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Cephalometric analysis of pharyngeal airway space dimensions in Turner syndrome

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SUMMARY Turner syndrome (TS) that is due to a total or partial lack of an X chromosome affects about 1 in 2000 girls. The syndrome is characterized by short stature and gonadal dysgenesis. Its documented craniofacial features include retrognathic jaws, a short mandible, and a large cranial base angle. Our aim was to find out whether the syndrome also has an effect on the pharyngeal airway space. We retrospectively analysed lateral cephalograms of 35 TS subjects whose age ranged from 6.5 to 21 years and of 35 healthy female controls matched for age. On those, we did 7 linear and 10 angular cephalometric measurements and 9 pharyngeal measurements. Differences between the subjects with TS and their controls were assessed by paired two-tailed *T*-test. In the girls with TS, both the maxilla and the mandible were more retrognathic (SNA, $P = 0.015$ and SNB, $P < 0.001$), the mandible was shorter (TM–Pgn, $P = 0.016$), and the cranial base angle was larger (SNBa, $P = 0.025$) than in the controls, confirming the results of earlier studies. Notably, all six pharyngeal airway measurements were smaller in girls with TS. Two of them, PNS–ad2 and PAS, were statistically significantly smaller ($P = 0.019$ and $P = 0.012$, respectively). Thus, a narrow pharynx, either as a primary finding or as a consequence of the maxillo-mandibular retrognathism, further delineates the phenotype. This may imply an elevated risk of sleep apnoea in females with TS.

Introduction

Turner syndrome (TS), the most common sex chromosomal disorder in women, was previously described as absence of one X chromosome. Later studies have shown that karyotype 45,X represents only about 50 per cent of cases, the other half consisting of mosaicisms where both 45,X and 46,XX cells are present, rarer karyotypes with an isochromosome of X and karyotypes with a Y or a part of a Y chromosome (Baena *et al.*, 2004). The phenotype is always female. The reported prevalence of TS is 1 in 2000 girls (Nielsen and Wohlert, 1991).

Short stature and gonadal dysgenesis are the most typical features in TS. The average height is 141.5 cm in women who have not been treated with growth hormone (Rochiccioli *et al.*, 1994). Other common dysmorphic features in TS are broad chest, cubitus valgus, low hairline, low and posteriorly rotated ears, hyperconvex nails, short forth/fifth metacarpal, and webbed neck (Donaldson *et al.*, 2006). About 50 per cent of patients with TS have heart malformations, coarctation of the aorta, and bicuspid aortic valve being the most common ones (Sybert, 1998).

Many of the typical features in TS can partly be explained by haploinsufficiency of the short stature homeobox-containing osteogenic (*SHOX*) gene contained in the PAR1 region of the X- and Y-chromosome (OMIM *312865). Corresponding haploinsufficiency occurs in Leri-Weill dyschondroosteosis. Even these patients have short stature, but the length difference compared to normal is not as great as in TS, indicating that the haploinsufficiency only partly explains the short stature in TS (Kosho *et al.*, 1999). Hence, the pathogenesis of the changes occurring in the syndrome is not fully elucidated.

Previous studies on the craniofacial phenotype in TS have shown that the cranial base angle (SNBa) is larger, the posterior cranial base shorter (S–Ba), both jaws more retrognathic, and the mandible more posteriorly rotated and shorter than usual, while the maxilla is of normal length. The mandibular retrognathism is explained both by a shorter than normal mandible and a higher than normal position of the condyles due to changes in the configuration of the cranial base. The abnormal craniofacial features in TS can therefore largely be explained as secondary to changes in the cranial base (Jensen, 1985; Peltomaki *et al.*, 1989; Rongen-Westerlaken *et al.*, 1992; Midtbo *et al.*, 1996; Dumancic *et al.*, 2010).

It has been suggested that a discrepancy in the cartilagenous growth is a factor involved in the development of the typical craniofacial morphology seen in TS since cranial base is one of the structures reaching a stable position already during the intrauterine period in the foetus (Diewert, 1985). The characteristic craniofacial features in TS are indeed established already in childhood (Rongen-Westerlaken *et al.*, 1992; Midtbo *et al.*, 1996). However, there is an association between some craniofacial measures (S–Ba, S–Go, SNB, and S–Art) of patients with TS and their mothers (Perkiomaki *et al.*, 2005). This implies that the syndrome

does not completely override the impact of the parental genetic factors on the craniofacial morphology.

Common malocclusions in TS include lateral crossbite, large horizontal overbite, distal bite (50–60 per cent), and a tendency to open bite, both anteriorly and laterally (Laine and Alvesalo, 1986; Laine *et al.*, 1986). The palate is narrow and the tongue position is lower in TS than normal, partly explaining the malocclusions associated with the syndrome (Perkiomaki and Alvesalo, 2008). Tooth morphology is affected as well; in comparison to controls, the teeth are smaller, have thinner enamel, and may have shorter roots, an abnormal number of roots and abnormal crown to root ratio (Alvesalo and Tammisalo, 1981; Varrela *et al.*, 1988; Varrela, 1990, 1992; Midtbo and Halse, 1994; Kusiak *et al.*, 2005; Rizell *et al.*, 2011).

Retrognathism of the maxilla and mandible, often found in TS, are also reported as typical craniofacial features in obstructive sleep apnoea syndrome (OSAS; Tangugsorn *et al.*, 1995; Ishiguro *et al.*, 2009). The airway space in OSAS also is narrower than normal. However, to our knowledge, pharyngeal airway dimensions have not been previously analysed in patients with TS. The aim of the present study was to investigate cephalometrically if TS has an impact on pharyngeal dimensions and if subjects with TS are therefore in an increased risk of developing sleep-disordered breathing or OSAS.

Subjects and methods

Study subjects

We studied lateral cephalograms of TS subjects that had been submitted for examination to the Department of Pedodontics and Orthodontics, Institute of Dentistry, University of Helsinki during the years 1973–96. The cephalograms of 38 subjects were retrospectively collected from patient files, and personal data were replaced by chronological age that ranged from 6.5 to 21 years. Three of the radiographs were excluded from the study due to poor quality. Of the 35 included, karyotypes for 30 were available. Of them, 25 were monosomic (45,X), 4 were mosaic (two having 45,X/46,X,r(X), one 45,X/46,XX, and one 45,X/46,XX/47,XXX), and 1 was isochromosomal 46,X,i(Xq). Most of the subjects had been treated with oestrogen and some with growth hormone. The radiographs of the known 45,X subjects were all from the seventies. Back then, patients with TS had received very small doses of purified human growth hormone, if any, because of its restricted availability and high price. The other subjects, born later, had received higher doses of recombinant human growth hormone. All lateral cephalograms were taken for diagnostic purposes at the Department of Radiology, Institute of Dentistry, University of Helsinki. Anonymously performed re-evaluation of the pre-existing radiographic data were approved by the Head of the Institute of Dentistry, University of Helsinki, Finland.

As paired controls, we used lateral cephalograms of 35 healthy girls who had participated in the Helsinki Longitudinal Growth Study, conducted during 1967–93, at the Institute of Dentistry, University of Helsinki under the approval of the Ethics Board of the Institute of Dentistry, University of Helsinki (Nyström *et al.*, 2001). The controls were age matched so that a maximum age difference of 0.25 years was accepted. The age distribution of the study subjects and controls is presented in Table 1.

All these cephalograms had been taken in Frankfurt horizontal plane parallel to floor in a rigid cephalostat by the same experienced staff at the Institute of Dentistry, University of Helsinki.

Measurements

The measurements from the radiographs were carried out by hand, and all linear measurements were adjusted for magnification. For cephalometric analysis, 10 angular and 7 linear measurements were carried out. The points and planes measured are presented in Figures 1 and 2. In addition, we calculated Harvold's difference, which is the difference between the length of the mandible and the effective length of the maxilla (Harvold, 1974), the ratio between lower anterior face height and total anterior face height, and the ratio between posterior face height and anterior face height. The explanations for the measurements are presented in Table 2.

Sagittal dimensions of the airway space were examined by six linear measurements at different pharyngeal sites. In addition, we measured the length and maximum thickness of the soft palate and the distance between hyoid bone and the mandibular plane. The points and lines used in the pharyngeal airway analysis are presented in Figure 3.

The measurements were done with the accuracy of 0.5 mm and 0.5 degrees by the first author and JWS until consensus was reached. They were not blinded for the group. To evaluate the repeatability of the measurements, cephalometric analysis of 10 randomly picked lateral cephalograms of the study material was repeated after 6 months. The error value was calculated using Dahlberg's formula $\sqrt{(\sum d^2 / 2N)}$, where d is the difference between the two measurements and N is the number of cephalograms

Table 1 Age distribution of the study subjects with Turner syndrome and their controls.

Age (years)	Turner syndrome (*n*)	Controls (*n*)
6.5–9.9	8	8
10–13.5	10	10
13.6–16.9	12	12
17–21	5	5
Total number	35	35
Mean age (years) ± SD	13.13 ± 3.99	13.16 ± 4.03

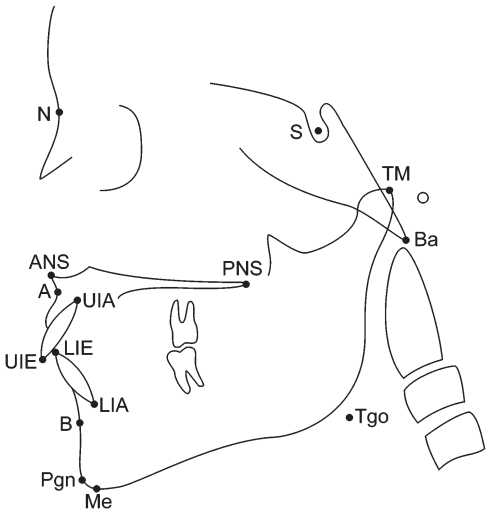

Figure 1 Cephalometric points in alphabetical order: A, the most posterior point on the anterior contour of the upper alveolar process; ANS, anterior nasal spine; B, the most posterior point on the anterior contour of the lower alveolar process; Ba, basion; LIA, lower incisor apex; LIE, lower incisor edge; Me, menton; N, nasion; Pgn, prognathion, a point on the contour of the bony chin indicating maximum mandibular length from the condyle; PNS, posterior nasal spine; S, sella; Tgo, constructed gonion, intersection of the tangents to mandibular ramus and corpus; TM, a point on the mandibular condyle indicating maximum mandibular length from prognathion; UIA, upper incisor apex; UIE, upper incisor edge. The points ANS(s) superior and ANS(i) inferior describe the points over (s) and under (i) ANS where height of spina nasalis anterior is 3 mm.

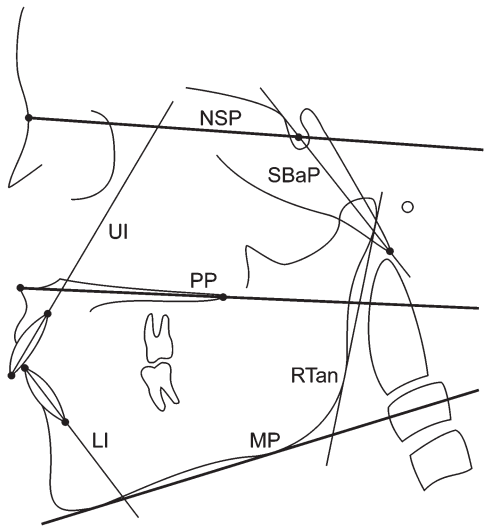

Figure 2 Cephalometric planes and their descriptions. NSP, anterior cranial base plane, crossing N and S; PP, palatal plane, crossing the points ANS and PNS; MP, mandibular plane, tangent to the lower border of the mandibular corpus; SBaP, posterior cranial base plane, crossing S and Ba; UI, Inclination of the upper first incisor, crossing UIA and UIE; LI, Inclination of the lower first incisor, crossing LIA and LIE; RTan, Tangent to the posterior border of the mandibular ramus.

(Dahlberg, 1948). The mean error value was 1.5 degrees for the angular measurements and 1.1 mm for the linear ones. The inclination of the upper incisors showed the biggest error value and ph1–ph2 the smallest one.

Statistical analysis

Descriptive statistics including mean and standard deviation were calculated for all measurements and calculated relationships. A paired two-tailed *T*-test was used to analyse whether there were statistically significant differences between the measurement values in subjects with TS and controls. We also specifically tested the differences between those with 45,X karyotype and their paired controls.

Results

The results of the cephalometric analysis are presented in Table 3. In the total sample of subjects with TS, both jaws were retrognathic in relation to the cranial base. SNB angle was, when comparing the averages, 3.5 degrees smaller in those with TS, which is statistically significant ($P < 0.001$). SNA also was smaller in TS, with a difference in the averages of 2 degrees ($P = 0.015$). The cranial base was flatter; the angle SNBa was on the average of 3.1 degrees larger in subjects with TS ($P = 0.025$). The smaller than normal size of the mandible and more posterior than normal position of the condylar fossa due to the flat anterior cranial base contribute to the diminished SNB value.

The length of the mandible (TM–Pgn) was significantly smaller, on the average of 4.9 mm, in females with TS ($P = 0.016$). The length of the maxilla (TM–ANS(i)) did not differ significantly. The combination of short mandible and normal maxilla also led to a mean Harvold's difference that was 3.7 mm smaller in those with TS ($P = 0.015$). The mean gonial angle was almost the same in both groups, but the standard deviation was almost twice as high in subjects with TS, indicating that larger variation in the shape of the mandible features TS. The inclination of the incisors did not differ between females with TS and controls.

All six pharyngeal measurements describing airway space (PNS–ad1, PNS–ad2, p1–p2, ve1–ve2, PAS, and ph1–ph2) were smaller in patients with TS than in controls. The soft palate was both shorter (PNS–ve1) and thicker (MPT) than in the controls. Both PNS–ad2 ($P = 0.019$) and PAS ($P = 0.012$) were significantly smaller in patients with TS. Mean PNS–ad2 differed by 12 per cent and PAS by 14 per cent between patients with TS and the controls.

Comparison of the subgroup with 45,X karyotype with their controls gave quite similar results with the following exceptions: maxillary retrognathism, flattening of the anterior cranial base, and narrowing of the PNS–ad2 measure did not reach statistical significance. Notably, however, the maximum palatal thickness was statistically significantly increased in this subgroup of TS subjects.

Discussion

This study showed that subjects with TS have sagittally narrower than normal pharyngeal airway space. Measuring

Table 2 The angular and linear measurements and their descriptions.

Angular measurements	
SNA	Sagittal location of maxilla in relation to the cranial base
SNB	Sagittal location of mandible in relation to the cranial base
ANB	Sagittal position of the jaws in relation to each other
NSBa	Cranial base angle
NSP–MP	Angle between the cranial base and the mandibular plane
PP–MP	Angle between the palatal plane and the mandibular plane
Gonial angle	Angle between the tangent to the mandibular ramus and the mandibular plane
UI–NSP	Angle between the upper first incisor axis and the cranial base
UI–PP	Angle between the upper first incisor axis and the palatal plane
LI–MP	The angle of the lower first incisor axis and the mandibular plane
Linear measurements	
TM–ANS(i)	Effective length of maxilla according to Harvold
TM–Pgn	Length of mandible according to Harvold
ANS(s)–Me	Total anterior height of the jaws according to Harvold
AFH	Anterior facial height, N–Me
PFH	Posterior facial height, S–Tgo
LFH	Lower facial height, the section from ANS to an imagined continuation of Me which is perpendicular to the line N–Me
S–N	Anterior cranial base length

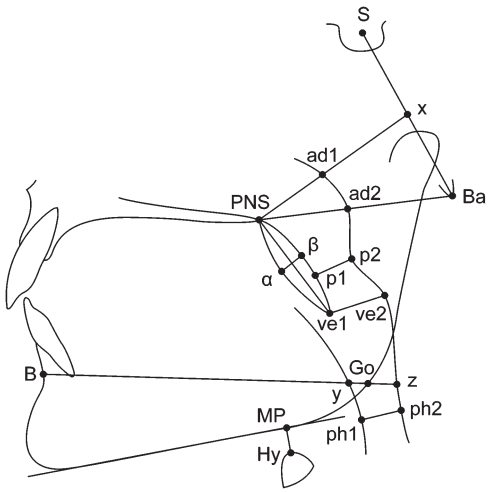

Figure 3 The measurements in the pharyngeal region: PNS–ad1, where ad1 is the point on the posterior pharyngeal wall where the line PNS-x crosses pharynx and the point x is the point at the middle of the line S–Ba; PNS–ad2, where ad2 is the point on the posterior pharyngeal wall where the line PNS–Ba crosses pharynx; p1–p2, the points that give rise to the shortest distance between the soft palate and posterior pharyngeal wall; ve1–ve2, where ve1 is the most inferior point of the soft palate and ve2 is the nearest point on the posterior pharyngeal wall; y–z, known as posterior airway space (PAS), the pharyngeal width on the line B–Go; ph1–ph2, the points that give rise to the shortest distance in pharynx below PAS but above the fourth vertebra; PNS–ve1, the length of the soft palate; α–β, the maximum thickness of the soft palate, perpendicular to PNS–ve1; Hy–MP, where Hy is the point on the hyoid bone closest perpendicular to the mandibular plane.

its size from lateral skull radiographs is sensitive to changes in head position (Muto *et al.*, 2002). In our material, both study subjects and controls were radiographed at the same radiological department by experienced staff who had been instructed to position Frankfurt horizontal plane and floor in parallel, and a rigid cephalostat was used. Therefore, no major variations in head position are expected to have occurred.

Whether or not the diminished pharyngeal width and increased thickness of the soft palate were associated with symptoms suggestive of nocturnal pharyngeal obstruction in these TS subjects remains an open question. Noteworthy, sleep apnoea was a less widely recognized phenomenon at the time the patients were examined. Consequently, all lateral skull radiographs had been taken in an upright position, which is not ideal when tracing anatomical risk for pharyngeal obstruction, and imaging had been limited to a two-dimensional view. Nevertheless, nasopharyngeal and retropalatal variables in cephalograms taken in upright position have been recently shown to significantly correlate with pharyngeal three-dimensional MRI variables in supine position within children suffering from sleep-disordered breathing (Pirilä-Parkkinen *et al.*, 2011).

There was no attempt to measure the overall size of the skull in this study, but several linear dimensions (TM-ANS(i), LFH, AFH, PFH, and S–N) suggest that there were no major differences in general size of the facial structures between girls with TS and the control group. This is also supported by the notion that the craniofacial dimensions are less affected by TS than growth in general (Peltomaki *et al.*, 1989). Most of the subjects in this study had been treated with oestrogen and minute doses of growth hormone. Although growth hormone treatment in sufficient doses affects height remarkably, it does not significantly affect the craniofacial structures. The characteristic features of both linear and angular cephalometric measurements remain (Hass *et al.*, 2001). The only measurement in the craniofacial region found out to vary before and after growth hormone therapy is mandibular length, due to vertical growth (Rongen-Westerlaken *et al.*, 1993).

We observed similar craniofacial features as reported in females with TS in earlier studies, namely that both jaws are retrognathic and mandible shorter than normal (Jensen, 1985; Peltomaki *et al.*, 1989; Rongen-Westerlaken *et al.*,

Table 3 Cephalometric values of the girls with Turner syndrome (TS) and the controls. Max, maximum; Min, minimum.

	TS ($n = 35$)				Controls ($n = 35$)				Difference of means	P ($n = 35$)	P_0 ($n = 25$)
	Mean	SD	Min	Max	Mean	SD	Min	Max			
Angular											
SNA (°)	79.5	4.5	73	90	81.5	3.6	74.5	87.5	−2	0.015*	0.174
SNB (°)	74.9	4.7	68	85.5	78.4	3.2	73	87	−3.5	0.000***	0.003**
ANB (°)	4.5	2.5	−2	11.5	3.2	2.4	−1.5	7	1.3	0.039*	0.033*
NSBa (°)	132.8	5.7	121.5	148	129.7	5.5	116	137	3.1	0.025*	0.144
NSP/MP (°)	32.8	7.7	20	48.5	30.7	6.0	21	44	2.1	0.191	0.300
PP/MP (°)	24.0	7.2	7	39	24.1	5.2	14	33	−0.1	0.929	0.970
Gonial angle (°)	127.2	8.9	104	145	127.6	4.8	117	136	−0.4	0.836	0.961
UI/NSP (°)	103.1	7.5	83.5	116.5	103.8	7.5	87	117	−0.7	0.655	0.819
UI/PP (°)	112.8	7.0	90	126.5	111.0	5.9	101	123	1.8	0.188	0.213
LI/MP (°)	99.3	7.6	84	120	98.3	8.2	80	117.5	1.0	0.621	0.422
Linear											
TM–ANS(i) (mm)	81.2	6.6	66.8	96.5	82.5	5.3	71.4	92.3	−1.3	0.347	0.558
TM–Pgn (mm)	99.6	8.9	80.5	112.2	104.5	8.1	88.2	117.7	−4.9	0.016*	0.032*
Harvold's difference (mm)	18.4	4.7	9.5	28.4	22.1	6.0	13.3	35.5	−3.7	0.015*	0.018*
S–N (mm)	65.1	3.9	56.8	72.4	65.4	3.0	59.6	71.8	−0.3	0.713	0.526
ANS(s)–Me (mm)	60.6	5.5	50.5	71.9	59.9	5.1	48.2	68.6	0.7	0.612	0.407
LFH (mm)	58.8	5.4	49.1	71	58.8	5.2	46.8	69.5	0	0.972	0.724
AFH (mm)	104.4	8.5	88.5	122.1	103.5	7.7	89.0	118.6	0.9	0.674	0.649
PFH (mm)	68.1	9.0	46.4	79.1	69.2	6.8	55.5	79.5	−1.1	0.545	0.470
LFH/AFH (ratio)	0.56	0.025	0.51	0.62	0.57	0.022	0.51	0.61	x	0.388	0.925
PFH/AFH (ratio)	0.65	0.068	0.52	0.77	0.67	0.050	0.57	0.75	x	0.218	0.151
Pharyngeal											
PNS–ad1 (mm)	15.2	3.8	8.0	21.3	15.8	3.4	6.2	22.7	−0.6	0.491	0.677
PNS–ad2 (mm)	18.1	4.8	8.9	29.3	20.5	4.3	7.1	27.3	−2.4	0.019*	0.198
p1–p2 (mm)	6.7	2.0	3.3	11.8	7.3	2.6	2.3	12.7	−0.6	0.339	0.233
ve1–ve2 (mm)	8.4	2.3	3.8	13.6	8.6	2.8	2.3	13.2	−0.2	0.625	0.349
PAS (mm)	9.5	2.7	3.8	13.7	11.0	2.6	5.9	16.4	−1.5	0.012*	0.029*
ph1–ph2 (mm)	7.9	2.8	2.8	13.7	9.1	2.7	3.6	14.2	−1.2	0.060	0.280
PNS–ve1	27.8	3.2	22.3	34.5	29.4	4.0	22.7	39.3	−1.6	0.105	0.350
MPT	8.3	1.2	6.4	11.4	7.8	1.2	5.5	9.5	0.5	0.078	0.008**
Hy–MP (mm)	10.5	5.8	−3.8	18.5	10.6	3.9	3.6	20.0	−0.1	0.966	0.797

P refers to statistical testing between the total subject sample and controls and P_0 to statistical testing between a subgroup of 25 subjects with 45,X karyotype and their controls.
***$P < 0.001$; **$P < 0.01$; *$P < 0.05$.

1992; Midtbo *et al.*, 1996). Any earlier data on pharyngeal dimensions in patients with TS was limited to the length between basion and PNS, which turned out to be significantly shorter in the group with TS (Jensen, 1985). In our study, all six pharyngeal airway measurements were smaller than in the controls, the difference for two of them being statistically significant, and the soft palate was significantly thicker in the ones with 45,X karyotype.

The relationship between pharyngeal airway dimensions and sagittal malocclusions has been analysed in many studies. In a study from 1995, the impact of various skeletal classes on the two-dimensional width of pharynx was examined, and it was suggested that the pharyngeal structures are unaffected by ANB value (Ceylan and Oktay, 1995). A more recent study, similarly based on two-dimensional lateral cephalograms, indicated no differences in airway dimensions between groups with Angle Classes I and II malocclusion. However, between patients with divergent and convergent patterns of growth rotation, a difference was found regardless of malocclusion type. The upper respiratory tract of those with a divergent growth rotation was found to be smaller, while the lower respiratory tract, at a level that roughly equivalents the PAS measurement in our study, was not affected (de Freitas *et al.*, 2006). However, the views about a connection are controversial. There are a few studies showing a link between orthognathic, retrognathic, and prognathic mandible and pharyngeal anterior–posterior width (Muto *et al.*, 2008; Kim *et al.*, 2010). Furthermore, sleep-disordered breathing has been reported in patients with retrognathia secondary to rheumatoid arthritis (Almoudi, 2006).

Three dimensionally, Alves *et al.* compared pharyngeal dimensions between patients with skeletal Classes II and III by computed tomography, and the results indicate that most of the dimensions of the pharynx are not associated with the skeletal class. They suggest that pharynx is a relatively autonomous structure in relation to the facial complex (Alves *et al.*, 2008). Another very comprehensive study done on

cone beam computed tomography images, where skeletal Classes II and III were compared and both the gender and the size of the skull were taken into account, suggested that the volume of the lower airway is related to the anterior–posterior jaw position and that the shape of the pharynx differs, so that the pharynx in skeletal Class III is more vertically oriented (Grauer *et al.*, 2009). Thus, the results are not entirely unambiguous even in these recent three-dimensional studies, which may partly depend on the methods not being all that developed yet.

The measurement PNS–ad2 represents the upper respiratory tract and PAS the lower respiratory tract in this study. Both these dimensions differed statistically significantly from the controls indicating that the airways are not only in a single point but also possibly over a longer distance, narrower than usual in TS. In the lower part, the abnormally low position of the tongue (Perkiomaki and Alvesalo, 2008) could play a role. In addition, it should be noted that we compared TS subjects with a mean ANB angle of 4.5 degrees with unaffected controls whose mean ANB was 3.2 degrees. Therefore, the study setting was different from several previous studies of pharyngeal dimensions where extremes of Classes II and III have been compared. In our study, the pharyngeal dimensions were narrower in TS subjects than in controls whose facial shape can be anticipated to represent the average of the Finnish population where Class I occlusion occurs in the majority (Myllärniemi, 1973). One can conclude that the syndrome has a greater impact on pharyngeal dimensions than the anterior–posterior position of the jaws normally does in healthy individuals. This conclusion is based on the conflicting earlier research results concerning the relationship between jaw position and pharyngeal dimensions. We tend to suggest that the craniofacial development probably differs between patients with TS and healthy patients with similar grade of retrognathism of the jaws.

Another possibility remains that the small pharyngeal dimensions in this study are secondary to the retrognathism. In that case, this study would support the theory that the jaws' anterior–posterior placement affects the pharyngeal dimensions. To confirm or to rule out such a direct relationship, one should investigate subjects with TS and healthy girls with similar craniofacial morphology in view of the SNA and SNB values for possible differences in pharyngeal airway dimensions.

It has been reported that 30 per cent of adolescent with TS are hypertensive, which is neither explained by the reported abnormalities in the heart nor the kidneys (Nathwani *et al.*, 2000). Interestingly, there is an association between OSAS and hypertension, which is explained by multiple mechanisms, the main one being an increase in sympathetic activity during the apnoeas (Baguet *et al.*, 2009). Our finding on the narrow pharynx is on the favour of the hypothesis that OSAS is partly responsible for the observed hypertension in TS. There is one case report on TS and associated OSAS. In this 34-year-old TS woman, OSAS was successfully treated first with CPAP and later with surgical maxillo-mandibular advancement (Orliaguet *et al.*, 2001).

In conclusion, we have shown that the pharynx is two dimensionally narrower in TS than in healthy subjects. We suggest that this anatomical predisposition for sleep-disordering breathing, OSAS, and hypertension may well be associated findings in TS. The prevalence of symptoms and signs of OSAS in patients with TS should be investigated in further studies, as well as pharyngeal size in a contemporary patient group that has received adequate growth hormone treatment. We propose that in clinical practice, doctors should ask their TS patients for eventual sleep problems or fatigue, so that they can be offered adequate examination and treatment in case of OSAS.

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