up: the most superior point of the posterior body of C3; C3ua: the most superior point of the anterior border of the body of C3; C4um: the middle of the upper border of the body of C4; C4am: the middle of the anterior border of the body of C4; SNA: Sella nasion A point angle; SNB: Sella nasion B point angle; ANB: Angel-Nose-Bite angle; FMA: Frankfort-mandibular plane angle; AFH: anterior facial height; PFH: posterior facial height; UAFH: upper anterior facial height; LAFH: lower anterior facial height; N::nasion; S: sella; Ar: articulare; ANS: anterior nasal spine; A: subspinale; B: supramental; Pog: pogonion; Me: menton; Go: gonion; G: glabella; N’: nasion of soft tissue; Prn: pronasale; Cm: columella; Sn: subnasale; UL: upper lip; Stoms: stomion superius; Stomi: stomion inferius; LL: lower lip; B’: soft tissue B point; Pog’: pogonion of soft tissue; Me’: menton of soft tissue; Sto: Stomi, stomion inferius.

TABLE 2. Sample characteristics.

Parameter	Female (N = 199)	Male (N = 141)	p
Age (yr, mean ± SD)	12.99 ± 0.17	12.69 ± 0.18	0.290
Subgroup			
<12 years old	73 (36.68%)	50 (35.46%)	0.817
≥12 years old	126 (63.32%)	91 (64.54%)	

SD: standard deviation.

TABLE 3. Sexual differences of distribution in different QCVM stages.

Subgroup	QCVM Stage	Female (N = 199)	Male (N = 141)	p
Overall				
	I	19 (9.55%)	49 (34.75%)	<0.001*
	II	51 (25.63%)	50 (35.46%)	
	III	68 (34.17%)	33 (23.41%)	
	IV	61 (30.65%)	9 (6.38%)	
<12 years old				
	I	17 (23.29%)	34 (68.00%)	<0.001*
	II	38 (52.05%)	13 (26.00%)	
	III	15 (20.55%)	3 (6.00%)	
	IV	3 (4.11%)	0 (0.00%)	
≥12 years old				
	I	2 (1.59%)	15 (16.48%)	<0.001*
	II	13 (10.32%)	37 (40.66%)	
	III	53 (42.06%)	30 (32.97%)	
	IV	58 (46.03%)	9 (9.89%)	

*Chi-square test and Mann-Whitney U test are used. *$p < 0.05$.*
QCVM: quantitative cervical vertebral maturation.

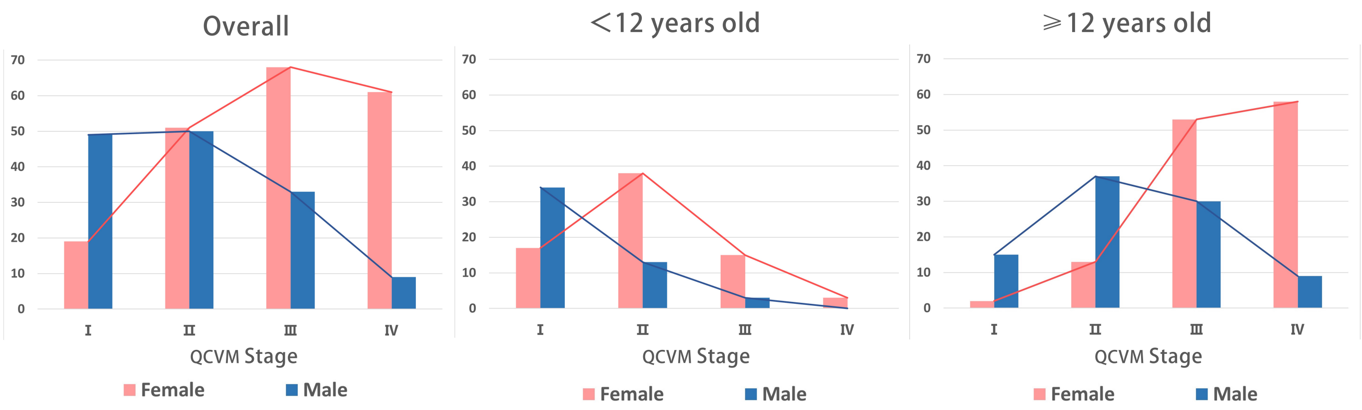

FIGURE 2. Distribution of females and males in different QCVM stages. QCVM: quantitative cervical vertebral maturation.

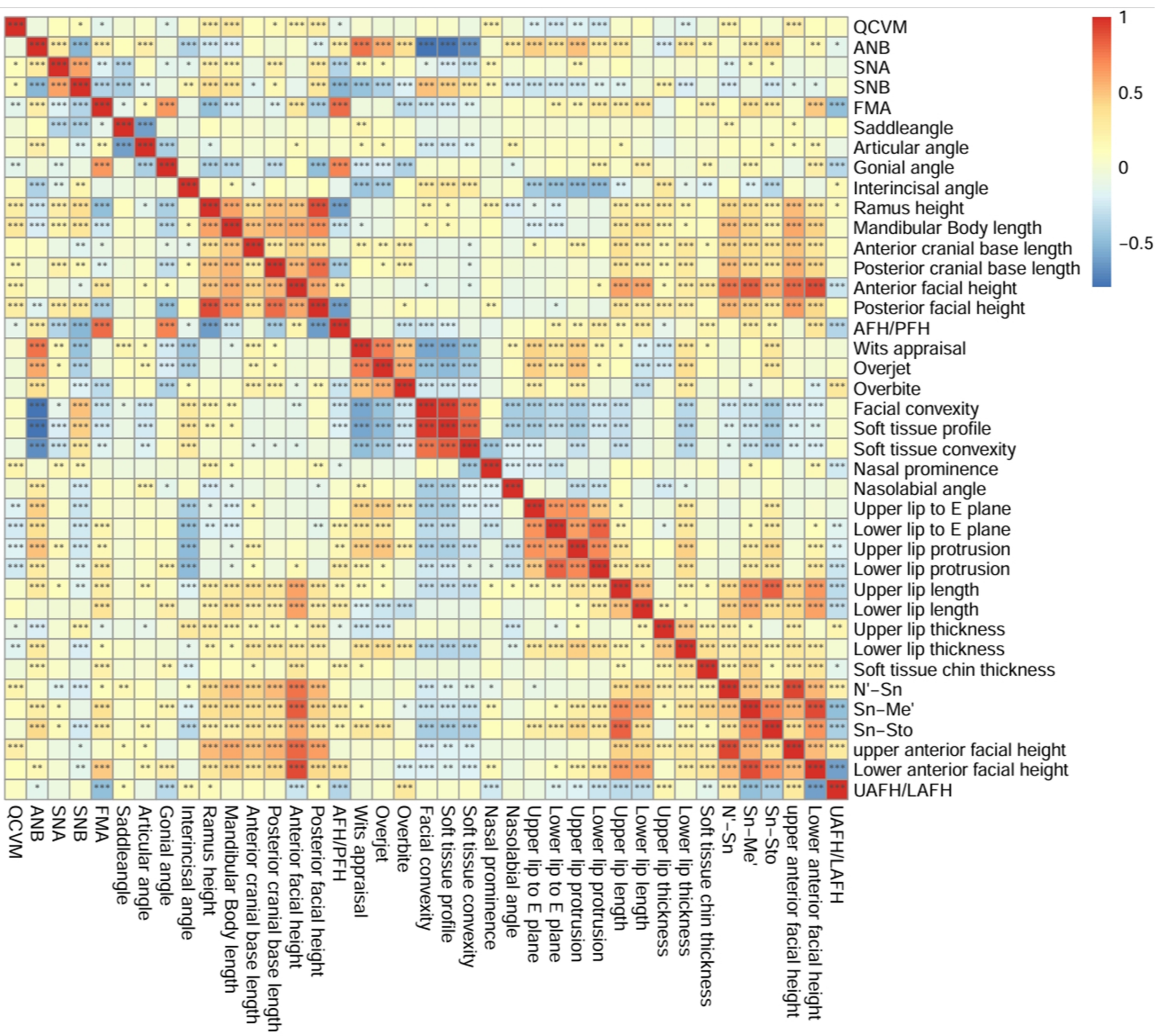

FIGURE 3. The heatmap of correlations among the craniofacial parameters and QCVM. Spearman's correlation analysis was used and the *p* values were adjusted with Benjamini and Hochberg method. *p value $<$ 0.05; **p value $<$ 0.01; ***p value $<$ 0.001. QCVM: quantitative cervical vertebrae maturation; FMA: Frankfort-mandibular plane angle; AFH: anterior facial height; PFH: posterior facial height; UAFH: upper anterior facial height; LAFH: lower anterior facial height. SNA: Sella nasion A point angle; SNB: Sella nasion B point angle; ANB: Angel-Nose-Bite angle; N': nasion of soft tissue; Sn: subnasale; Me': menton of soft tissue; Sto: Stomi, stomion inferius.

3.4 Overall sex comparison in craniofacial parameters

The overall statistical analysis yielded a total of 17 out of 38 craniofacial parameters showing significant and strong sex differences, including 7 hard tissue parameters and 10 soft tissue parameters, respectively ($p < 0.05$) (Table 4). The linear parameters accounted for size in the craniofacial region while angular parameters were for face convexity. Males significantly possessed greater linear parameters than females. However, facial convexity, the only sexually dimorphic angle measurement of soft tissue, is lower in males.

3.5 Sex comparison between age subgroups

There were obviously fewer significantly sex-different parameters in the younger subgroup. The <12 years old group presented 6 significantly sex-different parameters (6/38), and the ≥12 years old group showed 19 parameters (19/38) (Tables 5,6).

For the children group, there were only 6 linear parameters that showed significant sex differences, which were consistently larger in males (all $p < 0.05$) (Table 5). No angular measurement was significantly different.

For adolescents, 2 more linear parameters presented significant sex differences than the general subjects, including mandibular body length and AFH/PFH (the ratio of anterior facial height to posterior facial height) (Table 6). Linear parameters were consistently larger in males (all $p < 0.05$) and soft tissue convexity was significantly lower in males ($p < 0.038$) (Table 6).

3.6 Sex comparison between QCMV III patients

The QCMV III group had 12 significantly sex-different parameters (Table 7). In comparison with the results of craniofacial parameters in the overall analysis, QCMV III patients had slightly larger measurement values in craniofacial parameters, except for upper lip thickness. No significant sex difference was presented.

3.7 Sex comparison in craniofacial parameters without age effect

With age adjustment, 3 angular parameters were significantly larger in females including facial convexity, soft tissue profile and soft tissue convexity (Table 8). 18 linear measurements were significantly greater in males, which was most marked in anterior facial height and posterior facial height (all $p < 0.05$).

4. Discussion

Our findings support the hypothesis that there exists a positive correlation between sex and craniofacial growth and development of children and adolescents. In this study, we found that males had a larger head and longer face as well as a more protrusive face compared to female counterparts. However, the sex difference was indicated in a larger number of craniofacial parameters in adolescents than in children, which meant sex discrepancy was more obvious and diverse in the older group. Finally, girls presented earlier cervical vertebral maturation than boys before hitting adulthood.

Previous studies had manifested sex differences in craniofacial characteristics of children and youngsters [16, 17]. However, the literature exploring sexual dimorphic characteristics of the craniofacial region has lacked sufficient updates in recent decades. Our study advanced and enriched the relevant research by investigating a greater number of craniofacial variables, including linear and angle measurements, in both hard and soft tissues of a relatively large sample size of children and adolescents using a novel digital analysis tool. We also introduced the evaluation of craniofacial growth of individuals by the QCMV method which is an efficient and objective approach to assessing the level of cervical vertebral maturation during adolescence [15]. A subsequent sex comparison amongst QCMV III participants was made to investigate sex differences in subjects during the same skeletal maturation stage.

Our results coincide with Michael S. Cooke *et al.*'s [17] study in that males exhibit a variety of significantly greater craniofacial linear measurements than females, especially in anterior/posterior facial height, yet very few significant sex differences in angular measurements were found. We also found this agreement with research targeted at different ethnic samples [18, 19]. There is a significant sex difference between the size of the craniofacial region, and males are on average larger than females, especially in the vertical dimension. The sex difference in cranium size is considered not only on account of genetic and environmental factors but also the product of sexual selection under selective pressures due to male competition [20]. It is well acknowledged that sex determination of the normal craniofacial characteristics and measurements can play an important role in orthodontics, since it can provide useful information referring to the assessment of the growth and development of craniofacial structures. Given that our sample group was a population with needs for future orthodontic care or treatments, we are hoping that the current study can help in orthodontic treatment planning. Moreover, the different craniofacial characteristics are also applied for sex determination and estimation, which plays a crucial role in forensic science.

In our study, the significant sex difference in facial convexity is consistent with the findings of P. Yeong and J. Huggare's research [21], indicating that girls have straighter facial profiles. Interestingly, in their study, we noted opposite results regarding sex differences in convexity between soft and hard tissues of the craniomaxillofacial region. P. Yoeng *et al.* [21] reported that the girls possessed greater maxillary and mandibular protrusion in hard tissue, which contradicted the result in soft tissue facial convexity. Unfortunately, we did not include parameters to measure maxillary and mandibular protrusion in this study. However, the thicker upper and lower lip in males may account for the contradiction in the convexity-related sex difference between soft and hard tissues.

In this present study, more statistically significant sex differences were revealed with a greater number of significantly different parameters in the ≥12-year-old group compared with the younger group. This may be explained by the influence of hormones after puberty when active craniofacial growth

TABLE 4. Sex difference of the overall craniofacial parameters.

Craniofacial parameters	Female (N = 199)	Male (N = 141)	p
Hard tissue			
SNA	82.53 ± 3.08	82.44 ± 3.47	0.817
SNB	78.61 ± 3.60	78.36 ± 3.95	0.768
ANB	3.91 ± 2.85	4.08 ± 3.06	0.659
FMA	26.34 ± 5.93	25.70 ± 6.46	0.297
Saddle angle	122.28 ± 4.61	122.54 ± 4.87	0.643
Articular angle	151.95 ± 6.88	151.24 ± 5.79	0.382
Gonial angle	119.57 ± 6.97	119.75 ± 7.89	0.875
Interincisal angle	123.87 ± 11.26	122.84 ± 11.45	0.363
Ramus height	41.85 ± 4.46	44.36 ± 5.82	<0.001*
Mandibular Body length	67.33 ± 5.11	68.49 ± 6.05	0.110
Anterior cranial base length	62.07 ± 3.42	63.77 ± 4.74	<0.001*
Posterior cranial base length	32.95 ± 3.25	34.89 ± 3.32	<0.001*
Anterior facial height	110.05 ± 7.58	114.70 ± 9.38	<0.001*
Posterior facial height	72.48 ± 6.20	76.71 ± 8.08	<0.001*
AFH/PFH	1.52 ± 0.11	1.50 ± 0.12	0.050
Upper anterior facial height	50.63 ± 3.58	52.95 ± 4.41	<0.001*
Lower anterior facial height	61.43 ± 5.28	63.89 ± 5.95	<0.001*
UAFH/LAFH	0.83 ± 0.06	0.83 ± 0.06	0.582
Overjet	4.57 ± 2.81	4.83 ± 3.53	0.505
Overbite	2.35 ± 1.83	2.67 ± 1.98	0.119
Wits appraisal	0.53 ± 3.86	0.61 ± 4.28	0.696
Soft tissue			
Facial convexity	167.60 ± 5.57	166.15 ± 6.27	0.044*
Soft tissue profile	164.48 ± 5.87	163.12 ± 6.55	0.089
Soft tissue convexity	141.56 ± 5.59	140.31 ± 6.09	0.096
Nasolabial angle	90.34 ± 12.10	88.59 ± 12.31	0.122
Nasal prominence	14.74 ± 1.58	14.59 ± 2.01	0.287
Upper lip to E-plane	2.49 ± 1.76	2.77 ± 2.11	0.414
Lower lip to E-plane	2.90 ± 2.04	3.21 ± 2.31	0.314
Upper lip protrusion	6.61 ± 2.13	7.39 ± 2.08	0.003*
Lower lip protrusion	5.60 ± 2.31	6.20 ± 2.49	0.034*
Upper lip length	21.15 ± 2.16	22.04 ± 2.53	<0.001*
Lower lip length	15.84 ± 2.16	16.26 ± 2.56	0.095
Upper lip thickness	11.94 ± 1.98	13.39 ± 2.23	<0.001*
Lower lip thickness	13.87 ± 1.75	15.12 ± 2.22	<0.001*
Soft tissue chin thickness	12.31 ± 1.98	13.06 ± 2.44	0.001*
N'-Sn	53.97 ± 4.17	56.46 ± 5.44	<0.001*
Sn-Me'	68.64 ± 5.35	71.95 ± 6.54	<0.001*
Sn-Sto	22.23 ± 2.51	23.29 ± 2.97	<0.001*

*Independent samples t-test and Mann-Whitney U-test were used. *$p < 0.05$.*

FMA: Frankfort-mandibular plane angle; AFH: anterior facial height; PFH: posterior facial height; UAFH: upper anterior facial height; LAFH: lower anterior facial height; SNA: Sella nasion A point angle; SNB: Sella nasion B point angle; ANB: Angel-Nose-Bite angle; N': nasion of soft tissue; Sn: subnasale; Me': menton of soft tissue; Sto: Stomi, stomion inferius.

TABLE 5. Sex difference of the craniofacial parameters of <12 years old patients.

Craniofacial parameters	Female (N = 73)	Male (N = 50)	*p*
Hard tissue			
Anterior facial height	106.49 ± 6.53	109.56 ± 10.19	0.004
Lower anterior facial height	59.62 ± 4.79	61.65 ± 6.40	0.014
Soft tissue			
Lower lip protrusion	6.18 ± 2.48	6.62 ± 2.39	0.017
Lower lip thickness	13.91 ± 1.68	14.82 ± 2.14	0.024
N'-Sn	52.26 ± 3.70	53.49 ± 5.99	0.049
Sn-Me'	66.66 ± 5.02	69.37 ± 7.06	0.016

Independent samples t-test and Mann-Whitney U-test were used. Only measurements with statistical differences are illustrated. N': nasion of soft tissue; Sn: subnasale; Me': menton of soft tissue.

TABLE 6. Sex difference of the craniofacial parameters of ≥12 years old patients.

Craniofacial parameters	Female (N = 126)	Male (N = 91)	*p*
Hard tissue			
Ramus height	42.87 ± 4.35	46.64 ± 5.14	<0.001
Mandibular Body length	68.83 ± 4.64	70.73 ± 5.10	0.009
Anterior cranial base length	62.60 ± 3.46	64.61 ± 3.91	<0.001
Anterior facial height	112.12 ± 7.40	117.53 ± 7.59	<0.001
Posterior cranial base length	33.42 ± 3.34	35.91 ± 2.78	<0.001
Posterior facial height	73.95 ± 5.75	79.96 ± 6.78	<0.001
AFH/PFH	1.52 ± 0.11	1.48 ± 0.12	0.004
Upper anterior facial height	51.58 ± 3.30	54.44 ± 3.37	<0.001
Lower anterior facial height	62.47 ± 5.29	65.12 ± 5.34	<0.001
Soft tissue			
Soft tissue convexity	141.29 ± 5.48	139.76 ± 6.50	0.038
Upper lip protrusion	6.37 ± 2.17	7.09 ± 2.07	0.032
Lower lip protrusion	5.26 ± 2.14	5.98 ± 2.53	0.043
Upper lip length	21.51 ± 2.19	22.48 ± 2.44	0.001
Upper lip thickness	11.85 ± 1.94	13.78 ± 2.14	<0.001
Lower lip thickness	13.85 ± 1.79	15.29 ± 2.26	<0.001
Soft tissue chin thickness	12.38 ± 1.94	13.15 ± 2.37	0.007
N'-Sn	54.96 ± 4.12	58.08 ± 4.35	<0.001
Sn-Me'	69.79 ± 5.21	73.37 ± 5.81	<0.001
Sn-Sto	22.45 ± 2.40	23.62 ± 2.75	<0.001

Independent samples t-test and Mann-Whitney U-test were used. Only measurements with statistical differences are illustrated. AFH: anterior facial height; PFH: posterior facial height. N': nasion of soft tissue; Sn: subnasale; Me': menton of soft tissue; Sto: Stomi, stomion inferius.

TABLE 7. Sex difference of the craniofacial parameters of QCVM III patients.

Craniofacial parameters	Female (N = 68)	Male (N = 33)	*p*
Hard tissue			
Ramus height	42.78 ± 4.72	47.00 ± 6.33	<0.001
Anterior cranial base length	62.13 ± 3.63	64.38 ± 3.79	0.009
Posterior cranial base length	33.23 ± 3.35	35.99 ± 2.88	<0.001
Anterior facial height	73.67 ± 6.20	80.36 ± 8.17	<0.001
Posterior facial height	111.29 ± 8.13	117.14 ± 6.90	<0.001
Upper anterior facial height	51.09 ± 3.50	54.11 ± 3.36	<0.001
Lower anterior facial height	62.14 ± 5.87	64.99 ± 4.53	0.010
Soft tissue			
Lower lip protrusion	21.28 ± 2.28	22.73 ± 2.55	0.006
Upper lip thickness	11.62 ± 1.69	14.21 ± 2.04	<0.001
Lower lip thickness	13.96 ± 1.58	15.23 ± 2.23	0.006
N'-Sn	54.45 ± 4.28	57.45 ± 4.33	<0.001
Sn-Me'	69.20 ± 5.88	73.58 ± 5.01	<0.001

Independent samples t-test and Mann-Whitney U-test were used. Only measurements with statistical differences are illustrated.
QCVM: quantitative cervical vertebrae maturation. N': nasion of soft tissue; Sn: subnasale; Me': menton of soft tissue.

TABLE 8. Multivariate linear regression analysis between sex and cephalometric parameters, adjusted for age.

Craniofacial parameters	B (95% CI)	Adjusted *p* value
Hard tissue		
Ramus height	2.852 (1.908, 3.797)	<0.001
Mandibular Body length	1.515 (0.467, 2.564)	0.005
Anterior cranial base length	1.841 (0.995, 2.687)	<0.001
Posterior cranial base length	2.066 (1.384, 2.748)	<0.001
Anterior facial height	5.125 (3.481, 6.769)	<0.001
Posterior facial height	4.692 (3.361, 6.024)	<0.001
Upper anterior facial height	2.556 (1.787, 3.325)	<0.001
Lower anterior facial height	2.699 (1.552, 3.847)	<0.001
Soft tissue		
Facial convexity	−1.456 (−2.732, −0.181)	0.025
Soft tissue profile	−1.380 (−2.718, −0.041)	0.043
Soft tissue convexity	−1.382 (−2.626, −0.138)	0.030
Upper lip protrusion	0.748 (0.293, 1.203)	0.001
Lower lip protrusion	0.569 (0.053, 1.084)	0.031
Upper lip length	0.960 (0.471, 1.449)	<0.001
Lower lip length	0.507 (0.019, 0.996)	0.042
Upper lip thickness	1.455 (1.001, 1.909)	<0.001
Lower lip thickness	1.262 (0.837, 1.687)	<0.001
Soft tissue chin thickness	0.759 (0.285, 1.233)	0.002
N'-Sn	2.732 (1.784, 3.680)	<0.001
Sn-Me'	3.575 (2.373, 4.776)	<0.001
Sn-Sto	1.121 (0.542, 1.700)	<0.001

Adjusted model adjusts for age. Only measurements with statistical differences are illustrated.
CI: confidence interval; N': nasion of soft tissue; Sn: subnasale; Me': menton of soft tissue; Sto: Stomi, stomion inferius.

begins. Hormones affect craniofacial development in boys and girls, for example, the growth of the mandible, maxilla, upper face, height of the head, *etc*. [22]. Additionally, we first introduced and applied the QCVM method for the evaluation of skeleton growth and development in craniofacial sex difference analysis [15]. It is a simple but effective and feasible assessment approach designated for children and adolescents, resulting in a research protocol that is easy to duplicate. Besides, we found a difference in the maturation level of cervical vertebrae between sexes, where the majority of female participants reach a higher maturation degree of QCVM III and IV in contrast to that of males who were mostly diagnosed as QCVM I/II. Consistent with our finding, Magalhães *et al*. [23] also reported an earlier CVM in females. This phenomenon can also be explained by the hormone theory that active growth occurs earlier in women, while the growth in men continues from puberty and completes in early adulthood.

Limitations of the current study should be noted. Our study sample enrolled a population of children and teenagers from a region of southwestern China, they cannot fully represent the rest of the nation since factors like climate and genetics may affect the craniofacial structures. In future research, the problem can be improved by employing different regions of the Chinese population, and comparison of different regional groups will add diversity to the research results. Apart from that, another sample bias is that the lateral cephalometric radiographs recruited in this study were taken for diagnostic purposes, where although the subjects satisfy the inclusion criteria, they appear to have maxillary or mandibular structures that require orthodontic correction. This concern can be solved by further investigations into the craniofacial parameters of random individuals.

5. Conclusions

In this study, craniofacial characteristics and cervical vertebrae maturation of the southwestern Chinese children and adolescents exhibited significant sex differences, which were more obvious and diverse in adolescents than in children. In general, males showed a greater craniofacial size than their female counterparts, especially in the vertical dimension. And they also possessed a more protrusive face. In addition, though girls reached an earlier cervical vertebral maturation than boys, they showed smaller linear craniofacial features. Therefore, the sex difference in the craniofacial region and cervical vertebrae maturation should be considered when developing reference standards for young age cephalometric measurement. The findings of sex discrepancy also added understanding to craniofacial morphology study on the Chinese population and provided treatment references for clinical settings such as surgical planning.

ABBREVIATIONS

QCVM, quantitative cervical vertebral maturation; AFH, anterior facial height; PFH, posterior facial height; UAFH, upper anterior facial height; LAFH, lower anterior facial height; N'-Sn, nasion of soft tissue-subnasale; Sn-Me', subnasale-menton of soft tissue; Sn-Sto, subnasale-stomion inferius; CVMS, cervical vertebral maturation stage; SMI, Fishman skeletal maturity indicators.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

TXG—participated in project conceptualization, data collection, formal analysis, investigation, writing-original draft and data curation and approved the final manuscript to be submitted. SYZ—participated in data collection, formal analysis, investigation, writing-original draft and data curation and approved the final manuscript to be submitted. CQX—participated in methodology, resources, writing-review & editing and supervision and approved the final manuscript to be submitted. XX—provided the original idea for this project, participated in project conceptualization, methodology, resources, writing-review & editing and project administration and approved the final manuscript to be submitted. SSH—participated in investigation, writing-review & editing and supervision and approved the final manuscript to be submitted. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The current retrospective study was reviewed and approved by the Ethics Committee of West China School of Stomatology of Sichuan University (Ethics number: WCHSCRSE-2022110) and was conducted following the Declaration of Helsinki. All patients or legal guardians have signed an informed consent form and the patient's private information has been kept confidential.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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