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Craniofacial morphological characteristics in children with obstructive sleep apnea syndrome

A systematic review and meta-analysis

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ABSTRACT

Background. The authors conducted a systematic review to consolidate the current knowledge regarding craniofacial morphological characteristics associated with obstructive sleep apnea syndrome (OSAS) in nonsyndromic pediatric patients.

Types of Studies Reviewed. The authors included clinical studies in which participants were younger than 18 years, polysomnography was performed to determine the presence and severity of OSAS and the study group was compared with a control group or normative growth center data. The authors excluded studies with syndromic participants or participants who had received orthodontic treatment, orthognathic treatment or both previously.

Results. The authors identified nine articles. They conducted a meta-analyses of the data from all but one of the studies to evaluate the eight most common cephalometric variables in children with OSAS. The I^2 values were 79.53 percent for the angle from the basion point to the sella nasion (SN) line, 89.54 percent for the angle between the SN and palatal plane lines and 96.82 percent for the angle between the mandibular plane and SN lines (MP-SN). Therefore, for these three variables, the authors conducted a random-effect model meta-analysis. For the remaining five variables (MP-SN, the angle from SN to A point, the angle from SN to B point [SNB], the angle from A point to nasion point to B point [ANB] and the angle from articulare point to gonion point to gnathion point), I^2 values were all less than 40 percent, and therefore the authors conducted a fixed-effects model meta-analysis. Three of the evaluated cephalometric variables (MP-SN, SNB and ANB) had statistically significant differences in comparison with those in a control group. Although the values of these variables were increased in children with OSAS, results of the meta-analysis should be considered cautiously owing to the limited number of cephalometric variables included.

Practical Implications. Dentists who identify patients with a craniofacial morphology consistent with pediatric OSAS (retrusive chin, steep mandibular plane, vertical direction of growth and a tendency toward Class II malocclusion) should inquire further into their patients' medical histories. When the craniofacial morphology is accompanied by a history of snoring, inability to breathe through the nose, significant allergies, asthma or obesity, the dentist should refer the patient to an otolaryngologist for assessment.

Key Words. Cephalometry; sleep apnea syndrome; obstructive sleep apnea.
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Obstructive sleep apnea syndrome (OSAS) is a form of sleep-disordered breathing (SDB) characterized by recurrent episodes of partial or complete airway obstruction during sleep with associated abnormalities in gas exchange, sleep disruption or both.[1] Both adults and children can be affected; however, the prevalence, etiology and pathophysiology of the disease is different between the two groups. The prevalence of OSAS in

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children is reported to range from 1.0 to 2.2 percent.[2-5] In contrast to adults, the most common cause of pediatric OSAS is adenotonsillar hypertrophy.[6,7] Other risk factors include asthma, exposure to environmental tobacco smoke and low socioeconomic status.[8] In children, there also are several additional craniofacial risk factors such as macroglossia, mandibular or midface hypoplasia, obesity and other craniofacial anomalies.[9]

The subjective symptoms and clinical sequelae of OSAS vary according to the severity of the disease and patient-specific factors such as neuromotor tone and duration of disease. The most common symptoms are chronic snoring, increased work at breathing, daytime fatigue and sleepiness, nocturnal enuresis, irritability and other behavioral and neurocognitive changes.[10-12] In children, these changes often manifest as poor academic performance and social adjustment problems.[13] Successful treatment of OSAS has been associated with reversible improvement in these areas, with reported recurrence of these problems associated with recurrence of OSAS.[14] In severe cases of untreated or poorly controlled OSAS, more serious complications can occur such as failure to thrive, cor pulmonale, pulmonary hypertension and other significant cardiovascular complications.[11]

The interrelationships between craniofacial form and physiological function in the upper airway are central to understanding the etiology and treatment of a constricted upper airway in children. The focus of researchers has been directed largely toward structural narrowing and not the relationships that influence them. Cause-effect relationships between specific craniofacial growth patterns and the presence of SDB conditions such as OSAS in children have been the focus of the research. Across the preceding 43 years, investigators of a growing number of published articles have described specific patterns of craniofacial growth and development associated with SDB and other upper airway resistance syndromes (UARSs).[15-26] However, adult OSAS cannot be diagnosed unequivocally by means of only a lateral cephalogram. In contrast, anthropometric measurements have been used successfully to distinguish adult patients with OSAS from control patients with reasonable accuracy.[27]

Investigators in previous reviews discussed the relationship between pediatric OSAS and craniofacial morphology.[21,22] However, these reviews are dated and did not use systematic search methods. Therefore, we conducted a systematic review to consolidate the current knowledge of craniofacial morphological characteristics associated with upper airway constriction resulting in OSAS in children. Because of the significant differences in etiology and long-term impact on craniofacial morphology between pediatric and adult OSAS, the focus of our review was limited to studies of nonsyndromic pediatric patients.

METHODS

The search methods we used for our review included both electronic and manual searches of reference lists. Electronic database searches were conducted by using a series of key words and key word combinations based on knowledge of the subject-area controlled vocabulary and free-text terms, consultation with a specialized health-sciences librarian, use of Medical Subject Headings and reviews of reference lists in selected articles. Appropriate truncation and word combinations were used in each search. The electronic databases we searched from their inceptions until April 29, 2012, were MEDLINE, PubMed, Embase, All Evidence-Based Medicine Reviews, Scopus and Web of Science. The specific search strategies and terms and combinations used in each electronic database search are found in eTable 1 through eTable 6 in Appendix A in the supplemental data to the online version of this article (found at http://jada.ada.org).

We included only studies that reported cephalometric findings in nonsyndromic children with OSAS confirmed by means of polysomnography in our review. To identify these studies, we used the following inclusion criteria a priori and applied them to abstracts and articles we retrieved as soon as we completed the electronic database searches:

- all participants were younger than 18 years;
- polysomnography was performed to determine the presence and severity of a constricted upper airway in participants or both case participants and control participants;

ABBREVIATION KEY. ANB: Angle from A point to nasion point to B point. **AHI:** Apnea-hypopnea index. **Ar:** Articulare. **A:** A point. **ANS:** Anterior nasal spine. **B:** B point. **Ba:** Basion. **Gn:** Gnathion. **Go:** Gonion. **L1:** Lower incisor inclination. **MDAS:** Minimum posterior airway space. **Me:** Menton. **MP:** Mandibular plane. **MP-SN:** Angle between the mandibular plane and sella nasion lines. **N:** Nasion. **OSAS:** Obstructive sleep apnea syndrome. **PP:** Palatal plane. **PNS:** Posterior nasal spine. **S:** Sella. **SDB:** Sleep-disordered breathing. **SN:** Sella nasion. **SNA:** The angle from sella nasion to A point. **SNB:** Angle from sella nasion to B point. **T/A:** Tonsillectomy and adenoidectomy. **UARS:** Upper airway resistance syndrome.

- a comparison with an appropriate control group or with commonly accepted cephalometric normative data was conducted when appropriate for the study design;
- study samples did not include participants with craniofacial syndromes such as Down syndrome or those who had received orthodontic or orthognathic treatment before evaluation by the investigators.

Two reviewers (M.K. and a research assistant) applied these selection criteria separately to the retrieved abstracts from the electronic database searches. Treatment was not an inclusion criterion. Publication status and language were not exclusion criteria.

The first step of the selection process was based on reviews of the titles and abstracts of the retrieved abstracts and articles. We retrieved the abstract or article and reviewed it. When we needed more information to assess whether the article should be included in our review, we retrieved the entire article and contacted its authors if necessary. We settled discrepancies between the lists of abstracts and titles selected by the two reviewers by means of discussion.

We used a second similar selection phase to determine which of the retrieved articles to include finally in our review. Again, we resolved discrepancies between the lists of articles selected by the two reviewers by means of discussion. We also screened the reference lists of the selected articles at this stage for any article that we may have missed.

We conducted a meta-analysis when two or more of the selected studies used similar cephalometric values. When homogeneity between the studies was demonstrated, we used a fixed-effects model. When heterogeneity between the studies was demonstrated, we used a random-effects model.

RESULTS

The number of abstracts and titles obtained from each electronic database search are provided in eTable 1 through eTable 6 in Appendix A in the supplemental data to the online version of this article (found at http://jada.ada.org). Details about the selection process can be found in Appendix B in the supplemental data to the online version of this article (found at http://jada.ada.org). A list of excluded studies and the reasons for the exclusion are available on request. Nine articles[28-36] met the requirements of our four selection criteria. The investigators in seven of these articles specifically analyzed children with OSAS.[28,30,34,36]

We conducted a qualitative assessment of the nine retrieved articles on the basis of the degree to which they exhibited well-established and accepted requirements for clinical research in this area (Table 1[28-37]). The qualitative criteria for this assessment were as follows:

- Use of an appropriate control group. Children without OSAS were adequately matched for sex, age and body mass index. Of the nine selected studies, five[28,30,31,34,36] included a comparison between the study group and a control group. The investigators in all five studies reported age matching and sex matching between the two groups, but not body mass index.
- Stated definitions of OSAS with regard to polysomnographic findings. Investigators in two studies[28,36] conducted cross-sectional evaluations by using a single study group to assess correlations between cephalometric and polysomnographic data. Investigators in one of these studies used a sample of normative data from a different study for comparison with the study group,[36] and the investigators in the other study performed longitudinal cephalometric and respiratory evaluations of study group participants, with assessments before and after tonsillectomy, adenoid resection surgery or both for comparison.[28] Investigators in eight of the nine selected studies stated the polysomnographic thresholds used to establish the diagnosis of OSAS in study participants.
- Measurement of evaluator reliability. The investigators in six studies[29,31,33-36] reported an assessment of evaluator reliability.
- Evaluator masking. Investigators in two studies[30,35] also reported a method of evaluator masking.
- Definition of the cephalometric landmarks and angular and linear measurements used. The various linear and angular measurements making up the cephalometric analysis used were reported in all nine studies.

An aggregate list of the most commonly reported findings (those that appeared in three or more studies) across these selected studies is provided in the box (page 273). The cephalometric points we used are shown in the figure (page 274). In addition to these findings concerning the facial skeleton, investigators in several studies also reported that shorter anterior base and more acute cranial flexure angle were morphological characteristics associated with a constricted upper airway.[29,32,34] The results of one study showed no significant difference in mandibular size and shape between children with OSAS and healthy control children on the basis of three-dimensional imaging of the mandible.[33] However, the investigators did not evaluate the

TABLE 1

Outlines of the nine studies selected for the systematic review.

AUTHOR, YEAR	STUDY DESIGN	OSAS* GROUP†	CONTROL GROUP†	CEPHALOMETRIC FINDINGS
Agren and Colleagues,[28] 1998	Prospective evaluation of patients with OSAS before and after T/A‡	n = 20 Mean age, 6 Age range, 4-9	Age-matched healthy control participants and second measurement evaluation of OSAS group	OSAS/UARS§ group characterized by higher frequency of narrow maxillary dental arches and lateral crossbites, as well as reduction in vertical growth pattern of mandible to a more horizontal growth direction at one-year after T/A
Löfstrand-Tidström and Colleagues,[29] 1999	Cross-sectional comparison between participants and healthy control participants	n = 21 Mean age, 4.3 (4.0-4.9)	n = 40 Mean age, 4.1 (3.9-4.7)	OSAS/UARS group characterized by narrow maxilla, shorter mandibular dental arch, lateral crossbites, larger anterior face height, posterior rotation of the maxilla and mandible, and more acute cranial base angle
Zucconi and Colleagues,[30] 1999	Cross-sectional comparison of cephalometric variables between patients with OSAS and healthy patients	n = 26 Mean age, 5.1 ± 0.5 Age range, 4-7	n = 26 Age matched by categories (3.0-4.5, 4.6-6, > 6.0)	OSAS group characterized by high angle face (increased craniomandibular angle and intermaxillary angle), increased gonial angle, retrusion and clockwise rotation of the mandible, vertical growth pattern, increased size of the bony nasopharynx and higher prevalence of crossbite and labial incompetence
Kawashima and Colleagues,[31] 2000	Cross-sectional comparison between participants and healthy control participants	n = 15 Japanese children Mean age, 4.7 Age range, 3-5	n = 30 Age-matched healthy children	OSAS/UARS group characterized by posteriorly positioned and posteriorly rotated mandible, increased gonial angle, longer facial height, greater mandibular plane angle and a retrusive chin
Ozdemir and Colleagues,[32] 2004	Cross-sectional evaluation of correlations between cephalometric variables and AHI¶ scores in pediatric patients with OSAS	n = 39 Mean age, 7.5 ± 1.7 Age range, 4-12	Age-matched healthy control participants from longitudinal growth centers	Increased AHI scores (associated with increased severity of OSAS) were positively correlated with decreased cranial base angle, increased gonial angle, decreased length of mandibular plane and decreased minimal posterior airway space; protrusion of the maxilla and mandible did not correlate with AHI scores
Schiffman and Colleagues,[33] 2004	Cross-sectional three-dimensional evaluation and comparison of mandibular shape and size	n = 24 Mean age, 4.9 ± 1.7 Mean AHI, 9.8 ± 11.1	n = 24 Mean age, 4.9 ± 1.8 Mean AHI, 0.4 ± 0.3	Three-dimensional size and shape of analysis of the mandible showed no significant differences between the two groups; position of the mandible relative to the facial skeleton or cranial base was not evaluated
Zettergren-Wijk and Colleagues,[34] 2006	Cross-sectional and longitudinal comparisons between study patients and healthy control patients	n = 17 Mean age, 5.6	n = 17 Mean age, 5.8 Healthy age- and sex-matched control participants	At baseline (first measurement), the following significant differences were identified in the OSAS/UARS group: posteriorly positioned and inclined (clockwise) mandible, increased lower anterior facial height, reduced lower posterior facial height, shorter anterior cranial base, retroclined maxillary and mandibular incisors and narrower nasopharyngeal airways; at five years after treatment (T/A) follow-up, almost complete normalization of all cephalometric measures in the study group as compared with the control group, with the exception of length of the anterior cranial base and the nose, which remained shorter in the study group

* OSAS: Obstructive sleep apnea syndrome.
† Ages are presented as "year.month."
‡ T/A: Tonsillectomy and adenoidectomy.
§ UARS: Upper airway resistance syndrome.
¶ AHI: Apnea-hypopnea index.
# Tollaro and colleagues.[37]

position of the mandible relative to the rest of the facial skeleton or the cranial base. With the exception of this study, all of the studies relied on two-dimensional traditional cephalometric radiography for morphological assessment of study participants.

The most frequently used cephalometric variables (appearing in at least two of the nine

TABLE 1 (CONTINUED)

AUTHOR, YEAR	STUDY DESIGN	OSAS* GROUP†	CONTROL GROUP†	CEPHALOMETRIC FINDINGS
Juliano and Colleagues,[35] 2009	Cross-sectional comparison between children who were mouth breathers and nasal breathers	n = 15 Mean age, 9.5 ± 1.8	n = 12 Mean age, 10.3 ± 1.4	Mouth-breathing in OSAS/UARS group showed increased anterior facial height, greater clockwise inclination of the occlusal plane, retruded mandible and steeper mandibular plane, open bite tendency and lip incompetence and reduced pharyngeal airway spaces
Marino and Colleagues,[36] 2009	Cross-sectional comparison between participants and normative data from separate study	n = 21 white children Mean age, 4.56 ± 0.6 Age range, 3.11-5.9	Sample of healthy age-matched children obtained from another study[#] Mean age, 5.67	Normal maxillary proportions and position in the OSAS/UARS group; however, differences characterizing the OSAS group included retrognathic mandible in sagittal plane, strong posterior (clockwise) rotation of the mandible in relation to the anterior cranial base and increased lower anterior face height

studies), along with the number of studies that included each variable, are shown in Table 2 (page 275). We included in our results analysis eight variables, among them those that appeared most frequently in the selected articles: the angle between the mandibular plane (MP) and sella nasion (SN) lines (MP-SN), the angle from SN to A point (SNA), the angle from SN to B point (SNB) and the angle from A to nasion to B (ANB). We reviewed the cephalometric tracing methods used in each article to ensure that the same cephalometric landmarks were used across studies for each of the variables being considered. For the meta-analysis, we included data from only eight of the nine selected studies, as one study[28] did not include a control group. Investigators in one study[32] used age-matched healthy control participants from longitudinal growth centers.

The results of our meta-analysis can be seen in Table 3 (page 275). We used the I^2 value to test the heterogeneity of the selected studies for each of the eight variables. The I^2 values were 79.53 percent for the angle from the basion point to the SN line, 89.54 percent for the angle between the SN and the palatal plane lines, and 96.82 percent for MP-SN. Therefore, we conducted a random-effects model meta-analysis for these three variables. The I^2 values for the remaining five variables were all less than 40 percent (MP-SN, 0 percent; SNA, 0 percent; SNB, 33.68 percent; ANB, 35.48 percent; the angle from the articulare point to the gonion point to the gnathion point, 0 percent), and therefore we conducted a fixed-effects model meta-analysis. Three of the evaluated cephalometric variables (MP-SN, SNB and ANB) had statistically significant differences when compared with a control group.

DISCUSSION

To date, no cephalometric analysis has been validated or is widely accepted for use in evaluating the risk contribution of craniofacial morphology to OSAS or SDB in children. On the basis of the information compiled by means of our meta-analysis, we found that a few cephalometric characteristics were associated significantly with OSAS. A steep mandibular plane and a retrusive-tending chin common to "adenoid faces" were associated with OSAS.

BOX

Common reported findings across studies.

- Narrow maxillary dental arch with high palatal vault and posterior crossbites
- Longer lower anterior face height
- Steeper (more obtuse) gonial angle (vertical growth pattern)
- Posterior-inferior (clockwise) rotation of the mandible (mandibular plane angle)
- Retrusive chin
- Tendency toward anterior open bite and lip incompetence
- Smaller nasopharyngeal airway spaces

Our findings that children with OSAS are more likely to have a Class II malocclusion with vertical growth tendency than are children who do not have OSAS has been reported in the literature. Some authors have suggested that this altered craniofacial morphology is a result of airway dysfunction.[27,38-40] Unfortunately, the investigators of the studies in our meta-analysis did not comprehensively control for contributing environmental factors (for example, participants' environmental allergens, diet, sleeping conditions). Therefore, on the basis of available data, we were unable to determine whether airway dysfunction was the etiologic cause of altered craniofacial growth, whether a vertical Class II malocclusion was a craniofacial form that predisposes children to OSAS or whether craniofacial form and OSAS are related by

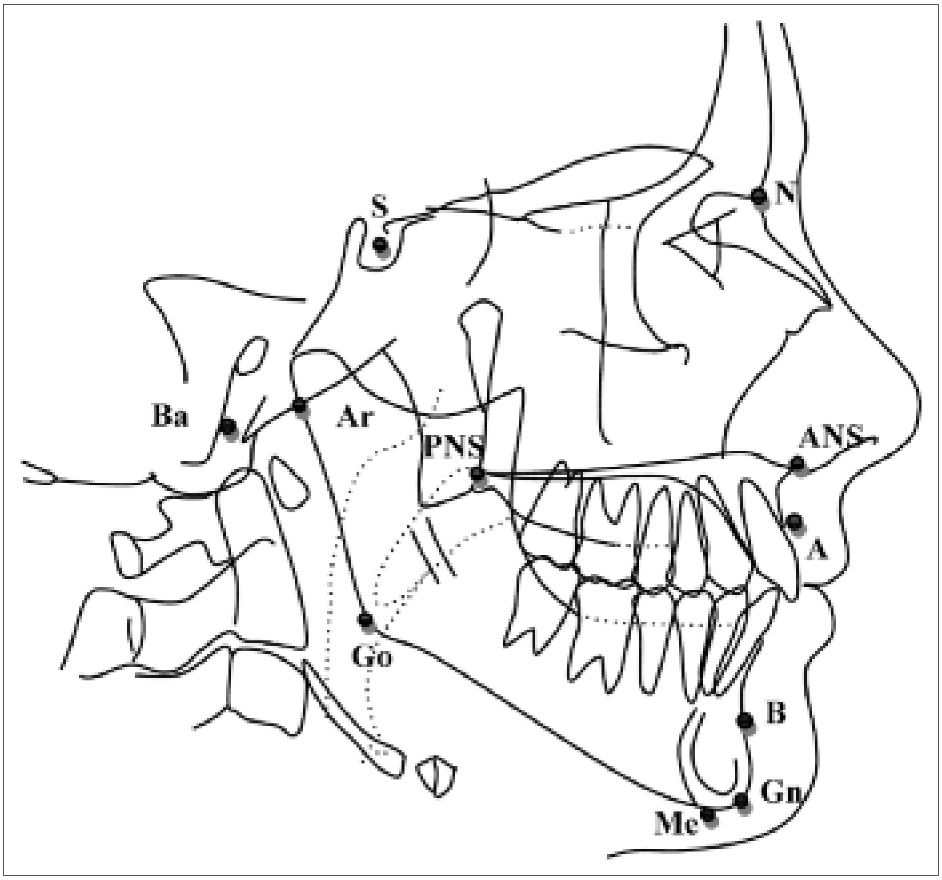

Figure. Diagrammatic representation of cephalometric variables. A: A point. ANS: Anterior nasal spine. Ar: Articulare. B: B point. Ba: Basion. N: Nasion. Gn: Gnathion. Go: Gonion. Me: Menton. PNS: Posterior nasal spine. S: Sella.

means of an unknown factor.

We found that two significant variables—SNB and ANB—appeared to demonstrate that mandibular retroposition or retrognathia was associated with OSAS in children. This finding is likely to be correct, because the inherent error in these two cephalometric variables is likely to underreport retrognathia in children with OSAS. In the orthodontic literature, it has been well established that the reliability of SNB and ANB as indicators of anteroposterior maxilla and mandible position is affected directly by vertical SN pitch and horizontal SN length.[41] Furthermore, other investigators have reported that children with OSAS are more likely to have a short SN measurement for anterior cranial base length than are children who do not have OSAS.[30,34] Therefore, this tendency toward a short cranial base in children with OSAS could demonstrate normal SNA, SNB and ANB values falsely despite the presence of true underlying retrognathism.

However, results of our meta-analysis should be interpreted with caution owing to the variability in magnification and calibration of radiographic equipment between studies, lack of standardization of measurements and differences in study sample parameters, among other reasons. In addition, we included only eight cephalometric variables in our meta-analysis, and a few of them were linked closely. Our cephalometric analysis should not be considered a comprehensive evaluation of the overall craniofacial morphological pattern associated with pediatric OSAS.

Reports of reductions in the severity of the morphological changes or even the near-total normalization of the craniofacial growth pattern in the lower face after successful treatment of the airway problem[19,34,42-44] suggest that an unfavorable growth pattern is a reversible outcome of the craniofacial musculoskeletal imbalances associated with postural changes that occur in response to OSAS. These findings also might suggest direct cause-effect relationships between OSAS and craniofacial growth changes, and some authors view them as such.[44-47] Correction of tonsil- and adenoid-caused OSAS can redirect craniofacial growth back toward a normal direction.[34,42,48,49] All of these findings have not been confirmed conclusively.

However, a different argument also can be made that specific morphologies—short cranial base, midface deficiency, retrognathic mandible, inferior positioned hyoid bone and perhaps obtuse gonial angle—are risk factors for pediatric OSAS.[23,50,51] As a result of our meta-analysis, we found that the saddle angle was not associated with OSAS, which supported this hypothesis since cranial base growth is unlikely to be affected by mode of breathing.

Whether a hyperdivergent Class II malocclusion facial morphology is a risk factor for developing OSAS or is an altered growth response to OSAS is not clear. There are logical reasons for believing that airway dysfunction could be the cause of altered craniofacial morphology, but there also are logical reasons for why specific genetically determined craniofacial morphologies could predispose children to OSAS. Etiologic connections between these morphological patterns and UARSs have not been established clearly. The connection between mode of breathing and postural changes, which is a basic premise of the associations between OSAS and craniofacial morphology has not been demonstrated clearly. Habitual open-mouth posture as seen in benign lip incompetence is not necessarily indicative of a predominantly oral respiratory pattern.[52,53] The impact of genetic variables also has not been studied directly. A deeper understanding of the pathophysiology of OSAS and its relationship to craniofacial form and function is required to determine the nature and extent to which craniofacial morphological patterns influence or are influenced by changes in upper airway function.

Although the results of our systematic review and meta-analysis integrate well with the existing airway function and craniofacial growth theory (a theory that has not been proven conclusively), we could not confirm a causative relationship between OSAS and craniofacial morphological features in the selected studies alone. Most of the studies had various methodological deficiencies such as inconsistent reporting of operator reliability and masking, inconsistent definitions of OSAS status and the lack of an appropriate control group. Other factors affected the strength of these conclusions, including the questionable relevance of static two-dimensional measurements (lateral cephalometry) to the status of a

TABLE 2

Number of studies incorporating the most commonly used cephalometric variables.

CEPHALOMETRIC VARIABLE ABBREVIATION*	NO. OF STUDIES	DESCRIPTION
MP-SN	6	The angle formed between the mandibular plane (MP) (line from the menton [Me] to the gonion [Go]) and the anterior cranial base (line from the sella [S] to the nasion [N])
SNA	5	Angle from S to N to the A point (A)
SNB	5	Angle from S to N to the B point (B)
ANB	5	Angle from A to N to B
BaSN	4	Angle from the basion (Ba) to S to N
ArGoGn	4	Gonial angle of the mandible (angle from the articulare [Ar] to Go to the gnathion [Gn])
SN-PP	3	Angle between the anterior cranial base (line from S to N) and the palatal plane (PP) (line from the anterior nasal spine [ANS] to the posterior nasal spine [PNS])
MP-PP	3	Angle between MP (line from Me to Go) and PP (line from ANS to PNS)
Gn-Go (Millimeters)	2	The linear distance (mm) from Gn to Go
Ba-S-PNS	2	Angle from Ba to S to PNS
L1-MP	2	Angle between lower (mandibular) incisor inclination relative to MP (line from Me to Go)
MPAS	2	Minimum posterior airway space

* The abbreviation key on page 270 contains the expanded version of these terms.

TABLE 3

Summary of meta-analysis for the eight most frequently reported variables in the selected articles.*

VARIABLE†	NO. OF STUDIES	MEAN DIFFERENCE, DEGREES (STANDARD ERROR)	*P* VALUE	95% CONFIDENCE INTERVAL
MP-SN	5	4.20 (0.45)	< .001	3.32 to 5.07
SNA	4	−0.32 (0.40)	.79	−1.10 to 0.46
SNB	4	−1.79 (0.42)	< .001	−2.61 to −0.97
ANB	4	1.38 (0.28)	< .001	0.83 to 1.92
BaSN	3	−1.12 (1.50)	.23	−4.06 to 1.82
ArGoGn	2	0.53 (0.89)	.28	−1.21 to 2.27
SN-PP	3	−0.77 (1.14)	.25	−3.01 to 1.47
MP-PP	2	7.12 (4.45)	.06	−1.60 to 15.84

* All of the measurements are angular.
† All of the variables are defined in Table 2.

dynamic structure like the upper airway, the lack of long-term follow-up in most studies and the lack of adequate exploration of alternative explanations for improvements in craniofacial growth and development after successful treatment of OSAS and vice versa. These alternate explanations include the role of growth hormones and genetics, as well as other growth mediators, in the growth and development of the lower face, and the metabolic and cardiovascular implications of improving sleep and oxygenation parameters on craniofacial growth and development. Although obesity has been linked to OSAS in children,[54] the role of obesity in OSAS was not considered by the investigators in any of the selected studies. Obesity is an important confounding factor because it likely affects the structural and functional relationships we discuss above.

The effect of treatment and how it alters the craniofacial structure and whether children with OSAS are predisposed to persistent UARS despite having undergone treatment have to be evaluated longitudinally. We speculate that this key finding will help determine who will need longer term follow-up and whose treatment will need special management.

Implications for clinical practice. Although some cephalometric variables have been shown to be associated with OSAS in children, none can be considered pathognomonic. The eight cephalometric variables we used in our meta-analysis are a limited and not comprehensive representation of the craniofacial structures. Lateral cephalometry alone should not be used as a diagnostic tool for OSAS in children because it lacks the sensitivity and specificity to act as a stand-alone tool. Instead, lateral cephalometry is useful as an adjunct meant to accompany a thorough medical history. Dentists who identify patients with a craniofacial morphology consistent with pediatric OSAS—a retrusive chin, steep mandibular plane, vertical direction of growth and a tendency toward Class II malocclusion—should inquire further into their patients' medical histories. When a suspicious craniofacial morphology is identified, dentists should inquire specifically about the patient's history of snoring, gasping for breath while sleeping, inability to breathe through the nose, significant environmental allergies (such as those to pets or dust or those that are seasonal), asthma or obesity. When such as thing is identified, the dentist should refer their patients to an otolaryngologist for assessment.

Implications for future research. Studies that single out specific factors are necessary to identify which factors are important contributors to the etiology and pathophysiology of OSAS. However, comprehensive evaluations conducted by a multidisciplinary research team that collectively addresses both form and function likely are needed to enable modeling to determine which aggregate factors contribute to OSAS in the affected children.

CONCLUSIONS

Although the values of some variables (MP-SN, SNB and ANB) suggested that children with OSAS grew more vertically and had more Class II skeletal malocclusions, the results of our meta-analysis should be considered cautiously owing to the limited number of cephalometric variables that were available for inclusion in our analysis. Identification of vertical growth with a retrusive chin alone is insufficient to diagnose OSAS in children. These craniofacial markers, however, are "red flags" that can direct dentists to inquire further into their patients' medical histories. ■

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