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REVIEW ARTICLES

Craniofacial features in children with obstructive sleep apnea: a systematic review and meta-analysis

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Study Objectives: This review aimed to evaluate the association between craniofacial features in children and adolescents with pediatric obstructive sleep apnea (OSA).

Methods: Seven databases were searched to fulfill our research objectives. Clinical studies that included participants younger than 18 years with fully diagnosed OSA or without OSA and that evaluated skeletal, soft craniofacial features, or dental arch morphology were considered for this review. The risk of bias and certainty of evidence were assessed. A meta-analysis was performed when low methodological and clinical heterogeneity were detected. This review followed the protocols recommended by the Preferred Reporting Items for a Systematic Review and Meta-analysis (PRISMA-2020) guidelines.

Results: Nine studies were identified at the end of the selection process, from which 5 did not report differences. Four studies reported differences between craniofacial features when OSA was compared to an asymptomatic control group. Mandibular retrognathia, reduced anteroposterior linear dimensions of the bony nasopharynx (decreased pharyngeal diameters at the levels of the adenoids), longer facial profile, and a narrower intercanine width were described among children with OSA. A meta-analysis was performed considering the studies with a similar methodological approach, and no differences were observed in all the considered cephalometric angles (SNA, SNB, ANB, NSBa, U1-L1, U1-SN). All the included studies were considered at low risk of bias even though some limitations were noted.

Conclusions: Due to the very low to moderate level of certainty, neither an association nor a lack thereof between craniofacial morphology and pediatric OSA can be supported by these data.

Keywords: obstructive sleep apnea, child, face, diagnoses

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BRIEF SUMMARY

Current Knowledge/Study Rationale: There is controversy regarding the association between pediatric obstructive sleep apnea (OSA) and craniofacial morphology. This systematic review adopted a reliable eligibility criterion to explore the possible link between fully diagnosed pediatric OSA and craniofacial morphology. After retrieving more than 8000 citations, 9 papers were identified. When qualitatively assessed, a specific subgroup of pediatric OSA presented with an increased mandible retrognathia, and/or an extended facial profile compared to children without OSA. However, while the present meta-analysis did not confirm this suggestion from a causality perspective, it supports previous studies that describe specific malocclusion phenotypes as frequent, but not consistently, comorbidities with sleep-disordered breathing and OSA.

Study Impact: Because of low to moderate certainty of the evidence, a clear causal relationship between craniofacial morphology and pediatric OSA cannot be supported at this time.

INTRODUCTION

Obstructive sleep apnea (OSA) is a respiratory sleep disorder resulting in partial or complete airflow obstruction.[1] Among children, OSA prevalence has been reported to vary from 1% to 5%.[2,3] In the absence of proper management of OSA cases, a typical result of underdiagnoses, several health conditions may arise, including growth impairment,[4] behavioral and cognition problems,[5,6] and respiratory and cardiac comorbidities.[7] From a social perspective, pediatric OSA is related to an increased cost of health care services and unsatisfactory academic progress.[8,9]

Previous cross-sectional studies suggested a subset of craniofacial features, such as increased facial height, labial incompetency, mandible retrognathia, increased overjet, higher mandible angle, and steeper mandibular plane presented in a higher frequency in children with OSA compared to a non-OSA control group.[10,11] The presence of these craniofacial features has been hypothesized as a possible cause or consequence of airway obstruction and OSA development.

A potential benefit of a craniofacial morphology evaluation to identify pediatric OSA is that it is accessible and convenient for routine clinical use in dental practices. The facial analysis can be performed by a clinical examination in the dental office and a craniofacial skeletal screening done by X-rays (ie, cephalometric analysis).

A systematic review and meta-analysis published 8 years ago summarized the differences in skeletal craniofacial features in children with OSA.[10] However, there was a paucity of

controlled studies with a definitive non-OSA control group (assessed through the nocturnal polysomnography [nPSG]). The nPSG is the standard exam to diagnose OSA in children and adults. Standardizing methodological approaches to analyze OSA patients and associated factors is important for fair comparison among groups. In addition, new studies have been published over the last 5 years, and other craniofacial techniques have been explored among children, such as the assessment of soft facial features, measurements of dental arches, and the evaluation of tooth position.[11,12] There is a need to update this literature synthesis.

This systematic review aimed to evaluate the association between craniofacial features in children and adolescents and pediatric OSA. The further investigation of pediatric OSA pathophysiology, specifically the craniofacial morphology role, may improve OSA screening methods and reduce the backlog of nPSG assessments by improving the referral algorithms.

METHODS

Protocol and registration

This systematic review has followed the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)[13] and was registered at PROSPERO database (University of York, York, UK) under the code CRD42020203051.

Search strategy and eligibility criteria

The definition of eligibility criteria was guided by a PECO (Population, Exposure, Comparison, and Outcome) question: "In children and adolescents, are specific craniofacial features linked to fully diagnosed pediatric OSA?" The studies focused on children or adolescents *(P)* in which the craniofacial features were assessed with a positive OSA diagnosis through nPSG *(E)* compared to those with a negative diagnosis for OSA through nPSG *(C)*, evaluating the differences in mean values of craniofacial variables *(O)*.

Observational studies were included if they evaluated OSA by a whole-night nPSG monitored by a sleep technician. To be considered for the non-OSA group, a participant had to have a negative diagnosis after an nPSG. As exclusion criteria in this review, we did not consider studies with adults (≥ 18 years) and without an nPSG non-OSA control group. We also excluded studies that evaluated only obese patients, children presenting with known craniofacial syndromes, or those who had received orthodontic or orthognathic treatment before craniofacial evaluation. No restrictions were made regarding the type of craniofacial assessment or craniofacial area that was considered. Studies using lateral cephalometrics, photographic analysis, and in vivo clinical evaluation were deemed eligible for this review. Reviews, letters, conference abstracts, and personal opinions were also excluded. No restriction of sex or ethnicity was considered.

Searches were conducted in 7 electronic databases until May 2021: PubMed, MEDLINE via OvidSP, Embase, Web of Science, The Cochrane Library, and LILACS. A narrow gray literature search was also performed in OpenGrey. According to the rules of each database and with the guidance of a health sciences librarian, all searches were conducted using a combination of controlled predefined MeSH (Medical Subject Headings) and free terms related to the topic (**Table S1** in the supplemental material). The results were imported to a reference manager software (Rayyan software; Qatar Computing Research Institute, Doha, Qatar),[14] and duplicate citations were excluded.

Study selection

The selection process was conducted in 2 phases by 2 reviewers (N.C.F.F. and S.G.C.) and checked by a third examiner (C.F.M.) in cases of disagreement. First, the citations were evaluated according to their title and abstract. Second, the selected articles were assessed through their full text. After these 2 steps, additional citations were sought by an analysis of the reference lists of all previously selected articles. Finally, the eligibility criteria, including the specified PECO strategy and study types, were considered the analysis of the articles in both phases.

Data extraction

A table was used to report the country, year of publication, demographic features (age, body mass index, and ethnicity), criteria adopted to define OSA, methods used to assess the craniofacial area, main results, and statistical analysis. This extraction was performed by 2 examiners (N.C.F.F. and S.G.C.). If necessary, in the case of lack of information, attempts to contact the authors were made by email. The contact attempts consisted of weekly emails for up to 3 consecutive weeks.

Outcomes

The main outcome considered was a finding of differences in the craniofacial abnormalities of children and adolescents with and without OSA. Secondary outcomes were the association of these results with demographic features and OSA severity.

Risk of bias among included studies

The risk-of-bias evaluation was performed using the Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-sectional Studies.[15] The articles included were judged as high risk (yes score ≥ 49%), moderate risk (yes score = 50%–69%), and low risk (yes score ≥ 70%).[16] The evaluation was performed by 2 reviewers (N.C.F.F. and S.G.C.), and disagreements were resolved by a third reviewer (C.F.M.).

Synthesis of results

The difference between craniofacial features of children with and without OSA was assessed using Review Manager software v.5.3 (Cochrane, London UK) when a low methodological and clinical heterogeneity was detected. The statistical heterogeneity significance was evaluated using the I^2 index. Thresholds for the interpretation of the I^2 statistic adopted from the Cochrane *Handbook for Systematic Reviews of Interventions* (www.training.cochrane.org/handbook; accessed January 28, 2022): 0%–40%: might not be significant, 30%–60%: may represent moderate heterogeneity, 50%–90%: may represent substantial heterogeneity, 75%–100%: considerable heterogeneity.

Risk of bias across studies

The overall strength of evidence was evaluated using the grading of recommendations, assessment, development, and evaluations tool (*GRADE Handbook*). [17] Included studies were evaluated according to their study design, risk of bias, inconsistent results, indirect evidence, imprecision, and publication bias.

RESULTS

Study selection

From electronic searches, 8288 citations were identified. After removing duplicate results, 3475 records were assessed by title and abstract, and out of these, 87 were considered for full-text reading. Among these, 76 studies did not meet our eligibility criteria and were excluded (**Table S2** in the supplemental material). In addition to the electronic searches, the 9 studies included in the previous version of this systematic review[10] were also screened in the full-text phase. However, none of these articles met the updated inclusion criteria proposed by the present review. After the selection process, 9 studies fit our criteria and were included[11,12,18–24] (**Figure 1**).

Study characteristics

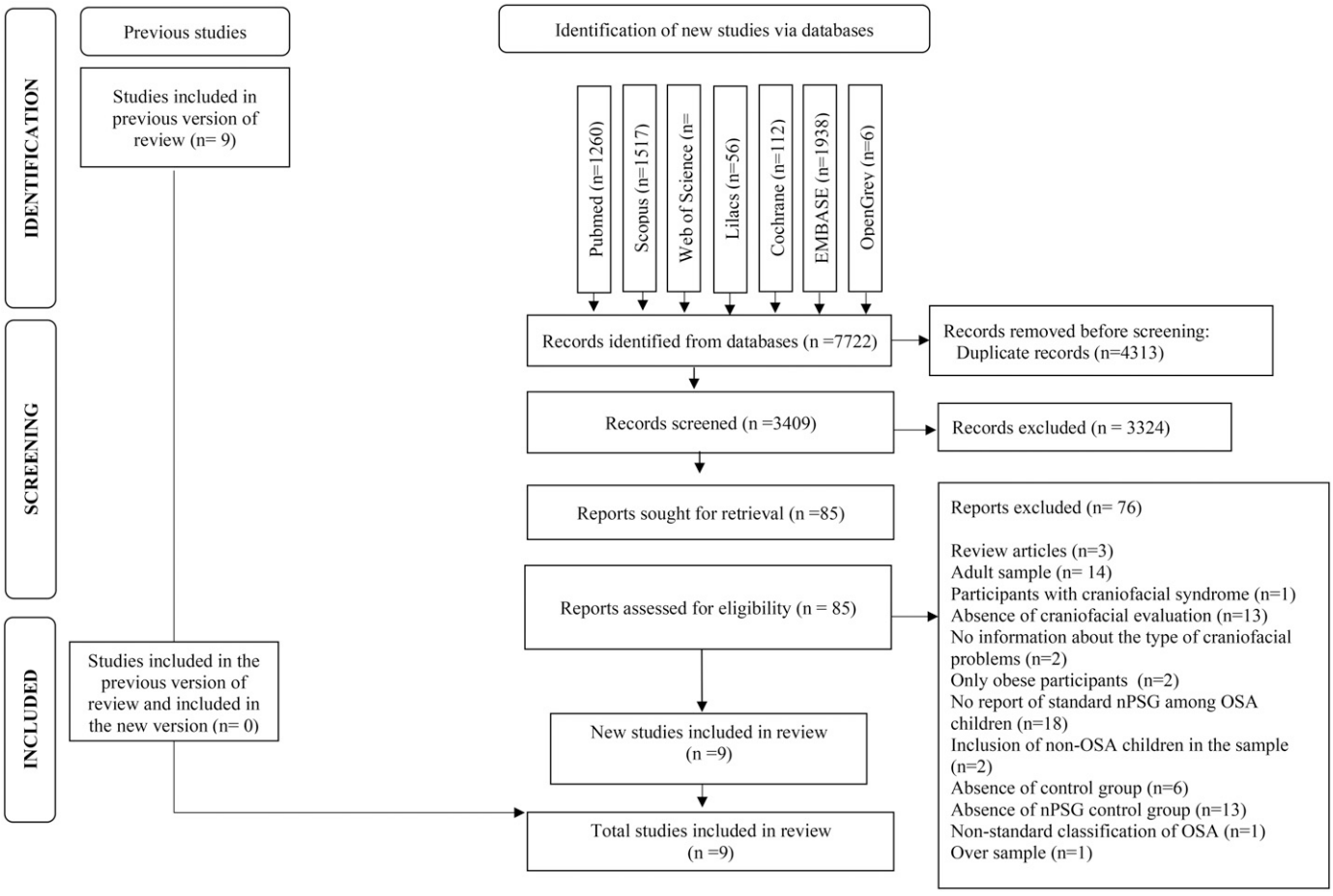
Among the 9 included studies, 4 presented a cross-sectional design,[11,19,23,24] 4 were case-control studies,[12,18,21,22] and one was a prospective cohort.[20] For the studies that were not cross-sectional, only the relevant information at the initial data gathering point was considered (at that data point cross-sectional in nature).

Six studies evaluated craniofacial skeletal features assessed through lateral cephalometrics.[18,19,21–24] Two studies analyzed dental arch dimensions and tooth position through dental models,[12,20] and 1 study performed evaluations of facial soft tissue features through 2-dimensional photo analysis[11] (**Table 1**).

In the 6 studies that evaluated skeletal craniofacial features, 182 children with OSA and 133 control children were screened. Three studies[18,19,21] found differences between children with OSA and the non-OSA control group. For example, children with OSA presented with:

- a retrusive mandible (reduced sella-nasion to B point angle [SNB] angle, OSA group = 75.8 ± 4.3 degrees vs control = 78.71 ± 2.6),[18]
- deficient chin (increased pogonion to nasion-B point line [PG-NB], OSA group = 1.3 ± 0.8 mm vs control = 0.62 ± 0.60 mm),[18] and

Figure 1—Flowchart according to PRISMA guidelines.



nPSG = nocturnal polysomnography, OSA = obstructive sleep apnea, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Table 1—Characteristics of the included studies.

Author/Year/ Study Design	Source of Sample	n	Age	Control Group Features	OSA Index	Ethnicity	BMI	Assessment of Adeno-tonsillar Size	Craniofacial Evaluation	Statistical analysis	Main Results
Deng 2012/CS 18	Beijing Children's Hospital (sleep center) and Department of Orthodontics, Peking University, China	Total: 30 OSA: 15 Control: 15	9.5 ± 1.0	Nonsnoring, first visit patients in Department of Orthodontics	Control group: AHI < 1; OSA: AHI = 6.29 ± 6.48	Asian	NI	NI	Cephalometric analysis (20 morphologic variables).	Paired *t* tests, ANOVA	SNB (78.71 ± 2.61 vs75.82 ± 4.30), PG-NB (0.62 ± 0.60 mm vs 1.32 ± 0.84), Na-Me (108.50 ± 6.93 mm vs 13.62 ± 10.0 mm), and ANS-Me (61.51 ± 3.22 mm vs 65.12 ± 5.91 mm) showed statistical difference between control and OSA groups. A more inferior and retrusive hyoid was described in OSA group.
Di Francesco 2012/CC 19	Otolaryngology Department of the University of São Paulo Medical School, Brazil.	Total: 77 OSA: 36 Control: 41	3.0–12.0	Children with OSA symptoms	NI	NI	BMI z-score Male: –0.5 (–1.38, 0); Females: 0 –1.5, 0)	Yes	Cephalometric analysis (6 skeletal craniofacial variables).	Spearman's rank correlation test	Facial depth (r = –.336), vertical growth tendency (r = –.337) and mandibular plane (r = .486) correlated with AHI in boys, but no correlations were found in girls.
Markkanen 2019/P-CH 20	Tampere University Hospital, Finland	Total: 27 OSA: 9 Control: 18	1.9–2.8	Nonsnoring children	Control group: NI; OSA: OAHI= 1.2–6.3 (median= 1.5)	NI	BMI: OSA group: 15.5–17.0; control: 16.0–17.8	Yes	Dental and face evaluated by wax bite and profile photograph	Mann-Whitney *U* test	Children with OSAS (median: 27.0 mm) had narrower intercanine width than nonsnoring children (median: 28.2 mm).
Caiza Rennella 2017/CC 23	Pontificia Universidad Javeriana, Colombia	Total: 43 OSA: 19 Control: 24	6.0–13.0	Children with an indication to nPSG	NI	NI	NI	NI	Cephalometric analysis (12 skeletal craniofacial variables).	Independent *t* test and Mann-Whitney *U* test	Children with OSAS had same features as controls.
Soares 2020/ CC 24	Centro do Respirador Bucal of the Clinics Hospital Ribeirão Preto Medical School, University de São Paulo, Brazil	Total: 76 OSA: 62 Control: 14	7.0–10.0	Children with respiratory and OSA symptoms	Control group: OAHI = 0.5 ± 0.2; OSA: OAHI = 13.0 ± 8.4	NI	BMI> 95th percentile patients were excluded.	NI	Cephalometric analysis (9 skeletal craniofacial variables).	Independent *t* test	There were no differences between the 2 groups for any craniofacial measure. Children with OSA showed a more inferior hyoid position in relation to the mandibular plane (HyMP: control group = 10.9 ± 0.9 and OSA group = 13.1 ± 0.5; 95% CI: 0.08; 4.32).
Sutherland 2019/CC 11	Melbourne Children's Sleep Centre for PSG, Australia.	Total: 59 OSA: 50 Control: 9	7.2 ± 3.4	Nonsnoring children	Control group: OAHI = 0.2 ± 0.3 for the control group; mild OSA group: OAHI = 2.8 ± 1.3; moderate-severe OSA group: OAHI= 14.5 ± 11.1	73.1% were Caucasian	BMI z-score: 0.6 ± 1.3 (− 3.7–3.3)	NI	Craniofacial measurements from 2-dimensional photography.	MANOVA	No association was observed between OSA and facial features. A direct association was observed between OSA severity and the inferior and posterior position of the hyoid bone.
Pirilä-Parkkinen 2009/CS 12	Children referred from primary health care units to the Department of Otorhinolaryngology of Oulu University Hospital, Finland	Total: 123 OSA: 41 Snoring: 41	3.8–11.4	Snoring children	Control group: AHI = 0.1 ± 0.2; OSA: AHI = 3.5 ± 3.60.	NI	NI	Yes	Dimensions of dental arches measured in upper and lower dental casts	ANOVA	Children with OSAS had same features as snoring children.

(continued on following page)

Table 1—Characteristics of the included studies. (*Continued*)

Author/Year/ Study Design	Source of Sample	n	Age	Control Group Features	OSA Index	Ethnicity	BMI	Assessment of Adeno-tonsillar Size	Craniofacial Evaluation	Statistical analysis	Main Results
Piriläa-Parkkinen 2010/CS 21	Children referred from primary health care units to the Department of Otorhinolaryngology of Oulu University Hospital, Finland	Total: 140 OSA: 26 Snoring: 27 Upper airway resistance syndrome: 17 Control: 70	4.7 ± 2.1	Snoring children	Control group: AHI = 0.2 ± 0.1; OSA group: AHI = 2.5 ± 1.2	NI	Only nonobese children	Yes	Cephalometric analysis (11 morphologic, 10 airway, 3 hyoid bone position, and 5 postural variables).	Paired *t* tests, ANOVA	Children with OSAS had same features than snoring children.
Wang 2012/CS 22	Qilu Hospital, Shandong University, Jinan, China	Total: 70 OSA: 24 Snoring:12 Control: 34	9.6 ± 1.9	Snoring children	Control group: AHI = 1.7 ± 1.2; OSA group: AHI = 8.5 ± 3.6	NI	OSA: 14.790 ± 1.125 control: 15.993 ± 1.303	NI	Cephalometric analysis (16 craniofacial skeletal variables, 7 craniofacial soft tissue variables).	ANOVA	Children with OSAS had same features as snoring children. A reduced anteroposterior linear dimensions of the bony nasopharynx (decreased pharyngeal diameters at the levels of the adenoids) was observed when children with OSA were compared to a non-nPSG group.

AHI = apnea-hypopnea index, ANOVA = analysis of variance, ANS-Me = anterior nasal spine to menton point, BMI = body mass index, CC = case-control study design, CH = prospective cohort, CS = cross-sectional, HyMP = hyoid position in relation to the mandibular plane, MANOVA = Multivariate Analysis of Variance, Na-Me = nasion-A point to menton line, **NI** = Not indicated, OAHI = obstructive apnea-hypopnea index, OSA = obstructive sleep apnea, OSAS = OSA syndrome, PG-NB = pogonion to nasion-B point, PSG = polysomnography, SNB = sella-nasion to B point angle.

- long lower face (increased anterior nasal spine to menton point [ANS-Me], OSA group = 67.4 ± 6.4 mm vs control = 62.2 ± 3.1 mm).[18]

In addition, among boys, some craniofacial features, including dolichocephaly facial pattern (r = –.33), mandibular plane (r = .48), and facial depth (r = –.33), were correlated to OSA in 1 study.[19] The other 3 studies did not report statistical differences in craniofacial skeletal features. A reduced anteroposterior linear dimensions of the bony nasopharynx (decreased pharyngeal diameters at the levels of the adenoids) was observed when children with OSA were compared to a non–polysomnography non-nPSG group:

- reduced PNS-ad1 (distance from the posterior nasal spine [the most posterior point of the bony hard palate] to the nearest adenoid tissue measured along the line PNS–Ba), OSA group = 17.3 ± 6.2 mm vs non-nPSG control = 20.9 ± 3.9 mm;
- reduced ve1-ve2 (minimal distance from the velum palatine to the posterior pharyngeal wall measured perpendicular to the direction of the airway), OSA group = 4.0 ± 3.0 mm vs non-nPSG control = 7.4 ± 2. 9 mm;
- reduced u1-u2 (airway space on a line from the tip of uvula to the posterior pharyngeal wall measured perpendicular to the direction of the airway), OSA group = 5.6 ± 3.3 mm vs non-nPSG control = 9.6 ± 3.4 mm;
- reduced rl1-rl2 (minimal distance from the radix linguae [base of the tongue] to the posterior pharyngeal wall measured perpendicular to the direction of the airway), OSA group = 12.7 ± 3.8 mm vs non-nPSG control = 10.1 ± 3.0 mm.[19]

Two studies analyzed dental arch dimensions and tooth position,[12,20] in which 35 children with OSA and 41 non-OSA snoring children were evaluated. Patients from different age groups were included in both studies. Compared to a negative nPSG control group, both studies did not show differences in the variables being assessed. In a group of 2.5-year-old children, a narrower upper intercanine width in the OSA group (median = 27 mm) compared to a nonsnoring group (median = 28.2 mm) was identified (P = .03).[20]

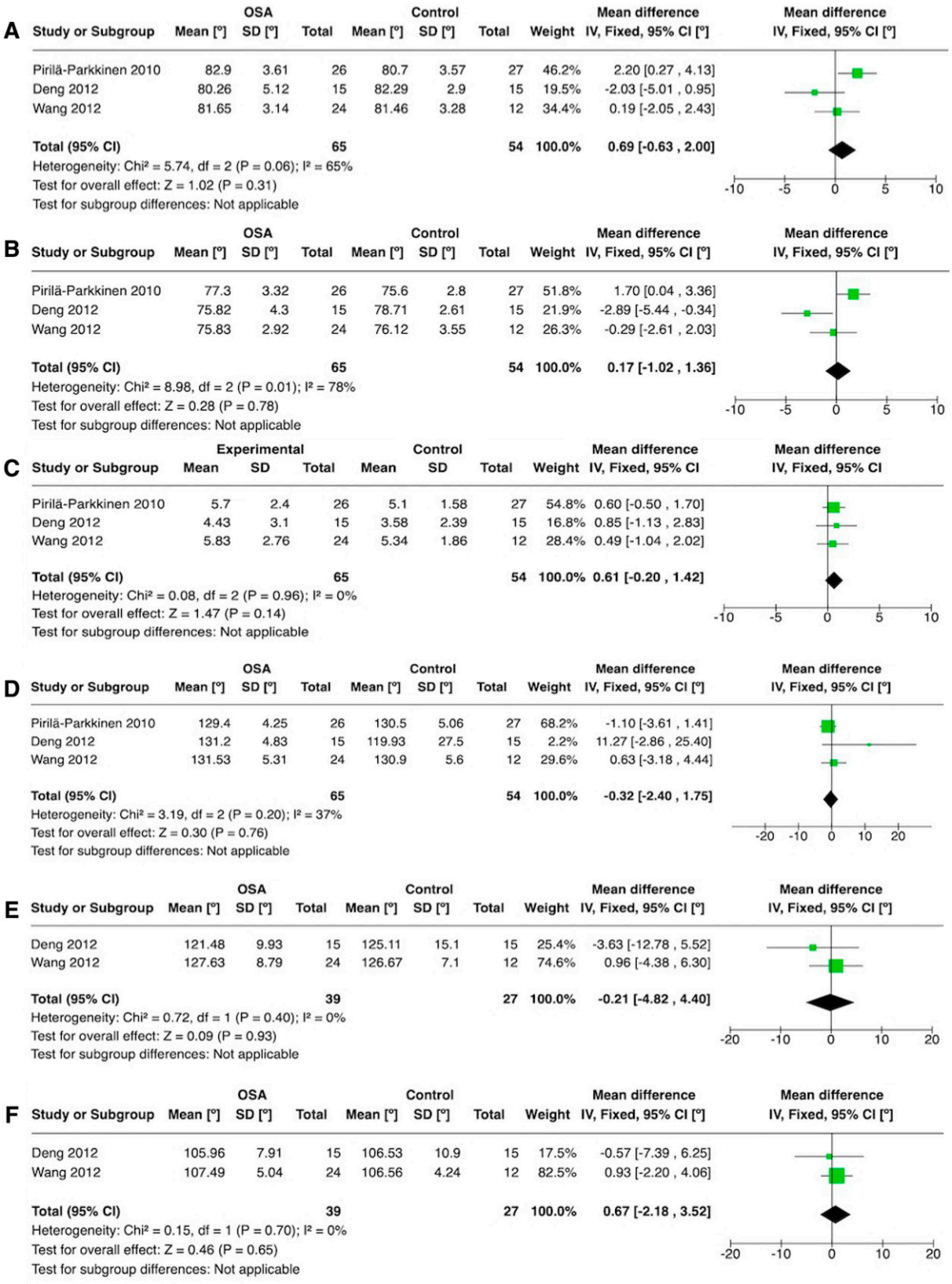
One study evaluated soft facial features of 59 children with OSA and 9 non-OSA, nonsnoring, control children by analyzing 2-dimensional facial photos. An increase in the obstructive apnea-hypopnea index (OAHI) was associated with an increase in the cervicomental angle (β = 0.18, 95% CI = 0.07, 0.29) and an increase in the ratio of upper to lower–face height (β = –37.16, 95% CI = –65.71, –8.62).[11]

Eight of the 9 studies included the evaluation of comorbidities associated with pediatric OSA (ethnicity, body mass index/obesity status, and adenotonsillar hypertrophy).

Three studies assessed the size of adenoids and tonsils in their sample without analyzing the interaction between OSA and craniofacial morphology.[20,21,25]

Regarding the characteristics of the non-OSA control groups, all studies included children with a negative nPSG result (apnea-hypopnea index < 1 or OAHI < 2). In addition, 3 studies included snoring patients,[21,22,25] 3 studies included children with respiratory or OSA symptoms,[19,23,24] and 3 studies had only nonsnoring children in the control group.[11,18,20]

Figure 2—Forest plot of meta-analysis.



Mean difference among OSA and control groups for the following skeletal angles: **(A)** SNA, **(B)** SNB, **(C)** ANB, **(D)** NSBa, **(E)** U1-L1, **(F)** U1-SN. ANB = A point-nasion-B point angle, CI = confidence interval, IV = inverse variance, NSBa = nasion-sella-basion angle (cranial base flexure angle), SD = standard deviation, SNA = sella-nasion to A point angle, SNB = sella-nasion to B point angle, U1-L1 = upper incisor to lower incisor angle, U1-SN = upper incisor to nasion-sella angle.

Table 2—Certainty assessment (GRADE tool) for the evaluation of skeletal, soft facial features, and dental arched morphology outcomes.

Outcome; Number of Participants (Studies)	Relative Effect (95% CI)	Certainty	What Happens
Skeletal features; 315 (6 observational studies)	Not estimable	⊕⊕◯◯ LOW[a]	Three studies found differences in the cephalometric features of children with OSA compared to a control group. Two studies reported a class II skeletal pattern and a vertical craniofacial growth tendency in the OSA group. One study also reported an inferiorly positioned hyoid in the OSA group.
Soft facial features; 59 (1 observational study)	Not estimable	⊕⊕⊕◯ MODERATE[b]	OSA probably results in little to no difference in soft facial features.
Dental arches morphology; 109 (2 observational studies)	Not estimable	⊕⊕◯◯ LOW[a]	Children with OSA may present little to no difference in dental arches morphology.

[a]Overlap among CIs was observed across studies. [b]Only 1 study was included and presented a wide variation among CIs. CI = confidence interval, GRADE = Grading of Recommendations, Assessment, Development and Evaluations, OSA = obstructive sleep apnea. Very low = The true effect is probably markedly different from the estimated effect, Low = The true effect might be markedly different from the estimated effect, Moderate = The authors believe that the true effect is probably close to the estimated effect, High = The authors have a lot of confidence that the true effect is similar to the estimated effect.

Risk of bias among included studies

The risk of bias was classified as low in all included studies. Nevertheless, specific problems were identified in some domains. None of the studies considered confounding factors. Rennella et al 2017[23] presented unclear information regarding how the nPSG diagnosed the OSA. Soares et al 2020[24] did not report the period of data collection (**Table S3** in the supplemental material).

Synthesis of results

Among the 6 studies which evaluated cephalometric parameters, 3 studies[18,21,22] reported a few consistent cephalometric variables and presented methodological and clinical comparable data to justify a quantitative synthesis. Six independent meta-analyses were performed to evaluate the mean differences of sella-nasion to A point angle (SNA) (1), sella-nasion to B point angle SNB (2), A point-nasion-B point angle (ANB) (3), nasion-sella-basion angle (cranial base flexure angle) (NSBa) (4), upper incisor to lower incisor angle (U1-L1) (5), and upper incisor to nasion-sella angle (U1-SN) (6). For the SNA, ANB, and NSBa, all 3 studies[18,21,22] were included. For the U1-L1 and U1-SN features, only 2 studies[18,22] were compared. The meta-analyses results did not show differences in any of the 6 evaluated features (**Figure 2**).

A quantitative evaluation was impossible among the studies that analyzed dental arches and tooth position because the age range in the 2 studies was not comparable. Markkanen et al (2019) included children at 2.5 years old, while Pirilä-Parkkinen (2009) evaluated children from 3–10 years old.[12,20]

Risk of bias across studies

Two certainty analyses were performed after data collection. Due to the small number of studies included on each outcome ($n < 10$), publication bias was not considered. In the first analysis, 3 main outcomes were considered: skeletal features, soft facial features, and dental arch morphology. A low to moderate certainty level was observed in which only the skeletal features reported some differences between OSA and non-OSA groups (**Table 2**).

A very low to moderate certainty level was detected among the 6 cephalometrically assessed outcomes following the meta-analyses results: SNA (1), SNB (2), ANB (3), NSBa (4), U1-L1 (5), and U1-SN (6). A serious and very serious inconsistency was observed in SNA and SNB outcomes due to moderate to high statistical heterogeneity. Another pitfall that downgraded the overall certainty was the presence of a serious imprecision in the ANB outcome and a very serious imprecision in the SNA, SNB, NSBa, U1-L1, and U1-SN outcomes (**Table 3**).

DISCUSSION

Previously, craniofacial morphology has been suggested as one of the potential causes of airway collapsibility during sleep. This systematic review screened over 8000 citations and identified 9 studies investigating this relationship. Among those, 5 articles reported no differences in the craniofacial features of OSA and control groups. The other 4 articles suggested that a specific group of children with OSA might present with a set of skeletal and craniofacial features suggestive of a class II tendency and a long facial profile. However, these results were not supported by meta-analyses. In sum, these results indicate that we should not suggest the existence of an association between specific craniofacial features and pediatric OSA. Even though a particular subgroup of pediatric OSA might present with an increased mandibular retrognathia, maxillary transverse deficiency, or a long facial profile, the investigation of associated clinical factors is needed to confirm or refute these features as possibly being causatively or consequentially associated with OSA in children. An important consideration is that this lack of strong association may reflect the methodological approaches. Lately, stronger arguments have arisen that imply that specific clinical phenotypes may have a stronger association with craniofacial features while other phenotypes do not.

The evaluation of the main features of craniofacial morphology included skeletal, soft features, and dental analyses. Regarding dental assessment, a narrower intercanine width was described among children with OSA.[20] The reported skeletal

Table 3—Certainty assessment (GRADE tool) for the quantitative cephalometric variables evaluated.

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With control	With OSA	Relative effect (95% CI)	Risk with control	Risk difference with OSA
SNA											
119 (3 observational studies)	not serious	serious[a]	not serious	very serious[b]	none	⊕○○○ VERY LOW	54	65	-	The mean SNA was **81.5**°	MD **0.69**° **higher** (0.63 lower to 2 higher)
SNB											
119 (3 observational studies)	not serious	very serious[c]	not serious	very serious[b]	none	⊕○○○ VERY LOW	54	65	-	The mean SNB was **76.81**°	MD **0.17**° **higher** (1.02 lower to 1.36 higher)
ANB											
119 (3 observational studies)	not serious	not serious	not serious	serious	none	⊕⊕⊕○ MODERATE	54	65	-	The mean ANB was **4.7**°	MD **0.61**° **higher** (0.2 lower to 1.42 higher)
NSBa											
119 (3 observational studies)	not serious	not serious	not serious	very serious	none	⊕⊕○○ LOW	54	65	-	The mean NSBa was **127.11**°	MD **0.32**° **lower** (2.4 lower to 1.75 higher)
U1-L1											
66 (2 observational studies)	not serious	not serious	not serious	very serious	none	⊕⊕○○ LOW	27	39	-	The mean U1-L1 was **125.89**°	MD **0.21**° **lower** (4.82 lower to 4.4 higher)
U1-SN											
66 (2 observational studies)	not serious	not serious	not serious	very serious[b]	none	⊕⊕○○ LOW	27	39	-	The mean U1-SN was **106.54**°	MD **0.67**° **higher** (2.18 lower to 3.52 higher)

[a]I^2 = 65%. [b]A large variation in 95% CI was detected. [c]I^2 = 78%.
CI: Confidence interval; **MD:** Mean difference.

differences suggest a class II malocclusion tendency (retruded mandible) and a vertical craniofacial growth tendency (long lower face, dolichocephaly facial pattern).[18,21] In concordance with skeletal results, the analysis of the soft features also suggested an increase in lower face height (relative to upper face height) among children with OSA.[11] However, when data of this review was quantitatively evaluated, none of the 6 skeletal variables (SNA, SNB, ANB, NSBa, U1-L1, and U1-SN) compared through a meta-analysis showed a difference between OSA and non-OSA groups. These findings indicate the need to further investigate craniofacial morphology as a clinical phenotyping factor in pediatric OSA. Even though some of the included studies reported differences, there is no consensus in the literature.

Our group conducted a previous systematic review on the same topic and only considered skeletal features, and no exclusion criteria were defined for non-PSG control groups.[10] Similarly to the results reported in the present review, a vertical direction of growth and a tendency to class II malocclusion were described.

We raise some hypotheses to justify a possible or lack of an association between some craniofacial features and pediatric OSA. One of them is the influence of craniofacial bones and position on airway size and contribution to airway obstruction. On the other hand, reduced mandibular growth might be a consequence of airway obstruction and sleep-disordered breathing (SDB). Children presenting with a mandible retrognathia, resulting in a class II, were associated with a narrower pharyngeal airway.[19] However, the association between a class II skeletal pattern and a reduced airway size among healthy children is still controversial.[26] Also, other craniofacial features, including the cranial base length, have not presented an association (or the lack of it) with SDB in children.[27] In summary, the differences in the craniofacial pattern observed in children with OSA might be linked to other factors not exclusively dependent on these anatomical features.

A vertical craniofacial direction of growth, and an increased lower anterior face height, could also represent a consequence of airway obstruction, as suggested by animal studies.[28] This feature was associated with multiple SDB signs and symptoms, including mouth breathing and adenotonsillar hypertrophy. To better understand a possible interaction between the vertical direction of growth and OSA, the causal relationship of this association should be explored in a longitudinal analysis.

The reported differences between craniofacial features of children with OSA and an nPSG-negative control group in only part of the studies included in this review could also be explained by the heterogeneity and multifactorial nature of OSA. Despite the abnormalities on craniofacial bones, other anatomical factors (ie, muscle tone), including obesity, adenotonsillar size, pharyngeal size, and genetic or biomechanical factors (ie, fluid dynamics), as airflow resistance, could be risk factors for pediatric OSA.[29]

Overall, there is limited knowledge of clinical and physiological phenotypes of OSA, and the majority of evidence is focused on nPSG sleep variables.[30] Available evidence suggests that lateral pharyngeal wall thickness and blood pressure are potential OSA phenotypes in children and adolescents.[31] There is a need to explore further the clinical phenotypes linked to pediatric OSA to improve the understanding regarding the role of craniofacial morphology in this disease.

Regarding the influence of other pediatric OSA risk factors on the craniofacial assessment, the adenotonsillar size and mouth breathing have been evaluated by the studies included in this systematic review. The adenotonsillar size was assessed in 2 studies. One of them reported no association between this variable and apnea-hypopnea index (AHI) values in a group of 4- to 11-year-old children.[12] The other study observed a larger adenoid size and increased mouth breathing among the OSA group in a group of 2.5-year-old children.[20] However, the interaction between those factors and craniofacial features was not explored in any of the included articles. In all selected studies, only nonobese or participants with matched body mass index values were included.

The influence of age has not been investigated in the papers included in this review. However, a wide age range has been considered in the studies. Three studies included participants from preschoolers until adolescence,[12,19,21] while 1 study included only minors younger than 3 years,[20] and the other 5 articles included children older than 6 years.[11,18,22–24] None of the included studies investigated the relationship between anatomical craniofacial changes and pediatric OSA over time. Understanding the effect of normal growth among children with and without OSA might explain the role of craniofacial growth in this population.

This systematic review aimed to evaluate the differences in craniofacial features among OSA and non-OSA groups of children. The criteria defined as control was the presence of a negative result in an nPSG evaluation. First, it is important to highlight the controversies associated with identifying a negative nPSG control group. Among the articles reviewed during our selection process, 12 studies reported healthy children without SDB symptoms and without an nPSG exam as a control group.[32–43] Among those, different results were also observed. While 5 studies reported no differences between OSA and the control group, the other 7 described differences in craniofacial morphology. Differences in craniofacial features were observed in the mandible, maxilla, facial height, nasopharyngeal airway at the adenoids, and position of the hyoid bone, and narrower intertooth distances for the first and second deciduous molars and the first permanent molars in children with OSA (**Table S5** in the supplemental material).

Adopting the nPSG-based diagnosis might also have limitations due to the reliance on a single sleep index, the AHI or the OAHI. In the review, all the selected studies used these indices to define an OSA case. The use of these indices alone for diagnostic and management approaches has been questioned.[44] Both AHI and OAHI are based only on the number of obstructive events, without further consideration of comorbidities, OSA symptoms, and quality of life. Other studies should explore the pediatric OSA in its multiple clinical features, including associated factors, for a more reliable diagnosis and understanding of the associated clinical and physiological phenotypes.

Collectively, despite myriad published studies over the previous 100 years within medical and dental journals indicating a secular trend toward a comorbid association of specific malocclusion phenotypes and SDB/OSA symptoms, the results of this

systematic review indicate that neither an association nor a lack thereof between craniofacial morphology and pediatric OSA can be supported or refuted. Some specific sets of craniofacial features, including mandible retrognathia, smaller cranial base angle, deficient intercanine width, and a long facial profile were more frequent among a specific subgroup of pediatric OSA. However, there is limited evidence of clinical phenotypes that would help understand the nature of this association. In the future, if this link is confirmed to be a reliable indicator of increased SDB/OSA risk, dental professionals may become even more helpful within collaborative efforts aimed at identifying children at high risk of OSA when SDB signs and symptoms are also identified in this group of children.[45] Children presenting these characteristics and other SDB signs and symptoms should be monitored by a sleep medicine or ear, nose, and throat specialist when justified.

Limitations

As a limitation of this systematic review, we may highlight the small sample size and the absence of a sample size justification in the included studies. These characteristics likely represent a bias in the interpretation of the results outside the study. One reason that might explain the difficulty of achieving larger sample sizes among children with pediatric OSA are the accessibility barriers to the nPSG exam, including the high cost and long wait lines for public health services.[46,47]

The eligibility criteria for the control group in this review was a negative nPSG result. However, only 3 of the selected papers reported that the participants from the control group did not present with any signs or symptoms of SDB.[11,18,20] The presence of these signs and symptoms may represent a confounding factor for the craniofacial assessment. Some of these features, such as mouth breathing, are associated with increased clockwise rotation of the mandible and increased lower facial height.[48]

Even though a low risk of bias was identified, some problems were found when confounding and controlling factors were defined in the analysis of the individual studies. That is why the certainty level for the conclusions was downgraded.

OSA has been associated with multiple comorbidities and disorders in children, including respiratory problems, obesity, adenotonsillar hypertrophy, and craniofacial and behavioral syndromes. The majority of the included studies reported excluding or matching participants regarding obesity, craniofacial syndromes, and adenotonsillar size.[4] However, none of the studies evaluated the influence of these features in their results. The consideration of other associated OSA risk factors, such as respiratory problems and behavioral conditions, could be included in future investigations to narrow the possible confounding factor for pediatric OSA.

CONCLUSIONS

Some specific craniofacial features, including mandibular retrognathia, reduced anteroposterior linear dimensions of the bony nasopharynx, smaller cranial base angle, deficient intercanine width, and a long facial profile, were more frequent, but not consistently, among a specific subgroup of pediatric OSA patients. However, due to the very low to moderate certainty level, neither an association nor a lack thereof between craniofacial morphology in pediatric OSA cases can be supported at this time.

ABBREVIATIONS

AHI, apnea-hypopnea index
nPSG, nocturnal polysomnography
non-PSG, non-polysomnography
NSBa, nasion-sella-basion angle (cranial base flexure angle)
OAHI, obstructive apnea-hypopnea index
OSA, obstructive sleep apnea
SDB, sleep-disordered breathing
SNA, sella-nasion to A point angle
SNB, sella-nasion to B point angle
U1-L1, upper incisor to lower incisor angle
U1-SN, upper incisor to nasion-sella angle

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