Formula for Cervical Vertebral Bone Age of Vietnamese People from 7 to 18 Years Old

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Introduction: The purpose of this study was to establish a formula for cervical vertebral bone age (CVBA) based on the morphological changes of cervical vertebrae on cephalometric radiographs in Vietnamese subjects between 7 and 18 years of age. Materials and Methods: This study included 180 children and adolescents (92 boys, 88 girls), between 7 and 18 years of age, selected from the craniofacial morphology studies of the Faculty of Odonto-Stomatology, Ho Chi Minh University of Medicine and Pharmacy. The cephalometric and hand-wrist radiographs of each subject were taken simultaneously and evaluated. Eleven hand-wrist skeletal maturity indicators of Fishman were grouped into five stages: initiation and acceleration, transition, deceleration, maturation, and completion stage. A multivariate regression analysis was conducted to assess the correlation between the stages of hand-wrist BA and the morphological characteristics of the second, third, and fourth cervical vertebrae on the cephalometric radiographs. Results: A formula for CVBA was proposed as follows: CVBA = 1.92 + 0.04 * α2 + 0.03 * α4 - 1.12 * AB3/BC3 + 3.17 * h4/w4, where α2 and α4 are anteroinferior border angles of C2 and C4; AB3/BC3 is the ratio of inferior to anterior dimension of C3; h4/w4 is the ratio of height to width of C4. The means and standard deviations of five stages of CVBA will be as follows: CVBA I = 1.527 ± 0.906; CVBA II = 2.732 ± 0.568; CVBA III = 3.762 ± 0.589; CVBA IV = 5.077 ± 0.840; and CVBA V = 5.820 ± 0.661. Conclusion: The quantitative CVBA method could be useful to assess the level of skeletal maturation in orthodontic and orthopedic treatments.

Keywords: Cephalometric radiograph, cervical vertebral bone age, Vietnam

INTRODUCTION

Since the chronological age does not closely correlate with the skeletal maturation, the evaluation of craniofacial growth according to the skeletal age is more appropriate in dentofacial orthopedic treatments, helping to improve the maxillomandibular imbalances. The assessment of bone age (BA) using hand-wrist radiographs has been considered a “gold standard” in determining the skeletal maturity of patients. However, to evaluate hand-wrist BA, we need to take extra hand-wrist X-rays which increase the incremental, unnecessary risk of radiation exposure for patients.

The developmental stages of cervical vertebrae during puberty can be easily observed on a cephalometric film, a common tool used for any orthodontic diagnosis and treatment planning. Many studies found strong level of agreement between hand-wrist and cervical vertebrae radiographic analysis in determining skeletal age, all

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How to cite this article: Ho TT, Lu LM, Luong QT. Formula for cervical vertebral bone age of Vietnamese people from 7 to 18 years old. J Int Soc Prevent Communit Dent 2022;12:49-57.
sugressing that cervical vertebrae radiography is a potential alternative to hand-wrist radiography.\cite{6-7}

There are two methods of assessing cervical vertebral bone maturation: the qualitative and quantitative methods. The qualitative methods analyze the appearance of the cervical vertebral bodies, including the concavity developed in the inferior border of the vertebra and the shapes of the vertebral bodies (trapezoid, horizontal rectangular, square, or vertical rectangular).\cite{8-10} The quantitative methods measure the dimensions, angles, or ratios of the dimensions of the cervical vertebrae.\cite{11-13} The advantage of qualitative methods is that they are time-saving as we do not need to take the cervical vertebrae measurement; however, one disadvantage of these methods is that they are subjective and require a lot of experience to make accurate judgment. In contrast, quantitative methods entail the measurement of cervical vertebrae dimensions which is time-consuming but objective and do not depend on one’s level of experience.\cite{14,15}

The previous literature included Chen’s suggestion of a quantitative cervical vertebral method to assess skeletal maturation of Chinese adolescence\cite{12} and Mito’s offer of a quantitative cervical vertebral BA (CVBA) formula for Japanese girls.\cite{11} Moreover, Ayach and Hadad\cite{16} presented a quantitative method to measure the volume of the fourth cervical vertebra on CBCT radiograph of Syrian adolescence. Because of difference in racial morphology, it is necessary to propose a quantitative method for assessing skeletal maturation in Vietnamese subjects based on the morphology of their cervical vertebrae. The quantitative assessment of cervical vertebral maturation will help growth modifications in dentofacial orthopedic treatment.

**Materials and Methods**

This retrospective and cross-sectional study was conducted with 180 subjects (92 boys and 88 girls) between 7 and 18 years of age, selected from the craniofacial morphology studies of Faculty of Odonto-Stomatolog, Ho Chi Minh University of Medicine and Pharmacy, Vietnam, in 15 years from 1996 to 2010.\cite{17} The chronological age was confirmed by the date of birth and the date of X-rays taken on each radiograph. The cephalometric and hand-wrist radiographs of each subject were taken simultaneously. The subjects were selected considering the following inclusion criteria: Vietnamese parents and grandparents; no cervical and craniofacial anomalies; no malformation of hand bones; and good quality lateral cephalometric and hand-wrist radiographs.

Hand-wrist radiographs were defined the skeletal maturation stages according to the Fishman classification.\cite{18} Eleven hand-wrist maturation stages or 11 skeletal maturation indicators (SMIs) were grouped by the researcher into five BA groups: BA I (SMI 1–4); BA II (SMI 5–6); BA III (SMI 7–9); BA IV (SMI 8–10); and BA V (SMI 11). About 180 lateral cephalometric radiographs that were divided into five BA groups above according to their hand-wrist radiographs. The 180 lateral cephalograms were included in 46 cephalograms of group BA I; 27 of group BA II; 24 of group BA III; 19 of group BA IV; and 64 of group BA V.

On each lateral cephalometric radiograph, the landmarks and tracings of three cervical vertebrae morphologies were identified and reviewed by a researcher. The tracings were scanned to a research computer, on 1:1 ratio, where the angles, distances, and ratios were measured on Autocad 2016, Autodesk Company, Vietnam. The 39 morphological characteristic parameters of the three cervical vertebrae (C2, C3, and C4) were measured and analyzed. A correlation equation was proposed that depicted the interrelationship between the 39 morphologic characteristic parameters of the three cervical vertebrae and the five BA groups of hand-wrist bone [Figure 1 and Table 1].

**Statistical analysis**

To determine the reliability or the reproducibility of the study, 18 hand-wrist radiographs and 18 cephalometric radiographs (10% sample size) were randomly selected 1 week apart to redefine the skeletal maturation index on hand-wrist radiographs and to retrace and redo all measurements of cervical vertebrae on cephalometric radiographs by the same operator. Intra-operator error between the two assessments of the skeletal maturation index was determined using Cohen’s kappa coefficient test, which revealed a high level of agreement (means of 0.93 at a \(P\)-value of 0.000). Intra-operator error between the two measurements was assessed using Dahlberg’s analysis that gave values between 0.061 and 0.404. These values indicated the adequate accuracy of measurement and reliability.

The data were analyzed by the statistical software SPSS Version 11.5 for Windows. The study power was set at 80% and a \(P\)-value of less than 0.05 was considered as significant (\(\alpha\) error – 95%). All 39 independent variables were analyzed the descriptive statistics (mean and standard deviation). The correlation coefficients between the dependent variable CVBA and 39 independent variables were calculated; analysis of variance and co-linearity.
diagnostics were employed for 39 independent variables of cervical vertebrae measurements. The means and standard deviations of CVBA between the male and female groups were compared by using two-tailed Student's $T$-test.

**RESULTS**

**Distribution of study sample**

The distribution of sample for gender and chronological age was shown in Tables 2 and 3.

The correlation of 39 independent variables and BA and formula of CVBA were presented in Tables 4 and 5.

In our study, 35 of 39 parameters of morphology of the C2, C3, C4 cervical vertebrae were correlated with hand-wrist BA [Table 5]. Of the 35 parameters, 27 were positively correlated with BA, whereas 8 were negatively correlated with BA. The variables related to the width of cervical vertebrae (w, AB, CD) had low or no correlation with BA, whereas the variables related
to the height (h3, h4, ah4, ph4, ph3, BC3, BC4, DA3, DA4) and the concavity of the inferior border (α2, α3, α4) of cervical vertebrae had a high correlation (r >0.847) [Table 5].

Using the multivariate regression analysis with the Enter method, the two groups of independent variables were identified as having significant correlation with BA, including group 1: ah4/ph4, AB3/BC3, h4/w4 and group 2: α2, α4, AB3/BC3, h4/w4, ah4/ph4. However, examination of co-linearity among the variables showed that there was no co-linearity phenomenon among the variables in group 2. Therefore, in group 2, we only chose the independent variables with high correlation coefficients above 0.85 (α2, α4, AB3/BC3, h4/w4 with r >0.85) and removed the variables with correlation coefficients below 0.85 (ah4/ph4 with r = 0.664 < 0.85).

Finally, we identified an equation which estimated the degree of correlation between CVBA and the four independent variables as follows:

\[
\text{CVBA} = \text{model} (\alpha_2, \alpha_4, \text{AB3/BC3}, \text{h4/w4})
\]
CVBA = 1.92 + 0.04 * α2 + 0.03 * α4 - 1.12 * AB3/BC3 + 3.17 * h4/w4,

with \( r = 0.957 \), \( r^2 = 0.916 \), and \( r^2 \) adjusted = 0.914.

Mean and standard deviation values of four independent variables in the equation (\( α2 \), \( α4 \), AB3/BC3, h4/w4) according to CVBA were presented in Table 6. Scatter plots of \( α2 \), \( α4 \), AB3/BC3, and h4/w4 variables according to CVBA were shown in Figures 2–5. The means and standard deviations of CVBA according to gender were presented in Table 7 and Figure 6.

**Table 6: Value of variables in the equation according to CVBA**

| BA  | N  | \( α2 \) (°), mean±SD | \( α4 \) (°), mean±SD | AB3/BC3 (%) , mean±SD | h4/w4 (%) , mean±SD |
|-----|----|----------------------|----------------------|-----------------------|----------------------|
| I   | 46 | 3.653 ± 5.133        | 2.747 ± 4.180        | 2.191 ± 0.504         | 0.593 ± 0.086        |
| II  | 27 | 9.633 ± 6.107        | 6.473 ± 4.689        | 1.658 ± 0.277         | 0.659 ± 0.066        |
| III | 24 | 13.6 ± 4.589         | 11.357 ± 7.466       | 1.380 ± 0.216         | 0.79 ± 0.084         |
| IV  | 19 | 22.547 ± 6.716       | 21.298 ± 8.706       | 1.087 ± 0.223         | 0.916 ± 0.131        |
| V   | 64 | 28.106 ± 8.732       | 29.269 ± 10.222      | 0.936 ± 0.086         | 0.954 ± 0.076        |

**DISCUSSION**

The period from 7 to 18 years is the pubertal growth stage of our body and consists of the prepubertal, circumpubertal, and postpubertal stages. The growth peak happens in the circumpubertal stage and is usually around years 11–13 for girls and 12–14 for boys.\(^{19}\) However, the growth peak is different from one person to another due to the difference in morphology and function. Some people have an early growth peak at 8 or 9 years, whereas others have a late peak at 13 or 14. The duration of the pubertal growth stage which composes of prepubertal, circumpubertal, and...
Figure 4: Scatter plot of AB3/BC3 variable according to CVBA

Figure 5: Scatter plot of h4/w4 variable according to CVBA

Figure 6: Graph of CVBA values in males and females
postpubertal periods is less or prolonged and varies among individuals. Despite some variations in the peak and duration of the pubertal stage, for most individuals, pubertal growth occurs from 7 to 18 years. Additionally, the craniofacial system also has its growth peak during the pubertal stage. Therefore, subjects of age between 7 and 18 were chosen for this study.

In 1972, Lamparski and Moca et al. demonstrated cervical vertebral morphological changes to chronological age between males and females. However, Hassel and Farman, San Román et al., and Baccetti presented cervical vertebrae changes during growth without mentioning gender difference. Besides, several quantitative CVBA methods have been introduced concerning with genders. Mito et al. studied on female groups from 8 to 14 years and suggested a quantitative CVBA method for Japanese girls. Therefore, when Caldas et al. applied Mito’s method derived from Japanese girls to Brazilian patients, this method was reliable only for Brazilian girls. Afterwards, Caldas et al. developed different formulae for both Brazilian genders. Further, Kumar et al. applied Mito’s formula to determine CVBA for the Asian North Indian people and concluded that Mito’s formula was reliable only for female patients. Therefore, Kumar et al.’s suggestion of a formula for Asian North Indian males was made. However, Chen suggested a quantitative cervical vertebral method for assessing skeletal maturation of Chinese adolescence without distinguishing between males and females. Ho and Hoang also suggested the cervical vertebral maturation assessment but did not deal with gender issue.

The results of our study demonstrated that there was no significant difference of CVBA between both sexes [Table 7 and Figure 6]. Subjects in our study were divided into five groups, which related to five pubertal growth stages: the initiation and acceleration stage (BA I), the transition stage (BA II) with growth peak, the deceleration stage (BA III), the maturation stage (BA IV), and the completion stage (BA V) with very little remaining growth. It meant that subjects were grouped into skeletal age (BA I–BA V). All parameters were analyzed according to skeletal age groups and not to chronological age groups [Table 2]. Additionally, the parameters in our proposed formula are angle ($\alpha_2$, $\alpha_4$) and ratio (AB3/CB3, h4/w4) measurements so that CVBA values did not depend on cervical vertebral dimensions that could be different for males and females. Therefore, CVBAs in our study were not significantly different between genders.

When analyzing the correlation of cervical vertebral morphological variables with BA, results presented that the variables describing the horizontal morphological characteristics of the cervical vertebrae were not correlated or less correlated with the CVBA, whereas those describing the vertical morphological characteristics and the inferior border angles of the cervical vertebrae were highly correlated with the CVBA [Table 5]. These could conclude that the cervical vertebral growth in the horizontal direction had completed in the early stage, but in the vertical direction growth occurred mainly during the adolescent period.

In our CVBA formula, the variables $\alpha_2$, $\alpha_4$, AB3/CB3, and h4/w4 had very high correlation with the BA [Table 5]. These ratio and angle parameters would be better than linear parameters in both comparability and validity. However, values of $\alpha_2$, $\alpha_4$, and h4/w4 increased, whereas value of AB3/CB3 decreased gradually from BA I to V [Table 6]. These results implied that the body heights of cervical vertebrae are gradually higher and the concavity of the inferior borders of cervical vertebrae are sequentially deeper during growth. These morphological changes were appropriate with cervical vertebral growth during pubertal stages. Our results were similar to those of studies that used qualitative methods: during growth, the concavity in the inferior border of the vertebra developed and the shapes of the vertebral bodies changed from trapezoid, horizontal rectangle, square, to vertical rectangle.
As described, there were slight differences between our CVBA formula and those by Mito and Chen. This could be explained by the differences in morphological characteristics and growth patterns between races and ethnics. Therefore, deriving a specific formula for the population of Vietnamese adolescents would be relevant and necessary.

The means and standard deviations of CVBA I to V vary from 1.527 ± 0.906 to 5.820 ± 0.661 [Table 7]. More specifically, the means and standard deviations of five stages of CVBA will be as follows: CVBA I= 1.527 ± 0.906; CVBA II= 2.732 ± 0.568; CVBA III= 3.762 ± 0.589; CVBA IV= 5.077 ± 0.840; and CVBA V= 5.820 ± 0.661. The aforementioned values of CVBA stages showed that there are some overlaps between the two adjacent stages. When a value belongs to overlapped areas, there could be some hesitation when deciding the exact stage of CVBA.

Qualitative methods depend a lot on experience and expertise in order to have high reliability and reproducibility. In contrast, quantitative methods like our CVBA index allow us to measure and calculate the parameters according to a formula making it more objective and reliable method for assessing the maturity of the cervical vertebra on cephalometric radiographs. Nonetheless, quantitative methods are not without limitations. Further division of CVBA subgroups to reduce overlapping areas may be needed to overcome a shortcoming of this quantitative method. Moreover, with the proposed CVBA formula, the growth peak of the maxilla and the mandible can be determined. Further studies of craniofacial growth according to CVBA can be conducted to determine the growth peak of the maxilla and mandible to help modify growth in class II or class III malocclusion patients.

CONCLUSION
A proposed formula of CVBA to assess skeletal maturation was established:

$$CVBA = 1.92 + 0.04 \cdot \alpha_2 + 0.03 \cdot \alpha_4 -1.12 \cdot AB3/BC3 + 3.17 \cdot \frac{h_4}{w_4},$$

for which $\alpha_2$ and $\alpha_4$ are anteroinferior angles of C2 and C4 vertebra; AB3/BC3 is the ratio of inferior to anterior dimension of C3; and $h_4/w_4$ is the ratio of height to width of C4 vertebra.

The quantitative CVBA method is an objective, reliable, and relatively simple method for evaluating skeletal maturation used in orthodontic and orthopedic treatments.

Acknowledgements
The authors wish to thank Professor Hoang Tu Hung, former Dean, Faculty of Odonto-Stomatology, University of Medicine and Pharmacy, Ho Chi Minh City, for his suggestion in the study.

FINANCIAL SUPPORT AND SPONSORSHIP
Nil.

CONFLICTS OF INTEREST
There are no conflicts of interest.

AUTHORS CONTRIBUTIONS
TT.T.H conceived the ideas. TT.T.H and L.M.L collected and analysed the data. TT.T.H and QT.T.L contributed to the writing. TT.T.H edited and reviewed.

ETHICAL POLICY AND INSTITUTIONAL REVIEW BOARD STATEMENT
This study was approved by the research committee of the University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam (244/QĐ-DHYD-SDH).

PATIENT DECLARATION OF CONSENT
The consent is not required as subject’s identify is not disclosed or compromised.

DATA AVAILABILITY STATEMENT
All data used to support the findings of this study are available from the corresponding author upon request.

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