
Growth in the Untreated Class III Subject

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The present study was designed to provide an estimate of growth in white subjects with Class III malocclusion by means of the analysis of lateral cephalograms in two samples: (1) 22 untreated Class III individuals followed longitudinally from a prepubertal observation through a postpubertal observation; and (2) a large cross-sectional population (n = 1091) of male and female untreated subjects at six consecutive developmental periods (CS1 through CS6 according to the cervical vertebral maturation method). Class III disharmony shows a significant tendency to worsen with growth, as assessed by means of the longitudinal portion of the study. The persistence of typical Class III growth characteristics well beyond the adolescent growth spurt into early adulthood was confirmed by the results of the large cross-sectional study. A long period of active mandibular growth, the absence of any catch-up growth in the maxilla, and the significantly more vertical direction of facial growth during late adolescence appear to be unfavorable aspects of Class III malocclusion in both genders during the postpubertal stages. Treatment planning by means of orthodontic/orthopedic appliances should take into account this pattern of prolonged mandibular growth in terms of duration of retention and timing for the evaluation of stability of treatment protocols and eventually for orthognathic surgery. (Semin Orthod 2007;13:130-142.) © 2007 Elsevier Inc. All rights reserved.

Knowledge of the physiologic growth changes of the dentofacial complex is fundamental to orthodontic treatment planning. In particular, growth trends in different malocclusions and skeletal disharmonies provide indica-

tions for the estimate of growth potential in patients with the same type of disharmony and represent adequate control data when evaluating treatment outcomes.

There are three methods of evaluating facial growth in individuals diagnosed as having a Class III malocclusion: classical growth studies, longitudinal data of untreated Class III individuals, and cross-sectional data from untreated Class III samples. The large North American growth studies have provided longitudinal data for untreated individuals with different types of malocclusion. These samples, however, consist primarily of individuals categorized as either having normal occlusion or Class I or Class II malocclusions. Individuals diagnosed as having a Class III malocclusion are represented less than the expected frequency of 1% to 5%.¹⁻⁴ In contrast, longitudinal studies comprised of individuals of Asian ancestry contain sample sizes adequate to describe Class III craniofacial growth.^{5,6}

Admittedly, the best method for studying facial growth and development is through the analysis of longitudinal data. Unfortunately, no

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major investigations have been performed in relation to untreated Class III malocclusion. There are two main reasons for this deficiency in the literature: the relatively low frequency of its occurrence (especially in white populations) and the well-recognized need for early intervention by both the public and dental professionals. In response, several investigators have attempted to contribute to the knowledge of Class III facial growth trends by assembling small groups of orthodontically untreated Class III individuals for use as controls groups when evaluating treatment effects. Again investigators evaluating predominantly Asian populations have led the way.⁵⁻¹⁰ Investigations collecting longitudinal data on those of European ancestry have arisen only within the last decade.¹¹⁻¹³

In an early attempt at quantification of white Class III growth, Chong and coworkers¹¹ collected cephalometric records and study models from the Burlington Growth Study at the University of Toronto and the Bolton-Brush Growth Study at Case Western Reserve University in Cleveland, Ohio. The assembled records of the 13 children suggested that between the ages of 6 and 11 and a half years maxillary length increased slightly more than 1 mm per year, lower anterior facial height increased more than 2 mm per year, and mandibular length increased by less than 3 mm per year.

Baccetti and coworkers¹² conducted an investigation of untreated Class III children in the mixed dentition stage of dental development. Thirty-two untreated Class III individuals from the University of Florence were divided into early and late mixed dentition groups. No statistically significant differences were found between these subgroups. Both samples displayed deficient maxillary advancement and excessive mandibular growth. Point A was found to advance at a rate of 1 mm per year, while mandibular length increased 4.5 mm per year. Macdonald and coworkers¹⁴ arrived at similar results when they gathered serial cephalometric records of Class III subjects from private orthodontic practices in the United States. They assembled cephalometric data from 27 individuals who had not received any orthodontic treatment. The total observation period was broken down into annualized changes, and these Class III individuals were compared with matched subjects (predominantly Class I) from the University

of Michigan Growth Study. The results of the comparison of untreated Class I and Class III subjects demonstrated significantly less forward movement of point A (0.6 mm) and greater forward movement of the mandible (1.3 mm) in the Class III group.¹⁴ The use of annualized changes involves the assumption that growth is linear over the observation interval. The major limitation of this method is that it may obscure changes in the rate of growth.

To clarify the weakness of these contributions further, these longitudinal studies are limited in many ways including the sample size or observation interval (or both), while they usually lack any information about the occurrence of the pubertal growth spurt. As a result, this methodology restricts the applicability of the outcomes to other Class III individuals meeting the same inclusion criteria.

Other investigators have chosen to collect data from a large number of Class III subjects at a single time-point and used these to make inferences on normal craniofacial growth. In 1986, Guyer and coworkers¹⁵ attempted to characterize Class III individuals at different developmental stages by studying lateral cephalograms of 144 Class III children between the 5 and 15 years of age. The sample was divided into four groups according to chronological age, and then compared with the so-called Bolton Standards.² The investigators reported that the differences in craniofacial form between Class I and Class III individuals were present in all four age groups. The excessive lower anterior facial height, dentoalveolar compensations, maxillary retrusion, and mandibular prognathism were evident in the Class III sample as early as 5 years of age. The early establishment of Class III characteristics and the tendency for the intermaxillary relationship to worsen is consistent with the findings in other populations.^{5,6}

Tollaro and coworkers¹⁶ conducted a study of Class III craniofacial development that was cross-sectional in nature. The 69 untreated northern European Class III children between the ages of 4 and 6 included in the study had full primary dentitions. The facial characteristics were compared with those of 60 subjects, matched for age and stage of dentition, presenting with a normal or Class I occlusion. Similar to the findings of Guyer and coworkers,¹⁵ these investigators observed that the signs of Class III skeletal imbal-

ance were present during the deciduous dentition phase.

An investigation of similar methodology was performed at the London Hospital Medical College Dental School.¹⁷ The study contrasted 285 Class III subjects with 210 normal controls; all subjects were white. Males and females were examined separately in each of four age groups: 7 to 10 years, 11 to 12 years, 13 to 14 years, 15 years and older. Although the data for the control subjects were longitudinal in nature and the Class III data were cross-sectional, their indirect comparison provided an estimation of the differences between age groups over time. Battagel¹⁷ reported that the Class III males at all age groups displayed retrusive maxillae and prominent mandibular positions relative to male controls. The investigator also noted an increase in lower anterior facial height and dentoalveolar compensations beginning at 11 years of age. With continued development, the Class III males demonstrated less forward growth of the maxilla and a more vertical growth pattern than their normal counterparts. Finally, the largest increment of change for mandibular length was between the last two age groups, suggesting peak growth at this age interval. The females presented a different growth pattern from the males. Relative to controls, the Class III females displayed more prominent mandibles, more proclined maxillary incisors, and similar lower anterior facial heights. The maximum change for facial characteristics occurred between the average ages 9.5 and 12 years, but continued after the age of 15 years. Although the data for the control subjects were longitudinal in nature and the Class III data were cross-sectional, their indirect comparison provided a rough estimation of the differences between age groups over time. Further, this study¹⁷ highlighted the presence of a sexual dimorphism in Class III malocclusion that was confirmed recently by Baccetti and coworkers.¹⁸

The largest cross-sectional Class III study to date was conducted by Miyajima and coworkers¹⁹ on a sample of 1376 Japanese females, 2.7 years to 47.9 years of age. These females were subdivided into groups based on the stage of dental development as described by Hellman.^{20,21} The results were congruent with the conclusions of other Class III investigations. In this sample of Japanese females, the maxilla as-

sumed a retrusive position at an early developmental stage and retained a fairly constant anteroposterior relationship to the cranial base structures with continued development. Likewise, the mandible was protrusive early in development and became increasingly prognathic with age. The characteristic of lower anterior facial height behaved similarly to the mandible with a steady increase in dimension with maturation.

Recently, Deguchi and coworkers²² used a large cross-sectional sample (562 subjects) as a control group in a long-term study on the effects of chin-cup therapy on Asian patients with Class III malocclusion. Three age periods were investigated (ie, 8 years, 13 years, 17 years), with no differentiation between males and females. Both ANB angle and the Wits appraisal worsened along with growth, mainly due to excessive mandibular growth in a forward direction.

The current article presents the results of two investigations on the growth characteristics of the untreated Class III patient: (1) A longitudinal study on 22 untreated Class III subjects of European ancestry; and (2) a cross-sectional study on a substantial group of individuals with untreated Class III malocclusions. Both investigations cover the circumpubertal period from early developmental phases (prepubertal) through late adolescence (postpubertal), as assessed by means of a reliable indicator of skeletal maturity, the cervical vertebral maturation method.

Longitudinal Data

A sample of 22 subjects with Class III malocclusion (8 females, 14 males) with availability of longitudinal records was obtained from the Department of Orthodontics at the University of Florence, The University of Michigan Growth Study,¹ and three private orthodontic practices in the state of Michigan. The lateral cephalograms of the examined subjects were evaluated at T₁ and at T₂, a long-term observation after completion of active growth. Mean ages were 8 years and 8 months \pm 2 years and 5 months at T₁ and 15 years and 2 months \pm 1 year and 11 months at T₂ with a mean duration of the observation period T₁-T₂ of 6 years and 5 months \pm 2 years and 2 months. Magnification was corrected to an 8% enlargement for all radio-

graphs. Although sexual dimorphism is known to be significant in Class III subjects,¹⁵ no attempt to evaluate females and males separately was performed because of the limited number of individuals in the collected sample.

The sample satisfied all of the following inclusionary criteria:

1. European-American ancestry (white);
2. No orthodontic treatment;
3. Class III malocclusion at the time of the first observation (T_1) characterized by an anterior crossbite or edge-to-edge incisal relationship and a Wits appraisal of -2 mm or less;
4. No permanent teeth congenitally missing;
5. Cephalograms of adequate quality available at T_1 and at the time of long-term observation T_2 ; and,
6. Patients had to present with postpubertal skeletal maturation at the final observation (T_2) based on the cervical vertebral maturation (CVM) method of developmental staging (stage CS5 or CS6 in CVM).²³

Cephalometric Analysis

A customized digitization regimen and analysis provided by Dentofacial PlannerTM (Dentofacial Software, Toronto, Ontario, Canada) was used for all the cephalograms that were examined in this study. The cephalometric analysis required the digitization of 77 landmarks and 4 fiducial markers. The customized cephalometric analysis containing measurements from the analyses of Steiner,²⁴ Ricketts,²⁵ Jacobson,²⁶ and McNamara²⁷ generated 36 variables, 13 angular and 23 linear, for each tracing.

Fiducial markers were placed in the maxilla and mandible on the T_2 tracing and then transferred to T_1 tracings in each subject's cephalometric series, based on superimposition of internal maxillary or mandibular structures. The maxillae were superimposed by registering on the bony internal details of the maxilla superior to the incisors and the superior and inferior surfaces of the hard palate. Fiducial markers were placed in the anterior and posterior part of the maxilla along the palatal plane. This superimposition describes the movement of the maxillary dentition relative to the maxilla.

The mandibles were superimposed posteriorly on the outline of the mandibular canal.

Anteriorly, they were superimposed on the anterior contour of the chin and the bony structures of the symphysis.^{25,28} A fiducial marker was placed arbitrarily in the center of the symphysis and another in the body of the mandible near the gonial angle. This superimposition facilitated measuring the movement of the mandibular dentition relative to the mandible.

Cranial base superimpositions assessed the movements of the maxilla and mandible relative to the basion-nasion line registered at the posterosuperior aspect of the pterygomaxillary fissure (PTM_{SP}).^{25,28} The posterior cranial outline also was used to verify the superimpositions. The movements of the maxilla and mandible were depicted by the direction and magnitude of displacement of the fiducial markers in the tracings of these bones relative to cranial base structures.

Staging of vertebral maturation was applied according to the most recent version of the method.²³

Statistical Analysis and Method Error

Descriptive statistics of the Class III group at T_1 and T_2 were calculated. The changes from T_1 through T_2 were analyzed statistically by means of a paired *t* test. Level of significance was set at $P < 0.05$.

McNamara and colleagues²⁹ have reported the error of the method previously. Accuracy of linear measurements ranged from 0.1 mm to 0.3 mm with a standard deviation of approximately 0.8 mm. Angular measurements varied 0.1° with a standard deviation ranging from 0.4 to 0.6° .

Results

Changes in craniofacial measures during the overall observation period (T_1 to T_2 , which covers an interval of approximately $6\frac{1}{2}$ years from the early mixed dentition through the permanent dentition) provide clear indication that the skeletal imbalance in Class III malocclusion is established early in life and is not self-correcting during development (Fig 1). In fact, the disharmony becomes more pronounced in the majority of patients during the pubertal peak and continues until skeletal maturation is complete. It is evident that Class III craniofacial measures display

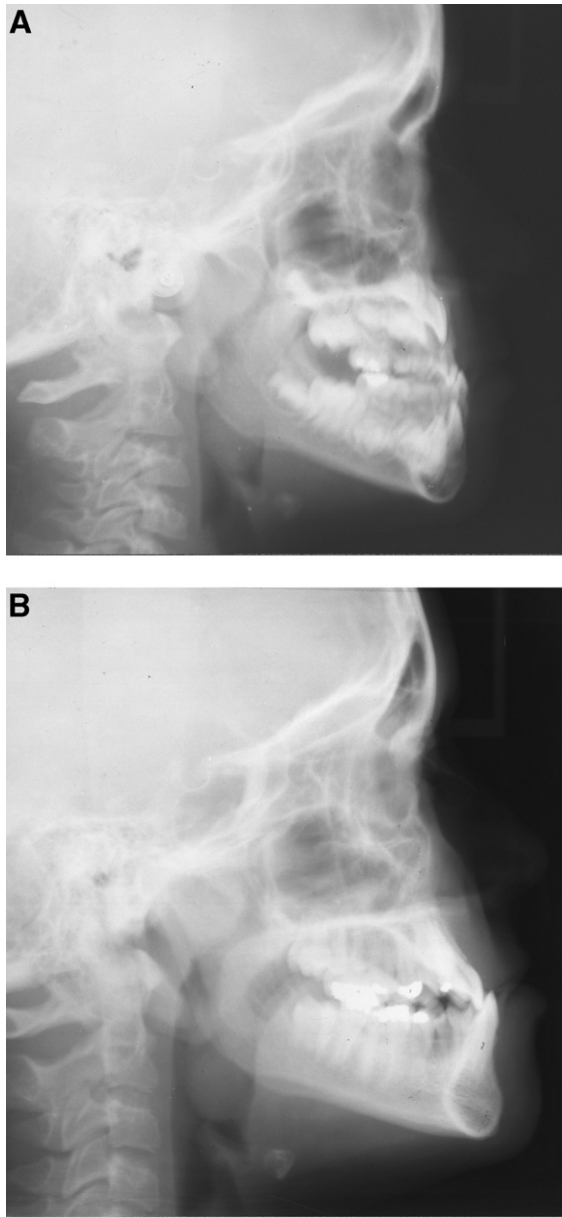


Figure 1. (A and B) Male subject with untreated Class III malocclusion: (A) T₁, CS 1; (B) T₂, CS 5. Observation interval: 6 years, 2 months.

a tendency to worsen with growth, thus supporting the findings of a previous cross-sectional study by Guyer and coworkers¹⁵ and a short-term longitudinal study by Baccetti and associates.¹² The present findings also are consistent with the conclusions of Bishara and Fernandez³⁰ that determined individuals possess a strong tendency to maintain the same facial type from 5 to 25 years of age.

In the sample with Class III malocclusion that was analyzed in the long term (Table 1 and Fig 2) the following was observed:

1. A slight closure of the cranial base angle, although not significant.
2. Changes in the maxilla relative to the cranial base (PtA-NaPerp) were similar to those expected for normal growth during the same observation period (0.5 mm compared with expected value of 0.7 mm). However, the early establishment of the retrusive maxillary position was maintained throughout skeletal maturity (-1.8 mm compared with expected position of +1 mm for adults with normal occlusion and well-balanced faces).³¹
3. An increase in the SNB angle that was more than twice that for the SNA angle.
4. The increase in mandibular projection (Pog-NaPerp) was more than double that of the expected value for normal growth during the same observation interval (6.3 mm compared with expected value of 3 mm).³¹
5. A statistically significant decrease of 2.7 mm in the value for the Wits appraisal and a statistically significant decrease of about 2° in the ANB angle.
6. A large amount of annual increases in total mandibular length (about 3 mm versus the average 2-2.5 mm increase in subjects with normal occlusion in the circumpubertal ages).³²
7. A closure of the mandibular plane angle equal to the amount expected for normal growth (about 2° in 6 years).³¹
8. The unfavorable growth changes in Class III malocclusion occurred concurrently with a statistically significant decrease in the overjet measurement in the long-term (-1.2 mm) and with a statistically significant worsening of the Class III molar relationship (3.3 mm).

The findings of the present investigation indicate that Class III malocclusion is not a self-correcting malocclusion at either the skeletal or the occlusal levels. On the contrary, mandibular projection, maxillo-mandibular differentials, negative overjet, and mesial molar relationship all tend to worsen during the developmental ages. The progressive closure of the cranial base angle is not helpful in the overall Class III growth pattern^{17,33-35} that leads to unfavorable skeletal and soft tissue relationships at the end of the period of active growth.

Table 1. Longitudinal study; statistical comparison on cephalometric measures in the untreated Class III sample at T₁ and T₂.

Cephalometric measures	Class III Group at T ₁ , n = 22		Class III Group at T ₂ , n = 22		T ₂ -T ₁ changes		Paired t-test
	Mean	SD	Mean	SD	Mean	SD	
<i>Cranial Base</i>							
Cranial flexure	129.9	5.1	127.8	5.1	-0.6	3.0	NS
<i>Maxillary Skeletal</i>							
Co-Pt A (mm)	78.5	4.6	87.1	5.4	7.6	2.9	***
SNA (°)	78.9	4.4	79.9	4.9	1.4	2.7	*
Pt A to Nasion perp (mm)	-1.8	2.7	-1.8	3.1	0.5	2.1	NS
<i>Mandibular Skeletal</i>							
Co-Gn (mm)	106.1	7.0	126.4	7.9	19.3	6.8	***
SNB (°)	79.8	4.4	82.0	5.2	3.3	2.9	***
Pg to Nasion perp (mm)	-2.1	6.6	2.0	9.0	6.3	4.5	***
Gonial Angle (°)	131.8	5.2	129.3	4.1	-2.4	3.3	**
<i>Maxillary/Mandibular</i>							
WITS (mm)	-7.5	3.9	-9.3	3.5	-2.0	3.1	**
Max/Mand difference (mm)	27.6	6.2	39.4	5.9	11.7	4.7	***
ANB (°)	-0.9	2.1	-2.1	2.8	-1.9	1.9	***
<i>Vertical Skeletal</i>							
FH to occlusal plane (°)	10.6	2.8	9.4	4.4	-2.0	3.1	**
FH to palatal plane (°)	0.0	2.1	-2.5	3.7	-0.6	2.3	NS
MPA (°)	29.3	4.5	28.2	5.7	-2.1	3.2	**
Nasion to ANS (mm)	47.2	4.0	55.8	2.4	6.7	4.0	***
ANS to Me (mm)	60.4	5.4	71.8	6.6	9.7	4.9	***
<i>Interdental</i>							
Overbite (mm)	1.0	1.6	0.8	2.3	0.7	2.0	NS
Overjet (mm)	-1.0	2.2	-2.3	3.1	-1.2	2.7	*
Interincisal angle (°)	137.4	12.8	134.6	11.0	-2.8	12.9	NS
Molar relationship (mm)	5.6	1.6	8.9	3.9	3.3	2.9	***
<i>Maxillary Dentoalveolar</i>							
U1 to Pt A vert (mm)	1.9	2.3	4.8	1.6	2.9	2.1	***
U1 to Frankfort (°)	109.4	6.3	115.8	4.4	6.4	6.6	***
<i>Mandibular Dentoalveolar</i>							
L1 to Pt A Pg (mm)	3.4	2.2	5.0	1.9	1.6	2.1	**
L1 to MPA (°)	83.0	7.1	81.4	7.4	-1.5	7.0	NS
<i>Soft Tissue</i>							
UL to E plane (mm)	-4.4	2.6	-7.7	3.3	-3.2	2.4	***
LL to E plane (mm)	0.1	3.3	-2.2	3.1	-2.3	2.5	***
Nasolabial angle (°)	106.7	11.2	104.4	11.9	-2.3	13.9	NS
Cant of upper lip (°)	8.0	7.0	9.9	10.3	1.9	9.2	NS

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Cross-Sectional Data

The parent sample consisted of 1549 pretreatment lateral cephalometric records of white Class III patients collected from twelve private orthodontic practices in Michigan and Ohio, the University of Michigan Graduate Orthodontic Clinic, and at the Department of Orthodontics of the University of Florence, Italy.

To be included in the final group, patients had to satisfy the following inclusion criteria:

1. White ancestry
2. No orthopedic/orthodontic treatment before taking the cephalogram

3. Diagnosis of Class III malocclusion:

- a. Anterior crossbite, with every attempt to exclude pseudo crossbites, or edge-to-edge incisor relationship
- b. Accentuated mesial step relationship of the primary second molars or permanent first molar relationship of at least one-half cusp Class III

4. No congenitally missing or extracted teeth

A final sample of 1091 subjects with Class III malocclusion met the inclusionary criteria. The sample consisted of 560 females and 531 males. The age range for female subjects was between 3 years 6 months and 57 years 7 months. The male

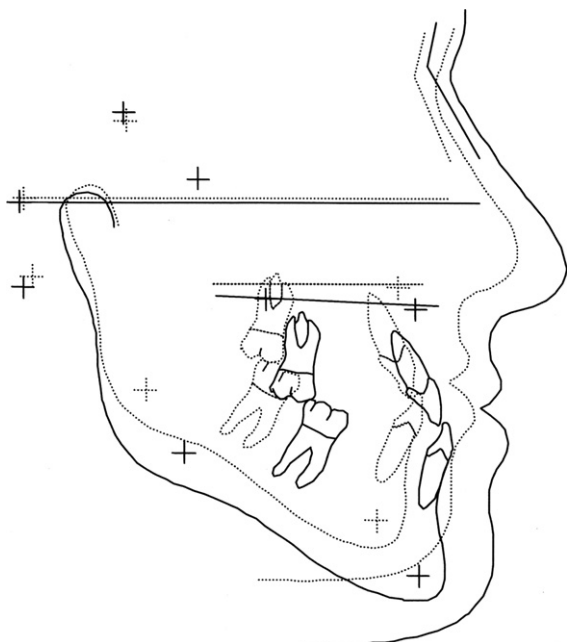


Figure 2. Longitudinal study: superimposed mean tracings of the 22 untreated Class III subjects at T_1 (dotted line) and T_2 (continuous line).

subject group ranged from 3 years 3 months and 48 years 5 months.

The lateral cephalograms of Class III individuals were staged according to the cervical vertebral maturation method.²³

Cephalometric Analysis

Lateral cephalograms were hand traced using 0.003-inch matte acetate and a sharpened 2H lead drafting pencil. The descriptive cephalometric analysis required the digitization of 71 landmarks on each tracing. A cephalometric analysis including measures adopted from the analyses of Steiner,²⁴ Ricketts,²⁵ Jacobson,²⁶ and McNamara²⁷ was performed on each tracing included in the investigation.

Statistical Analysis

With the sample categorized according to indices of skeletal maturity (ie, 6 stages of cervical vertebral maturation), descriptive statistics for the cephalometric measures were calculated for each stage group in male and female subjects separately. The data were analyzed with a commercial social science statistical

package (SPSS for Windows Version 12.0, SPSS, Inc, Chicago, IL).

Initially, gender differences were tested using Hotelling T² test to see if the differences between male and female subjects were statistically significant with respect to the collection of cephalometric measures. The results of this test indicated statistically significant differences and dictated that male and female groups should be analyzed separately, thus confirming previous data.¹⁸ Consequently, one-way analysis of variance was used to identify statistically significant differences ($P < 0.05$, and $P < 0.01$) between the means for each cephalometric variable in consecutive developmental groups. A Bonferroni correction assisted in the identification of statistically significant differences. Despite the cross-sectional nature of the present study, the terms “increase” and “decrease” will be used in the results and discussion sections to depict positive and negative differences, respectively, as these terms are more reader-friendly.

The error of the method for the cephalometric measurements was evaluated by repeating the measures in 100 randomly selected cephalograms. Error was on average 0.6° for angular measures and 0.9 mm for linear measures.

Results

Male Subjects

As with the female groups, no statistically significant difference for any of the examined cephalometric variables was assessed in the transitions from CS1 through CS2 and from CS2 through CS3. The comparison between CS3 and CS4 revealed statistically significant increases for total mandibular length (Co-Gn), maxillo-mandibular differential, upper and lower anterior facial heights (N-ANS and ANS-Me), and dentoalveolar height at the upper molar (U6-PP) and at the lower incisor (L1-Me). A statistically significant decrease was recorded for the molar relation. During the transition from CS4 through CS5, statistically significant increases were found for total mandibular length (Co-Gn), upper and lower anterior facial heights (N-ANS and ANS-Me), and dentoalveolar height at the upper molar (U6-PP) and at the lower incisor (L1-Me). The transition from CS5 through CS6 exhibited statistically significant increases in the position

of the chin in relation to the Nasion perpendicular (Pog-NaPerp), Co-Gn, maxillo-mandibular differential, and protrusion of the lower lip relative to the E-plane. The decreases in the ANB angle and Wits appraisal were statistically significant as well when CS5 was compared with CS6.

As staged through the CVM method, the male groups exhibited the most evident trends of growth in the Class III sample. No statistically significant changes along with subsequent CVM stages were found for cranial base and maxillary measurements. Cranial flexure was reduced when compared with values for normal subjects at all developmental stages. The atlas by Riolo and coworkers¹ reports a value of about 130° for the cranial flexure angle at all ages, whereas the mean value in the male Class III samples investigated here ranged consistently between 121° and 122°, with no statistically significant changes at subsequent stages. The presence of a reduced cranial flexure and consequently an advanced position of the glenoid fossa is confirmed as an anatomical characteristic of Class III malocclusion throughout the developmental stages.^{16,36}

Particularly interesting were the findings related to the changes in the mandibular region (Fig 3). The between-stage differences in total mandibular length became statistically significant starting at the CS3-CS4 interval. At this interval mandibular length in male Class III subjects exhibited the greatest difference between CVM stages: approximately 8 mm. Therefore, Class III individuals present with the peak in mandibular growth at the same maturation stage as individuals with normal occlusion,^{23,37} that is,

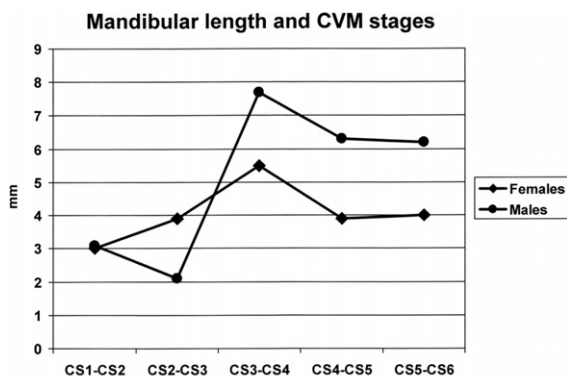


Figure 3. Cross-sectional study: average differences between cervical vertebral maturation (CVM) stages for mandibular length in Class III females and males.

from CS3 through CS4 in cervical vertebral maturation. The pubertal peak in mandibular growth occurred between the ages of 11 years 4 months and 12 years 10 months in the female Class III subjects and between 12 years 8 months and 14 years 2 months for the male Class III subjects.

These data also show that the duration of the peak interval is approximately 6 months longer in both female and male Class III individuals than in individuals with normal occlusion who present with an average CS3-CS4 interval of 1 year. The longer interval in part can account for the large increases in mandibular dimensions in Class III subjects during the growth spurt, as assessed in the present study. The increases in mandibular length continued to be statistically significant also at later maturational intervals in the examined Class III samples. Total mandibular length exhibited between-stage differences of about 6 mm from CS4 to CS5, and of about 7 mm from CS5 to CS6.

Female Subjects

No statistically significant difference for any of the examined cephalometric variables was assessed in the transitions from CS1 through CS2 and from CS2 through CS3. The comparison between CS3 and CS4 revealed statistically significant increases for total mandibular length (Co-Gn), maxillo-mandibular differential, lower anterior facial height (ANS-Me), and dentoalveolar height at the upper molar (U6-PP). The same comparisons were statistically significant for the transition from CS4 through CS5. In addition to the same statistically significant comparisons, the increases in upper anterior facial height (N-ANS), extrusion of upper incisors (U1-ANS) and of lower incisors (L1-Me), as well as the protrusion of the lower lip in relation to the E-plane (LL-E plane, respectively) became statistically significant during the transition from CS5 through CS6.

In the Class III female samples, a growth trend similar to the male samples was found. Despite differences between the two genders in the “amount” of between-stage changes (in agreement with previous evidence of sexual dimorphism in Class III malocclusion),¹⁸ from CS3 to CS4 (“peak” interval) total mandibular length exhibited a statistically significant differ-

Table 2. Cross-sectional study: descriptive statistics and comparison of craniofacial measurements at subsequent stages in Cervical Vertebral Maturation (CS)

Females	CS 1 (n = 167) mean age: 8 ys 2 mos		CS 2 (n = 51) mean age: 10 ys 8 mos		CS 3 (n = 60) mean age: 11 ys 8 mos		CS 4 (n = 85) mean age: 12 ys 10 mos		CS 5 (n = 90) mean age: 14 ys 1 mos		CS 6 (n = 107) mean age: 17 ys 2 mos		1 vs 2	2 vs 3	3 vs 4	4 vs 5	5 vs 6
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD					
Cranial Base																	
SNFH (°)	8.9	2.9	9.5	2.7	8.6	3.1	9.8	2.8	9.2	3	9.1	2.9	ns	ns	ns	ns	ns
S-N (mm)	67.9	3.5	68.5	3.5	70.2	4.3	71.1	3.4	71.5	3.6	72.4	3.6	ns	ns	ns	ns	ns
Cranial Flexure (°)	121.8	5.4	122	4.9	123.1	5.2	122.9	5.4	123.2	5.5	123	5.6	ns	ns	ns	ns	ns
Maxillary Skeletal																	
SNA (°)	80.3	3.3	80.2	3.9	80	4.6	79.8	3.1	81	3.9	80.7	3.6	ns	ns	ns	ns	ns
PtA to NaPerp (mm)	-0.7	2.6	-0.3	3.6	-1.4	3.5	-0.5	3.2	0.2	3.7	-0.4	3.7	ns	ns	ns	ns	ns
PP-FH (°)	-0.5	3.2	-1.1	3.2	-0.1	4.1	-1	3.3	-0.4	2.9	0.5	3.9	ns	ns	ns	ns	ns
Co-Pt A (mm)	82.1	4.5	83.3	4.6	86.3	5.9	88.7	5.2	90.5	5.1	90.4	4.7	ns	ns	ns	ns	ns
Mandibular Skeletal																	
SNB (°)	79.4	3.2	79.9	3.5	79.8	3.7	79.7	3.1	80.9	3.7	81.2	3.6	ns	ns	ns	ns	ns
Pog-Na Perp (mm)	0.4	1.2	0.9	1.4	1.4	2.5	1.5	1.6	1.5	1.8	2.4	1.8	ns	ns	ns	ns	ns
Facial Angle (°)	88.5	2.9	90	3.5	89.1	3	90.3	3	90.9	3	91.4	3.4	ns	ns	ns	ns	ns
Co-Gn (mm)	106.4	6.3	109.4	6.5	113.3	7.7	118.8	7.8	122.7	6.7	126.7	6.2	ns	ns	*	*	*
Maxillary/Mandibular																	
MPA (°)	25.9	4.3	24.7	5	25.7	4.9	26.9	5.6	25.8	5.4	25.7	5.6	ns	ns	ns	ns	ns
ANB (°)	0.9	2.2	0.3	2	0.2	2.7	0.1	2	0.1	2.2	-0.5	3	ns	ns	ns	ns	ns
Wits (mm)	-4.2	2.5	-4.6	2.4	-4.9	2.8	-5	2.8	-5.1	2.9	-5.7	4.1	ns	ns	ns	ns	ns
Mx-Md Diff (mm)	24.4	3.9	26.1	3.5	27.1	3.9	30.1	4.3	32.3	4.6	36.3	4.6	ns	ns	*	*	**
Molar relation (mm)	-3.9	1.7	-4.1	1.8	-4.2	2	-5.1	1.5	-5.5	1.9	-6.1	2.5	ns	ns	ns	ns	ns
Vertical																	
Nasion to ANS (mm)	47.2	3.8	48.4	3.2	50.4	3.6	52.2	3.1	53.2	3.4	55.1	3.7	ns	ns	ns	ns	*
ANS to Me (mm)	60.3	4.6	60.8	5	62.6	4.7	66.3	5.6	68.4	5.7	71.2	5.9	ns	ns	*	*	**
UFH/LAFH ratio	82.4	7.2	83.2	7.9	83.9	6.4	82.5	7.2	80.9	7.3	80.4	7.9	ns	ns	ns	ns	ns
U1 - ANS (mm)	24.5	2.7	25	2.8	25.6	3	27.8	3.6	25.5	2.9	29.6	3.1	ns	ns	ns	ns	*
U6 - PP (mm)	18.3	2	19.4	2.2	19.8	2.2	22	2	23.6	2.2	25.5	2.4	ns	ns	*	**	**
L1 - Me (mm)	36.2	2.4	36.3	2.3	37.5	2.8	38.9	2.6	40	3	41.3	3.2	ns	ns	ns	ns	*
Dentoalveolar																	
U1 - Pt A (V) (mm)	1.1	2.7	2.2	2.4	2.9	1.9	3.3	2.3	4.3	2.4	4	2.9	ns	ns	ns	ns	ns
U1 - SN (°)	100.3	9	103.3	8.5	105	5.6	103.3	5.4	106.3	6.5	105	7.2	ns	ns	ns	ns	ns
IMPA (°)	88.2	7	87.6	6.7	88	8.4	84	6.3	85.8	7.6	83.9	8.3	ns	ns	ns	ns	ns
FMIA (°)	65.9	6.9	67.7	6.9	66.3	8.8	68.9	6.9	68.4	8.1	70.4	8.4	ns	ns	ns	ns	ns
L1 - A Pog (mm)	3	1.9	2.8	2	3.3	2.7	2.8	2.4	3.5	2.6	3.2	2.6	ns	ns	ns	ns	ns
Interincisal angle (°)	136.6	11.7	134.9	11.2	132.6	8.8	135.9	9.2	132.9	11.7	136.3	10.8	ns	ns	ns	ns	ns
Soft Tissue																	
UL - E plane (mm)	-4	2.3	-4.3	1.8	-5.1	2.3	-5.5	2.6	-6.4	2.7	-8.0	2.9	ns	ns	ns	ns	ns
LL - E plane (mm)	-0.7	2.4	-1	2.2	-1.6	2.7	-2.1	2.5	-2.4	3	-4	2.9	ns	ns	ns	ns	*
Nasolabial angle (°)	112.4	12.8	112.8	11.8	112.2	14.9	111	12.2	109.7	12.3	109.8	12	ns	ns	ns	ns	ns

Males	CS 1 (n = 163) mean age: 8 ys 10 mos		CS 2 (n = 62) mean age: 11 ys 3 mos		CS 3 (n = 61) mean age: 12 ys 9 mos		CS 4 (n = 82) mean age: 14 ys 2 mos		CS 5 (n = 65) mean age: 15 ys 4 mos		CS 6 (n = 98) mean age: 18 ys 3 mos		1 vs 2	2 vs 3	3 vs 4	4 vs 5	5 vs 6
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD					
<i>Cranial Base</i>																	
SNFH (°)	8.3	2.7	8.2	3.6	8.5	3.1	9.2	2.5	8.6	2.7	7.7	3.5	ns	ns	ns	ns	ns
S-N (°)	71.2	3.6	71.8	3.5	71.8	3.6	73.7	3.6	76	3.9	77.3	4.2	ns	ns	ns	ns	ns
Cranial Flexure (°)	121	4.7	121.1	5.4	122.1	4.8	122.3	4.6	122.9	5.2	121.8	6	ns	ns	ns	ns	ns
<i>Maxillary Skeletal</i>																	
SNA (°)	80.2	3.7	80.5	3.6	79.3	4.5	81	3.5	81.8	4.6	81.1	4.4	ns	ns	ns	ns	ns
PtA to NaPerp (mm)	-1.4	2.8	-1.3	2.8	-2.3	4.2	-0.8	3.2	-0.3	4.4	-1.5	4.6	ns	ns	ns	ns	ns
PP-FH (°)	-0.5	3.2	-0.2	2.8	0.3	3.4	0.0	3.2	0.8	3.5	0.9	4.4	ns	ns	ns	ns	ns
Co-Pt A (mm)	84.8	4.6	86.1	5	87.8	4.8	89.1	4.1	92.3	6.3	94.1	5.6	ns	ns	ns	ns	ns
<i>Mandibular Skeletal</i>																	
SNB (°)	79.5	3.5	80	3.2	79.4	3.2	80	3.1	80.5	3.8	82.4	4.5	ns	ns	ns	ns	ns
Pog-Na perp (mm)	0.3	1.2	0.7	0.9	0.8	1.3	1.2	1.6	1.3	1.3	2.9	2.1	ns	ns	ns	ns	*
Facial Angle (°)	88	2.9	88.5	2.6	88.4	2.7	89.9	2.8	89.7	3.7	91.4	4	ns	ns	ns	ns	ns
Co-Gn (mm)	111.3	6.2	114.4	6.6	116.5	7.3	124.2	5.9	130.5	6.5	137.7	8.4	ns	ns	**	**	**
<i>Maxillary/Mandibular</i>																	
MPA (°)	26.5	4.5	26.5	5	27.5	4.5	27.2	4.5	27.2	5.4	25.4	6.1	ns	ns	ns	ns	ns
ANB (°)	0.7	2.2	0.5	2.3	-0.1	2.7	0.9	2.5	1.2	2.5	-1.3	2.8	ns	ns	ns	ns	*
Wits (mm)	-4.4	2.4	-4.6	2.6	-5.3	2.7	-4.4	3	-3.7	3.7	-5.9	4.5	ns	ns	ns	ns	*
Mx-Md Diff (mm)	25.3	3.8	27.3	3.8	29.3	4.1	32	4.1	34.2	4	41	6	ns	ns	*	*	*
Molar relation (mm)	-3.8	1.7	-4.1	1.9	-4.4	2.2	-6.1	3	-5.4	1.9	-6.9	3.6	ns	ns	*	ns	ns
<i>Vertical</i>																	
Nasion to ANS (mm)	48.4	3.4	50.4	4.9	51.9	4.2	55.9	3.3	57	3.6	58.7	4.3	ns	ns	**	ns	ns
ANS to Me (mm)	62.6	4.9	64.9	5.2	66.9	5.5	71	5.5	74.7	6.8	77.6	6.6	ns	ns	**	*	ns
UFH/LAFH ratio	81.3	6.8	81.4	7.5	81.3	7.9	82.3	6.9	80.1	6.8	78.7	7.6	ns	ns	ns	ns	ns
U1 - ANS (mm)	25.6	2.9	26.8	3.1	27.6	3.4	29.3	2.9	30.2	3.5	31.2	3.5	ns	ns	ns	ns	ns
U6 - PP (mm)	19.1	2.3	20.7	2.8	21.9	2.8	23.9	2.5	25.8	2.9	27.9	3.2	ns	ns	**	**	ns
L1 - Me (mm)	37.9	2.6	39	2.5	39.6	3	42.1	3.1	44.1	3.3	45.6	3.3	ns	ns	**	*	ns
<i>Dentoalveolar</i>																	
U1 - Pt A (V) (mm)	0.7	2.4	1.7	2.6	2.3	2.3	3.6	2.5	3.8	2.6	4.4	2.1	ns	ns	ns	ns	ns
U1 - SN (°)	99.7	8.8	102.1	6.9	102.4	6.4	103.9	6.3	105.1	6.4	106.1	7.9	ns	ns	ns	ns	ns
IMPA (°)	87.3	6.3	86.2	7.3	85.8	6	85.9	7.3	85.3	7.1	83.6	6.9	ns	ns	ns	ns	ns
FMIA (°)	66.2	6.3	67.3	6.8	66.7	6.2	66.9	8.2	67.4	7.6	71	7.7	ns	ns	ns	ns	ns
L1 - A Pog (mm)	3.1	1.7	3.3	2	3.6	2.2	3.6	2.5	3.3	2.4	3.7	2.9	ns	ns	ns	ns	ns
Interincisal angle (°)	138.2	11.6	137	10.2	135.8	8.7	133.8	9.8	133.7	9.3	137.2	10.4	ns	ns	ns	ns	ns
<i>Soft Tissue</i>																	
UL - E plane (mm)	-3.3	2.2	-4.1	2.4	-4.3	2.7	-5	2.7	-6.3	2.7	-8.1	3.4	ns	ns	ns	ns	ns
LL - E plane (mm)	0.1	2.3	-1	2.4	-0.7	3.2	-1.3	2.9	-1.9	3.4	-4	2.9	ns	ns	ns	ns	*
Nasolabial angle (°)	112.4	12.7	114.2	15.5	114.5	12.5	116.2	9.8	111.6	9.7	106.7	12.8	ns	ns	ns	ns	ns

*($P < .05$; ** $P < .01$).

ence of 5.5 mm in Class III females, and CS4-CS5 and CS5-CS6 differences were both about 4 mm (Fig 3). These data suggest that the amount of increase in mandibular length at postpeak intervals is much greater in Class III individuals (both males and females) with respect to Class I individuals, where both CS4-CS5 and CS5-CS6 increases in Co-Gn are expected to range between 2 and 3 mm.^{23,37} Active, clinically significant growth in the mandible, especially with respect to normal trends of growth in subjects with Class I occlusion, appears to continue for a long period after the adolescent growth spurt in Class III malocclusion (up to the age of about 18 years in the present samples).

It must be noted that the average duration of the CS5-CS6 interval in both male and female samples was approximately 3 years, while the duration of between-stage intervals before CS5 never exceeded 2 years. The longer duration of the most mature interval may account, at least in part, for the substantial amount of growth found at this developmental stage.

When the lack of statistically significant between-stage differences for maxillary growth/advancement are considered, it is easily understood that excessive amounts of mandibular lengthening from the pubertal intervals onward were responsible for significant concurrent worsening of the maxillomandibular differential in Class III subjects of both genders when analyzed by means of CVM stages. At the final stages, a statistically significant protrusion of the lower lip relative to the E-plane became apparent as well, thus indicating a late worsening of the Class III profile.

Discussion

The outcomes of the present investigation are in agreement with the observations by Deguchi and coworkers²² who described a worsening of the Class III skeletal characteristics along with growth, mainly due to continuous advancement of the mandible relative to the maxilla. The Class III sample investigated by Battagel¹⁷ also showed that the maximum change for facial characteristics in the female groups occurred between the average ages 11 and 12 years, but continued after the age of 15 years. In Class I females at the age of 14 years to 17 years, facial

growth essentially had ceased, but development remained active in the Class III group.

The Japanese female sample with Class III malocclusion that was studied by Miyajima and coworkers¹⁹ with the use of dentitional stage categorization showed similar trends: the maxilla exhibited a retrusive position at an early developmental stage and retained a fairly constant anteroposterior relationship to the cranial base structures with continued development, while mandibular position worsened along with growth.

None of these previous studies, however, had analyzed growth trends in Class III malocclusion by means of a reliable indicator of skeletal maturity (eg, the CVM method).

As for the vertical measurements, between-stage differences became statistically significant during the peak interval (CS3-CS4) in both males and females with Class III malocclusion. These increases were found in both skeletal and dentoalveolar measures for vertical development. However, late stage intervals (CS5-CS6) presented once again with statistically significant increases in vertical dimensions, in correspondence with the completion of the permanent dentition, thus confirming previous findings by Miyajima and coworkers¹⁹ in Japanese female Class III subjects.

Conclusions

The results of the longitudinal study presented here demonstrated that Class III disharmony tends to worsen along with growth and that the need of appropriate orthopedic intervention in growing Class III individuals is warranted. The persistence of typical Class III growth characteristics well beyond the adolescent growth spurt into early adulthood as found in the large cross-sectional study entails important clinical consequences. A much longer period of active mandibular growth, the absence of any catch-up growth by the maxilla, and a significantly more vertical direction of facial growth during late adolescence appear to be unfavorable aspects of Class III malocclusion in both genders during the postpubertal stages.

Treatment planning by means of orthodontic/orthopedic appliances should take into account this pattern of prolonged mandibular growth in terms of duration of retention and

timing for the evaluation of stability of treatment protocols. The timing for orthognathic surgery in Class III patients, as well as the appropriate "surgical age" for other procedures in dentistry (eg, implants in the mandibular arch), should be considered also with particular attention in the light of the findings of the present study that indicate mandibular growth continued into young adult ages in males and females with Class III malocclusion (Table 2).

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