Title: Absence of a Discernible Secular Trend in CVM Stages in American Blacks and Whites

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Abstract: Purpose: The dual purposes were (1) to estimate chronological ages at attainment of cervical vertebral maturation stages (CVM) and (2) to test for a secular trend between an older cohort treated between 1980-1984 and a recent group treated between 2010-2014 from the same clinic. Methods: CVM stages were scored from lateral pretreatment cephalograms of orthodontic patients (n=343) between 10 and 15 years of age. Both males and females, American blacks and whites (race determined by self-identification) were examined singly. CVM were scored per the 6-stage method of Baccetti et al. (2005). Median age of each stage was estimated with survival analysis, by cohort, race, and sex, and logistic regression analysis compared groups. Results: No significant difference was found between the two cohorts. There also was no significant race difference between the CVM tempos of American blacks and whites. However, the subject's sex was statistically important. All sex differences had girls achieving a CVM stage earlier than boys. American whites exhibited greater sexual dimorphism (~13%) than blacks (~4%). Conclusions: There was no discernible difference in the CVM ages of attainment between the two cohorts that were 30+ years apart. The tempo of cervical vertebral maturation has not been altered in this population, and can be applied equally to both American blacks and whites. Girls achieve CVM stages earlier than boys, and ought to be treated earlier to harness their parapubertal growth.
Absence of a Discernible Secular Trend in CVM Stages in American Blacks or Whites

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\textbf{KEY WORDS:} Bone age, physiological age, Sexual dimorphism, Age at treatment, Maturation

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The study tested CVM stages for differences between two cohorts, by race and sex.

No difference in CVM ages between the two cohorts that were 30+ years apart.

American blacks and whites had almost-identical tempos of CVM maturation.

Sex greatly affected rate of CVM maturation: girls developed much faster than boys.
INTRODUCTION

Over the past century, broad-spread evidence has accumulated for the earlier maturation of children, termed a secular trend of earlier maturation. “Secular” is an adjective referring to a period of time, and a secular trend is a change in occurrence of some thing or event over that time.\(^{1,2}\) Secular trends towards earlier maturation have been attributed to the attenuation of developmental constraints through improved nutrition, healthcare, and socio-economic environments.\(^{3,4}\) Other factors such as more sedentary lifestyles and increased body mass indexes have also been shown to be related to secular trends of earlier maturation.\(^{5}\) The concept is that, with environmental improvements, children are able to more fully attain their genetic growth potential, resulting in increases in the size of skeletal and dental structures.\(^{6}\)

We are unaware of secular studies for cervical vertebrae, but arguing from hand-wrist bone-age studies,\(^{7,8,9}\) trends show earlier maturation. Hand-wrist (boer age) studies by Hawley et al.\(^{10}\) (South African white and black girls and boys), So et al.\(^{11}\) (Chinese girls in Hong Kong), and Himes et al.\(^{1}\) (British boys and girls) document significant secular quickening in skeletal maturity. Changes in bone age were greater for black than white children and for black females in particular.\(^{10}\)

In the past, hand-wrist films were more widely used by orthodontists to estimate skeletal maturity, often focusing on the pubertal spurt in mandibular growth.\(^{13,14}\) Cervical Vertebral Maturation (CVM) methods are now advocated as a suitable method for the detection of peak mandibular growth,\(^ {15,16,17}\) negating the need for a hand wrist film.

Intents of the present study were (1) to estimate median chronological ages at attainment of cervical vertebral maturation stages (CVM) in samples of adolescent
orthodontic patients and (2) to test for a secular trend between an older cohort treated between 1980-1984 and a recent group treated between 2010-2014 from the same clinic. Cohorts were composed of both males and females and of American blacks whites, all evaluated separately.

MATERIALS AND METHODS

Patient records were analyzed from the Department of Orthodontics at ••••••. Demographic data and CVM scores were collected from pretreatment cephalograms (one per person). Two cohorts were constructed, an older group that began treatment between 1980 and 1984 and a more recent group, started between 2010 and 2014. This span of 30+ years—more than a generation—used the oldest records archived in this clinic. Females and males, and two ethnicities were examined, American blacks and whites, determined by self-identification. Subjects subsequently received comprehensive orthodontic treatment that began between the chronological ages of 10 and 15 years (Table I). Cases had a negative medical history; subjects with a syndrome, cleft, or hypodontia (ignoring third molars) were excluded. Recent cohort cephalograms were retrieved from Dolphin Imagining® (Dolphin Imaging & Management Solutions, Chatsworth, CA). The digital files were transferred to a computer folder without identifiers (except record number) so they could be analyzed while blinded to the subject’s demographics. The older cohort’s cephalograms were collected from archived records; these film cephalograms—labeled with patient record number—were scored using a light box, while blinded to the subjects’ demographics. HIPAA approval was obtained prior to the study (IRB # 14-03180-XM). There were 154 individuals in the 1980-1984 cohort and 189 in the recent 2010-2014 cohort. The paucity of black
patients in the earlier cohort (n = 37) was a limiting factor. Cervical vertebrae morphology was scored using the 6-stage method of Baccetti and coworkers.\textsuperscript{17} In brief, the visually-defined, ordinal grades of the cervical vertebrae (C2-C4) were:

**CVM 1 (CS1):** Caudal borders of all three vertebrae (C2-C4) are flat. Bodies of C3 and C4 are trapezoid (superior border of the vertebral body is tapered from posterior to anterior).

**CVM 2 (CS2):** A concavity is present at lower border of C2. Bodies of C3 and C4 are trapezoid in shape.

**CVM 3 (CS3):** Concavities occur at lower borders of C2 and C3. Bodies of C3 and C4 are either trapezoid or rectangular-horizontal.

**CVM 4 (CS4):** Concavities at lower borders of C2, C3, and C4 are present. Bodies of C3 and C4 are rectangular-horizontal.

**CVM 5 (CS5):** Concavities at lower borders of C2, C3, and C4 are present. At least one of the bodies of C3 and C4 is square in shape. If not square, the body of the other vertebra is rectangular-horizontal.

**CVM 6 (CS6):** Concavities at lower borders of C2, C3, and C4 are evident. At least one of the bodies of C3 and C4 is rectangular-vertical. If not rectangular-vertical, the body of the other cervical vertebra is square.

The kappa statistic for agreement was calculated from double determinations of CVM scores on 35 cephalograms.\textsuperscript{19} Data were analyzed using survival analysis to calculate the median ages at attainment of each stage\textsuperscript{20} and Cox’s proportional hazards model\textsuperscript{21} to test for group differences. Inferential statistics were evaluated at the conventional alpha level of 0.05; tests were two-tail.
RESULTS

Cases (n = 35) were randomly selected and re-scored after a wash-out period of several weeks. Most repeated CVM scores were identical (86%, 30/35), and none differed by more than one grade. Kendall’s tau, a measure of association, was 0.95 (SE = 0.02) and the kappa statistic was 0.84 (SE = 0.06). Landis and Koch\textsuperscript{22,23} suggest that repeatability values above 0.81 be labelled “almost perfect agreement.” The chronological age distribution for each CVM stage was tested for normality using the Shapiro-Wilk goodness-of-fit test. None departed significantly (P > 0.50).

Survival analysis was used to estimate median ages at attainment of each CVM stage, by cohort, race, and sex (Table II). Pooling the sample (n = 343 subjects), median ages span the interval from about 12 to 15 years (Fig. 1). Using the data plotted in Fig. 1, intervals between stages are all less than a year (Fig. 2), with the duration between stages 2 and 3 being the shortest (0.03 years).

Cohort differences were of major interest in this study, but, statistically (Table II), proportional hazards tests were negative. None of the 8 race-stage comparisons between the older and recent cohort approached significance (Fig. 3). The biggest change was for black boys (a quickening in tempo), but none of the cohort tests (controlling for race and sex) was statistically different.

So too, there was no discernible race difference between the CVM tempos of American blacks and whites (Table II). American black girls were trivially slower than whites to attain most CVM stages (Fig. 3), while American black boys were insignificantly older at each CVM stage than American whites.
Sex of the adolescent was statistically important (Table III), and the relationship differed by race (Fig. 4). For whites, 3 of the 4 tests were significant (P < 0.001), and 1 of the 4 tests was sexually dimorphic for the American black sample. All significant sex differences had girls achieving a stage earlier than boys. The striking difference was the greater sexual dimorphism among American whites than blacks (Fig. 4). White boys were the slowest group to attain each CVM stage, while white girls were the fastest—achieving CVM stages at the youngest chronological ages. American black boys were generally quicker to achieve stages than white boys but slower than black girls. Indeed, the American black samples are within the age interval bounded by the white samples. Using the formula, \( \frac{(\text{median}_{\text{boys}} - \text{median}_{\text{girls}})}{\text{median}_{\text{girls}}} \times 100 \), percent sexual dimorphism averaged 4.4% for blacks and 13.1% for whites.

**DISCUSSION**

Keying orthodontic treatment to the patient’s maturational status facilitates the orthodontic outcome,\(^{24,25,26,27}\) since it capitalizes on the person’s growth to enhance occlusal and bony changes. The use of biological age has a long history in the healthcare sciences,\(^{28}\) and it is argued that biological age is a better predictor of a patient’s growth status than chronological age.\(^{29,30}\)

CVM are ordinal-scale grades. Conformation of each morphological grade depends on criteria that distinguish it from others. The number of stages and the criteria of each stage depend on the researcher. The aim generally is to develop as many stages as possible to heighten discrimination, but only as many as can be reliably distinguished to reduce misclassification. The ordinal series—as defined by Lamparski\(^{15}\) or Baccetti et al.\(^{17}\) — are not equidistant, and the use of numerals to
designate them is misleading. The grades are monotonic, meaning that each child’s vertebrae will successively exhibit the grades in the same invariant order. What varies is the rate at which subjects achieve the stages.

With the CVM method used in this study, the metameric cline of morphological differences among the vertebrae (i.e., more mature caudal vertebral centra\textsuperscript{31} is incorporated into one scoring system.\textsuperscript{17} This contrasts with studies by Lamparski\textsuperscript{15} and others,\textsuperscript{16,32} who scored each vertebra separately.

With cross-sectional data, ages of the marginal stages cannot be accurately estimated. For example, all children will exhibit CVM 1 for about a decade—until CVM 2 occurs, so estimation of average age depends on the age distribution sampled. Likewise, CVM 6—once attained—persists throughout the person’s lifetime. It is necessary to use longitudinal data to estimate the onset of these marginal maturational events.\textsuperscript{33} Therefore, just CVM 2 through 5 were analyzed in this study.

Intervals between CVM stages were generally less than a year (Fig. 4), but this is somewhat misleading since individuals probably do not mature as quickly as suggested by the averages, but it does suggest that the orthodontist has only a short time to capitalize on the enhanced growth that is anticipated to occur between CVM stages 2 and 3.\textsuperscript{34} Thereafter, craniofacial growth slows, and orthodontic correction becomes primarily dental rather than skeletal.\textsuperscript{35}

Most maturational studies have focused on American whites. This seems to be the first CVM aging study of American blacks, though they constitute about 1/8 of the US population.\textsuperscript{36} There were few non-whites in the early cohort (1980-1984), reflecting their under-utilization of orthodontic treatment\textsuperscript{37} and that limited our sample size for
blacks (Table I). It was surprising to us that no hint of a black-white difference in the tempo of vertebral maturation was found (Table III). This vertebral measure is distinct from tooth mineralization\textsuperscript{38,39} and tooth emergence,\textsuperscript{40,41} where American blacks develop quicker. This emphasizes the modest concordance among different physiological measures, and it argues for a multifactorial approach to age estimation\textsuperscript{42} if the estimate has important consequences.\textsuperscript{43,44} Different aging methods are controlled by different endocrine systems and are not strongly inter-correlated either within an individual or across groups.\textsuperscript{46,47,48,49} Measures of physiological age all progress during a person’s ontogeny, but they are dissociated, often responding to different biochemical cues. This perspective may seem counter to studies reporting statistically significant correlations among aging techniques, but a correlation measures the strength of a relation between two variables, not the agreement between them.

A shortcoming of this study was the restriction of examinations to the age span of 10.0 to 15.0 years because this misses the occurrence of CVM stages before and after this interval. This could alter the age estimates (Table II) by upward-biasing early-maturers and attenuating the age estimates of late maturers. However, tests for normality were quite acceptable, and patients presenting for orthodontic treatment typically range between 10 and 15 years of age.

The principal source of variation was subject’s sex, not race (Fig. 4). Girls (black and white) and boys (black and white) matured at more diverse ages than between races. Girls achieved CVM stages at significantly younger ages than boys, but it mattered little whether subjects were black or white. It is more important, in terms of maturational status, to focus on the patient’s sex than whether the subject is American
black or white. Sexual dimorphism averaged 4.4% for blacks and 13.1% for whites. It is known that girls mature more quickly than boys, but this magnitude of difference among whites was unanticipated.

**CONCLUSION**

This retrospective study of cervical vertebrae (n = 343 children) tested for age differences in CVM stages between two cohorts (1980-1984 versus 2010-2014), and/or between races (American blacks, whites), and/or between sexes (boys, girls). Subjects were between the ages of 10 and 15 years.

1. There was no discernible difference in the CVM ages of attainment between the two cohorts that were 30+ years apart.
2. American blacks and whites exhibited no statistically significant difference in their tempos of CVM maturation.
3. The subject’s sex significantly affected the rates of CVM maturation (girls faster than boys). Sexual dimorphism was greater in whites than blacks.
REFERENCES CITED


Fig. 1. Boxplots of the subject's age by CVM stage (cohorts combined) to give a sense of the variability in ages among males (M) and females (F) by CVM stage. Sample was limited to those between 10 and 15 years of age.
Fig. 2. Plots of race against median CVM age (cohorts combined). **Top:** plot for girls alone. **Bottom:** plot for boys alone. Error bars are 1 SD and are only shown in one direction to avoid clutter.
Fig. 3. Plots of CVM stage against chronological age (years) between cohorts ("recent" = 2010-2014; "older" = 1980-1984), by race and sex. Graphs are on the same scale. Error bars are interquartile distances; errors are only plotted in one direction to diminish overlap and confusion. None of the cohorts differed significantly.
Fig. 4. Plot of median ages (years) of the cervical vertebral stages, by race and sex. Races are American whites (W) and American blacks (B). Error bars are omitted for clarity.
Table I. Descriptive statistics for chronological ages (years) at examination of the pretreatment cephalograms.

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Table II. Results of proportional hazards tests for cohort difference, while controlling for ethnicity and sex.\(^1\)

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\(^1\)Each row was a separate analysis. Statistics are sample size (n), chi-square test statistic (1 degree of freedom), and two-tail probability value (P value).
Table III. Descriptive statistics for CVM stages, by race.\(^1\)

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\(^1\)Calculated from product-moment survival analysis. Log rank tests (1 degree of freedom) tested for a statistically significant difference between sexes within race. Statistics are sample size (n), 50th percentile (median), lower and upper 95th percentiles (L\(_1\) 95\%, L\(_2\) 95\%), arithmetic mean (mean), and standard error of the mean (SE).
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