

Facial soft tissue changes during the pre-pubertal and pubertal growth phase: a mixed longitudinal laser-scanning study

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Summary

Background/objectives: Facial soft tissues changes during growth roughly tend to mimic the underlying hard tissues, but not completely. The aim of this mixed longitudinal study was to assess facial growth among pre-pubertal and pubertal subjects without malocclusion using a non-invasive three-dimensional laser scanning system.

Subjects/methods: Fifty-nine subjects (30 females and 29 males) aged at baseline 5.4–8.9 years with normal occlusion were clustered into the younger, older pre-pubertal, and pubertal groups according to age and the absence/presence of a standing height growth spurt. Three-dimensional facial images were obtained using laser scanners for five consecutive years. Several transversal, sagittal, and vertical parameters were assessed for between and within group comparisons.

Results: Significant overall changes of almost all parameters were seen within each group ($P < 0.05$) without any group differences ($P > 0.05$). The younger pre-pubertal group showed greater annual growth rates of lip prominence; both pre-pubertal groups showed greater rates in facial middle third height. The pubertal group showed greater annual rates in facial profile angle changes during the growth peak.

Limitations: A high standing height increment (7 cm) was used as the threshold for subject allocation in the pubertal group.

Conclusions: Soft tissue facial growth has generally similar amounts and rates irrespective of the pubertal growth spurt. Pre-pubertal subjects show greater annual rates of facial middle third height changes while pubertal subjects show greater annual rates of chin protrusion.

Introduction

Traditional longitudinal cephalometric growth studies (1) gave insight into craniofacial growth and it has been hypothesized that growth of the hard tissues of the face has its accelerations and decelerations, while the soft tissues of the face roughly tend to mimic the underlying hard tissues, but not completely (2, 3), mainly because of the variation in the thickness of the soft tissues (2). On the contrary, more recent studies reported that soft tissue thickness is indeed related to various craniofacial skeletal dimensions (4) and approximately 50 per cent of the variability of the

soft tissue shape might be related to the underlying skeletal and dental structures (5).

Due to the importance of facial soft tissue appearance in orthodontic treatment planning, it is necessary to determine, whether a subject is merely at the extreme of normal variation or is outside the normal range (6). Therefore, longitudinal assessment of soft tissue changes is needed to better understand its dynamics during normal growth and development.

In the literature, longitudinal changes of the soft tissues during growth were analysed mainly on facial photographs, but most

frequently by the use of lateral cephalometry (7, 8). Although cephalometric analysis is an important diagnostic tool in orthodontics it has some disadvantages in evaluating facial soft tissues (9). Indeed, being a two-dimensional method lateral cephalometry has some limitations in assessing the three-dimensional (3D) morphology and growth changes of the face (10). Furthermore, longitudinal growth studies among normal subjects based on cephalometric analysis are nowadays ethically questionable due to radiation at regular intervals and the use of alternative non-invasive techniques seems to be the best way to understand how the face develops and changes with time (6). Recently, several studies evaluated 3D facial soft tissue morphology among different populations (11) and cross-sectional growth changes (6). Moreover, 3D changes after surgical (12, 13) and non-surgical (14, 15) treatment were also analysed.

However, only a few studies aimed to assess longitudinal changes of facial morphology in terms of facial asymmetry (16, 17), or surface facial changes (6) in growing subjects. Nevertheless, the reported studies either analysed mainly pre-pubertal subjects (17) or subjects of a specific age group (6, 16), not considering the subjects' individual maturation phase. As the growth pattern is almost unique for each subject, having its accelerations and decelerations according to the individual maturation phase, it is very important when analysing data not to group subjects in terms of their chronological age but rather use a skeletal maturation indicator.

Therefore, the aim of the present mixed longitudinal study was to assess facial growth changes among pre-pubertal and pubertal subjects without malocclusion using a non-invasive three-dimensional laser scanning system.

Subjects and methods

Subjects and study design

Ethical approval for this study was gained from the Slovenian Ethical Committee of the Medical Faculty, University of Ljubljana, Slovenia, and informed consent was obtained from the parents of all subjects. All of the children were randomly selected from a local kindergarten and school. Only subjects showing a Class I facial profile without malocclusion clinically assessed by an experienced orthodontist (MO) and having a good general health with no respiratory, deglutition, or mastication problems were included. According to the mixed longitudinal design, the whole sample was then divided into three cohorts (groups), as younger pre-pubertal, older pre-pubertal, and pubertal, each followed prospectively and annually for 5 consecutive years. Children were clustered in each group according to age and dentition phase, and presence of a growth velocity peak in standing height (peak height velocity; PHV) during the observational period (assessed retrospectively). In particular, children in the younger pre-pubertal group had to have 5.0–7.0 years and being in the primary or early mixed dentition phase; children in the older pre-pubertal group had to have 7.1–9.0 years, being in the intermediate or late mixed dentition phase and had to not show any PHV during the observational period; finally, the children in the pubertal group had to have 7.1–9.0 years, being in the intermediate or late mixed dentition phase and had to show a clear PHV during the observational period. A total of 77 children were examined of which, after drop-out and considering two subjects with unclear PHV also excluded (see below), 59 (30 females and 29 males) aged between 5.4 and 8.9 years had full data and were included in the study.

At each time point, standing height and facial parameters were recorded.

The annual increments in standing height were assessed for the presence of the pubertal growth spurt, and individual time intervals for the ascending and descending PHV were derived. Therefore, the time intervals for the pubertal group were defined as the PHV interval, that is pubertal growth spurt, and PHV (–1 year) and PHV (+1 year) for the previous and subsequent intervals, respectively. In particular, a pubertal growth spurt was assessed when the annual increment in standing height was at least 7 cm over the previous recording. Only two subjects with unclear PHV in the pubertal group, were further excluded from the study. Changes of each facial parameter were assessed among three time intervals defined as Main, Main (–1 year), and Main (+1 year). In the pubertal group, the Main interval corresponded to the PHV, while in the younger and older pre-pubertal groups, such time intervals have been selected to have, at each time point, similar mean ages between the older pre-pubertal and pubertal groups, and different mean ages between these 2 groups and the younger pre-pubertal group (Table 1).

Clinical recordings

Surface facial images were obtained using two Konica/Minolta Vivid 910 laser scanners angled to capture left and right sides of the face with significant overlap in the anterior part of the face to facilitate registration and merging of the two images to produce one facial shell (18).

These devices are eye safe and have a reported manufacturing accuracy of 0.3 mm (<http://www.konicaminolta.com>). The technique for positioning the subjects and image capture has been validated and described elsewhere (15, 18).

The 3D data were imported to a reverse modeling software package, Rapidform™ 2006 (@ INUS Technology Inc., Seoul, Korea). Each scan of the face (left and right images) was pre-processed in order to remove unwanted data, registered and merged to produce a complete facial shell. The facial shell was aligned to three reference planes: the mid-sagittal plane (Y–Z), the coronal plane (X–Y), and the transverse plane (X–Z) (19). At every time point, each 3D facial shell was analysed by measuring different transversal, sagittal, and vertical parameters, both linear and angular, between reference facial points (Figure 1). In the transverse plane (Figure 1A), inter-eye distance [between the left (EnL) and right (EnR) endocanthi], nose width [between the left (AIL) and right (AIR) alare points] and mouth width [between the left (ChL) and right (ChR) cheilion points] were measured. Furthermore, the asymmetry of the face was measured by the eyes/mouth angle (Figure 1B) between the average lines through the eyes' (endo- and exocanthi points [left (ExL) and right

Table 1. Definition of the different time intervals for the groups.

Group	Time interval		
	Main (–1 year)	Main	Main (+1 year)
Younger pre-pubertal	T1–T2	T2–T3	T3–T4
Older pre-pubertal	T2–T3	T3–T4	T4–T5
Pubertal	PHV (–1 year)	PHV	PHV (+1 year)

PHV, peak height velocity defined as interval corresponding to an annual increment in standing height of at least 7 cm (mostly between T2 and T3). Main, previous [Main (–1 year)] and subsequent [Main (+1 year)] time intervals were selected for the younger pre-pubertal group as to have lower ages as compared to those of the older pre-pubertal group. For the older pre-pubertal group, the corresponding time intervals were selected as to have similar ages as compared to those of the pubertal group.

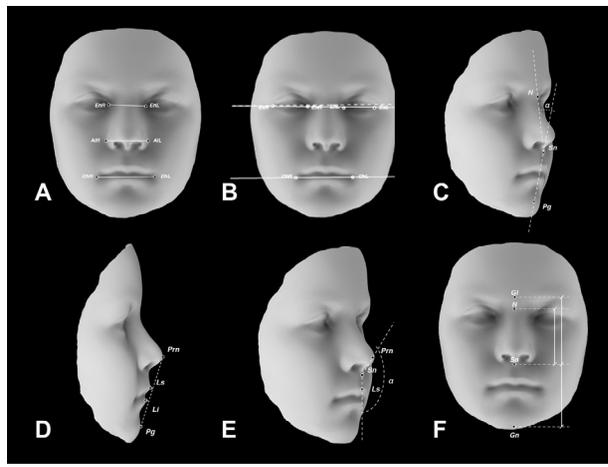


Figure 1. Facial parameters assessed on three-dimensional facial scans: (A) inter-eye distance between the left (EnL) and right (EnR) endocanthi, nose width (between the left (AIL) and right (AIR) alare points and mouth width between the left (ChL) and right (ChR) cheilion points; (B) eyes/mouth angle between the average lines through the eyes' (endo- and exocanthi points [left (ExL) and right (ExR)]) and through the mouth [through ChL and ChR and Stomion (Sto)]; (C) facial profile angle between the lines through nasion (N) and subnasale (Sn) and Sn and Pogonion (Pg); (D) distances of the upper (Labii superior, Ls) and lower (Labii inferior, Li) lips to the esthetic line [line through Prn and Pogonion (Pg)]; (E) nasolabial angle between the lines through Sn and pronasale (Prn) and Sn and Ls; (F) nose height between nasion (N) and subnasale (Sn), middle third height between Glabella (Gl) and Sn and lower third height between Sn and Gnathion (Gn).

(ExR)]) and through the mouth [line through ChL and ChR and Stomion (Sto)]. In the sagittal plane, the facial profile angle [angle between the line through nasion (N) and subnasale (Sn) and the line through Sn and Pogonion (Pg), Figure 1C] was assessed. The distances of the upper (Labii superior, Ls) and lower (Labii inferior, Li) lips to the esthetic line [EL; line through pronasale (Prn) and Pg; Figure 1D] were measured and the ratio between these two distances was also calculated. Moreover, the nasolabial angle (angle between the line through Sn and Prn and the line through Sn and Ls; Figure 1E) was assessed. In the vertical plane (Figure 1F), nose height (linear distance between N and Sn), middle third height [linear distance between Glabella (Gl) and Sn] and lower third height [linear distance between Sn and Gnathion (Gn)] were measured and the ratio between the middle and lower thirds' heights was further calculated.

Sample size calculation and method error analysis

A sample size of at least 17 subjects *per* group was necessary to detect an effect size coefficient (20) of 1.0 for changes in every facial parameter in any comparison between the groups, within each time interval, with an alpha set at 0.05 and a power of 0.8 (21). The ES coefficient is the ratio of the difference between the recordings of the two groups, divided by the within-subject standard deviation (SD). An effect size of at least 0.8 is regarded to as a 'large effect' (20).

With the aim of quantifying the full method error of the recordings for each recorded parameter, the method of moments (MME) variance estimator (22) was used on a random sample of 25 replicate measurements. Therefore, the mean error and 95% confidence intervals (CIs) between the repeated recordings were calculated using the MME variance estimator, and were expressed as percentages (23). The MME variance estimator has the advantages of not being affected by any unknown bias, that is systematic errors,

between pairs of measurements (22). Method errors as mean (95% CI) ranged from 5.8% (2.5–9.3) to 8.4% (3.7–11.6) for the middle third height and eyes/mouth angle, respectively.

Statistical analysis

The SPSS software, version 13.0 (SPSS® Inc., Chicago, Illinois, USA) was used to perform the statistical analyses. The balance of experimental groups according to gender (at each time point, considering drop out) was tested with a chi-square test, while the significance of the differences in age (at each time point, considering drop out) was assessed by a Student's *t*-test.

After testing the normality of the data with the Shapiro–Wilk test and Q–Q normality plots, and the equality of variance among the datasets using a Levene test, parametrical tests were used for the absolute standing height data at each time point, and non-parametric methods were used for all the other data sets. Nevertheless, mean and SDs are reported for descriptive purposes.

A repeated measures one-way analysis of variance (ANOVA) was used to assess the significance of the differences in standing height among the five time points within each group. When significant interactions were seen, a Bonferroni corrected paired sample test was used for pairwise comparisons. A one-way ANOVA for independent data was also used to assess the significance of the differences among the three groups within each time point followed by a Bonferroni corrected *t*-test for independent data used for pairwise comparisons.

Facial parameters were initially analysed as overall changes, that is as recorded at T1 and T5. Within each group, a Wilcoxon test was used to assess the significance of the differences between T1 and T5. Moreover, a Kruskal–Wallis test assessed the significance of the differences among the three groups within either T1 or T5. When significant interactions were seen, a Bonferroni-corrected Mann–Whitney *U*-test was used for pairwise comparisons.

Subsequently, annual changes of each facial parameter, corresponding to the Main time intervals [Main, Main (–1 year), and Main (+1 year)] as defined in Table 1, were computed and expressed as growth rates in percentages. A Friedman test was also used to assess the significance of the differences among the three time intervals within each group followed by a Bonferroni-corrected Wilcoxon test used for pairwise comparisons. The Kruskal–Wallis test was also used to assess the significance of the differences among the three groups within each time interval followed by the Bonferroni-corrected Mann–Whitney *U*-test used for pairwise comparisons. A similar analysis was performed to assess the significance of the differences in annual increments in standing height among the groups within each time interval.

A *P* value less than 0.05 was used in the rejection of the null hypothesis.

Results

Demographic and standing height details of the groups over time are summarized in Table 2. The distribution of the genders was similar among the groups and over time. As *per* protocol, at each time point, the mean age in the younger pre-pubertal group was significantly lower as compared to both those of the older pre-pubertal and pubertal groups ($P = 0.000$, at least), while the older pre-pubertal and pubertal groups had similar ages. Standing height underwent significant increase over time in each group and also showed statistically significant differences among the groups at each time point ($P = 0.000$, at least). Moreover, at each time point the standing height was significantly lower, intermediate, and greater in the younger

Table 2. Demographic and standing height statistics of the groups according to each time point.

Parameter	Group	Time point					Diff.
		T1	T2	T3	T4	T5	
F/M (<i>n</i>)	Younger pre-pubertal	10/10	10/10	10/10	10/10	10/10	—
	Older pre-pubertal	12/9	12/9	12/9	12/9	12/9	—
	Pubertal	8/10	8/10	8/10	8/9	5/6	NS
		NS	NS	NS	NS	NS	
Age (years)	Younger pre-pubertal	6.0 ± 0.3	7.0 ± 0.3	8.0 ± 0.3	9.0 ± 0.3	10.0 ± 0.3	0.000
	Older pre-pubertal	8.0 ± 0.7 a	9.0 ± 0.7 a	10.0 ± 0.7 a	11.0 ± 0.7 a	12.0 ± 0.7 a	0.000
	Pubertal	8.4 ± 1.0 a	9.4 ± 1.0 a	10.4 ± 1.0 a	11.3 ± 0.9 a	11.8 ± 0.7 a	0.000
	Diff.	0.000	0.000	0.000	0.000	0.000	
Standing height (cm)	Younger pre-pubertal	121.3 ± 5.3	126.8 ± 5.4	132.0 ± 6.2	137.7 ± 6.6	144.4 ± 7.1	0.000
	Older pre-pubertal	131.9 ± 4.6 a	137.7 ± 4.8 a	143.9 ± 5.6 a	150.0 ± 6.0 a	156.6 ± 7.5 a	0.000
	Pubertal	135.5 ± 6.7 a,b	141.3 ± 7.0 a,b	155.7 ± 9.4 a,b	161.2 ± 10.1 a,b	164.6 ± 9.2 a,b	0.000
	Diff.	0.000	0.000	0.000	0.000	0.000	

Age and standing height presented as mean ± SD. Diff., significance of the difference over time within each group, or among the groups within each time point; NS, not statistically significant difference. Notes on results of pairwise comparisons between the groups for each time point: a, different from younger pre-pubertal group; b, different from older pre-pubertal group.

pre-pubertal, older pre-pubertal, and pubertal groups, respectively, with all the pairwise comparisons showing statistically significant differences ($P < 0.05$, at least).

Standing height increments corresponding to the Main, Main (-1 year), and Main (+1 year) intervals for each group are shown in Figure 2. Among the three time intervals, no significant differences were seen for the younger and older pre-pubertal groups, while significant differences were seen for the pubertal group ($P = 0.000$). Moreover, significant differences were seen among the groups at the Main time interval, with the pubertal group showing a greater increment as compared to the other groups ($P = 0.000$).

The mean values of the recorded facial parameters at T1 and T5 for each group are summarized in Table 3. Generally, all the transversal and vertical facial parameters underwent a significant increase over time ($P = 0.019$, at least). Few exceptions with unchanged mean values over time were seen for the middle/lower third ratio in the younger and older pre-pubertal groups, and for the eyes/mouth angle in all the groups. On the contrary, the sagittal facial parameters generally showed no significant differences over time for all the groups. Exceptions were seen for the facial profile angle that underwent a significant reduction in the younger pre-pubertal and pubertal groups ($P = 0.011$, at least), and for the upper lip/EL distance that underwent a significant increase in the pubertal group ($P = 0.035$). When comparing the groups within each T1 and T5, generally statistically significant differences were seen only for the vertical and not for the transversal and sagittal facial parameters. Of note, within the vertical facial parameters, the middle third height was similar among the groups both at T1 and T5. At the pairwise comparisons, nose height and lower third height, but not the middle third height, were significantly smaller in the younger pre-pubertal group, as compared to the other two groups. Moreover the middle/lower third ratio was significantly greater in the younger pre-pubertal group as compared to the other two groups.

Annual growth rates of the facial parameters according to the time intervals [Main, Main (-1 year) and Main (+1 year)] are summarized in Table 4. In only few cases, the facial parameters underwent significant growth rate changes over the three time intervals. In particular, in the younger pre-pubertal group, the middle third height and the mouth width showed significant growth rate changes

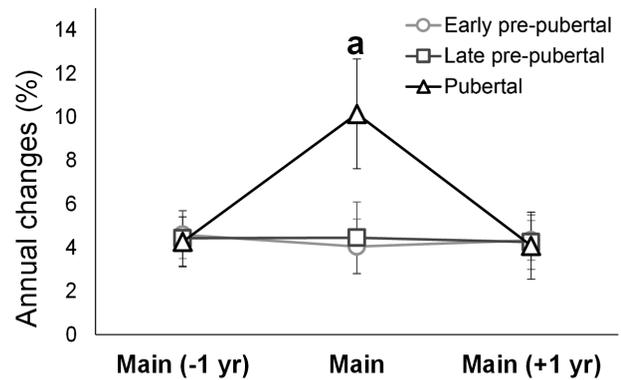


Figure 2. Changes in the standing height of the groups according to the time intervals: data are presented as mean ± standard errors. Notes on results of pairwise comparisons between the groups for each time interval: a, different from younger and older pre-pubertal groups.

($P = 0.011$, at least). In the older pre-pubertal group, the upper and lower lip/EL distances also showed significant growth rate changes over the time intervals ($P = 0.013$, at least). In the pubertal group, the nose width and the facial profile angle underwent significant growth rate changes over the time intervals ($P = 0.043$, at least). When comparing the groups within each time interval, no significant differences were seen for any parameter at the Main (-1 year) time interval. Regarding the Main time interval, significant differences among the groups were seen for: 1) nose height where in the older pre-pubertal group rates were lower as compared to the younger pre-pubertal group, 2) middle third height where in the pubertal group the rate was lower as compared to the younger pre-pubertal group, 3) upper, and 4) lower lip/EL distances where in the older pre-pubertal group rates were lower as compared to the younger pre-pubertal group. Finally, regarding the Main (+1 year) time interval, significant differences among the groups were seen for: 1) nose height and 2) lower third ratio where in the older pre-pubertal group rates were greater as compared to the younger pre-pubertal group, and 3) mouth width where in the pubertal group the rate was greater as compared to the younger pre-pubertal group.

Table 3. Mean values (\pm standard deviation) of the facial parameters according to group at T1 and T5 along with between and within group comparisons.

Parameter	Group	Time point		Diff.
		T1	T5	
Transversal				
Intereye distance (mm)	Younger pre-pubertal	31.79 \pm 3.29	35.52 \pm 1.97	0.000
	Older pre-pubertal	34.13 \pm 2.54	35.48 \pm 2.34	0.019
	Pubertal	33.97 \pm 2.21	35.40 \pm 2.98	0.005
	Diff.	0.046	NS	
Nose width (mm)	Younger pre-pubertal	28.72 \pm 2.06	30.2 \pm 2.0	0.004
	Older pre-pubertal	29.79 \pm 2.11	31.5 \pm 2.2	0.000
	Pubertal	29.53 \pm 2.33	31.7 \pm 3.2	0.002
	Diff.	NS	NS	
Mouth width (mm)	Younger pre-pubertal	37.42 \pm 2.72	41.88 \pm 3.95	0.000
	Older pre-pubertal	37.21 \pm 3.15	41.88 \pm 3.70	0.000
	Pubertal	37.19 \pm 3.70	42.83 \pm 4.16	0.000
	Diff.	NS	NS	
Eyes/mouth angle (°)	Younger pre-pubertal	3.04 \pm 1.58	2.85 \pm 1.51	NS
	Older pre-pubertal	2.56 \pm 1.62	3.10 \pm 2.09	NS
	Pubertal	3.83 \pm 1.93	3.18 \pm 1.83	NS
	Diff.	NS	NS	
Sagittal				
Facial profile angle (°)	Younger pre-pubertal	20.0 \pm 2.8	16.95 \pm 4.64	0.011
	Older pre-pubertal	18.3 \pm 4.5	17.27 \pm 5.27	NS
	Pubertal	18.4 \pm 4.9	13.86 \pm 6.34	0.000
	Diff.	NS	NS	
Upper lip/EL distance (mm)	Younger pre-pubertal	1.78 \pm 0.77	2.01 \pm 1.19	NS
	Older pre-pubertal	1.68 \pm 1.02	2.09 \pm 1.32	NS
	Pubertal	1.39 \pm 1.13	2.17 \pm 1.15	0.035
	Diff.	NS	NS	
Lower lip/EL distance (mm)	Younger pre-pubertal	2.26 \pm 1.29	1.76 \pm 1.10	NS
	Older pre-pubertal	1.64 \pm 0.97	1.59 \pm 1.15	NS
	Pubertal	1.47 \pm 1.11	1.86 \pm 1.44	NS
	Diff.	NS	NS	
Upper lip/lower lip ratio	Younger pre-pubertal	1.13 \pm 0.93	2.19 \pm 2.97	NS
	Older pre-pubertal	1.82 \pm 3.10	1.98 \pm 1.61	NS
	Pubertal	2.41 \pm 4.86	1.50 \pm 1.09	NS
	Diff.	NS	NS	
Nasolabial angle (°)	Younger pre-pubertal	96.77 \pm 3.37	96.4 \pm 3.1	NS
	Older pre-pubertal	95.86 \pm 3.83	97.6 \pm 4.0	NS
	Pubertal	97.46 \pm 4.55	96.2 \pm 5.3	NS
	Diff.	NS	NS	
Vertical				
Nose height (mm)	Younger pre-pubertal	34.27 \pm 2.16	38.99 \pm 2.76	0.000
	Older pre-pubertal	36.84 \pm 3.72 a	42.75 \pm 4.33 a	0.000
	Pubertal	37.37 \pm 2.78 a	40.76 \pm 2.43 a	0.000
	Diff.	0.003	0.002	
Middle third height (mm)	Younger pre-pubertal	57.21 \pm 3.42	62.95 \pm 3.62	0.000
	Older pre-pubertal	56.26 \pm 3.20	61.89 \pm 3.28	0.000
	Pubertal	55.23 \pm 2.89	61.96 \pm 3.04	0.000
	Diff.	NS	NS	
Lower third height (mm)	Younger pre-pubertal	44.19 \pm 2.63	47.37 \pm 2.89	0.000
	Older pre-pubertal	47.33 \pm 4.01 a	53.19 \pm 3.33 a	0.000
	Pubertal	47.01 \pm 3.27 a	50.85 \pm 3.57 a	0.002
	Diff.	0.013	0.000	

Table 3. Continued

Parameter	Group	Time point		Diff.
		T1	T5	
Middle third/lower third ratio	Younger pre-pubertal	1.30 ± 0.13	1.33 ± 0.12	NS
	Older pre-pubertal	1.20 ± 0.13	1.17 ± 0.11 a	NS
	Pubertal	1.18 ± 0.10	1.22 ± 0.10 a	0.041
	Diff.	0.013	0.000	

Data are presented as mean ± standard deviation. Diff., significance of the difference between T1 and T5 within each group, or among the groups within each T1 and T5; NS, not statistically significant difference. Notes on results of pairwise comparisons between the groups for each time interval: a, different from younger pre-pubertal group.

Table 4. Annual growth rates of the facial parameters according to group at different time intervals along with between and within group comparisons.

Parameter	Group	Time interval			Diff.
		Main (-1 year)	Main	Main (+1 year)	
Transversal					
Intereye distance (%)	Younger pre-pubertal	8.11 ± 3.13	4.20 ± 1.39	-1.41 ± 0.91	NS
	Older pre-pubertal	0.72 ± 1.37	0.17 ± 1.61	3.95 ± 1.69	NS
	Pubertal	1.92 ± 1.76	3.75 ± 1.90	-0.37 ± 1.75	NS
	Diff.	NS	NS	NS	
Nose width (%)	Younger pre-pubertal	1.86 ± 0.89	0.69 ± 1.67	0.03 ± 0.50	NS
	Older pre-pubertal	1.38 ± 0.81	2.03 ± 1.33	0.13 ± 1.31	NS
	Pubertal	4.03 ± 1.34	0.66 ± 1.36	0.60 ± 1.21	0.035
	Diff.	NS	NS	NS	
Mouth width (%)	Younger pre-pubertal	-0.33 ± 1.85	5.63 ± 1.50	-0.50 ± 1.30	0.011 b
	Older pre-pubertal	2.83 ± 1.81	5.51 ± 2.64	1.54 ± 1.59	NS
	Pubertal	5.24 ± 3.32	2.03 ± 2.40	6.28 ± 1.51 a	NS
	Diff.	NS	NS	0.015	
Eyes/mouth angle (%)	Younger pre-pubertal	43.46 ± 31.86	0.58 ± 15.37	25.22 ± 15.22	NS
	Older pre-pubertal	69.74 ± 32.22	-30.27 ± 18.63	378.85 ± 147.25	NS
	Pubertal	0.44 ± 25.96	-5.69 ± 12.94	54.50 ± 41.42	NS
	Diff.	NS	NS	NS	
Sagittal					
Facial profile angle (%)	Younger pre-pubertal	-0.14 ± 0.96	-2.32 ± 1.92	0.58 ± 1.51	NS
	Older pre-pubertal	-2.42 ± 0.94	-2.51 ± 1.29	2.10 ± 1.38	NS
	Pubertal	-2.02 ± 1.22	-8.84 ± 2.97	1.50 ± 4.35	0.043
	Diff.	NS	NS	NS	
Upper lip/EL distance (%)	Younger pre-pubertal	-11.60 ± 13.17	193.10 ± 107.90	-4.76 ± 7.06	NS
	Older pre-pubertal	22.49 ± 16.47	-46.42 ± 8.55 a	244.86 ± 93.49	0.028 c
	Pubertal	289.61 ± 272.59	25.68 ± 37.28	615.94 ± 411.19	NS
	Diff.	NS	0.000	NS	
Lower lip/EL distance (%)	Younger pre-pubertal	0.19 ± 18.66	31.39 ± 22.24	13.36 ± 18.12	NS
	Older pre-pubertal	37.59 ± 21.93	-51.40 ± 7.04 a	144.83 ± 60.87	0.013 c
	Pubertal	56.77 ± 42.24	-4.07 ± 20.93	389.89 ± 174.38	NS
	Diff.	NS	0.002	NS	
Upper lip/lower lip ratio (%)	Younger pre-pubertal	23.58 ± 20.18	220.77 ± 115.84	2.23 ± 10.50	NS
	Older pre-pubertal	30.71 ± 30.30	73.35 ± 53.68	132.88 ± 56.77	NS
	Pubertal	289.30 ± 238.75	138.34 ± 82.20	76.96 ± 45.58	NS
	Diff.	NS	NS	NS	
Nasolabial angle (%)	Younger pre-pubertal	-0.08 ± 1.06	0.68 ± 0.86	-0.58 ± 0.92	NS
	Older pre-pubertal	-0.47 ± 0.97	-1.08 ± 0.87	1.87 ± 0.76	NS
	Pubertal	-0.92 ± 1.20	-0.34 ± 1.19	0.19 ± 0.55	NS
	Diff.	NS	NS	NS	

Table 4. Continued

Parameter	Group	Time interval			Diff.
		Main (-1 year)	Main	Main (+1 year)	
Vertical					
Nose height (%)	Younger pre-pubertal	4.12 ± 1.30	5.20 ± 1.18	1.27 ± 0.79	NS
	Older pre-pubertal	4.19 ± 1.88	0.19 ± 1.08 a	6.87 ± 1.34 a	NS
	Pubertal	1.65 ± 1.43	-0.76 ± 1.65	5.43 ± 1.76	NS
	Diff.	NS	0.013	0.02	
Middle third height (%)	Younger pre-pubertal	2.64 ± 0.72	5.44 ± 0.77	1.86 ± 0.51	0.002 b
	Older pre-pubertal	2.50 ± 0.57	3.80 ± 1.10	2.15 ± 1.19	NS
	Pubertal	3.71 ± 0.65	1.72 ± 0.60 a	2.33 ± 0.21	NS
	Diff.	NS	0.07	NS	
Lower third height (%)	Younger pre-pubertal	1.17 ± 1.02	3.79 ± 1.04	1.10 ± 0.53	NS
	Older pre-pubertal	3.88 ± 1.00	2.27 ± 0.46	3.35 ± 0.74 a	NS
	Pubertal	2.85 ± 0.93	2.02 ± 0.52	1.13 ± 0.60	NS
	Diff.	NS	NS	0.036	
Middle third/lower third ratio (%)	Younger pre-pubertal	1.63 ± 1.07	1.90 ± 1.20	-0.34 ± 0.87	NS
	Older pre-pubertal	-1.17 ± 0.97	1.50 ± 1.21	-1.01 ± 1.14	NS
	Pubertal	0.89 ± 0.96	-0.17 ± 0.73	1.20 ± 0.58	NS
	Diff.	NS	NS	NS	

Data are presented as mean ± standard error. Diff., significance of the difference among the time intervals within each group, or among the groups within each time interval; NS, not statistically significant difference. Notes on results of pairwise comparisons between the groups for each time interval or between time intervals within each group: a, different from younger pre-pubertal group (within each time interval); b, significant difference between Main and Main (+1 year) (within each group); c, significant difference between Main and other time intervals (within each group).

Discussion

The present study aimed to assess soft tissue facial changes in the transverse, sagittal, and vertical planes among pre-pubertal subjects in comparison to subjects in whom a clear PHV was observed, according to a mixed longitudinal design. Soft tissue facial growth showed a generally similar amount and annual growth rates irrespective of the pre-pubertal/pubertal maturation phase, with only a few clinically relevant exceptions including the facial profile angle, upper and lower lip/EL distances, and middle third height.

Standing height increments were used as a skeletal maturation indicator, as it has been reported previously (24, 25) to be a valid and reliable tool for skeletal maturation assessment. Moreover, as only subjects with normal occlusion without any need for orthodontic treatment were included in the present study, the use of others, that is radiographic diagnostic tool, would have been ethically questionable.

Due to the importance of soft tissue esthetics in orthodontic treatment planning, several studies of facial profile changes during growth have been performed. However, these investigations were limited to analysis on 2D (invasive) lateral cephalograms (2, 8, 9, 26). As the face is a 3D object, the measurements performed on 2D recordings could be subjected to bias due to head position or angulation (15, 18). To overcome this limitation, non-invasive 3D facial scans were used herein that allow for a more precise placement of reference points and more realistic linear and angular measurements not distorted by projection phenomena.

In the present study, facial changes were observed over time in three groups of subjects: the younger pre-pubertal, defined by an early age and no evident PHV during the observational period and significantly older pre-pubertal and pubertal groups (with similar age ranges), in which the PHV was missing or evident, respectively, during the observational period. As expected, overall increment of standing height over time (T1–T5; Table 2) was observed in all three

groups, although only in the pubertal group a clear PHV (as defined above) was seen. In particular, the present study is among the few investigations (25) in which facial changes were analysed according to a clear absence or presence of PHV, thus capturing the pubertal growth effects.

In all three groups, significant overall changes of several facial parameters over the 5-year observation period were seen (Table 3). More in detail, significant overall changes were seen for most of the transverse facial parameters, including the inter-eye distance, nose width and mouth width that significantly increased. On the contrary, the eyes/mouth angle did not undergo significant overall changes, consistent with previous studies that showed no significant variations in facial asymmetry for either pre-pubertal (27) or pubertal (16) subjects. According to the present evidence, transverse growth of the face is present during different growth age ranges from 6 to 12 years, and similar between pre-pubertal and pubertal subjects (Table 3).

In the sagittal plane, a decrease of the facial profile angle was seen for all groups, even though difference did not reach statistical significance for the older pre-pubertal group (Table 3). According to previous longitudinal studies (3, 28) changes of facial convexity have been demonstrated in pre-pubertal subjects and relative stability in facial convexity after 6 years of age has been reported (8). Although in the present study, a decrease of the overall facial profile angle was observed in younger pre-pubertal subjects, a further marked decrease of the profile angle was seen in the pubertal group. As the soft tissue profile is primarily related to the underlying skeletal configuration, changes in facial convexity would be expected after maxillary and/or mandibular growth increments. However, not all parts of the soft tissue profile directly follow the underlying hard tissue (3), mainly due to the variation in the thickness of soft tissue (2). Therefore, some changes in the profile angle are likely dependent on the thickening of the soft tissue of the philtrum and chin

during growth (9). According to this previous evidence, the greatest decrease in the overall facial profile angle seen herein in the pubertal group, might be due to a combination of mandibular growth peak occurring at puberty (29) and soft tissue thickness changes in the philtrum and chin area (9). Regarding lip profile, in the present study no significant overall changes in upper or lower lip prominence or nasiolabial angle were observed over time. This might be due to the concept that thickening of the upper and lower lips occur concomitantly with nose and chin growth that influences the position of the esthetic line (9). Indeed, as previously reported, nose prominence also significantly influences the lip profile (9).

In the vertical plane, significant changes were seen in all groups for all the facial parameters with the exception of the middle/lower third ratio (Table 3). This results were expected and in line with previous evidence (30). In particular, increases of nose height (and width), as previously reported, might be an adaptation to higher functional demands due to increases of lung volume (31) and pulmonary function that reach stability only after puberty (32).

When analysing the facial growth according to the pre-pubertal and pubertal growth phases, an interesting evidence is derived from the annual growth rates at different time intervals (Table 4), with relevance to the Main interval of the pubertal group (including the standing height peak). Indeed, comparisons of rates among groups according to the different time intervals may clearly define whether the pubertal spurt has an influence not only on the total amount of growth, but also on growth timing from pre-pubertal to post-pubertal phases (33). Herein, few significant differences were seen in terms of annual growth rates among the Main (-1 year), Main and Main (+1 year) intervals, meaning that the amount and velocity of facial growth (as defined here) appears to be similar throughout 6–12 years of age, irrespective of the presence of a pubertal growth spurt (Table 4). The only relevant exception was seen for the annual facial profile angle rates in that they were similar among time intervals for both the pre-pubertal groups, while it showed a greater value in the Main interval for the pubertal group. This evidence would be consistent with a slight chin protrusion during the pubertal growth phase, likely coincident with the skeletal mandibular growth spurt (34).

Similarly, no statistically significant differences were noted in annual growth rates among the groups within the Main (-1 year) interval. The concept that all the subjects in each group during the Main (-1 year) interval were in the pre-pubertal growth phase would justify the very similar growth rates, irrespective of chronological age. On the contrary, some statistically significant and likely clinically relevant differences among the groups were seen within the Main and Main (+1 year) intervals and only in the sagittal and vertical directions. In particular, the annual growth rates of upper and lower lip/EL distances were negative and significantly lower in the older pre-pubertal group at the Main time interval only. This lip retrusion can be accounted for by the increase in nasal depth and height (26) accompanied by the anterior growth displacement of the chin (9). However, while no significant differences were seen between the younger pre-pubertal and pubertal groups, lower annual growth rates were seen for the latter group, meaning that during the pubertal growth spurt lips may have a slower protrusion rate. A possible explanation of the greater rates of lip prominence seen in the younger pre-pubertal group may reside in the eruption of the permanent upper and lower incisors. Therefore, changes in lip prominence in very young subjects may be more related to dental rather than skeletal maturation.

The nose parameters showed some significant different annual growth rates both in the transversal and vertical directions. Within each

group, the annual rate of nose width was greater in the Main (-1 year) interval as compared to the other intervals only for the pubertal group (Table 4). On the contrary, the annual growth rates of nose height also showed generally greater values in the pre-pubertal groups, as compared to the pubertal group, with significant differences at both the Main and Main (+1 year) intervals. The present evidence would be consistent with previous reports showing that the pubertal growth spurt has a greater effect on anterior nasal growth (not included in the present investigation) than on the height and width of the nose (35). Contrasting the present results are reports of significant increments in nose length during puberty (35, 36). However, the different facial parameters used to assess nose height among studies may explain such inconsistency.

Moreover, the middle third height showed generally greater annual rates in the pre-pubertal groups as compared to the pubertal group, even though the difference reached significance in the Main interval only. This evidence is thus consistent with the greater skeletal maxillary growth seen at very early developmental stages (37). On the contrary, annual growth rates for the lower third height showed only little differences with limited clinical relevance, as the pubertal growth spurt did not appear to have influence on its behavior.

In the present study the peak of standing height increment was observed at an early age, confirming that puberty might occur at large age ranges. A clear peak in standing height (i.e. more than 7 cm over the previous recording) was used as a threshold to allocate the subjects in the pubertal group. However, while the use of such a threshold has the advantage of being highly specific, that is true positives were detected in the pubertal group, it has the disadvantage of including some true pubertal subjects into the pre-pubertal groups (false negatives). Therefore, results on the older pre-pubertal group may be considered less reliable as compared to the other groups.

Clinical implications

Contemporary orthodontic diagnosis and treatment planning should be based not only on the assessment of skeletal parameters but also on soft tissue appearance. As orthopedic treatment is frequently performed during growth and development, it is very important to consider changes also of the soft tissue profile according to different developmental phases. Younger pre-pubertal subjects show greater annual growth rates in lip prominence, mainly occurring concomitantly with permanent incisors' eruption. Furthermore, greater annual growth rates in middle third height are to be expected during the pre-pubertal phase, while a decrease of the facial profile angle is to be expected during puberty. This should be considered in orthopedic treatment of either maxillary or mandibular retrusion at early developmental stages. However, other maturation indicators rather than standing height might be better correlated with soft tissue facial changes.

Conclusions

In subjects with normal profile, soft tissue facial growth has generally similar amount and rates irrespective of the ages herein investigated and pubertal growth spurt, with only few exceptions. Earliest pre-pubertal subjects show greater annual growth rates of lip prominence. Pre-pubertal (younger and older) subjects show greater annual growth rates in middle third height; on the contrary, pubertal subjects show greater annual growth rates in chin protrusion.

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