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Airways and malocclusion: etiology and treatment outcomes

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Airways and malocclusion: etiology and treatment outcomes

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Editorial: Airways and malocclusion: etiology and treatment outcomes

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The correlation between the upper airway and malocclusion is still a controversial issue. Craniofacial abnormalities and dental malocclusions, such as mandibular retrusion, maxillary constriction, and vertical skeletal discrepancies, are strongly associated with reduced airway patency and increased pharyngeal collapsibility. This relationship underscores the importance of evaluating craniofacial morphology in both the diagnosis and management of OSAS. Treatment aims not only to reduce apneic events and improve sleep quality but also to restore normal breathing dynamics and prevent long-term cardiovascular, metabolic, and neurocognitive complications. Achieving these goals requires a multidisciplinary approach that integrates orthodontics, surgery, otolaryngology, and sleep medicine to provide effective and long-term outcomes.

KEYWORDS

malocclusion, orthodontic, airway obstruction, craniofacial growth and development, sleep-related breathing disorders

Editorial on the Research Topic
Airways and malocclusion: etiology and treatment outcomes

Introduction

The craniofacial morphology may have an important role in upper airway anatomy. The reduction of the upper airway space may increase the risk of Obstructive Sleep Apnea start. Obstructive sleep apnea syndrome (OSAS) has increasingly been recognized as a highly prevalent and multifactorial disorder with significant clinical and socioeconomic implications. In Europe, it affects an estimated 44.3 million adults, posing a substantial clinical and socioeconomic burden (1). The pathogenesis reflects the interplay of anatomical predispositions that narrow the upper airway and the sleep-related decline in dilator muscle tone, particularly of the genioglossus, which together promote pharyngeal collapse (2). Affecting both pediatric and adult populations, OSAS is associated with cardiovascular and metabolic morbidity, impaired neurocognitive development, behavioral disturbances, reduced quality of life, and increased healthcare costs. The heterogeneous nature of this condition requires a personalized, multidisciplinary approach that draws upon the expertise of pediatricians, otolaryngologists, orthodontists, pulmonologists, radiologists, and maxillofacial surgeons.

Special issue evidence

This Special Issue brings together a total of nine articles, including two corrigenda, reflecting the breadth and diversity of current research in the field. The contributions stem from international teams based in China, Italy, Switzerland, the United States, and Thailand, underscoring the global relevance of obstructive sleep apnea research. The articles, published between March 2023 and September 2025, collectively provide a timely and comprehensive overview of diagnostic and therapeutic advances across different age groups and clinical settings.

Two articles focus specifically on the pediatric population. Wei et al. explored the application of drug- induced sleep endoscopy (DISE) in infants with dynamic upper airway collapse. The study demonstrates how DISE, by reproducing sleep conditions pharmacologically, provides real-time visualization of airway dynamics. This technique allows clinicians to localize the precise site and degree of obstruction, which is particularly crucial in very young patients where traditional assessments are limited by age and cooperation. Complementing this, Shi et al. investigated the diagnostic value of morphological data derived from volumetric computed tomography, integrated with clinical indices. The results suggest that quantitative imaging parameters, such as airway volume, cross-sectional area, and craniofacial characteristics significantly enhance diagnostic accuracy when combined with clinical evaluation. Importantly, this approach can help distinguish children who are likely to benefit from surgical interventions, such as adenotonsillectomy, from those requiring alternative or adjunctive therapies.

The pediatric section of this Special Issue also addresses therapeutic strategies, combining critical reflection with long-term clinical evidence. Rinchuse et al. examined the role of the orthodontist in pediatric OSAS. The authors emphasize that while orthodontic interventions such as rapid maxillary expansion or mandibular repositioning appliances hold promise for improving airway dimensions, the evidence supporting their effectiveness remains limited. Authors argue that orthodontics must not be practiced in isolation but rather integrated within an interdisciplinary framework that includes pediatricians, otolaryngologists, and sleep specialists. Sriboonyong et al. provided a compelling 20-year experience with CPAP administered via tracheostomy in children with tracheomalacia. This rare and severe condition is associated with recurrent airway collapse and life-threatening events. The authors demonstrate that long-term CPAP, even when delivered through tracheostomy, can significantly improve survival, growth, and neurodevelopmental outcomes. The complexity of chronic tracheostomy care is evident, involving substantial psychosocial and logistical challenges for families.

Finally, Guerin et al. presented a corrigendum to a case report on long-term non-invasive ventilation (NIV) in an infant with Hallermann–Streiff syndrome. The correction highlights the importance of precision in reporting but also reiterates a key clinical message: syndromic patients often require highly personalized, prolonged ventilatory strategies. The case underscores the necessity of tailoring interventions to genetic and craniofacial anomalies, reinforcing the heterogeneity of pediatric OSAS and the need for flexible, individualized management approaches.

Orthodontic and surgical approaches in adults

In the adult population, three articles explore innovative therapeutic strategies. Ciavarella et al. investigated sleep position shifts in patients with OSA treated with mandibular advancement device (MAD). The study expands the current understanding of MAD, traditionally evaluated for the ability to maintain upper airway patency. MAD therapy may also influence positional behavior during sleep, suggesting a broader mechanism of action that integrates mechanical and behavioral effects. This finding opens new avenues for evaluating oral appliances not only in terms of respiratory indices but also in their impact on sleep architecture. A corrigendum (Ciavarella et al.) was later published, ensuring transparency and accuracy in reporting.

Cretella Lombardo et al. compared twin-block appliances with mandibular advancement achieved through clear aligners, a modality gaining increasing popularity in orthodontics. The comparative study is highly relevant, as it explores both incremental and maximal mandibular advancement strategies. The results provide novel insights into how different appliance designs affect airway volume, helping clinicians balance therapeutic efficacy with patient comfort and long-term dental stability.

Li et al. offered an anatomic and aerodynamic assessment of a modified maxillomandibular advancement (MMA) procedure in East Asian patients with moderate to severe OSAS. The study recognizes that craniofacial morphology varies significantly across ethnic groups and that surgical approaches must be adapted accordingly. By tailoring MMA to East Asian anatomical characteristics, authors demonstrated improved airway outcomes and reduced pharyngeal collapsibility.

Although addressing different aspects of the disorder, the articles in this Special Issue converge on a central message: the management of OSAS must be individualized, grounded in an accurate assessment of each patient's anatomical, functional, and clinical characteristics. Diagnostic innovations, ranging from DISE to volumetric imaging, are opening new avenues for more targeted interventions. At the same time, the diversity of therapeutic options, from orthodontics and mandibular advancement to surgery and long-term ventilatory support, highlights the need for effective multidisciplinary integration.

Conclusion

This Special Issue offers a comprehensive perspective on the evolving landscape of obstructive sleep apnea management

across age groups and clinical settings. Taken together, the articles highlight that OSAS cannot be managed through a uniform strategy; instead, effective care requires individualized approaches informed by each patient's anatomical, functional, and clinical characteristics. Advances in diagnostic techniques are opening new avenues for earlier and more accurate patient identification and treatment planning. At the same time, the broad range of therapeutic strategies, which includes orthodontics, mandibular advancement devices, surgical innovations, and long-term ventilatory support, underscores the essential role of multidisciplinary collaboration.

Author contributions

MT: Writing – original draft, Writing – review & editing. ML: Writing – original draft. DC: Writing – review & editing, Writing – original draft.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Diagnostic value of upper airway morphological data based on CT volume scanning combined with clinical indexes in children with obstructive sleep apnea syndrome

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Background and purpose: Early diagnosis is important for treatment and prognosis of obstructive sleep apnea (OSA)in children. Polysomnography (PSG) is the gold standard for the diagnosis of OSA. However, due to various reasons, such as inconvenient implementation, less equipped in primary medical institutions, etc., it is less used in children, especially in young children. This study aims to establish a new diagnostic method with imaging data of upper airway and clinical signs and symptoms.

Methods: In this retrospective study, clinical and imaging data were collected from children ≤10years old who underwent nasopharynx CT scan(low-dose protocol)from February 2019 to June 2020,including 25 children with OSA and 105 non-OSA. The information of the upper airway (A-line; N-line; nasal gap; upper airway volume; upper and lower diameter, left and right diameter and cross-sectional area of the narrowest part of the upper airway) were measured in transaxial, coronal, and sagittal images. The diagnosis of OSA and adenoid size were given according to the guidelines and consensus of imaging experts. The information of clinical signs, symptoms, and others were obtained from medical records. According to the weight of each index on OSA, the indexes with statistical significance were screened out, then were scored and summed up. ROC analysis was performed with the sum as the test variable and OSA as the status variable to evaluate the diagnostic efficacy on OSA.

Results: The AUC of the summed scores (ANMAH score) of upper airway morphology and clinical index for the diagnosis of OSA was 0.984 (95% CI 0.964–1.000). When sum=7 was used as the threshold (participants with sum>7 were considered to have OSA), the Youden's index reached its maximum at which point the sensitivity was 88.0%, the specificity was 98.1%, and the accuracy was 96.2%.

Conclusion: The morphological data of the upper airway based on CT volume scan images combined with clinical indices have high diagnostic value for OSA in children; CT volume scanning plays a great guiding role in the selection of treatment scheme of OSA. It is a convenient, accurate and informative diagnostic method with a great help to improving prognosis.

KEYWORDS

CT volume scan, upper airway morphology, children, OSA, diagnosis

Highlights

- Early diagnosis of OSA in children is very important for the treatment.
- However, the traditional diagnostic gold-standard PSG is difficult to implement.
- This study aims to explore convenient and reliable diagnostic methods for children.
- A new diagnostic model was established combining CT with signs and symptoms.
- The diagnostic method in this study is highly effective, informative, and convenient.

1. Introduction

Obstructive sleep apnea (OSA) in children is a series of pathophysiological changes caused by frequent partial or complete upper airway obstruction during sleep that interferes with sleep architecture and ventilation in children (1–3). The prevalence of OSA in children is about 2%–4%, and it is on the rise (1). Its main clinical manifestations include sleep dyspnea/apnea habitual snoring, mouth breathing, sleep awakenings, daytime weakness and drowsiness. Habitual snoring is present in almost all children with OSA. Habitual snoring and sleep apnea are often the first symptoms, but are easily ignore (4). Without timely treatment, the long-term course of the disease can lead to a variety of complications such as developmental abnormalities, cognitive dysfunction, cardiovascular disorders, as well as mood disorders such as irritability, aggressive behavior, anxiety, and depression (5). Therefore, early identification, definite diagnosis and timely treatment are important to improve the prognosis of children with OSA.

At present, the clinical definite diagnosis of OSA in children depends on Polysomnography (PSG). The American Academy of Pediatrics (AAP) suggests that OSA should be screened in children as part of routine health maintenance. PSG should be performed for a definitive diagnosis in children with typical symptoms (e.g., snoring, sleep disturbance, or daytime hyperactivity) or risk factors (e.g., craniofacial, neurological, or genetic disorders) (6). However, it is difficult to implement PSG because of the long monitoring time, high cost, the need for the subject to sleep naturally throughout the night during the examination, and a well cooperation from parents and children. In addition, due to the lack of standard sleep monitoring conditions in some medical institutions, clinicians, especially pediatricians and ear, nose and throat (ENT) clinicians, diagnose the OSA mainly based on imaging examinations such as lateral cephalometric X ray films, CT scans of the head and neck, and clinical symptoms and signs of the child patients. Unfortunately, there is still a lack of satisfactory screening tools and objective scoring criteria in clinical practice yet (7). And consequently the accuracy of disease diagnosis much depends on the clinicians' subjective cognition and experience of the disease. This paper aimed to explore a diagnostic method of combining upper airway morphological data with clinical symptoms and signs to predict OSA in children by analyzing the nasopharyngeal CT examination data and clinical data of children under 10 years of age with OSA.

1.1. Methods

This is a retrospective study. This study was approved by the Ethics Committee of Zhengzhou Central Hospital Affiliated to Zhengzhou University (approval number: 201978). The legal guardians of all subjects had singed the informed consents. All methods have been performed in accordance with the relevant guidelines and regulations.

1.2. Subjects

Clinical and imaging data were collected from children ≤10 years old who underwent nasopharynx CT scan at Zhengzhou Central Hospital Affiliated to Zhengzhou University from February 2019 to June 2020. The reasons for choosing the age range of the subjects are: adenoids develop rapidly after birth, reach their maximum size in early childhood, begin to regress around 8–10 years of age (8). In addition, OSA has a peak incidence around 2–8 years of age (9). Exclusion criteria: (i) nasopharyngeal cavity bleeding; (ii) immunodeficiency; (iii) previous history of turbinatectomy or adenoidectomy; (iv) nasopharyngeal or cervical masses or occupying lesions involving the upper airway; (v) skull base fracture or craniofacial malformation; (vi) chondrodysplasia, hypothyroidism and acromegaly; (vii) various central nervous system diseases.

2. Materials and methods

2.1. Imaging indexes and detecting methods

The measurement indexes and the corresponding methods are shown in Table 1; Figure 1.

All the imaging data were obtained from high-resolution CT volume scan images with a Siemens Somatom definition flash CT scanner, installed in June 2018.The detector combine with Siemens' proprietary Ultra Fast Ceramics scintillator the SOMATOM Definition Flash acquires 2 × 128 slices per rotation at outstanding dose efficiency. Except for children under 3 years of age who breathe naturally, all the children were given a CT scan of nasopharynx when deep inhaling and breathy holding (the volume of nasopharynx is the largest at this time) in static and supine position. During scanning, all children were in supine position, with the audio-orbital line

Abbreviations: OSA, obstructive sleep apnea; PSG, Polysomnography; AAP, American Academy of Pediatrics; ENT, Ears, nose, and throat; DLP, Dose length product; MPR, Multi-planar reformation; VR, Volume rendering; AASM, American Academy of Sleep Medicine; ROC, Receiver Operating Characteristic; AUC, Area under the curve; SpO2, Oxygen saturation of pulse; AHI, Apnea-hypopnea index.

TABLE 1 Measurement of morphological data of the upper airway based on CT volume scan images.

Measurement image source	Measurement indicators	Specific observations	Measurement methods	Reference illustrations
Median sagittal position: positive mid-sagittal images were obtained by positioning the upper edge of the soft and hard palate in the transverse axis position	N line	Nasopharyngeal cavity width	Distance from the lower border of the pterygo-occipital cartilage junction (point O) to the upper border of the soft and hard palate junction (point H) in line	Figure 1A
	A line	Adenoid thickness	Make an extension line (L) along the inferior border of the occipital bone and a vertical line of the extension line through the most convex point of the adenoids	Figure 1A
	Nasal gap	Mean of left and right posterior nostril gap sizes	Parallel inferior turbinate sagittal images measuring the distance from the posterior margin of the left and right inferior turbinates to the anterior margin of the adenoids	Figure 1B
Coronal images: sagittal image reconstruction of the coronal image *via* the most convex point of the adenoids, perpendicular to the long axis of the airway	Upper airway area	Minimum cross-sectional area of upper airway	Coronal image reconstruction *via* the most convex point of the adenoids, perpendicular to the long axis of the airway	Figure 1C
	Upper and lower airway diameters and right and left diameters	Upper airway minimum cross-sectional dimensions upper-lower diameter and left -right diameter	Coronal images were reconstructed *via* the most convex point of the adenoids, perpendicular to the long axis of the airway, and the size of the upper- lower and right–left trajectories of the airway at this level	Figure 1D
Original axial images: parallel inferior turbinate level	Upper airway volume	VR images and volume size of the nasopharyngeal cavity in the upper airway	The posterior border of the inferior turbinate was used as the anterior border, the parietal wall of the nasopharynx as the posterior superior border, and the level of the soft palate at the level of the uvula not connected to the oropharynx as the inferior border, and the area of interest was outlined along the edge of the airway layer by layer, then the volume was calculated by the post-processing software of the CT device workstation.	Figures 1E,F

perpendicular to the examination bed surface, the midsagittal position of the head and body coincident with the table top. All children were fixed with head rest to avoid artifacts caused by head movement Cases with image artifacts such as swallowing and respiratory movement were excluded. The scanned part was the nasopharynx, from the upper limit of the nasopharyngeal apex to the lower limit of the epiglottis. All children were examined by low-dose scanning protocol: tube voltage 100KV, Care Dose 4D automatic tube current technology and iterative reconstruction algorithm, scanning layer thickness 1.0 mm, layer spacing 0.6 mm, scan length 11.2–13.6 cm, and scanning time 3-4S. The min-max dose length product(DLP)is 49-56 mGy.cm (see Figure 2 patient protocol). Each indicator was measured twice and averaged by two radiologists double-blindly. Paired *t*-test was used to test the consistency between two experts, showing good agreement ($t = -1.716 \sim 1.916$, $p > 0.05$). The mean of data measured by the two experts was used as the final value of the indicator.

Referring to the method in previous research (10), the original images were reconstructed into coronal and sagittal images by

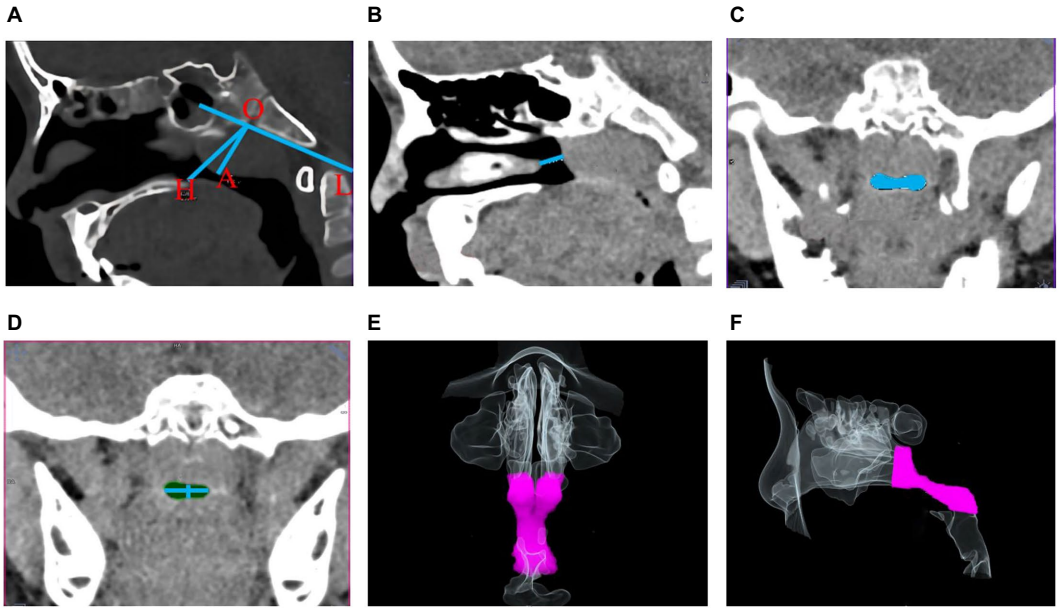

FIGURE 1
Schematic diagram of morphological indicators of the upper airway. **(A)** Nasopharyngeal cavity width (OH) and adenoids thickness (OA); **(B)** Right nasal gap size; **(C,D)** Minimum cross-sectional area of the upper airway in coronal position and its upper-lower, right–left diameters; **(E,F)** Coronal (E) and sagittal (F) upper airway volume model VR plots.

A

Total mAs 219 Total DLP 49 mGycm

	Scan	kV	mAs / ref.	CTDIvol* mGy	DLP mGycm	TI s	cSL mm
Patient Position H-SP							
Topogram	1	120	35 mA	0.29 S	4.7	1.7	0.6
Sinus	2	100	45 / 67	3.97 S	44.5	1.0	0.6

B

Total mAs 257 Total DLP 56 mGycm

	Scan	kV	mAs / ref.	CTDIvol* mGy	DLP mGycm	TI s	cSL mm
Patient Position H-SP							
Topogram	1	120	35 mA	0.29 S	6.0	2.2	0.6
Sinus	2	100	41 / 67	3.64 S	49.5	1.0	0.6

FIGURE 2
Patient protocol. **(A)** The smallest DLP across all study subjects, was obtained from a 1-year-old child. **(B)** The largest DLP of all study subjects, was obtained from a 10-year-old child.

multi-planar reformation (MPR). Imaging of the upper airway was measured in the original transaxial and reconstructed coronal and sagittal images. VR images of the upper airway were reconstructed based on the original axial images by volume rendering (VR).

A/N represented the adenoid size. According to A/N, participants were classified into mild adenoid hypertrophy group($A/N \geq 0.6$) and severe adenoid hypertrophy group ($A/N \geq 0.7$) (11).

2.2. Clinical indexes and evaluation methods

Collect clinical information of children, including whether it exists habitual snoring, mouth breathing, adenoidal facies, chronic sinusitis and secretory otitis media.

Chronic sinusitis, secretory otitis media and adenoid face were diagnosed according to the guidelines and consensus of imaging diagnostics experts (12–16).The information of clinical signs, symptoms and others were obtained from the medical records. Habitual snoring was categorized into <3 months and ≥ 3 months according to its duration. OSA was diagnosed by two ENT clinicians according to the diagnostic criteria and opinions of OSA published by the AAP and the American Academy of Sleep Medicine (AASM) (4, 17). Subjects were grouped into the OSA or non-OSA based on the diagnosis. When the two independent diagnoses of chronic sinusitis or secretory otitis media or adenoid face or OSA in the same patient were inconsistent, the two clinicians discussed and made a final diagnosis.

3. Sample size

Based on the diagnostic model, the sample size was calculated by the formula (1), where $\alpha = 0.05$, allowable error $\delta = 0.15$, and p is the sensitivity or specificity of the method to be tested. Previous findings (18) showed that the sensitivity and specificity of diagnosis on OSA with combined adenoid and upper airway morphology were 90.0% and 79.8%, respectively. The minimum sample size of the OSA group was 16, and that of the non- OSA group was 28. A margin of 20% was used for the sample size to account for any invalid samples. Therefore, the minimum sample size was 20 for the OSA group and 34 for the non-OSA group.

$$n = \left(\frac{z_\alpha}{\delta}\right)^2 (1-p)\,p \tag{1}$$

3.1. Statistical analysis

Statistical analyses were performed with IBM SPSS Statistics 23.0 software. Single-factor unconditional logistic regression was used to screen the risk factors for OSA. Statistically significant variables were assigned values. For categorical data, each category was assigned a value based on the magnitude of the regression coefficient (0–5 points). For quantitative variables, logistic regression analysis was performed with the presence or absence of OSA as the dependent variable, and diagnostic probabilities were calculated, and quantitative variables were assigned a value (0–5 points) after transformed into categorical variables based on the diagnostic probability values. All indicators were scored and summed up. Receiver Operating Characteristic (ROC) analysis was performed with sum as the test variable and OSA as the state variable, and the optimal cut-off value of the sum was determined based on the Youden's index. And the diagnostic efficacy was assessed in terms of area under the curve (AUC), sensitivity, specificity, and accuracy. All the above statistical tests were two-sided with test level $\alpha = 0.05$.

4. Results

4.1. General characteristics of subjects

Based on the inclusion criteria, a total of 140 subjects imaging and case information were collected, out of which 2 and 8 subjects were excluded due to adenoidectomy and nasopharyngeal hemorrhage respectively, resulting in the inclusion of 130 subjects. There were 50 males and 80 females, aged 1–10 years with a mean age of 5.01 ± 2.19 years. There were 92 (70.8%) and 19 (14.5%) patients with chronic sinusitis and secretory otitis media, respectively. There were 25 patients in the OSA group with a proportion of 19.2%, including 17 males and 8 females with a mean age of 5.56 ± 2.20 years. There were 105 in the non-OSA group, 63 and 42 males and females, respectively, with a mean age of 4.88 ± 2.17 years. There was no statistical difference in age and gender distribution between the OSA and non-OSA groups (age: $t = 1.410$, $p = 0.162$; gender: $\chi^2 = 0.546$, $p = 0.461$).

4.2. Univariate logistic regression analysis of the relationship between clinical information and OSA

The results of logistic regression analysis with the presence or absence of OSA as the dependent variable are shown in Table 2. Five statistically significant variables were found: A-line, nasal gap, mouth breathing, adenoidal face and habitual snoring. The results showed that the risk of OSA increased 1.047-fold (95% CI 1.509–2.776) for each 1-mm increase in the A-line (adenoid thickness) and decreased 39.4% for each 1-mm increase in the nasal gap (OR = 0.606, 95% CI 0.475–0.774). The risk of OSA in mouth breathers was 7.778 times greater than in those without mouth breathing (OR = 7.778, 95% CI 2.223–27.217). The risk of OSA was 25.000 times higher in those with adenoidal facies than in those without this sign (OR = 25.000, 95% CI 3.664–170.586). The risk of OSA was 50.500 and 168.333 times higher in those who snored for <3 months and ≥ 3 months, respectively, than in those who did not snore ($p < 0.05$).

4.3. Assignment for variables

Based on the results of the univariate analysis, five statistically significant variables were included and assigned.

4.3.1. Assignment for categorical variables

Values of categorical variables were assigned according to the magnitude of the regression coefficient. The reference group was assigned a score of "0"(all the regression coefficients needed to be greater than 0; if the regression coefficient was less than 0, the direction of the variable assignment was reversed for dummy variables). If there was no statistical difference between the category and the reference group, "0"was assigned. The other categories were rounded to the closest value according to the regression coefficient

TABLE 2 Univariate logistic regression analysis of the relationship between clinical information and OSA (n=130).

variable	β	S.E.	Wald	OR	95% CI	p
Age	0.144	0.103	1.957	1.154	0.944–1.412	0.162
Upper airway volume	0.000	0.000	0.353	1.000	1.000–1.000	0.553
Upper airway area	−0.005	0.004	1.948	0.995	0.987–1.002	0.163
A line	0.716	0.155	21.242	2.047	1.509–2.776	<0.001
N line	0.044	0.098	0.207	1.045	0.863–1.266	0.649
Nasal gap	−0.500	0.125	16.128	0.606	0.475–0.774	<0.001
Male	0.349	0.473	0.543	1.417	0.561–3.578	0.461
Mouth breathing	2.051	0.639	10.303	7.778	2.223–27.217	0.001
Chronic sinusitis	0.074	0.494	0.023	1.077	0.409–2.837	0.880
Secretory otitis media	0.276	0.673	0.169	0.759	0.203–2.835	0.681
Adenoidal facies	22.721	28420.722	0.000	$7.37*10^9$	--	0.999
Habitual snoring			37.887			<0.001
<3 months	3.922	0.788	24.769	50.500	10.777–236.633	<0.001
≥3 months	5.126	1.130	20.583	168.333	18.384–1541.355	<0.001

95% confidence interval for OR not calculated because the standard error is too large.

TABLE 3 Assignments for clinical information.

variable	Original values	n	Assignments
A line(mm)	<12	62	0
	[12, 13.5)	28	1
	[13.5, 15)	14	2
	≥15	26	5
Nasal gap(mm)	≤2.5	8	3
	(2.5, 5.5]	42	2
	(5.5, 8.5]	54	1
	>8.5	26	0
Mouth breathing	No	118	0
	Yes	12	2
Adenoidal facies	No	128	0
	Yes	2	5
Habitual snoring	No	107	0
	< 3 months	12	4
	≥ 3 months	11	5

value as a score: "close 1" was assigned "1"; "close 2"was assigned "2," and so on; if $\beta \geq 5$, "5"was assigned. For example, those who sleep with mouth breathing were assigned "2," and those without mouth breathing were assigned "0." Although the logistic regression showed that the *OR* value for adenoidal facies contained 1, but considering that there were only 2 cases of adenoid facies in this study, which may result in a false negative error; and previous studies (16, 19, 20) have reported a significant association between adenoid facies and OSA, "5" was assigned to those with adenoid facies in the later analysis, otherwise "0" was assigned.

4.3.2. Assignment for quantitative variables

Logistic regression analysis was performed and diagnostic probabilities were calculated with the presence or absence of OSA as the dependent variable. Decile splits were performed according to diagnostic probabilities, with probabilities 0.1, 0.2,0.3, 0.4,0.5 as splits. There were 6 groups with probability ranges of (0–0.1), [0.1–0.2], [0.2–0.3], [0.3–0.4), [0.4–0.5), and ≥0.5. The original quantitative variables were then grouped according to probabilities against the original quantitative variables, rounding up the original values to the closest and regrouping. The logistic regression was performed again with the new categorized ordinal variable as dummy variable. And each category were assigned according to the regression coefficients in the same way as for the categorical variables. The assignment of statistically significant variables in the univariate analysis is shown in Table 3.

4.3.3. Diagnostic effectiveness of sum of 5 variables on OSA

The scores for the five variables of A-line, nasal gap, mouth breathing, adenoidal facies and habitual snoring were summed up. Here, we simply call it "ANMAH score." ROC analysis was performed and the curves were plotted with sum as the test variable and OSA as the status variable (Figure 3) to test the diagnostic efficacy of sum on OSA. The results showed that the AUC was 0.984 (95% CI 0.964–1.000). The diagnostic efficacy of the model at different cut-off points is shown in Table 4. When cut-off points is 7 (patient with 'sum >7' could be considered to have OSA), the Youden's index reached the maximum, the sensitivity was 88.0%, the specificity was 98.1%, and the accuracy was 96.2%.

5. Discussion

Early diagnosis is a prerequisite for reducing the complications and improving the prognosis of OSA. Though PSG is recognized as

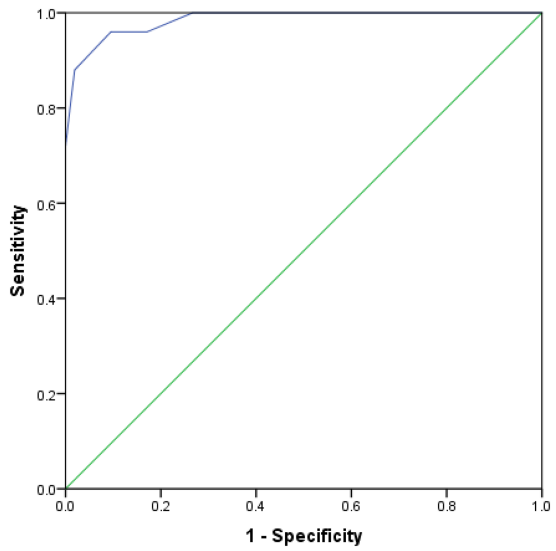

FIGURE 3
ROC curve for the diagnosis of sum on OSA.

TABLE 4 The diagnostic efficacy of the model at different cut-off points.

Cut-off point	Sensitivity	Specificity	Youden's index	Accuracy
>4	100.0%	73.3%	0.733	78.5%
>5	96.0%	81.9%	0.779	84.6%
>6	96.0%	89.5%	0.855	90.8%
>7	88.0%	98.1%	0.861	96.2%
>8	76.0%	99.0%	0.750	94.6%
>9	68.0%	100.0%	0.680	93.8%

the gold standard for the diagnosis of OSA (7, 9, 21), for various reasons, it is difficult to implement in children, especially preschool-aged patients. Exploring a less costly, convenient and highly accurate method for the diagnosis of OSA in children that can replace PSG has been the goal of researchers in recent years. In this study, the method of combining CT volume scan data (adenoid thickness and posterior nasal gap size), with clinical indexes(mouth breathing, sleep habitual snoring symptoms and adenoid facial signs) was found to have high sensitivity, specificity, and accuracy (the sensitivity the specificity and the accuracy was 88.0%, 98.1%, and 96.2%, respectively) for the diagnosis of OSA, which could be a convenient and effective way to diagnose OSA in children. Moreover, CT volumetric scan can not only determine the site and degree of upper airway obstruction, but also evaluate the complications such as chronic sinusitis and secretory otitis media comprehensively, which can provide more information for the choice of OSA treatment plan.

Other studies about the diagnosis of OSA in children and their defects. At present, some other diagnostic models of OSA in children have limitations. Jing Zhang et al. (22) collected clinical data information of 136 habitual snoring children(1–12 years)and establish a diagnosis model of OSA with pediatric sleep questionnaire, minimum nocturnal transcutaneous oxygen saturation of pulse (SpO2) monitoring,age and neck circumference. Its sensitivity was 80.9% and specificity was 76.2%. However, the large age span of subjects in the study may affect the authenticity of the results, furthermore nocturnal SpO2 monitoring still needs to be performed all night, which is difficult to implement. Lai CC et al. (7) collected data of BMI Z-score, tonsil volume, updated Friedman tongue position, snoring visual analog scale, nasal obstruction and mouth breathing in children, and established a diagnostic model by calculating and analyzing apnea-hypopnea index (AHI). The sensitivity of its AHI ≥ 5 and AHI ≥ 10 for diagnosing OSA was 75.6% and 84.6%, while the specificity was 61.7% and 56.5%, respectively. The unsatisfactory diagnostic efficacy of model in this study may be related to the adenoid hypertrophy, an important factor to trigger OSA in children, was not included.

Therefore, in an excellent diagnostic model pathophysiological mechanism should be considered. Computerized tomography is often used to evaluate the upper airway in the research about pathophysiology of OSA. Several studies have explored their diagnostic potential (23). Van Holsbeke et al. (24) found that functional 3D imaging parameters from computed tomography (CT) scans of upper airway better predicted obstructive sleep apnea (OSA) severity than standard clinical markers in children. Some subjects in the study had a history of upper respiratory surgery, and whether this factor would affect the accuracy of the study results is unknown. Alsufyani et al. (25) tested the feasibility in using cone beam CT (CBCT) to analyze the nasal and pharyngeal airway space post-surgery with meaningful methods of analyses, and correlating imaging findings with clinical outcomes in children with SDB(sleep disordered breathing) symptoms and maxillary-mandibular disproportion. They found that using point-based analyses, new imaging airway measures including constriction and patency better explained changes in clinical symptoms compared to conventional measures. However, patients need to have a higher degree of cooperation in the process of CT examination in this study. Our study is different from theirs because we mainly focus on the convenient and reliable diagnosis of OSA in children. And our research has been able to meet the requirements of diagnosis.

It is just based on the comprehensive consideration of pathophysiology to select CT volume scan data of upper airway morphology as the model indexes in this study. Adenoid hypertrophy is a major causative factor for OSA in children (6, 9, 21, 23, 26, 27). It is reported that structural abnormality of the upper airway caused by adenoid hypertrophy is the major factor in the pathogenesis of OSA in children. Resection of hypertrophic adenoids can rapidly relieve upper airway obstruction, which remains the first-line treatment of adenoid hypertrophy-induced OSA (1, 4, 9, 26, 27). CT volume scan can rapidly obtain images of the nasopharynx of children, clearly display the morphological characteristics of the upper airway. It can not only provide detailed anatomical data of the axial, sagittal and coronal surfaces of the upper airway, but also determine whether pathogenic factors causing OSA were existed such as adenoid hypertrophy, pharyngeal space-occupying lesion, etc.

Although the symptoms and signs of OSA are important, they must be combined with other objective criteria to diagnose OSA accurately. Several studies (9, 21, 27) pointed out that the symptoms and signs of the disease should be paid much attention to because they are important basis for the initial diagnosis of OSA in children. This study also demonstrated that symptoms such as sleep with mouth breathing, habitual snoring and adenoid facies increased the risk of

OSA exponentially. However, SLAATS et al. reported (23) that symptoms/signs alone or being combined were not satisfactory in diagnosing OSA and predicting therapeutic effect. The subjective assessment of adenoid size does not correlate significantly with OSA severity, while the objective measurement of adenoid volume can well determine the severity of OSA. A combination of clinical features with other diagnostic tools was recommended. The univariate analysis in this study revealed that adenoid thickness was positively associated with OSA, whereas nasal gap size was negatively associated with it, which is consistent with previous findings that OSA is almost always associated with adenoid hypertrophy without severe malformations or complications (23, 26). In this study, both the upper airway morphological data and clinical indicators were included. Based on CT volumetric scan image data, this study quantifies the morphology and size of upper airway structures combining with clinical symptoms and signs, which can scientifically and accurately evaluate the role of different indicators on the diagnosis of OSA in children.

The CT scanning technology is advanced and the radiation used in this study is at a safe dose. In recent years, the application of ultra-high-speed CT, advances in examination techniques and optimization of protocols have made it possible to obtain clear, large amounts of image data at lower radiation doses (28, 29). The min-max dose length product(DLP) on all subjects is 49-56 mGy.cm, below the internationally recommended reference levels for children aged 1,5,10 (50, 60, 100 mGy.cm) (30). CT volume scan is a fast, convenient and noninvasive examination that can be performed both during wakefulness and sleep and be available in most medical institutions.

One of the advantages of this study Is the high diagnostic efficiency. In this study, rich morphological data of the upper airway and clinical symptoms and signs were included. Finally, five important indicators were screened out by univariate analysis to establish a diagnostic model (ANMAH score), in which adenoid thickness (A-line), nasal gap, mouth breathing, adenoid facial appearance and habitual snoring were scored and summed up. When 'sum>7', the accuracy rate for OSA reached 96.2%. This method has high sensitivity and specificity for diagnosing OSA in children and is superior to previous studies in diagnostic efficacy (7, 22). In addition, the diagnosis by the ANMAH score is easy for clinicians to operate, which can exclude the interference of subjective factors and improve the stability of diagnosis greatly.

The second advantage of this study is that CT scan can also provide much important information and diagnose complications, which is conducive to the choice of treatment plan. Although adenoidectomy remains one of the primary treatments for OSA in children with adenoid hypertrophy, there is no definitive conclusion on whether adenoidectomy will affect children growth and development. Adenoids are immune tissue. There is still disagreement on whether adenoidectomy should be performed and the extent of resection (31). The 2012 edition of the AAP guidelines (4) noted that adenoidectomy was used as the primary treatment method in moderate and severe OSA children with adenoid hypertrophy and no surgical contraindication. However, endoscopic or imaging evaluation of the upper airway conditions (including the nose, nasopharynx, oropharynx, larynx, and throat) is required. Adenoidectomy is also written into the guidelines as an important treatment in several countries for the management of child secretory otitis media, especially in children with nocturnal habitual snoring and nasopharyngeal infections (32). Gulottal et al. (3) suggested that recurrent otitis media and adenoid hypertrophy should also be taken into account as an important influencing factor in the diagnosis and treatment of OSA disease. Therefore, individualized and precise diagnosis is a prerequisite for treatment (6, 26). Before making an appropriate treatment plan, doctors need to accurately master the patient's disease-related information. For example, whether the upper respiratory tract is unobstructed, whether there is nasopharyngeal mass, whether there is chronic sinusitis and otitis media, etc. All this information can be obtained by volumetric CT scanning. In this study, 92 cases (70.8%) of chronic sinusitis and 19(14.6%) cases of secretory otitis media were detected from 130 subjects. This provides an important reference for the formulation of personalized treatment plan.

However, this study has some weakness. First, obesity is one of risk factors for OSA in children. OSA has a high prevalence in obese children. Some studies suggested that obesity and mild adenoid hyperplasia can cause another type of OSA (1, 33). Obesity was not included in this study as an indicator, so its role in OSA could not be distinguished. More attention on obesity needs to be paid in future studies. In addition, the nasopharynx CT of some children under the age of three is scanned when natural breathing, so the upper airway volume may be slightly smaller than that when deep inhaling and breathy holding, which may result in some bias. Finally, the sample in this study was derived from a single center and has not been confirmed in other countries or regions, therefore future verifying in multicenter studies with large sample is needed.

In conclusion, morphological data of the upper airway based on CT volume scan combined with clinical indicators are of high value in the diagnosis of OSA in children. It is simple, reliable, informative and easy to implement in most medical institutions. This method is expected to be of high benefit in the diagnosis and treatment of OSA in children.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors upon request. Requests to access these datasets should be directed to XX, xiaoxinguang126@126.com.

Ethics statement

The studies involving human participants were reviewed and approved by This study was approved by the Ethics Committee of Zhengzhou Central Hospital Affiliated to Zhengzhou University (approval number: 201978). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

YS performed data collection, analysis and explanation, reviewed the literature, and wrote most of the manuscript. MG and XZ participated the suggestion of the concept, design of experimental suggestions of the research procedures. MW participated in the revision of the article. YW and CL made much contributions to data collection and analysis. RL, XW, and RY participated in the research procedures and made some data analysis and explanation. XX participated in the study conception, design, and reviewed the final manuscript. XX was responsible for the content of the manuscript and the integrity of the data analysis. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Long-term sleep apnea CPAP via tracheostomy in children with tracheomalacia: 20-year experience

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Introduction: Children with severe tracheobronchomalacia may need placements of tracheostomies and long-term mechanical ventilation. Due to financial constraints, continuous positive airway pressure (CPAP) machines commonly used to treat obstructive sleep apnea in adults have been utilized to deliver positive distending pressure to such children at our institution for more than 20 years with favorable outcomes. We, therefore, reported our experience with 15 children using this machine.
Methods: This is a retrospective study during 2001–2021.
Results: Fifteen children, 9 boys, aged ranged 3 months–5.6 years, were discharged home with CPAP via tracheostomies. All had co-morbidities including gastroesophageal reflux ($n = 9$, 60%), neuromuscular disorders ($n = 6$, 40%), genetic abnormalities ($n = 6$, 40%), cardiac diseases ($n = 4$, 27%) and chronic lungs ($n = 3$, 20%). Eight (53%) children were aged less than 1 year old. The smallest child was aged 3 months old, weighing 4.9 kg. All caregivers were relatives and non-medical health professionals. The 1-month and 1-year readmission rates were 13% and 66% respectively. No factor-associated unfavorable outcomes were statistically identified. No complications related to CPAP malfunction were found. Five (33%) were weaned off CPAP, and 3 died (2 from sepsis and 1 from a sudden unknown cause).
Conclusion: We first reported the use of sleep apnea CPAP via tracheostomy in children with severe tracheomalacia. In limited-resource countries, this simple device may be another option for long-term invasive ventilatory support. The CPAP use in children with tracheobronchomalacia requires adequately trained caregivers.

KEYWORDS

tracheostomy, tracheomalacia, children, continuous positive airway pressure, invasive ventilatory support

1. Introduction

Tracheomalacia is a condition of excessive tracheal collapsibility. European Respiratory Society defines tracheomalacia as collapsibility greater than 50% expiratory decline in the cross-sectional luminal area during silent respiration. Either a bronchoscopic or radiological examination can be used to assess the severity of tracheomalacia. Although flexible bronchoscopy is the most often utilized modality, there is no one "gold standard" diagnostic test that is accepted worldwide (1). Mild cases can usually be treated without intervention. However, severe cases can result in life-threatening cyanotic attacks,

Abbreviations
CPAP, continuous positive airway pressure; HMV, home mechanical ventilation.

necessitating immediate intervention to stabilize the airway. Because the causes differ, so as a result, the treatments differ such as surgical stabilization, stabilization with removable stents, and conservative intervention such as continuous positive airway pressure (CPAP) (2). Severe tracheomalacia has been managed with many forms of positive pressure therapy (3) (CPAP, bilevel airway pressure, pressure support, full ventilation). Clinical studies have shown that increasing CPAP with tracheomalacia increases forced expiratory flows at functional residual capacity and it has been suggested that CPAP prevents airway collapse by stenting the airway open (4). To adjust CPAP, bronchoscopy or imaging may be used (1). Severe tracheomalacia with chronic respiratory failure may require a tracheostomy with mechanical ventilator support (1). Some of the children with severe tracheomalacia need long-term mechanical ventilation which is indicated when the patients cannot be weaned from mechanical ventilation.

In developing countries because of limited financial resources for homecare mechanical ventilation, it is difficult to send patients back home with mechanical ventilator support. Consequently, CPAP originally designed as a non-invasive ventilator was intentionally used as an invasive ventilator alternative via tracheostomy.

This retrospective study aims to report our twenty-year experience with fifteen children using this CPAP machine to treat severe tracheobronchomalacia and to identify factors associated with unfavorable outcomes.

2. Materials and methods

2.1. Study population

This study was approved by the Ethical Clearance Committee on Human Rights Related Research Involving Human Subjects, Faculty of Medicine Ramathibodi Hospital, Mahidol University (COA MURA2021/887). This was a retrospective study of all children with tracheomalacia that were treated with home continuous positive airway pressure via tracheostomy in the Ramathibodi pediatrics home mechanical ventilation program between February 2, 2001, and October 31, 2021. The research followed the international recommendations for Strengthening the Reporting of Observational Studies in Epidemiology (5). The following criteria were required for inclusion: (1) All children with tracheomalacia, aged 0 to 18 years, included in this study, and had a confirmed diagnosis by flexible bronchoscopy in spontaneous breathing, the current gold standard (1); and (2) Children have been treated with CPAP via tracheostomy for more than a year. Children who lost to follow-up were excluded. The age of home CPAP started from the time the patient was first sent home with CPAP. The causes for nonscheduled readmission in 1-year were categorized as respiratory problems (acute lower respiratory tract infection, atelectasis), mechanical CPAP-related problems, and other reasons.

2.2. Characteristics of home CPAP via tracheostomy

At our hospital, long-term home mechanical ventilation (HMV) was indicated when the patients could not wean from mechanical ventilation or showed progressive respiratory failure. Tracheostomy with invasive ventilation was used when patients had evidence of inadequate ventilation with non-invasive ventilation, risk of aspiration, dependence on ventilation for more than 16 h, and/or ineffective secretion drainage (3). Depending on their budget, the Philips Respironics REMstar Pro C-Flex, Fisher and Paykel CPAP Machines, and Weinmann CPAP were chosen as CPAP devices. The sleep apnea CPAP was a non-invasive ventilator. We modified CPAP to deliver positive airway pressure through a tracheostomy tube instead of the nasal mask in children. The non-invasive CPAP through tracheostomy system comprises of a CPAP machine, a heated humidifier, a single limb circuit, and a tube that ends at the tracheostomy. To reduce rebreathing and avoid excessive carbon dioxide levels, we connect an exhalation port to the tracheostomy in the single limb circuit closet.

The final decision to initiate HMV was made after a detailed discussion with their parents and multidisciplinary team. The settings of home CPAP were established by bedside titration and monitoring (including clinical symptoms, chest x-ray, laboratory studies, vital signs, and end-tidal carbon dioxide monitoring) that were all within normal range. The discharge occurred when the caregiver's competence was assessed and believed to be safe. The first visit was planned 1–3 months after discharge, depending on the clinical condition of the patient. Successful CPAP weaning was defined as being off from CPAP for 7 consecutive days without concomitant clinical or laboratory signs of chronic ventilatory insufficiency (6).

2.3. Data collection

We obtained information on patients using a CPAP machine to treat severe tracheomalacia by retrospectively reviewing medical records. Data included demographic data, baseline clinical characteristics including age, gender, underlying disease, age at initiation of CPAP, age at tracheostomy, and weight. Initial CPAP settings, including duration of CPAP per day, CPAP pressure setting was collected at the time of discharge. Additional data gathered included caregivers, educational level of caregivers, hospital stay before discharge with CPAP, and cuffed tracheostomy tube.

2.4. Outcome variable

The primary outcomes were to report twenty-year experience with all children using this CPAP machine to treat severe tracheobronchomalacia that met inclusion and exclusion criteria. Factors including age, weight, underlying disease, CPAP pressure, caregiver, and education of caregivers associated with unfavorable outcomes. Unfavorable outcomes were defined as death or readmission within 6 months after discharge.

2.5. Statistical analysis

Statistical analysis was performed using the SPSS (version 22.0) statistical software. Descriptive data were presented as mean ± standard deviation (SD) or median (min, max), depending on normality. Continuous data were compared by using Mann–Whitney tests.

The χ^2 test was used for categorical data. For all analyzed parameters, $p < 0.05$ was considered statistically significant.

3. Results

Out of a total of 15 patients, 9 were boys (60%). All of them used home CPAP via tracheostomy. Their main underlying disorders were gastroesophageal reflux ($n = 9$, 60%), neuromuscular disease ($n = 6$, 40%), genetic abnormalities ($n = 6$, 40%), cardiac disease ($n = 4$, 27%) and chronic lung disease ($n = 3$, 20%). The patient's characteristics are shown in Table 1. The median age at initiation of home CPAP was 1 year and the median weight was 7.5 kg. The youngest patient was a 3-month-old girl and her body weight was 4.9 kg. The follow-up period for CPAP usage ranged from 2.01–18.77 years. CPAP pressure setting when discharged ranged from 5 to 12 cmH_2O. Indications for tracheostomy and home CPAP were tracheomalacia and bronchomalacia, 80% and laryngomalacia, 53%. The median length of hospitalization in the critical care unit and ward before home CPAP onset was 101 days (IQR: 23–351). Eighty percent of their caregivers were parents and 67% of caregivers had high school graduate or lower. At discharge, all patients needed 24-hour CPAP support, and of those 4 patients required oxygen supplementation (Table 2). Intermittent weaning from CPAP and oxygen was performed by caregivers as tolerated at home.

TABLE 1 Demographic characteristics.

Clinical characteristics	$N = 15$
Age at initiation of CPAP (years)	1.0 (0.3, 5.6)
Age less than 1 year	8 (53%)
Age at tracheostomy (months)	1.8 (0.3, 4.1)
Sex (male), *n* (%)	9 (60)
Weight (kg)	7.5 (4.9, 12)
Body mass index (kg/m^2)	17.0 (10, 22)
Underlying diseases, *n* (%)	
Neuromuscular disorders	6 (40)
Chronic lungs	3 (20)
Cardiac diseases	4 (27)
Genetic abnormalities	6 (40)
Gastroesophageal reflux	9 (60)
Esophageal atresia with tracheoesophageal fistula	1 (7)
Locations of airway malacia	
Laryngomalacia	8 (53)
Tracheomalacia	15 (100)
Bronchomalacia	12 (80)

Values are median (min-max), number (%).
CPAP, continuous positive airway pressure.

TABLE 2 Initial CPAP settings and caregivers.

Initial CPAP settings and caregivers	$N = 15$
CPAP pressure setting when discharged (cmH_2O)	9 (5, 12)
Duration of CPAP per day (h)	24
Cuffed tracheostomy tube, *n* (%)	5 (33)
Oxygen supplement	4 (26)
Caregivers, *n* (%)	
Parents	12 (80)
Relatives	2 (14)
Unrelated	1 (7)
The educational level of caregivers, *n* (%)	
Primary school	4 (27)
High school	6 (40)
Bachelor	5 (33)
Hospital stay before discharge with CPAP (days)	101 (23, 351)

Values are median (min-max), number (%).
CPAP, continuous positive airway pressure.

There was a 13% rate of readmission within 1 month after discharge. The 1-year readmission rate was 66%. The most common causes of readmissions in 1-month and 1-year were pneumonia, followed by tracheitis. Five (33%) children have been weaned off their devices. Ten (67%) have been dependent on CPAP. Three (20%) died due to 2 from sepsis and 1 from an unknown cause (Table 3).

Bivariable analyses of risk factors found no significant predictor of death or readmission identified any factor whether it was age, weight, underlying diseases, or CPAP pressure itself because our admission rate was very low (Table 4).

4. Discussion

To the best of our knowledge, this is the first report of using adult sleep apnea CPAP to treat children with severe

TABLE 3 Clinical courses and outcomes of home continuous positive airway pressure.

Outcomes	*N* (%)
Weaned from CPAP	5 (33)
Decannulation of tracheostomy	3 (20)
Remaining on CPAP	10 (67)
Decreasing the duration of CPAP usage	5 (33)
1-month readmission after discharge	2 (13)
Readmission in 1 month due to	2 (13)
Lower respiratory tract infection	
Readmission in 6 months due to	7 (47)
Lower respiratory tract infection	6 (40)
Secretion obstruction causing atelectasis	1 (7)
1-year readmission after discharge	10 (66)
Readmission in 1 year due to	
Lower respiratory tract infection	9 (60)
Secretion obstruction causing atelectasis	1 (7)
Death	3 (20)
At the hospital, sepsis	2 (13)
At home, unknown	1 (7)

CPAP, continuous positive airway pressure.

TABLE 4 Factors associated with unfavorable outcomes.

Number	Outcomes		*p*-value
	Favorable (*N* = 7)	Unfavorable (*N* = 7)	
Age less than 1 year	3	5	0.315
Male	7	2	0.041
Weight ≤7 kg	2	5	0.132
Underlying diseases			
Gastroesophageal reflux	3	6	0.119
Neuromuscular disorders	2	4	0.315
CPAP pressure ≤7 cmH_2O	2	3	0.608
Cuffed tracheostomy tube	4	1	0.282
Non-parent caregivers	1	2	0.569
Educational ≤ secondary school	4	6	0.282
Complication			
≥5 events of lower respiratory tract infection	3	2	1
Granulation tissue formation at tracheostomy	4	4	1

Unfavorable outcomes defined by death or readmission within 6 months after discharge.
CPAP, continuous positive airway pressure.

tracheobronchomalacia via tracheostomy. We had to employ this simple device due to the limited financial resources of our country. In Thailand, home mechanical ventilators are not supported by the government or any health insurance. Therefore, if caregivers/parents would like their children to go home, they have to cover all the expenses of home respiratory care. Otherwise, all these children will have an extended hospital stay under the universal health coverage scheme. The benefits of HMV were shorter hospital stays and lower medical expenses (7–9).

CPAP creates distending pressure that prevents excessive collapse of the tracheal wall during inspiration due to tracheomalacia (10). In this study, for severe tracheomalacia often in combination with bronchomalacia or laryngomalacia, CPAP was applied via tracheostomy to stent the airway. CPAP was used at very young ages, and the youngest patient was a 3-month-old girl, with a body weight of 4.9 kg and there were no complications related to CPAP use. An exhalation port was attached in the single limb circuit closest to the tracheostomy to minimize rebreathing and prevent elevated carbon dioxide. More importantly, this exhalation port also allows excessive inspiratory flow generated from an adult sleep apnea CPAP to be released into the atmosphere. This technique prevents pneumothorax. To ensure safety, a chest x-ray was done to make sure the CPAP setting did not cause overinflation. Heated humidification systems were connected to the inspiratory circuit to prevent dry airways and oxygen source can be connected to a heated humidified circuit.

CPAP pressure setting when discharged ranged from 5 to 12 cmH_2O which were established by bedside titration and cardiopulmonary monitoring (including chest wall movement, chest x-ray, pulse oximeter, vital signs, and capnometry and machine output). An official American Thoracic Society Clinical Practice Guideline: Pediatric Chronic Home Invasive Ventilation, and professional in-home caregivers (e.g., nurses) as required to support the family were arranged before discharge or at least two family caregivers should have had specialized training for the child's care (11). Eighty percent of caregivers were parents and 67% of caregivers were only high school graduates or lower, more than the findings of Kim, Hyang Sook et al. (12). Therefore, even with a lack of well-trained nursing staff, HMV education for caregivers was successful. This comprehensive HMV training program was done by a multidisciplinary team comprising physicians, nurses, and social workers. The program took roughly a month to complete before discharge. Checklists were provided for the HMV training program.

Tracheomalacia's symptoms typically improve or resolve over time because the child grows, and the tracheal cartilage strengthens and stiffens (2). In our study, the 1-month readmission rate was 13% from pneumonia. The rate of nonscheduled hospital admission was lower in our study. Sheila S et al. (13), in their study consisting of 19 children with home mechanical ventilators via tracheostomy, determined the incidence of hospital admissions in the first month after discharge as 42%, and pneumonia and tracheitis were the most common reasons for admission. In Gizem et al.'s (14), study of 70 children with invasive HMV, 30% of them were readmitted to the hospital within 1 month mostly because of tracheostomy-related complications. Thirteen percent of children died at our hospital due to sepsis and 7% died at home with unknown causes. There was no complication related to CPAP use. Compared to the literature review from Edwards JD, et al., 47 of 228 children on chronic positive-pressure ventilation via tracheostomy died over 22 years. They found the commonest cause of mortality was a progression of the reason for chronic respiratory failure or underlying condition (34%) (15).

In limited-resource countries, this sleep apnea CPAP, which was initially intended to be a non-invasive ventilator, was used for long-term invasive ventilatory support via tracheostomy. The cost of a CPAP machine and heated humidified is around 1,000 US dollars which is much cheaper than a regular home mechanical ventilator approximately one-third of a conventional home ventilator. More importantly, no CPAP-related problems occurred over the 20-year experience of 15 patients.

This study has several limitations. The first limitations are the small sample and heterogeneity by age and co-morbidities, which may not have sufficient power to identify risk factors for poor outcomes and prevent readmission and may be selection bias. Second, the study was conducted at a single center and may reflect center-specific procedures for managing CPAP via tracheostomy, an HMV training program, and follow-up care. Third, since this was a retrospective study, we were unable to control for several confounding factors, including caregiver knowledge, home environment, and family members, which might have affected readmission outcomes. Lastly, this study focused only on death or readmission. Future studies should consider multicenter studies and investigate the caregiver's

HMV skill, quality of care, and quality of life for both the patient and the caregiver.

5. Conclusion

In conclusion, a non-invasive CPAP ventilator via tracheostomy in children with tracheomalacia may be safely used as a substitute for an invasive long-term home mechanical ventilator in a country with limited resources. The CPAP use in children with tracheobronchomalacia requires adequately trained caregivers.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Ethical Clearance Committee on Human Rights Related Research Involving Human Subjects, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand (COA MURA2021/887). Written informed consent from the participants' legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

Author contributions

The authors' contributions are as follows: AP, TS, and MN contributed to conceptualization, study design, data curation, and supervision. TS contributed in manuscript preparation and manuscript revision. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Comparison between twin block appliance and mandibular advancement on clear aligners in the improvement of airway dimension: incremental versus maximum bite advancement

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Objective: The aim of the present retrospective study was to compare the changes resulting from treatment using the MA and the TB with special regard to the oro-and naso-pharyngeal sagittal airway dimensions in subjects with dentoskeletal Class II malocclusions and positive history of Sleep Disorder Breathing (SDB) diagnosed through the Pediatric Sleep Questionnaire (PSQ).
Materials and methods: This retrospective study involved 2 groups of subjects: patients treated with Twin Block (TB group: $n = 22$, 10 males, 12 females; mean age 12.0 ± 1.3 years) and patients treated with Mandibular Advancement (MA group: $n = 23$, 11 males, 12 females; mean age 12.2 ± 1.1 years). Pretreatment (T1) and posttreatment (T2) lateral cephalograms were analyzed. All patients underwent the PSQ to diagnose SDB.
Results: In both treated groups there was an increase in the airways dimensions and an improvement in symptoms related SDB. The statistical comparison of the changes between T1 and T2 in the TB group showed a significant increment in upper airway size (PNS-AD2, +1.50 mm + −3.30; McNamara's upper pharynx dimension, +2.21 + −4.21) after active treatment. The MA group showed similar results during active treatment with a significant increase in both upper (PNS-AD2, +2.72 + −2.65; McNamara's upper pharynx dimension, +2.97 + −3.07) and lower (PNS-AD1, +2.17 mm + −3.54) airway size.
Conclusions: Despite the different structure of these two devices and the different advancement protocols, both appliances were valuable as a suitable treatment option for Class II patients with respiratory disorders, inducing an increase of upper and lower airway size and a significant reduction in diurnal symptoms.

KEYWORDS

class II, aligners therapy, cephalometric analysis, sagittal airway dimensions, growing patients

Abbreviations
TB: twin block; MA: mandibular advancement; SDB: sleep disorder breathing; PSQ: pediatric sleep questionnaire; T1: pre-treatment; T2: post-treatment; OSA: obstructive sleep apnea; CVM: cervical vertebral maturation; PNS: posterior nasal spine; AD1: the nearest adenoid tissue measured through the PNS-Ba line; AD2: nearest adenoid tissue measured through a perpendicular line to S-Ba from PNS; Ba: Basion; H: Hormion, point located at the intersection between the perpendicular line to S-Ba from PNS and the cranial base.

Introduction

Sleep-disordered breathing (SDB) involves a range of respiratory problems during sleep, including snoring and obstructive sleep apnea (OSA) (1). These conditions are particularly concerning in pediatric populations due to their potential impact on cognitive development, growth, and overall health (2–4). Mandibular advancement devices have emerged as a promising non-invasive treatment option for managing SDB in growing patients. These devices by anterior posturing of the mandible, enlarge the upper airway and reduce the airway obstruction during sleep.

The use of orthodontic appliances for mandibular advancement in pediatric patients has been supported by several studies (5–9). A study by Villa et al. (10) demonstrated the effectiveness of oral appliances in reducing respiratory disturbances in children with OSA. Similarly, Cozza et al. (11) pointed out that functional appliances could significantly improve airway dimensions and respiratory parameters in growing patients. These findings highlight the potential benefits of mandibular advancement in managing SDB in pediatric populations (10).

In recent years, improvement in orthodontic technology have introduced clear aligners, such as Invisalign, which are primarily used for dental alignment. However, these aligners can also be designed to incorporate mandibular advancement features (12, 13). This feature allows to induce the advancement of the mandible which shifts incrementally in its proper position. This dual functionality could offer a convenient and aesthetically pleasing option for patients requiring both orthodontic treatment and SDB management.

The use of clear aligners for mandibular advancement is a relatively new area of research, in a controlled retrospective study published by Cretella et al. in 2022 (12), the authors analyzed the effects of treatment performed with the Twin Block (TB) and mandibular advancement on clear aligners (MA) in Class II subjects, concluding that both functional appliances produced a significant elongation of the mandible with an improvement in sagittal relationship, overjet, and vertical overbite values (12).

To our best knowledge, only one study, published by Yue in 2023 (14), investigated the effects of MA about the changes of upper airway morphology. In the cited study, Yue et al. performed a comparison between MA and TB appliances for the treatment of Class II patients and they concluded that both devices were effective in increasing airway dimensions (14).

Due to the widespread application for this new type of appliance and considering the impact of respiratory disorders on the health of growing patients, further studies are necessary to evaluate the effect of MA on airway dimensions and the possible positive impact on patients with breathing difficulties.

It is interesting to better understand if the different structure of this new appliance and the different advancement protocol compared to other conventional devices has an effect on its effectiveness.

Thus, the aim of the present retrospective study was to compare the changes resulting from treatment using the MA and the TB with special regard to the oro-and naso-pharyngeal sagittal airway dimensions in subjects with dentoskeletal Class II malocclusions and positive history of SDB diagnosed through the PSQ (15).

The null hypothesis tested was that both types of functional appliances were equally effective in inducing an improvement of airway size.

Materials and methods

The study design received approval from the Ethics Committee at the Rome "Tor Vergata" Hospital, and informed consent was secured from the participants' parents for both the treatment and the potential use of their data for research purposes.

In this retrospective clinical trial, the cephalometric records of 45 patients with Class II division 1 malocclusion treated consecutively either with the TB (TB group: $n = 22$, 10 males, 12 females; mean age 12.0 ± 1.3 years), or the MA (MA group: $n = 23$, 11 males, 12 females; mean age 12.2 ± 1.1 years) were collected. Class II subjects were retrieved from the records of patients treated at the Department of Orthodontics at the Hospital of "Tor Vergata". Participants were selected based on the following inclusion criteria: overjet ranging between 5 and 8 mm, bilateral full Class II or end-to-end molar relationships, ANB angle greater than 4°, improvement in facial profile when the lower jaw was postured forward, and cervical stage 3 in cervical vertebral maturation (CVM) at T1 (16).

Parents of all participants filled in a version of the pediatric sleep questionnaire, PSQ-SRBD Scale by Ronald Chervin (Italian version in 22 items) pre and post treatments. The questions sought information about the child's daytime symptoms (such as sleepiness, irritability, fatigue, school problems, morning headache, mouth breathing, and nasal congestion) and nighttime symptoms (including habitual snoring, apnea, restless sleep, and nightmares) (15).

Teleradiography were available at two observation points: T1, at the onset of treatment; and T2, at the conclusion of functional therapy, before orthodontic treatment with either fixed appliances or the finishing phase with additional aligners. Functional treatment ceased with a Class I molar relationship.

Study samples were selected based on skeletal maturity at the beginning of treatment, assessed using the CVM method. The CVM method can identify individual skeletal maturity in growing patients, replacing the need for hand-wrist radiographs. CVM staging was conducted by an experienced evaluator (ECL).

Demographic data for the TB and MA groups are reported in Table 1. All patients were treated by two skilled orthodontist, whose experience in managing the two functional appliances was comparable in terms of years of practice and the number of patients treated with functional devices.

Treatment protocol

Patients in the TB group were treated with a TB device designed according to Clark's original concept (Figure 1).

TABLE 1 Demographics of the TB and MA groups.

	Age at T1, y		Age at T2, y		T1-T2, y	
	Mean	SD	Mean	SD	Mean	SD
TB Group ($n = 22$; 12 f, 10 m)	12.0	1.3	13.8	1.3	1.8	0.5
MA Group ($n = 23$; 12 f, 11 m)	12.2	1.1	13.7	1.2	1.5	0.6
P-value	0.5797		0.7898		0.0761	

y, indicates years; SD, standard deviation; f, female; m, male.

The appliance consisted of maxillary and mandibular plates fitting against the teeth, alveolus, and other supporting structures. Delta or Adams clasps were constructed on both sides to anchor the upper plate to the first permanent molars, and 0.030-inch ball clasps (or arrow clasps) were placed in the anterior interproximal spaces. The precise arrangement of the clasps depended on the state of dentition at the time of TB construction. In the mandibular arch, Clark suggested placing ball hooks between the canines and incisors.

For each patient, the construction bite was created in a single step, with maximum bite advancement. The construction bite allowed for a 5–7 mm vertical opening in the area of the posterior bite blocks. An important advantage of the twin block is the ability to guide the vertical eruption of posterior teeth through selective removal of acrylic during therapy. In hypodivergent patients with short lower anterior facial height and/or a deep curve of Spee, the acrylic on the posterior area of the upper bite block was trimmed to encourage the eruption of the lower posterior teeth. All subjects in this study were advised to wear the device full-time for a minimum of 22 h a day (excluding meals and sports) until the end of therapy (17).

Patients in the MA group were treated with the Mandibular Advancement (MA) appliance (Figure 2). The aligners feature precision wings made from the patented SmartTrack® material, located between the premolars and first molars, to hold the mandible in a forward position. With the MA appliance, mandibular advancement was not programmed in a single step but incrementally. While the aligners worked on orthopedic correction, they also aligned and leveled the teeth simultaneously. An initial pre-MA phase was automatically applied in specific situations (deep bite >7 mm, molar rotation >20°, Class II division 2, and cross-bite) to allow for wing placement or the first advancement. After mandibular advancement, a transitional phase was planned to hold the mandible in the advanced position while awaiting the delivery of standard or additional aligners. As with regular aligner treatment, patients were instructed to wear the aligners for a minimum of 22 h a day, removing them only to eat, drink, brush, and floss. Aligners were changed weekly (12).

Cephalometric analysis

All lateral cephalograms of each patient were manually traced in a single session. The tracings were performed by one investigator, and the accuracy of landmark locations and anatomical outlines was verified by a second investigator. Any

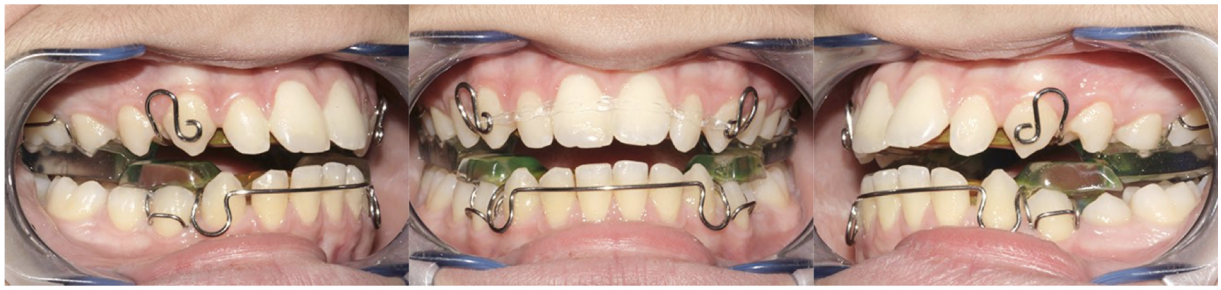

FIGURE 1
Frontal and lateral views of a twin block (TB) appliance.

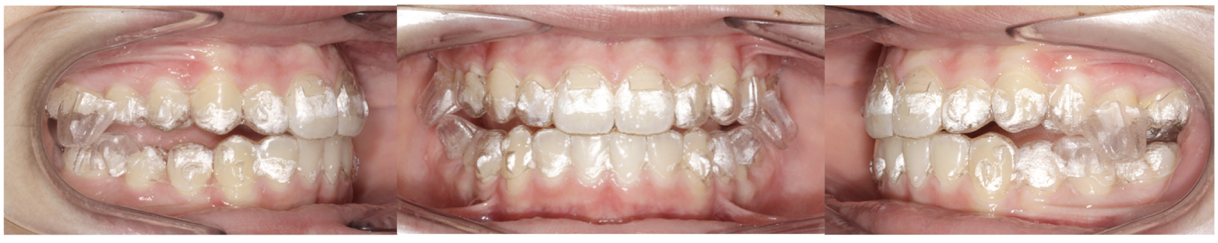

FIGURE 2
Frontal and lateral views of a mandibular advancement (MA) appliance.

discrepancies in landmark placement were resolved through mutual agreement. A customized digitization regimen (Viewbox, version 4.0, dHAL Software, Kifissia, Greece) was created and utilized for the cephalometric evaluation.

The cephalometric measurements used were (Figure 3) (18, 19):

1) PNS-AD1: lower airway dimension; the distance between the Posterior Nasal Spine (PNS) and the nearest adenoid tissue measured through the PNS-Ba line (AD1).
2) AD1-Ba: lower adenoid size; defined as the soft tissue thickness at the posterior nasopharynx wall through the PNS-Ba line.
3) PNS-AD2: upper airway dimension; the distance between the PNS and the nearest adenoid tissue measured through a perpendicular line to S-Ba from PNS (AD2).
4) AD2-H: upper adenoid size; defined as the soft tissue thickness at the posterior nasopharynx wall through the PNS-H line (H, Hormion, located at the intersection between the perpendicular line to S-Ba from PNS and the cranial base).
5) McNamara's upper pharynx dimension: the minimum distance between the upper soft palate and the nearest point on the posterior pharynx wall.
6) McNamara's lower pharynx dimension: the minimum distance between the point where the posterior tongue contour crosses the mandible and the nearest point on the posterior pharynx wall.

Statistical analysis

The Fisher Exact test was used to compare gender distribution. Descriptive statistics and statistical comparisons between the TB and MA groups at T1 (starting forms) and for the T2-T1 inter and intra-group changes were assessed using Independent samples *t*-test, with the *P*-value set at $P \leq 0.05$.

Method error

Fifteen lateral cephalograms, randomly selected, were re-measured after a washout period of 2 weeks by the same operator (ECL). Intraobserver reproducibility was assessed with the intraclass correlation coefficient (ICC), while the method of moments' estimator (MME) was applied for assessing random error.

Results

The demographic data of the treated and the control groups are reported in Table 1. No significant between-group differences were found either for chronologic age at T1 ($P = 0.5797$), at T2

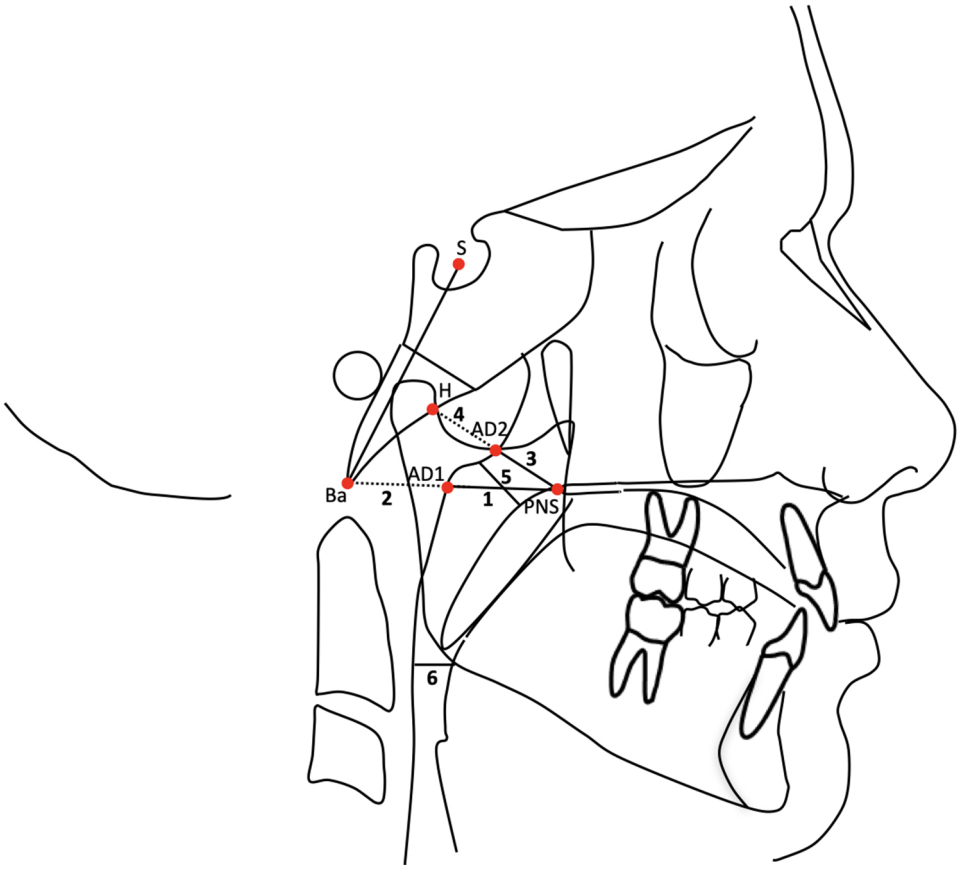

FIGURE 3
Cephalometric measurements for the analysis of airway dimensions.

($P = 0.7898$) and for gender distribution ($P = 1.000$). The duration of treatment was similar for both groups ($P = 0.0761$).

For each patient included in the present investigation, the Pediatric Sleep Questionnaire (PSQ) indicated a positive result for sleep-related breathing disorders before treatment.

The analysis of the starting forms showed no significant differences between groups for any airway measurements (Table 2).

The statistical comparison of the changes between T1 and T2 in the TB group (Table 3) showed a significant increment in upper airway size after active treatment (PNS-AD2, upper airway dimension; distance between the PNS and the nearest adenoid tissue measured through a perpendicular line to S-Ba from PNS: +1.50 mm + −3.30; McNamara's upper pharynx dimension, the minimum distance between the upper soft palate and the nearest point on the posterior pharynx wall: +2.21 + −4.21), no significant differences were found in lower airway size.

The MA group showed similar results during active treatment (T1-T2; Table 4), with a significant increase in both upper (PNS-AD2, upper airway dimension; distance between the PNS and the nearest adenoid tissue measured through a perpendicular line to S-Ba from PNS:+2.72 + −2.65; McNamara's upper pharynx dimension, the minimum distance between the upper soft palate and the nearest point on the posterior pharynx wall: +2.97 + −3.07) and lower (PNS-AD1, lower airway dimension; distance between the PNS and the nearest adenoid tissue measured through the PNS-Ba line: +2.17 mm + −3.54) airway size (Figure 4).

The statistical comparison of T2-T1 changes between the TB and MA groups showed no statistically significant differences for any airway analyzed measurements (Table 5).

At the end of the treatment, the children's parents again completed the same questionnaire and a significant reduction in diurnal symptoms was observed in all the treated patients.

TABLE 2 Descriptive statistics and statistical comparisons (independent-samples *t*-tests) of the starting forms (cephalometric values at T1).

Variables	TB (*n*: 22)		MA (*n*: 23)		Difference	*P*-value	95% CI of the difference	
	Mean	SD	Mean	SD			Lower	Upper
AD1-Ba	19.24	3.12	20.07	3.77	0.83	0.427	−1.19	2.85
AD2-H	14.94	1.87	15.00	3.52	0.06	0.944	−1.58	1.70
McNamara's lower pharynx	9.77	2.00	10.94	2.02	1.17	0.058	0.00	2.34
PNS-AD1	20.47	4.08	21.43	3.64	0.96	0.409	−1.30	3.22
PNS-AD2	15.70	2.98	15.69	3.17	−0.01	0.991	−1.81	1.79
McNamara's upper pharynx	10.20	2.80	11.47	1.82	1.27	0.077	−0.12	2.66

SD, standard deviation; CI, confidence of interval; $P < 0.05$.

TABLE 3 Descriptive statistics and statistical comparisons (independent-samples *t*-test) of the T2-T1 changes in the TB.

Variables	T1 ($n = 22$)		T2 ($n = 22$)		Difference	*P*-value	95% CI of the difference	
	Mean	SD	Mean	SD			Lower	Upper
AD1-Ba	19.24	3.12	18.45	3.96	−0.79	0.355	−2.371	0.791
AD2-H	14.94	1.87	13.39	4.03	−1.55	0.068	−2.943	−0.157
McNamara's lower pharynx	9.77	2.00	10.43	3.92	0.66	0.473	−0.720	2.040
PNS-AD1	20.47	4.08	21.58	6.00	1.11	0.416	−1.165	3.385
PNS-AD2	15.70	2.98	17.20	3.67	1.50	0.045*	0.018	2.982
McNamara's upper pharynx	10.20	2.80	12.41	5.06	2.21	0.022*	0.397	4.023

SD, standard deviation; CI, confidence of interval; $P < 0.05$.
Asterisks are used to indicate the level of significance associated with *P*-values in the results of statistical analyses; one asterisk (*) indicates a $P < 0.05$.

TABLE 4 Descriptive statistics and statistical comparisons (independent-samples *t*-test) of the T2−T1 changes in the MA.

Variables	T1 ($n = 23$)		T2 ($n = 23$)		Difference	*P*-value	95% CI of the difference	
	Mean	SD	Mean	SD			Lower	Upper
AD1-Ba	20.07	3.77	18.99	3.86	−1.07	0.110	−2.730	0.570
AD2-H	15.00	3.52	13.7	3.34	−1.3	0.206	−0.739	3.339
McNamara's lower pharynx	10.94	2.02	11.63	2.47	0.70	0.180	−0.286	1.666
PNS-AD1	21.43	3.64	23.60	3.79	2.17	0.008**	0.563	3.777
PNS-AD2	15.69	3.17	18.40	3.30	2.72	0.000***	1.311	4.109
McNamara's upper pharynx	11.47	1.82	14.43	3.22	2.97	0.000***	1.829	4.091

SD, standard deviation; CI, confidence of interval; $P < 0.05$.
Asterisks are used to indicate the level of significance associated with *P*-values in the results of statistical analyses; two asterisks (**) indicate a $P < 0.01$; three asterisks (***) indicate a $P < 0.001$.

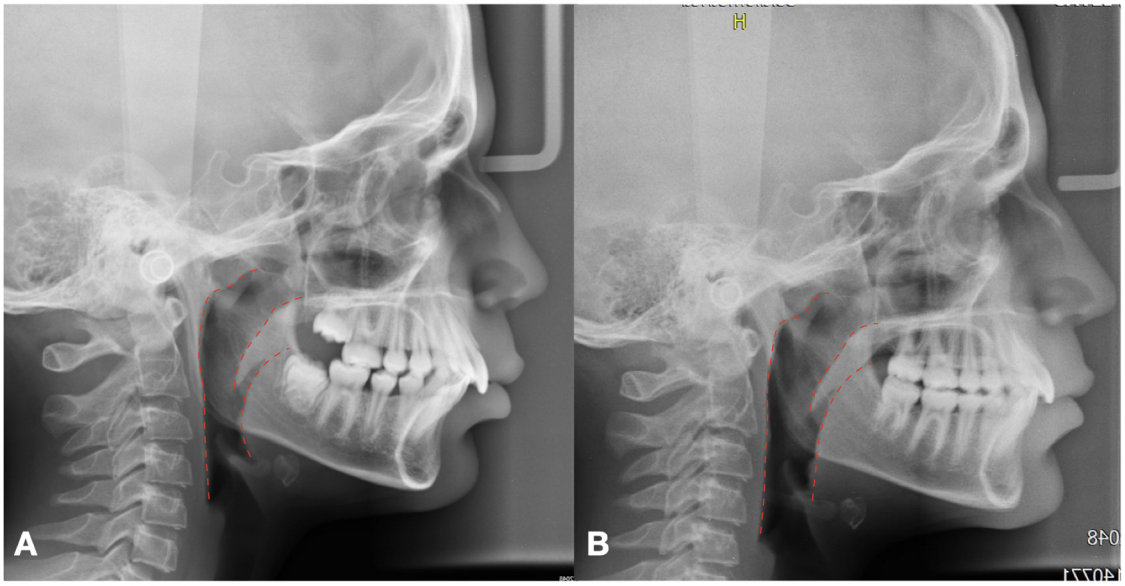

FIGURE 4
Increase of airway dimensions on Pre (A) and post (B) treatment lateral cephalogram.

TABLE 5 Descriptive statistics and statistical comparisons (independent-samples *t*-test) of the T2-T1 changes in the TB vs. the MA.

Variables	TB (*n*: 22)		MA (*n*: 23)		Difference	*P*-value	95% CI of the difference	
	Mean	SD	Mean	SD			Lower	Upper
AD1-Ba	−0.88	4.06	−1.07	3.10	−0.19	0.86	−2.31	1.93
AD2-H	−0.31	3.64	−1.30	2.63	−0.99	0.299	−2.89	0.91
McNamara's lower pharynx	1.25	4.59	0.70	2.41	−0.55	0.615	−2.71	1.61
PNS-AD1	1.46	5.66	1.27	3.05	−0.19	0.888	−2.86	2.48
PNS-AD2	1.36	4.18	2.34	2.81	0.98	0.359	−1.11	3.07
McNamara's upper pharynx	2.19	3.42	3.19	2.33	1.00	0.256	−0.72	2.72

SD, standard deviation; CI, confidence of interval; $P < 0.05$.

Discussion

Functional appliances are orthodontic devices designed to modify the position of the mandible and stimulate the growth. Nowadays, mandibular advancement is an orthodontic practice used not only to improve the sagittal skeletal relationship of growing patients, but also to treat respiratory disorders. Indeed, Mandibular advancement with functional appliances aims to reduce the obstruction of the upper airways, improving airflow during nocturnal breathing.

Several studies in literature analyzed the effects of different devices for mandibular advancement in increasing airway dimensions. For the existing literature, functional appliances have stronger scientific evidence supporting their effectiveness, with numerous papers confirming their efficacy (20–24).

On the contrary, very poor is the literature supporting the positive effects induced by Mandibular advancement with Clear Aligners on the sagittal airway dimension in growing patients (14).

Therefore, the objective of the present research was to compare the effects resulting from treatment with the MA and the TB given the differences in terms of material and advancement protocols. The TB appliance induces a maximum bite advancement in a single step, while with the MA the jaw shift incrementally forward. In the literature there are very conflicting opinions on which is the most effective advancement protocol. Nowadays there is greater scientific evidence in favor of incremental mandibular advancement in terms of mandibular response and increase in mandibular length. It is interesting to note that on the basis of our results, the different advancement protocol applied by these two devices did not produce differences in the improvement of airways dimension and SDB symptoms.

The results of the present study concluded that both TB and MA were able to induce an increasing of airway dimension. In particular TB group showed an improvement of the airway size mainly located in the upper adenoid tissue whereas MA patients showed a reduction of adenoid tissue both at upper and lower level.

As reported in literature, the reduction of adenoid tissue through the use of functional appliance occurs primarily by improving the patency of the upper airway. This enhancement

can decrease the hypertrophy of adenoid tissue caused by chronic obstruction. The main mechanism behind this phenomenon lies in the ability of functional appliances to advance the mandible and tongue, thereby increasing the airway space and reducing the likelihood of airway collapse during sleep (25, 26).

Mandibular advancement can result in a significant increase in the volume of the upper airway, including both the upper and lower oropharynx. However, the effect is often more pronounced in the superior adenoid tissue, which is directly involved in the obstruction of the upper airway. This is due to the increased airflow and the reduction of negative pressure that contributes to adenoid hypertrophy (25, 26).

Moreover, our results could be explained by a better management of inflammatory response of adenoid tissue performed with incremental mandibular advancement compared to single-phase maximum protrusion. Incremental advancement allows for gradual adaptation of the tissues, reducing the risk of excessive inflammation (27, 28).

According to our research, a study conducted by Iwasaki et al. demonstrated that the use of functional appliances can significantly increase the dimensions of the upper airways in patients with OSA. The results showed an increase in pharyngeal volume and a reduction in OSA symptoms, confirming the effectiveness of functional appliances in improving respiratory function (29–31).

A further study by Pavoni et al, published in 2017 found that the treatment with functional appliances produced significant favorable changes during active treatment in the oro- and nasopharyngeal sagittal airway dimensions in subjects with dentoskeletal Class II subjects when compared with untreated controls. The favorable changes obtained during T1-T2 interval were maintained in the long-term observation after puberty (22).

Aligners with an integrated mandibular advancement mechanism have been recently introduced, combining the benefits of invisible orthodontics with mandibular advancement to improve airways.

Similar to our study, the paper published by Yue et al. in 2023 compared the effects of Invisalign with mandibular advancement and Twin Block appliance. The cited study evaluates and compares the improvement of upper airway morphology and hyoid bone position in children with Class II mandibular retrusion treated with these two types of appliances, by means of cone beam computed tomography (CBCT) (14).

The authors, according to our results, found that both MA and TB appliances effectively improved the structural narrowness of the upper airway and reduced respiratory resistance, thus improving breath quality with a better comfort and adherence to treatment by patients with Invisalign system. However, in the study performed by Yue, MA showed more effectiveness in improving the narrowest part of the hypopharynx compared to TB (14).

In conclusion, mandibular advancement represents an effective strategy to increase airway dimensions with solid scientific base supporting the effectiveness of functional appliances. It is important to consider that studies on Invisalign MA are still limited and further research is needed to confirm its long-term effectiveness. Mandibular advancement with aligners offers advantages in terms of comfort and treatment adherence, but the high cost can represent a barrier for some patients.

The choice of the most appropriate device depends on the individual needs of patients, considering factors such as the severity of OSA, aesthetics, comfort, and costs.

It is fundamental to carefully evaluate these variables to provide the appropriate treatment for patients.

A primary limitation of this study is the small sample size, which should be increased in future research. Additionally, the absence of a control group and the short-term nature of the study are significant constraints. Having a control group is crucial as it allows for comparison against a baseline, thereby enhancing the validity of the results by isolating the effect of the intervention. Evaluating the long-term stability of the findings is also important to determine the persistence and durability of the observed effects, which would provide a more comprehensive understanding of the intervention's impact over time. Future studies will aim to overcome these limitations to validate the current results and assess their long-term stability.

Conclusions

Functional therapy performed with TB and MA produce the following:

- Despite the different structure of the analyzed devices and the different advancement protocols, both appliances were suitable treatment options for Class II patients with respiratory disorders, inducing an increase of the airway dimension and a significant reduction in diurnal symptoms in all patients;
- Patients treated with the TB appliance showed a significant improvement of airway dimension after active treatment mainly located in the upper adenoid tissue whereas MA patients showed a reduction of adenoid tissue both at upper and lower level probably as a consequence of a better adaptation of the tissue to incremental advancement.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by Ethical Committee of the Hospital of Rome "Tor Vergata" (Protocol number: 48/23). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or

the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

Author contributions

EC: Investigation, Writing – original draft, Writing – review & editing. LL: Formal Analysis, Resources, Software, Writing – original draft, Writing – review & editing. PC: Supervision, Validation, Visualization, Writing – review & editing, Writing – original draft. RL: Data curation, Formal Analysis, Methodology, Supervision, Validation, Writing – review & editing, Writing – original draft. SL: Conceptualization, Data curation, Resources, Writing – original draft, Writing – review & editing. CP: Methodology, Supervision, Validation, Visualization, Writing – review & editing, Writing – original draft.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/froh.2024.1463416/full#supplementary-material

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Avoid overstepping the bounds of evidence: the role of the orthodontist in managing pediatric Obstructive Sleep Apnea

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Introduction: Pediatric Obstructive Sleep Apnea (OSA) is a common sleep-related breathing disorder often linked to distinct craniofacial features and malocclusions. While orthodontic treatments, particularly maxillary expansion and mandibular advancement, have been suggested for managing this condition, the results remain controversial and are based on low-quality evidence. This paper aims to summarize the ongoing debates on this topic by reviewing relevant literature and highlighting the role of the orthodontist in diagnosing and managing OSA in daily clinical practice.

Discussion and conclusions: According to the present review, there is insufficient evidence to either confirm or deny the effectiveness of oral appliances for treating pediatric OSA due to significant methodological limitations, such as small sample sizes, inadequate control groups, short study durations, and a lack of long-term follow-up. Additionally, this condition cannot be diagnosed solely based on craniofacial morphology, but an interdisciplinary evaluation is strictly required. In addition, orthopedic treatment may be considered only as an adjunct therapy for children with craniofacial anomalies increasing the risk for OSA, and the combination of multiple therapeutic approaches may be necessary to achieve effective treatment outcomes.

KEYWORDS

airway, OSA, orthodontics, evidence, breathing disorder

1 Introduction

Obstructive Sleep Apnea (OSA) is a multifactorial breathing sleep disorder, consisting in partial or intermittent complete blockage of the upper airways during sleep, which affects about 1%–4% of children, with a slightly higher prevalence in males than in females (1). This causes a reduction or absence of airflow despite continuous respiratory effort and is usually associated with reduced peripheral oxygen saturation and hypercapnia (2). To date, several risk factors, such as adenotonsillar hypertrophy, obesity, neuromuscular tone, rostral fluid shifts, genetic diseases like Down syndrome, asthma and allergies have been identified. Moreover, since this condition has been associated with some craniofacial features (3–5), such as maxillary transverse deficiency, mandibular hypoplasia or retrusion, hyperdivergent skeletal pattern (6), some authors have promoted orthodontic treatment for the management of child breathing problems (7–9), however such results are quite controversial, and most studies are based on low

quality of evidence. Therefore, the aim of this paper is to summarize the current debates on this topic by reviewing relevant literature and highlighting the role of the orthodontist in diagnosis and management of OSA in daily clinical practice.

2 OSA and orthodontics

In 2019 because of the controversial role that dentistry and particularly orthodontics played in the diagnosis, management, and treatment of OSA and airway problems, the American Association of Orthodontists taskforce published a white paper on OSA and orthodontics (10). The main point from this paper was, "Orthodontists should not assume responsibility for the definitive diagnosis of OSA." Dental professionals can assume a screening role such as the use of the STOP-Bang questionnaire for adults and the Pediatric Sleep Questionnaire (PSQ) for children since the diagnosis of OSA in children is confirmed by the gold standard PSG (polysomnography). Therefore, the definitive diagnosis is appropriately made by a physician.

At least four relatively recent narrative reviews addressed the OSA debate (11–14). Rinchuse (12) challenged the "airway friendly" orthodontic movement from an evidence-based perspective and suggested that studies should explore the sources and reasons for misinformation being circulated to dental and orthodontic practitioners, and even patients. Kazmierski (14) emphasized the role of the orthodontist as screening for obvious OSA signs and symptoms and if necessary to make appropriate referral to a physician. To emphasize that the diagnosis and treatment of OSA is a medical condition, not dental, Kandasamy factiously added, "If our colleagues want to play medical doctor, then they should consider going to medical school. If our colleagues want to carry out orthodontic treatment to treat medical problems based on anecdotal claims and beliefs unsubstantiated by the evidence, such as expansion and growth modification at all costs, then this is not only unethical but grossly misleading to the public."

The recent American Academy of Dental Sleep Medicine (AADSM) consensus panel of 12 experts reviewed literature relating to numerous therapies for OSA and snoring in both adults and children (15). This consensus paper is believed to be the first to evaluate novel therapies in both children and adults. Modalities of interventions reviewed were: myofunctional orthodontics, expansion for maxillary constriction, myofunctional therapy for tongue motor immaturity, lingual and buccal releases for tethered tissue, ablative and nonablative lasers for elongated or edematous soft palate and adjacent tissue, and extractions. There was agreement among panelists that none of the reviewed therapies were considered appropriate as first-line single therapies. They however may be appropriate as possible secondary, tertiary, or rescue options. Limitations of this paper were mentioned as well as the requirement for additional long-term RTCs with larger sample sizes.

The contretemps regarding OSA and airway parallels the early controversy concerning the diagnosis and treatment of TMDs (Temporomandibular Disorders), which centered on a dental, occlusal, gnathological, and jaw function philosophical perspective. Now the definition of TMD has involved into a more complex disorder as a group of muscular and neuromuscular conditions that include the muscles of mastication, the TMJ, and associated structures. From an evidence-based perspective TMDs are now viewed from a medical and biopsychosocial perspective (16). Likewise, OSA is more complicated and multifactorial in etiology. Adenotonsillar hypertrophy, neuromuscular tone, obesity, rostral fluid shifts, genetic predisposition influencing craniofacial anatomy and other related factors account for etiologies. In particular, adenotonsillar hypertrophy, which typically occurs during the period of significant lymphoid tissue growth, between the ages of 8 and 10, is recognized as the leading cause of sleep-disordered breathing (SDB) in children (17). Also obesity is considered an independent risk factor for the onset and progression of sleep-disordered breathing (17), while a reciprocal interaction between Pediatric OSA and asthma has been reported, whereby each disease impacts the severity of the other (18). In addition to risk factors, collapsibility of the upper airway is influenced further by OSA severity, which is heterogeneous among patients with the disorder. Pediatric OSA can be generally categorized into mild [AHI or respiratory disturbance index (RDI) between 1 and <5 events per hour], moderate (AHI between 5 and <10 events per hour), and severe (AHI ≥10 events per hour). This wide range of presentation leads to variations in management approach and differences in treatment response (10).

Even though impaired neuromuscular tone is a more valid assessment of OSA than airway volume (10), airway volume still seems to be the focus of some contentious groups and individuals for the management and treatment of OSA. For instance, maxillary expansion in the transverse dimension and advancement of the maxilla and/or mandible in the sagittal is recommended for increasing airway volume whereas orthodontic extractions are condemned for reducing airway volume and causing harm.

Recently there have been claims even for maxillary expansion in children as early as 3 years of age (19). This advocacy for early expansion has been dispelled by both Rinchuse (12) and Kandasamy (13). Rinchuse argued that caution should be advised, especially aggressive treatment for young children, without high quality investigations and particularly "long-term follow-up." Therefore, when evaluating expansion, or craniofacial growth modification claims for pre-school children relative to airway development and decrease in the size of enlarged adenoids and palatine tonsils, it is imperative to consider long-term maintenance and stability. Successful short-term outcomes may have relative statistical significance, but no clinical significance, and no long-term stability and pertinence. For instance, as Lyle Johnston argued it may be a "mortgage on growth" like ostensibly successful early Class II Phase I treatments (20). Meaning there is a temporary effect that is paid back later with no overall net gain. Or a "Soft Tissue Paradigm" (21) in which the stability of results is related primarily to soft tissue pressure and equilibrium effects, with relapse seen years later, like very young children outgrowing treatment. Finally, the American Academy of Dental Sleep Medicine (AADSM) consensus panel concluded that maxillary constriction is not a factor that contributes to pediatric OSA. "There was insufficient

evidence to support RME as a treatment to cure pediatric OSA and stressed that expansion should only be considered in those patients who demonstrate maxillary constriction, independent of having pediatric OSA" (15). In addition, extractions were evaluated as to whether they decrease airway and tongue volume leading to pediatric OSA. The overall conclusion was that extractions in children are not a risk factor for OSA. Malocclusion and craniofacial morphologies identified as predisposing for OSA and airway problems include "retrognathia, long and narrow faces, dolichocephalic facial type, narrow and deep palate, steep mandibular plane angle, anterior open bite, midface deficiency, and lower hyoid position. It should be noted, however, that the strength of the relationship between these craniofacial morphologies and the development of OSA is not well established" (10).

Functional appliances have been advocated as useful in the treatment of breathing sleep disorders, however, while mandibular advancement has shown some benefits in treating primary snoring (22) and mild-to-moderate Obstructive Sleep Apnea (23) in adults, the situation appears more complex in pediatric patients. Currently, there is no robust, evidence-based support for its benefits in children, if compared with adenotonsillectomy (AT), which remains the first-line therapy for pediatric OSA (24). Notably, no studies have demonstrated that functional appliances are superior to AT in children with an Apnea-Hypopnea Index (AHI) >10 (15).

Furthermore, while the persistence of sleep-disordered breathing after surgery has been linked to pre-existing craniofacial characteristics that contribute to a reduced upper airway size (25, 26), a clear cause-and-effect relationship has not been firmly established (27). In fact, systematic reviews (28–32) indicate that due to strong limitations such as small sample sizes, inadequate control groups, short study durations, and a lack of long-term follow-up, there is insufficient evidence to either confirm or refute the effectiveness of oral appliances for treating pediatric OSA. Moreover, although some studies reported the reduction of at least 50% in respiratory events in compliant patients, this treatment alone does not guarantee a cure for OSA (AHI <1 event/h) and the conclusion was, "It may be necessary to combine therapies to achieve a cure" (28).

While most research has focused on mandibular advancement, few papers have evaluated the effect of maxillary protrusion. The conclusion of a systematic review and meta-analysis on this topic indicated that "maxillary protraction appliances can only increase pharyngeal airway dimensions in the short term" (33). Unfortunately, analyzing changes in posterior airway space through 2D or 3D radiography is insufficient for evaluating OSA, as it lacks pre- and post-intervention AHI data and does not accurately reflect the supine sleep airway anatomy due to altered physiological states and head positions (15). Accordingly, OSA cannot be confirmed by craniofacial morphology alone and, based on current scientific evidence, orthopedic treatment might be considered in specified cases as an auxiliary treatment for children with craniofacial anomalies that are risk factors for OSA, but combining multiple therapies might be necessary to achieve successful treatment outcomes.

Nevertheless, orthodontists should be well-versed in the signs and symptoms of Obstructive Sleep Apnea (OSA) and capable of conducting clinical risk assessments for the condition. It is highly recommended that orthodontists refer patients who may be at risk to a qualified physician for a definitive diagnosis (10). In cases where a physician identifies a skeletal discrepancy contributing to pediatric OSA, orthodontists may play a key role in treatment if the patient is referred back to them for intervention.

3 Discussion and conclusions

This paper has provided a concise, provocative review of OSA and airway problems particularly in children. Regrettably knowledge alone may have little impact on changing attitudes and certainly not behaviors. Biases and misconceptions are still pervasive in medicine and dentistry (34). Maybe even in the health sciences, it may be as Cavett Robert (35) pointed out in reference to social proof that, "95% of people are imitators and only 5 percent initiators, people are persuaded more by the actions of others than any proof we can offer." Adherence to unproven claims can have serious health related consequences such as increased burden of care (time, finances, extended treatments), and inappropriate and unnecessary treatments. As dentistry and orthodontics move closer to being as an evidence-based health care profession, we may observe less ambiguity, confusion and uncertainty.

Based on the above considerations, the following conclusions can be drawn:

- The diagnosis of OSA in children is confirmed by the gold standard PSG (polysomnography) and by a physician.
- Dental professionals and orthodontists may have a supporting role to screen for OSA.
- Airway volume is not a reliable and valid assessment tool for the diagnosis of OSA.
- Maxillary expansion solely for OSA is inappropriate.
- Extractions in children are not a risk factor for OSA.
- Malocclusion and craniofacial morphologies may be associated with OSA and airway problems, but not a cause and effect.
- An interdisciplinary approach to treating Obstructive Sleep Apnea (OSA) ensures that patients receive the most comprehensive and effective care.

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Evaluation of sleep position shifts in patients with obstructive sleep apnea syndrome with the use of a mandibular advancement device

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Background: The aim of this study was to evaluate position shifts during sleep of patients with obstructive sleep apnea (OSA) syndrome both with and without the use of a mandibular advancement device (MAD).
Methods: In total, 73 adult Caucasian patients diagnosed with obstructive sleep apnea syndrome confirmed by polysomnography were retrospectively enrolled. Inclusion criteria were as follows: age >20 years, body mass index <34 kg/m^2, polysomnographic diagnosis of OSA, non-smoker, absence of comorbidities at diagnosis, and treatment with a MAD. Two polysomnographic monitoring were performed: one at the time of diagnosis (T0) and another after 3 months of treatment (T1). The parameters evaluated were the apnea-hypopnea index, oxygen desaturation index, the total number of position shifts, and position shift index (number of shifts per hour). Since the variables failed the normality test, the Wilcoxon test was performed to analyze the correlation between the mean of polysomnographic parameters at T0 and T1. The difference between the T1 and T0 values for each variable was evaluated using Spearman's rho correlation test. Statistical significance was set at $p < 0.05$.
Results and conclusions: All the parameters, including respiratory and positional measures, were significantly reduced after the use of a MAD compared to the beginning. Spearman's correlation test revealed a relationship between the total number of sleep position shifts and the sleep position shift index with the oxygen desaturation index. However, no significant correlation was observed between the apnea-hypopnea index and the positional values.

KEYWORDS

obstructive sleep apnea (OSA), apnea-hypopnea index (AHI), oxygen desaturation index (ODI), sleep position shifts, mandibular advancement device (MAD)

1 Introduction

Obstructive sleep apnea syndrome (OSAS) is a sleep-related breathing disorder characterized by repeated episodes of partial or total obstruction of the upper airway during sleep, thus leading to phenomena defined as hypopnea and apnea. An apnea episode, by definition, is the cessation of breathing for at least 10 s. Hypopnea is defined as a reduction in airflow of at least 50%, associated with a reduction in oxygen saturation of >4%. The apnea-hypopnea index (AHI), i.e., the total number of hypopneas and apneas per 1 h of sleep, is used to indicate the severity of obstructive

sleep apnea (OSA). There are different categories of sleep apnea depending on the OSA index: normal sleep has an AHI of fewer than 5 events, mild sleep apnea has an AHI of 5–15 events, moderate sleep apnea has an AHI of 15–30 events, and severe apnea has an AHI of more than 30 events per hour (1–3).

1.1 Epidemiology

The prevalence of OSA is approximately 22% in men and 17% in women with a gender distribution of 2:1 (4). This distribution is perhaps related to different hormonal effects that induce an increase in upper airway muscle collapsibility, body fat distribution, and different anatomy. Hormonal effects have an important role in OSA pathogenesis, particularly in post-menopausal women compared to pre-menopausal women. Unfortunately, the role of hormones in OSA pathogenesis is still unclear (5).

1.2 Comorbidities

Obstructive sleep apnea syndrome is becoming an increasingly studied condition because of its many comorbidities and consequences, although there is a high prevalence of undiagnosed and untreated patients (6). Because of sleep deprivation and daytime sleepiness, patients with OSA have a higher risk of car accidents (7). Cardiovascular disease is correlated with OSA, with sympathetic activation, oxidative stress, and systemic inflammation defined as the main causes of this association. OSA is an independent risk factor for hypertension, coronary artery disease, heart failure, cardiovascular and cerebrovascular diseases (CVDs), and atrial fibrillation (8, 9). OSA is related to many metabolic complications such as type 2 diabetes mellitus (T2DM) (10). The prevalence of T2DM in patients with OSA is higher than in the general population (11). Current research suggests that arousals and sleep fragmentation may have effects on systemic inflammation, sympathetic surges, glucose intolerance, β-cell dysfunction, and insulin resistance (12). Narkiewicz et al. (13) suggested an alternative way to explain the relationship between T2DM and OSA. Oxyhemoglobin desaturation and hypercarbia may alter epinephrine, norepinephrine, and cortisol secretion, which leads to increased gluconeogenesis and decreased glucose uptake.

1.3 Symptoms and diagnosis

Sleep fragmentation in patients with sleep apnea can also lead to neurocognitive and behavioral consequences (14, 15). Although there are questionnaires and several risk factors (age >40 years, male sex, obesity, smoking) and symptoms (snoring, nocturia, nocturnal gasping, daytime sleepiness) to identify patients with obstructive sleep apnea, the diagnostic standard to diagnose the condition is nocturnal polysomnography (16, 17). OSA is evaluated by many questionnaires that focus on daytime sleepiness and health-related quality of life (HRQoL) (18, 19). The Epworth Sleepiness Scale (ESS) and the STOP-Bang and Berlin questionnaires are the main questionnaires used to evaluate daytime sleepiness (20, 21). Other questionnaires investigate the HRQoL of patients with OSA [i.e., short form 36 health survey questionnaire (SF36), short form 12 health survey questionnaire (SF12), sleep apnea quality of life index (SAQLI), functional outcomes of sleep questionnaire (FOSQ), and OSA wellness scale (OWS)] (22). A complete overnight sleep test, i.e., polysomnography (PSG), is conducted to evaluate OSA severity. PSG evaluates at least seven different physiological signals. PSG is the "gold standard" in objective-based sleep studies. There are four levels of sleep studies:

1. Type 1: full attended polysomnography (≥7 channels) in a laboratory setting;
2. Type 2: full unattended polysomnography (≥7 channels);
3. Type 3: limited channel devices (usually using 4–7 channels);
4. Type 4: 1 or 2 channels, usually with oximetry as one of the parameters (23).

The home sleep apnea test (HSAT) is the most frequently used test to reduce the patient's discomfort and provide the most effective evaluation of OSA. The HSAT is a type 3 level of evaluation and gives information to screen the patients in aspects such as oximetry, respiratory monitoring [(a) effort, (b) airflow, (c) snoring, (d) end-tidal CO_2, and (e) esophageal pressure], cardiac monitoring [(a) heart rate or heart rate variability and (b) arterial tonometry], measures of sleep-wake activity [(a) electroencephalography and (b) actigraphy], body position, and other (24).

1.4 Treatment

Continuous positive airway pressure (C-PAP) is the first-line treatment for patients with obstructive sleep apnea. It is a non-invasive treatment method used to maintain airway patency by delivering constant airway pressure. Other alternative methods, such as oral appliances, are also used in patients with apnea, especially for those who do not tolerate the C-PAP mask. Surgery is only used in cases with anatomic obstructions that need to be corrected (25). The oral appliances used are tongue retainer devices (TRDs) and mandibular advancement devices (MADs). A TRD is made of a flexible material with a bulb-like receptacle in the anterior portion. It maintains the tongue in a forward position during sleep, reducing stress on the upper airway and against the posterior pharyngeal wall (26). A MAD has been recommended by the American Academy of Sleep Medicine as a treatment for mild to moderate OSA (27). Some studies suggest that it also has an excellent effect on severe apnea. A MAD is a device with important advantages: low cost, simple production, and portability (28). The effect of a MAD is to increase the upper airway space through a forward and vertical movement of the jaw along with a repositioning of the hyoid bone and tongue (29). A MAD is built as two occlusal splints, fully covering the teeth, allowing for an increase in mandibular sagittal movement and free vertical/transversal movement of the jaw (30). The role of the dentist is becoming increasingly important for both the diagnosis and treatment of snoring and obstructive sleep apnea (31).

1.5 Research aim

It is well-known that obstructive sleep apnea causes restless sleep, tossing and turning, circadian misalignment, and daytime sleepiness. Therefore, sleep deficiency and poor sleep quality are closely linked to OSA (32, 33). OSA is associated with several other sleep disorders (e.g., insomnia and restless legs) and sleep-related problems [e.g., excessive daytime sleepiness (EDS)] (34).

In the International Classification of Sleep Disorders second edition (ICSD-2), the IV group describes the most common symptoms of dyssomnias (insomnia and EDS) and parasomnias (abnormal physiological events) such as sleep-related movement disorders (SRMDs), restless legs syndrome, periodic limb movement disorder, sleep-related leg cramps, and sleep-related bruxism (35). Sleep-related movement disorders involve characteristic body movements that alter sleep. When these disorders coexist, there is an increase in cumulative morbidity, and they are likely to negatively affect each other (36).

Sleep position has already been associated with sleep apneas, defined in most studies in the literature as an increase in AHI in the supine position, later coming to define positional apneas and subsequent positional therapy (37). Restless sleep, however, and constant position changes have been less investigated in the literature, except for the association with other types of pathologies.

A modification of nervous activation may be correlated to the night shifts in sleep time, as documented during the periodic limb movements during sleep (PLMS) and other SRMDs. PLMS are repetitive, stereotypical limb movements that can lead to arousals and sleep fragmentation. PLMS are also more prevalent among patients with OSA than in the general population (38). PLMS are strongly associated with increased sympathetic activity. The correlation between the PLMS and sympathetic activation is still debated (39). The sympathetic activation may be due to PLMS-triggered arousal. It is well-known that sympathetic activation is correlated to blood pressure, vascular inflammation, hypercoagulation, and dyslipidemia (40, 41).

Khan hypothesized that an increase in position shifts during sleep (PSDS) may be correlated with a modification of the nervous system activation, as PLMS and SRMD treatment with a reduction of movement is correlated with a reduction of sleep arousals and cardiorespiratory efforts (42). The effects of oral treatment on OSA and SRMDs are still a controversial issue. Bariani et al. (43) showed that rapid maxillary expansion (RME) treatment had effects in children with OSA and PLMS. Other research studies have tried to evaluate the effects of a MAD on PLMS. The effect of a MAD on PLMS was to reduce the body movement events, similar to C-PAP treatment (44). In the present paper, the authors evaluated the effect of MAD treatment on patients with mild to severe OSA, focusing on cardiorespiratory effects [i.e., AHI and oxygen desaturation index (ODI)] and position shifts during sleep. The frequency of position shifts during sleep may be correlated to stress during sleep caused by the number of apnea events and oxygen desaturation. Using the HSAT, the present study aimed to investigate the correlation between position shifts during sleep caused by OSA and their modification due to treatment with a MAD.

2 Materials and methods

2.1 Study population

This study was reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational studies (45). This retrospective study involved 73 adult Caucasian patients (43 men and 30 women; mean age 46 ± 4 years) selected from patients with OSA treated at the Department of Orthodontics, University of Foggia, Italy. All patients consented to be included in the present research. Patients were selected using the following inclusion criteria: age >20 years, body mass index <34 kg/m^2, diagnosis of OSA by nocturnal polysomnography, absence of comorbidities at the time of diagnosis, non-smoker, treatment with a mandibular advancement device, and treated from February 2021 to March 2023. All the procedures described in the present research protocol adhered to the Declaration of Helsinki (1975) (and the subsequent revisions) and were approved by the Ethics Committee of the University of Foggia (Approval no. 43/CE/2019) and all patients gave their informed consent to participate. A power analysis (G*Power 3.1.9.2, Franz Faul, Universitat Kiel, Germany) revealed that to detect a large effect size of 0.5 (46) with the Wilcoxon signed-rank test, an α error probability of 0.05, and a power (1 − β error prob) of 0.95, 47 participants would be needed.

2.2 Methods and parameters

All patients underwent drug-induced sleep endoscopy (DISE) to assess their upper airway closure type and position. A split-night polysomnogram test (SN-PSG) was conducted in a sleep laboratory for each patient before treatment (T0) using a type 2 portable device (Embletta X-100 system, Flaga, Reykjavik, Iceland) that recorded electroencephalograms, electrooculograms, electromyograms, pulse oximetry channels, abdominal respiratory effort bands, body position sensors, nasal cannulas, and oral thermistor. Another SN-PSG was conducted after 3 months of treatment with a mandibular advancement device (T1). The parameters extracted from the night records were the following: AHI, ODI, the number of position shifts (NPS), and the position shifts index (PSI) (Table 1).

ODI was calculated based on oxygen desaturation being lower than 3%, as recommended by the American Academy of Sleep Medicine (47).

TABLE 1 Description of the indices recorded during the overnight polysomnography.

Polysomnographic evaluation	Description
AHI	Number of apnea and hypopnea events per hour of sleep
ODI	Number of oxygen desaturations
NPS	Number of sleep body movements
PSI	Number of sleep body movements/hour

The primary outcome of the study was to evaluate changes in polysomnographic indices and positional shifts after treatment with a MAD. The secondary outcome was to analyze the correlation between positional changes and polysomnographic indices.

The device used was a customized and adjustable device called IMYS (It Makes You Sleep), ideated by Professor D. Ciavarella (Figures 1, 2). It consists of two resin splints connected by two vertical stainless-steel bars and two lateral screws, and the inclusion of these components facilitated the adjustment of mandibular advancement. The design of the vertical arms had a top end that fitted into a vertical space (mesial to the screw) set in the resin of the upper splint, and a bottom end incorporated in the resin of the lower splint. These arms allowed a slight vertical mandibular movement, preventing a full mandibular opening. Moreover, the vertical space in which the upper arm was set, enabled slight lateral movements for the mandible. To enhance the tongue's position, a vertical palatal spot was added to the upper splint (29). A functional mandibular evaluation was conducted on each patient. An irreversible hydrocolloid material (Orthoprint Zhermack®) was used to take the impressions of both the upper and lower arches of each patient, employing non-perforated Rim Lock trays. Cast models were generated through impressions using high-strength type IV dental stone (such as Fujirock, Vel-Mix, and Suprastone), and these models were subsequently mounted on an articulator. An initial advancement of 70% of the total was established for each patient using an intraoral gauge (Occlusion®, Nonrusso+®, Dr. Giuseppe Burlon, Belluno, Italy) (Figure 3). The occlusion gauge (OG) features a millimetric grid for assessing sagittal mandibular shifts, along with engravings for both upper and lower incisors. The lower part of the gauge was designed to allow for sagittal movement. Before recording the effective mandibular protrusion, patients were instructed to move their jaw forward and backward. An initial advancement of 70% of the total mandibular movement, both backward and forward, was applied. The occlusion position with 70% activation using Occlufast [Zhermack Spa, Via Bovazecchino, 100–45021 Badia Polesine (RO), Italy] was then recorded. Every 2 weeks, the MAD was adjusted in increments of 0.25 mm to achieve the most functional and comfortable position for the patient.

Patients used the device overnight for at least 8 h.

2.3 Statistical analysis

Data distribution analysis was conducted using the Shapiro–Wilk normality test. Descriptive statistics were also performed. Because the variables failed the normality test, a Wilcoxon signed-rank test was used for comparison of the polysomnographic parameters taken at T0 (pre-treatment) and T1 (3 months after treatment). Spearman's rho correlation test was performed to assess the relationship between the

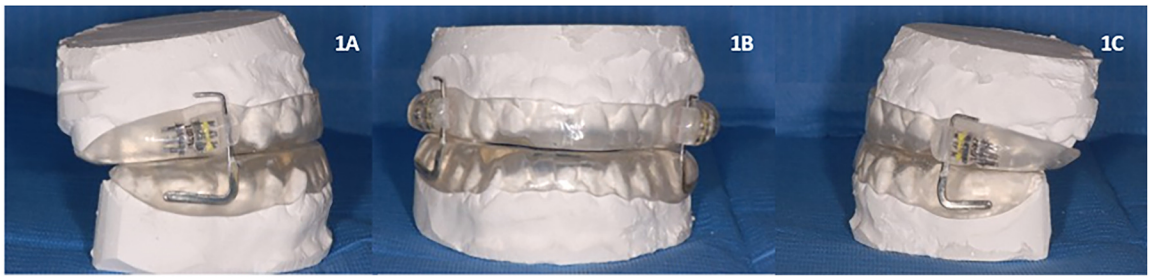

FIGURE 1
IMYS device (It Makes You Sleep). **(A)** Right lateral view, **(B)** frontal view, and **(C)** left lateral view.

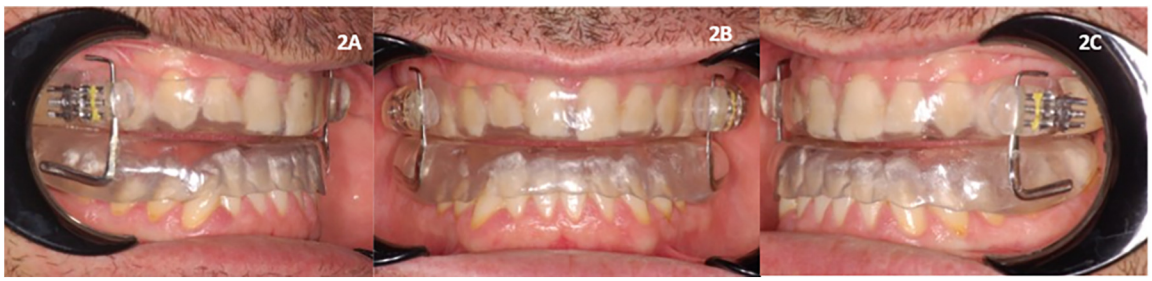

FIGURE 2
IMYS device (It Makes You Sleep) in a patient's mouth. **(A)** Right lateral view, **(B)** frontal view, and **(C)** left lateral view.

FIGURE 3
The OCCLUSION® device was used to register the ideal mandibular protrusion and to transfer the desired mandibular position to the dental laboratory for the manufacturing the MAD device.

polysomnographic variables at T1 and T0. The significance index was set to $p < 0.05$. Data were analyzed using GraphPad Prism software 6.0 (GraphPad Prism Software, San Diego, CA, USA).

3 Results

Table 2 shows the polysomnographic data distribution of all variables before and after MAD treatment. The patients had mild OSA overall (mean AHI 25.2 e/h and mean ODI 18.8 e/h). The mean NPS was 479.2 and the mean PSI was 69.56 (Table 2). Following MAD treatment, a reduction of both the AHI (−16.36 e/h, $p < 0.01$) and ODI (−9.556 e/h, $p < 0.01$) was observed (Table 2).

After MAD treatment, a decrease in the number of sleep shifts was observed, with NPS decreasing by −402.5 ($p < 0.01$) and PSI decreasing by −58.35 ($p < 0.01$) as indicated in Table 2.

The authors evaluated the correlation between NPS and PSI (difference between T1 and T0) with the AHI and ODI (T1 and T0). The test demonstrated that the reduction in the ODI was correlated with both NPS (rho 0.447 NPS to ODI, $p < 0.01$) and PSI (rho 0.416, $p < 0.01$). No statistical correlation between positional indicators (i.e., NPS and PSI) and the AHI was observed (NPS to AHI: rho 0.216, p = n.s.; PSI to AHI rho 0.182, p = n.s.) (Table 3).

4 Discussion

Recently, OSA has increasingly attracted interest because of its serious health impact, particularly the association between obstructive sleep apnea and increased cardiovascular risk. OSA has been defined as an independent risk factor for hypertension, stroke, coronary artery disease, heart failure, and arrhythmias (8, 9, 48). Moreover, there is much evidence supporting the association between OSA and metabolic disorders such as diabetes and impaired glucose control (12, 49, 50). In addition, repeated arousals and sleep fragmentation can lead to neurocognitive and mood deterioration including depression and anxiety (51). Daytime sleepiness may affect daily activities by reducing performance and causing occupational accidents, injuries, and car accidents (7, 52). In this context, the treatment of obstructive sleep apnea becomes crucial for the patient's health. Although C-PAP is still the treatment of choice for sleep apnea therapy, the use of mandibular advancement devices is increasingly common. A MAD ensures mandibular protrusion to keep upper airways open during sleep, improving oxygenation; reducing the number of apneas, hypopneas, and arousals; and improving the associated subjective and objective symptomatology (30, 53). Therefore, there is substantial evidence demonstrating the efficacy of these devices. The present study highlighted a new feature of MADs: the ability to reduce the number of shifts during sleep. Sleeping position and body posture are closely linked to the occurrence and severity of sleep apnea (54, 55). The body's nocturnal movements are linked to brain arousal. Nevertheless, it remains unclear whether the number of position shifts during sleep can influence arousals and daytime quality of life (22). Zhang et al. (56) monitored 13 subjects, without sleep disorders, using a sleeping-position monitoring device to determine the impact of sleeping positions and turning shifts on sleep quality. They found that patients with a higher turning frequency had poor sleep quality. De Koninck et al. (57) agreed with one of the initial studies on sleep and body position conducted by the Health Physics Society (58), finding that poor sleepers had more frequent position changes during sleep compared to good sleepers, who spent more time in the same position. The present study correlates the high number of position shifts during sleep in patients suffering from apnea with OSA severity. Although it is common to change positions several times during sleep, the number of shifts appears to vary among individuals and differs among specific groups. According to Skarpsno et al. (59), the number of shifts during sleep is higher in young people than in

TABLE 2 Descriptive statistics, normality test, and Wilcoxon signed-rank test for polysomnographic variables ($n = 73$) before treatment with a MAD (T0) and after treatment (T1).

Descriptive statistics	AHI T0 (e/h)	AHI T1 (e/h)	ODI T0 (e/h)	ODI T1 (e/h)	NPS T (events)	NPS T1 (events)	PSI T0 (e/h)	PSI T1 (e/h)
Mean	25.2	9.30	18.8	7.10	479.2	73.88	69.56	12.18
Std. deviation	11.4	10.7	10.0	9.98	111.8	171.8	80.73	17.93
Median	23.6	6.05	18.7	3.50	108.0	13.85	39.50	5.95
Lower 95% CI of the mean	21.0	5.43	15.2	3.51	76.20	11.95	40.45	5.71
Upper 95% CI of the mean	29.3	13.1	22.5	10.7	882.2	135.8	98.67	18.64
Difference	−16.35		−9.556		−402.5		−58.35	
p-value (Wilcoxon test)	**		**		**		**	

**$p < 0.01$.

TABLE 3 Spearman's rho correlation test between the patient's sleep movement and the polysomnography indexes ($n = 73$).

Variables	NPS	PSI	AHI	ODI
NPS		0.975°	0.216°	0.447**
PSI	0.975°		0.182°	0.416**
AHI	0.216°	0.182°		0.767°
ODI	0.447**	0.416**	0.767°	

°n.s., **$p < 0.01$.

older people. In addition, women experience fewer nocturnal movements compared to men, and a high BMI is associated with fewer shifts in sleep position. Skarpsno et al. reported an average number of 1.6 position shifts per hour, with 1.77 in men and 1.36 in women. The mechanisms underlying the frequency of positional changes during sleep are not fully understood. Tossing and turning generally occur during "arousals". It 's possible that cortical signals swiftly transition from the sleep state to waking actions, causing the person to change positions and resume sleep without remembering the position shift. Sleep fragmentation is a common condition in sleep breathing disorders such as OSA (17). On the one hand, arousal is an important lifesaving mechanism to overcome narrowing and stabilize breathing, but, on the other hand, it is associated with increased activity of the sympathetic nervous system (60). PLMS is a movement disorder that causes repetitive and involuntary arm movements during sleep.

This disorder is commonly linked to other conditions such as Parkinson's disease and narcolepsy. In such cases, it is referred to as secondary PLMDS. However, at times, it is not associated with other diseases and has no known cause, leading to its classification as primary PLMDS. The literature indicates that patients with OSAS often suffer from PLMS. The mechanisms have not yet been fully discovered; an over-activation of the sympathetic system is likely an underlying factor. However, OSAS patients with PLMS tend to be older, have shorter rapid eye movement (REM) duration, and have a higher AHI (60). All these characteristics of patients with OSA may be predisposing factors for restless sleep and an increased number of sleep positions. Consequently, sleep quality in OSA patients also seems to be associated with the number of position changes during sleep.

The number of sleep movements may impact patients' sleep quality, directly affecting their quality of life and cardiovascular function. The authors evidenced how OSA led to significant changes in patients' nightly body positions, which were correlated with their ODI. This aspect needs further clarification due to its potential relevance to factors such as daytime sleepiness, nocturnal agitation, and heart rate modifications.

4.1 Limitations of the study

The limitation of this study is due to the retrospective nature of patient recruitment, although care was taken to avoid any selection bias thanks to the use of a rigid chronological criterion. Due to the retrospective nature of this study, it is difficult to understand which other unanalyzed variables might have influenced the relationship between the polysomnographic variables and the MAD effects. Since only one type of MAD was used, the results obtained could differ if other devices were used. Future studies should implement a longitudinal case–control design and a long-term follow-up.

5 Conclusions

In the present paper, the authors showed how MAD treatment may modify the severity of OSA by reducing polysomnographic parameters (i.e., AHI and ODI). In addition, a mandibular advancement device has the capability to decrease the number of positional shifts during sleep, resulting in an improved quality of sleep.

In this paper, the reduction of respiratory effort events was correlated with a decrease in patient night shifts. The conclusions regarding patients with OSA treated with a MAD are as follows:

- a reduction in the AHI and ODI;
- a reduction of NPS and the PSI;
- a statistical correlation between the reduction of the ODI and NPS;
- a statistical correlation between the reduction of the ODI and PSI.

Position shifts are yet another consequence of the poor sleep quality experienced by patients with sleep apnea and a MAD may be the key to achieving restorative sleep.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the Ethics Committee of the University of Foggia (approval number 43/CE/2019). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

DC: Conceptualization, Data curation, Writing – original draft, Writing – review & editing. DF: Conceptualization, Data curation, Writing – original draft, Writing – review & editing. CF: Formal analysis, Writing – review & editing, Data curation. GM: Data curation, Writing – review & editing. GB: Data curation,

Investigation, Writing – review & editing. MLa: Methodology, Project administration, Writing – review & editing. LL: Project administration, Resources, Writing – review & editing. FE: Resources, Writing – review & editing. MT: Supervision, Validation, Writing – review & editing. MLo: Validation, Visualization, Writing – review & editing, Writing – original draft.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Publisher's note

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Corrigendum: Evaluation of sleep position shifts in patients with obstructive sleep apnea syndrome with the use of a mandibular advancement device

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KEYWORDS

obstructive sleep apnea (OSA), apnea-hypopnea index (AHI), oxygen desaturation index (ODI), sleep position shifts, mandibular advancement device (MAD)

A Corrigendum on
Evaluation of sleep position shifts in patients with obstructive sleep apnea syndrome with the use of a mandibular advancement device

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In the published article, there was an error in Table 3 as published. Incorrect negative values were entered when copying the results into the table. The corrected Table 3 and its caption appear below.

TABLE 3 Spearman's rho correlation test between the patient's sleep movement and the polysomnography indexes ($n = 73$).

Variables	NPS	PSI	AHI	ODI
NPS		0.975°	0.216°	0.447**
PSI	0.975°		0.182°	0.416**
AHI	0.216°	0.182°		0.767°
ODI	0.447**	0.416**	0.767°	

°n.s., **$p < 0.01$.

In the published article, there was an error. The incorrect values in Table 3 were reported to **Results**, *paragraph 3*.

The corrected sentence appears below:

"Table 2 shows the polysomnographic data distribution of all variables before and after MAD treatment. The patients had mild OSA overall (mean AHI 25.2 e/h and mean ODI 18.8 e/h). The mean NPS was 479.2 and the mean PSI was 69.56 (Table 2). Following

MAD treatment, a reduction of both the AHI (−16.36 e/h, $p < 0.01$) and ODI (−9.556 e/h, $p < 0.01$) was observed (Table 2). After MAD treatment, a decrease in the number of sleep shifts was observed, with NPS decreasing by −402.5 ($p < 0.01$) and PSI decreasing by −58.35 ($p < 0.01$) as indicated in Table 2. The authors evaluated the correlation between NPS and PSI (difference between T1 and T0) with the AHI and ODI (T1 and T0). The test demonstrated that the reduction in the ODI was correlated with both NPS (rho 0.447 NPS to ODI, $p < 0.01$) and PSI (rho 0.416, $p < 0.01$). No statistical correlation between positional indicators (i.e., NPS and PSI) and the AHI was observed (NPS to AHI: rho 0.216, p = n.s.; PSI to AHI rho 0.182, p = n.s.)."

The authors apologize for these errors and state that this does not change the scientific conclusions of the article in any way. The original article has been updated.

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Modified maxillomandibular advancement for Eastern Asian patients with moderate or severe OSA: an anatomic and aerodynamic assessment of the upper airway

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Background/purpose: Maxillomandibular advancement (MMA) is widely used for treating obstructive sleep apnea (OSA) patients. However, conventional MMA may not be suitable for Eastern Asian patients with moderate or severe OSA, as it can lead to unsatisfactory postoperative facial appearance. Hence, modified MMA was reported. Our study aims to evaluate the therapeutic effects of modified MMA on OSA and patient satisfaction with facial appearance. In addition, anatomic and aerodynamic changes in the upper airway were explored.

Materials and methods: This retrospective study included 13 patients with moderate or severe OSA. Overnight polysomnography and the Epworth Sleepiness Scale (ESS) scores were recorded before operation and 6 months after operation to evaluate therapeutic outcomes. Spiral CT scans were performed for all patients to reconstruct 3D configurations of the bony structures and the upper airway. Computational fluid dynamics was performed to analyze aerodynamic characteristics. In addition, correlations between bone segment movements and improvement in airway parameters were examined.

Results: Modified MMA achieved successful therapeutic and esthetic outcomes in all cases. The apnea–hypopnea index (36.05 ± 17.68 vs. 5.72 ± 4.76, $p < 0.001$) and the ESS (13.23 ± 8.9 vs. 6.23 ± 6.81 events/h, $p < 0.05$) decreased significantly, while the lowest oxygen saturation ($76.54 \pm 10.26\%$ vs. $84.77 \pm 6.02\%$, $p < 0.05$) improved greatly. Modified MMA significantly increased the total volume ($6{,}716.55 \pm 1{,}357.73$ vs. $11{,}191.28 \pm 2{,}563.79$ mm^3, $p < 0.001$) and the averaged cross-sectional area (117.38 ± 24.25 vs. 201.58 ± 35.76 mm^2, $p < 0.001$) of the upper airway. After modified MMA, the pressure drop, gas velocity, and resistance in the upper airway were all significantly decreased ($p < 0.05$). Among all the maxillary and mandible sections, the strongest correlation was observed between the advanced movement of the anterior mandible segment and anatomical characteristics of the upper airway.

Conclusion: Modified MMA is an excellent therapeutic method for Eastern Asian patients with skeletal class II dentomaxillofacial deformity suffering from moderate to severe OSA; it achieves a balance between esthetic improvement and therapeutic efficacy for OSA both anatomically and aerodynamically.

KEYWORDS

obstructive sleep apnea, skeletal class II dentomaxillofacial deformity, modified maxillomandibular advancement, three-dimensional reconstruction, computational fluid dynamics

Background

Obstructive sleep apnea (OSA) is a condition characterized by repetitive episodes of apnea or hypopnea caused by pharyngeal collapse during sleep. OSA can lead to oxygen desaturation, hypercapnia, and sleep fragmentation, which contribute to cardiovascular, metabolic, and neurocognitive diseases (1). Thus, OSA is considered a potentially life-threatening disease. Multiple factors, such as obesity, excessive soft tissue in the upper airway, retrusive jaw, and dysfunction of the upper airway dilator, might contribute to the occurrence of OSA (2, 3). Currently, nasal continuous positive airway pressure (CPAP) is the first-line treatment for OSA, especially in moderate-to-severe cases. However, not all patients can tolerate lifelong CPAP use (4, 5). Since its introduction by Riley et al. in 1984, maxillomandibular advancement (MMA) has been widely used in treating OSA patients, especially in patients with retrusive maxilla and mandible (6). MMA increases the upper airway volume and reduces the upper airway collapsibility by enlarging the oral cavity, therefore alleviating OSA in patients. Over nearly 40 years of practice, MMA has been proven to be highly effective and stable for selected OSA patients (7, 8). However, in the Eastern Asian population, OSA patients more frequently present with features such as a flat nose, protrusive upper jaw, and weak chin. Thus, the conventional MMA procedure might cause adverse esthetic outcomes in these patients. Several studies reported that MMA, when modified by segmentation of the maxilla or mandible, can achieve maximal advancement while preserving a balanced facial appearance and functional dental occlusion (9–11). However, it has also been reported that a decreased oral cavity volume increases the risk of flow resistance and upper airway collapse (12, 13). We hypothesize that the airway enlargement by maxillomandibular advancement might be neutralized by the segmental setback of the anterior jaw, as the actual oral cavity volume does not change significantly.

Hence, in this study, we evaluated the clinical outcomes of modified MMA, including its therapeutic effect on OSA and patient satisfaction with facial appearance. In addition, we evaluated the airway configuration anatomically and simulated airflow changes using the computational fluid dynamics (CFD) method to gain a better understanding of the aerodynamic effects of modified MMA.

Methods and materials

Participants

This is a retrospective study, approved by the institutional review board of the Hospital of Stomatology, Sun Yat-sen University. Between May 2020 and March 2024, patients referred to the Hospital of Stomatology, Sun Yat-sen University, who met the following criteria were enrolled in our study:

1. Patients of either sex aged between 18 and 60 years.
2. Patients with moderate to severe OSA combined with class II skeletal dentomaxillofacial deformity, who were intolerant of other conservative treatments (e.g., CPAP, weight loss, or oral appliances).

Exclusion criteria are as follows:

1. Patients with any genetic syndromes.
2. Patients with systemic diseases contraindicating orthognathic surgery under general anesthesia.
3. Patients with uncontrolled temporomandibular disorders or periodontitis.
4. Patients with uncontrolled psychological diseases.
5. Patients who were unwilling or unable to participate in this study.

Informed consent was obtained from all participants. Approval for this research was obtained from the Institutional Research Ethics Committee (KQEC-2024-117-01).

Orthodontic and orthognathic treatment

All patients received combined orthodontic and orthognathic treatment using a surgery-first or early approach. When necessary, limited preoperative orthodontic treatment was performed to align the dentition without further decompensation. All patients underwent modified MMA, which included conventional MMA combined with upper and lower subapical osteotomy and premolar extraction to achieve maximal mandibular and posterior maxillary advancement while avoiding postoperative bimaxillary protrusion. Genioplasty was performed when further advancement of the chin was required. Postoperative orthodontic alignment, leveling, and space management were performed to establish the final occlusion.

Virtual surgical planning

Preoperatively, surgical simulation was performed using the Dolphin platform. Spiral CT data, digital dental casts, and 3D facial photographs were integrated into the Dolphin platform. The head orientation was set parallel to the FH plane laterally and the interpupillary line frontally. A stepwise surgical workup, including setup, cropping, cleaning, osteotomy design, landmark identification, treatment planning, presentation, and splint fabrication, was performed. An intermediate splint was designed for mandibular movement, and a final splint was designed for maxillary movement. Occlusal splints were printed by stereolithography and sterilized before surgical use.

Assessment of patients and evaluation of sleep status

Preoperatively, the medical history and comorbidity profiles of all enrolled patients were reviewed. Physical examinations, sleep-related questionnaires, and sleep studies were conducted before and after surgery. First, physical characteristics, such as height, weight, and body mass index (BMI), were recorded. Preoperative symptoms were also carefully inquired. Then, self-evaluation of sleep quality was performed using the Epworth Sleepiness Scale (ESS) questionnaire. Finally, the apnea–hypopnea index (AHI) and lowest oxygen saturation (LSAT) were recorded using polysomnography (PSG).

Evaluation of patients' satisfaction

Patients' satisfaction with their postoperative facial appearance was evaluated using a five-point Likert scale (1 = very dissatisfied; 5 = very satisfied).

Assessment of the surgical movement of landmarks

After three-dimensional reconstruction of preoperative and postoperative spiral CT images, landmarks were labeled to assess the surgical movements of the jaw segments. The movement of the anterior maxillary section was measured using the A (subspinale), ANS (anterior nasal spine), and U1 (upper incisor) points, while the posterior section was marked using the U6 (maxillary first molar) and PNS (posterior nasal spine) points. The B (supramental) and L1 (lower incisor) points were regarded as landmarks of the anterior mandible segment, while the L6 (mandible first molar), Menton, Pogonion, and mental foramen points were set as landmarks of the posterior mandible segment. A schematic diagram of the bony landmarks in modified MMA is shown in Figure 1.

Airway measurement

Preoperative and postoperative spiral CT data were imported into the Mimics 20.01 platform to reconstruct the jaw, airway,

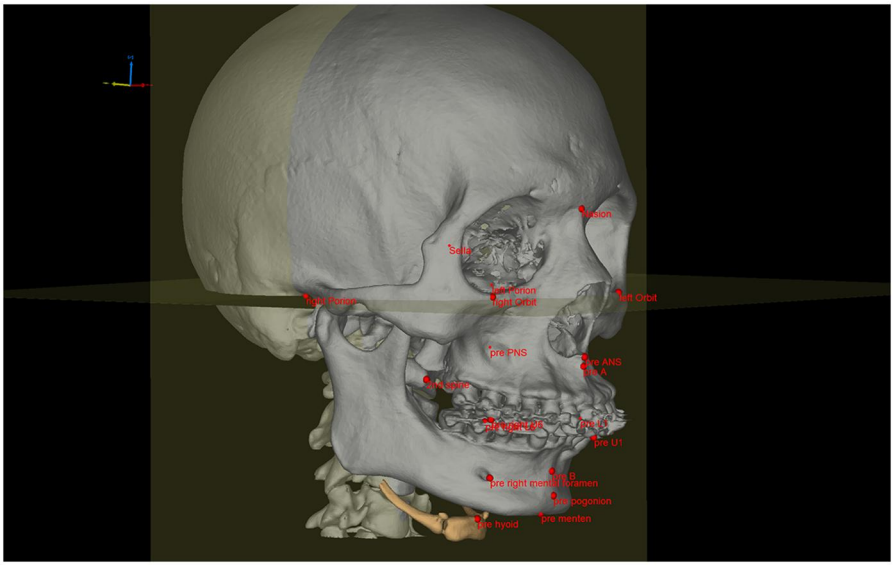

FIGURE 1
Schematic diagram of bony landmarks in modified MMA. Landmarks of the anterior maxillary segment: A point-subspinale; ANS point-anterior nasal spine; U1 point-mesioincisal angle of the upper central incisor. Landmarks of the posterior maxillary segment: U6-mesiobuccal cusp of maxillary first molar; PNS-posterior nasal spine. Landmarks of the anterior mandible segment: B-point supramental, L1-mesioincisal angle of the lower incisor. Landmarks of the posterior mandible segment: L6 point-mesiobuccal cusp of mandibular first molar; Menton point-the lowest point of mandible; Pogonion point-the most prominent point of the chin; mental foramen point-mental foramen.

and hyoid. Image segmentation of these structures was performed based on the threshold values from their DICOM image series. A three-dimensional airway model was created for the region between the nostrils and the infraglottic cavity, excluding the paranasal sinuses. Then, the airway model was smoothed while preserving patient-specific characteristics. The airway was further divided into the nasal airway, postpalatal airway, and postlingual airway using three virtual planes, which were defined as parallel to the FH plane and passing through the PNS, uvula tip, and epiglottic tip, respectively. Preoperative and postoperative jaws, airways, and hyoids were matched by point-based registration of orbital and cranial landmarks. Landmarks (Figure 1) of preoperative and postoperative jaws were analyzed. Pre- and postoperative airway configuration changes were quantified by measuring total airway volume, postpalatal volume, postlingual volume, total airway surface area, postpalatal surface area, postlingual surface area, mean airway cross-sectional area, cross-sectional area at the PNS level, cross-sectional area at the uvula level, and cross-sectional area at the epiglottic level. A schematic diagram of the upper airway segmentation is shown in Figure 2.

Computational fluid dynamics analysis

Preoperative and postoperative airway models were exported as STL files and further smoothed in the Geomagic platform. Each airway was then meshed into numerical computational cells. Laminar and turbulent CFD simulations were performed on the 3D airway models to predict the flow field in the nasal and upper airway of 13 patients before and after MMA. For numerical simulations, the inlet air pressure at the nostrils was set to ambient pressure (1 atm). A steady airflow rate of 700 mL/s, representative of adult inhalation, instead of dynamic tidal air flow, was used to calculate flow fields and pressure distributions. The same airflow rate was used for all cases. The simulation was designed to model human inspiration at rest under atmospheric pressure (1.013×10^5 Pa) and atmospheric temperature (20°C). The coefficients of viscosity (1.822×10^5 Pas) and density ($1.205\ kg/m^3$) were provided as fluid data.

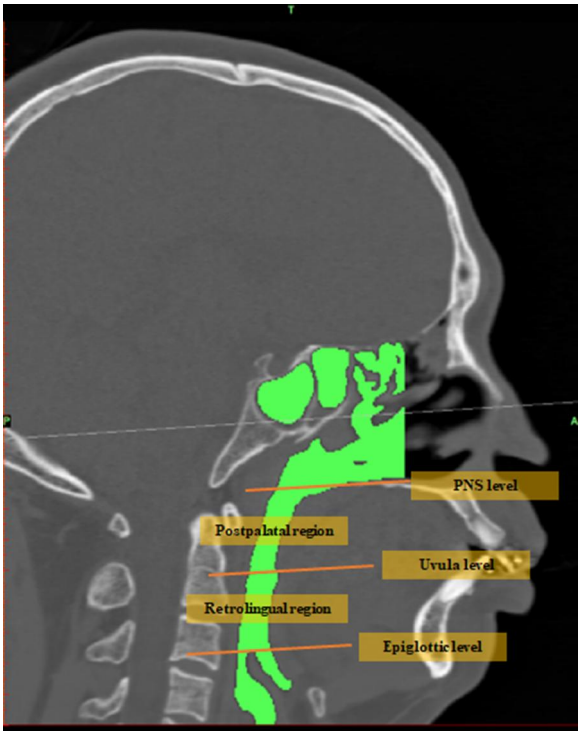

FIGURE 2
Schematic diagram of upper airway partition.

Statistical analysis

All statistical analyses were performed using GraphPad Prism 8.0 and SPSS 25.0 software. The Shapiro–Wilk (S-W) test was used to evaluate the normality of data distribution. For comparison between two groups, a two-tailed paired *t*-test was applied for the data with normally distributed differences, and the Mann–Whitney *U*-test was used for non-normally distributed ones. To analyze correlations between two groups, Pearson correlation analysis was used for normally distributed continuous data, while Spearman correlation analysis was used for ordinal variables. A p-value <0.05 was considered statistically significant.

Results

Patient characteristics

A total of 13 patients with skeletal class II dentomaxillofacial deformity were enrolled in this study. All patients presented with both mandibular retrusion and sleep apnea. Three of them also reported maxillary protrusion. Patient characteristics are summarized in Table 1. Four patients had undergone tonsillectomy, and two had tried but eventually discontinued CPAP due to intolerance. Snoring was the most frequent symptom, followed by excessive daytime sleepiness, frequent awakenings, morning headaches, and nighttime urination. One patient had systemic diseases secondary to OSA, including hypertension and stroke.

The mean BMI before surgery was $24.58 \pm 2.82\ kg/m^2$. Height and weight were remeasured 6 months after surgery when the patients conducted the postoperative PSG. The mean postoperative BMI was $25.10 \pm 3.49\ kg/m^2$. No significant differences were observed.

Satisfaction with facial appearance

All patients reported being “satisfied” or “very satisfied” with their postoperative facial appearance (Table 2). Radiographic records of a typical case are shown in Figure 3. None of the

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TABLE 1 Participant characteristics before surgery.

Participant characteristics before surgery, *n* (%)	
Age (years), mean ± SD (range)	27.85 ± 6.52 (20–41)
Sex, *n* (%)	
Male	9 (69.2)
Female	4 (30.8)
BMI (kg/m^2), mean ± SD (range)	24.58 ± 2.82 (20.57–29.98)
Degree of OSA	
Mild	0 (0)
Moderate	6 (46.2)
Severe	7 (53.8)
Vertical skeletal type	
Hypodivergent	0 (0)
Normally divergent	2 (15.4)
Hyperdivergent	11 (84.6)
Preoperative symptoms	
Loud snoring	13 (100)
Awakening	7 (53.8)
Nighttime urination	1 (9.1)
Excessive daytime sleepiness	8 (72.7)
Morning headaches	6 (46.2)
Previous OSA treatment	4(30.8)

TABLE 2 Likert scale for evaluating facial appearance satisfaction.

Satisfaction with facial appearance, *n* (%)	
Very satisfied	9 (69.2)
Satisfied	4 (30.8)
Neutral	0
Dissatisfied	0
Very dissatisfied	0

patients reported that their appearance had changed to bimaxillary protrusion after surgery.

Treatment effectiveness

Results of preoperative and postoperative PSG were presented in Table 3. All preoperative symptoms resolved, with only two patients complaining of slight snoring. Significant improvement was observed after modified MMA. Following the criteria of a ">50% improvement in AHI" or "post-treatment AHI < 15 events/h," modified MMA achieved successful therapeutic outcomes in all cases. Seven patients achieved complete resolution (AHI < 5 events/h). The average reduction in the AHI was 30.32 events/h. Recovery of the LSAT during PSG was at an average of 8.23%. The ESS score decreased by an average of 8.44.

Surgical movement of the landmarks

Surgical movement of key landmarks was also measured. The hyoid point was displaced forward by about 5.06 ± 5.09 mm and lifted up by about 4.94 ± 5.51 mm. Other detailed data are presented in Table 4.

Morphological characteristics of the upper airway

The 3D morphological characteristics of the upper airway are presented in Table 5, and the three-dimensional reconstruction of the upper airway is shown in Figure 4. The volume, surface area, length, and average cross-sectional area of the upper airway were measured. The postpalatal, retrolingual, and total parameters were evaluated separately. In addition, the axial area of the upper airway was evaluated at the PNS level, the uvula level, and the epiglottic level.

Modified MMA significantly increased the volume, cross-sectional area, and average cross-sectional area of the upper airway. The postpalatal and total surface areas of the upper airway were also significantly increased after surgery. However, no significant differences were observed in the retrolingual level surface area of the upper airway between the preoperative and postoperative measurements. The length of the upper airway tended to be shortened, with no significant difference, except at the retrolingual level.

Aerodynamic characteristics of the upper airway

Patient upper airway aerodynamic characteristics during inspiration are summarized in Table 6. Pressure drop, gas velocity, and resistance in the upper airway were significantly decreased after modified MMA. The simulation results of upper airway pressure and gas velocity are shown in Figure 5.

Correlation analysis between surgical movements of bone segments and changes in airway characteristics

A correlation between surgical movements of bone segments and changes in airway morphologic features was observed. In detail, the change in total volume ($r = 0.6044$, $p = 0.0287$) and retrolingual surface area ($r = 0.6447$, $p = 0.0174$) exhibits a positive correlation with the degree of forward movement of the hyoid bone (Figure 6A). A negative correlation was observed between the upward movement of the hyoid bone and changes in retrolingual length ($r = -0.5659$, $p = 0.0473$) and total length ($r = -0.6538$, $p = 0.0182$) (Figure 6B). No significant correlation was found between the movement of the anterior maxillary segment and changes in any airway morphological characteristic ($p > 0.05$). Unexpectedly, aside from postpalatal length ($r = -0.5974$, $p = 0.0311$), total surface area ($r = 0.6241$, $p = 0.0226$), and retrolingual surface area ($r = 0.5582$, $p = 0.0474$), no other morphological feature showed a significant correlation with the movement of the posterior maxillary segment (Figure 6C). A strong correlation was identified between the

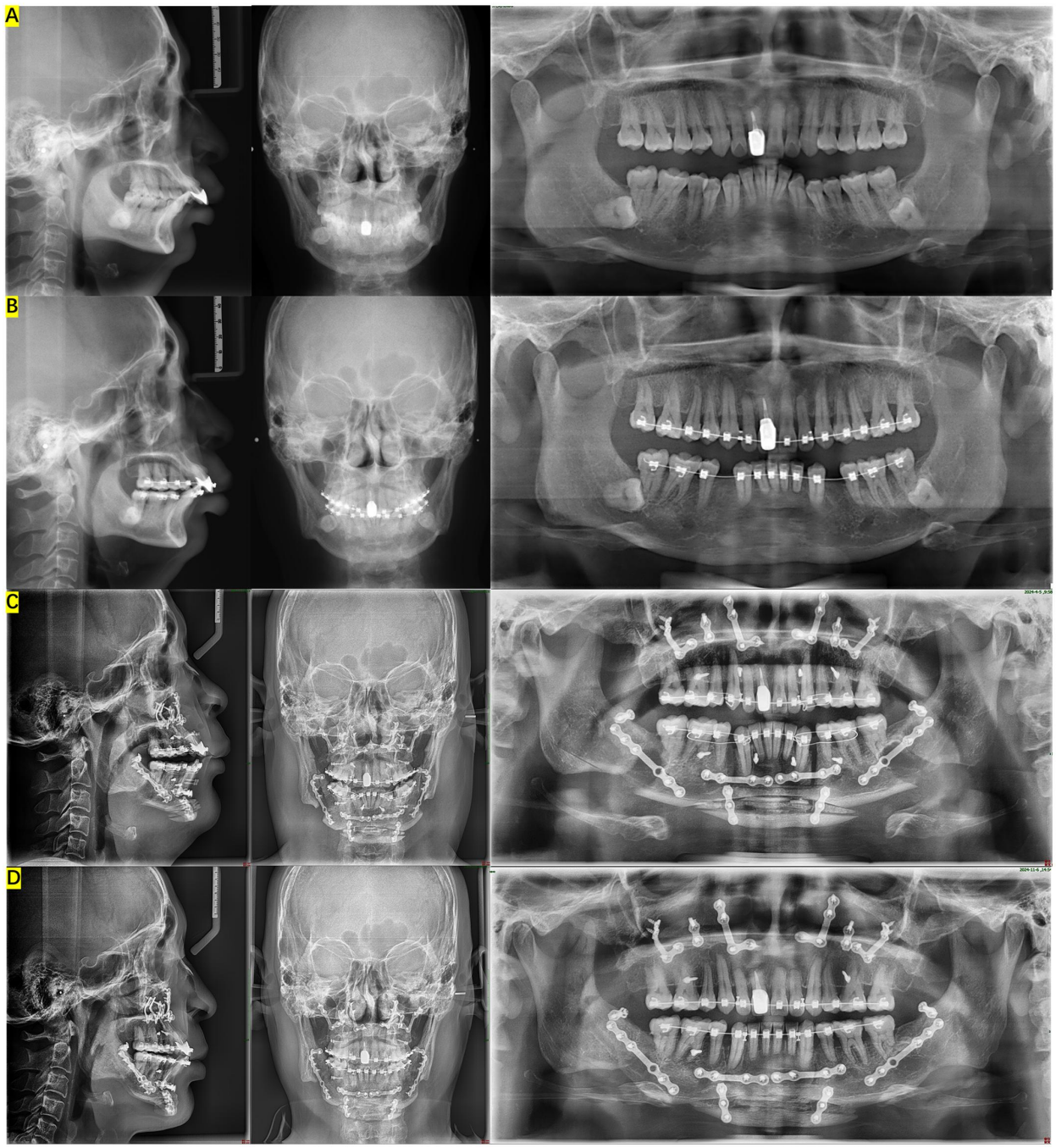

FIGURE 3
Lateral cephalometric radiograph, posteroanterior cephalometric radiograph and panoramic radiograph during orthodontic-surgical combined therapy. **(A)** Before pre-orthognathic orthodontics, **(B)** 1 week before orthognathic surgery, **(C)** 1 week after orthognathic surgery, **(D)** 6 months after orthognathic surgery.

TABLE 3 Preoperative and postoperative PSG results.

Results of PSG	Preoperative		Postoperative		*p*-value
	Mean	Standard deviation	Mean	Standard deviation	
AHI (events/h)	36.05	17.68	5.72	4.76	<0.001[a]
LSAT (%)	76.54	10.26	84.77	6.02	0.018[b]
ESS	13.23	8.90	6.23	6.81	0.001[b]

[a]Paired sample *t*-test.
[b]Wilcoxon rank-sum test.

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advanced movement of the anterior mandible section and several airway characteristics, including postpalatal volume ($r = 0.6572$, $p = 0.0147$), postpalatal surface area ($r = 0.7603$, $p = 0.0026$), postpalatal average cross-sectional area ($r = 0.6817$, $p = 0.0103$), and cross-sectional area at the uvula level ($r = 0.7205$, $p = 0.0055$). Furthermore, the total average cross-sectional area demonstrated a moderate correlation with the movement of the anterior mandible section ($r = 0.5575$, $p = 0.0487$) (Figure 6D). In contrast, weaker correlations were observed between similar airway characteristics and the movement of the posterior mandible segment (Figure 6E). No correlations were found between surgical movement of bone segments and sleep-related indicators or aerodynamic parameters.

TABLE 4 Surgical movement of important anatomical landmarks.

Surgical movement of the landmarks		Mean ± SD (range)
Forward movement (mm)	A point	−1.18 ± 1.46 (−3.41 to 1.19)
	U1 point	−1.15 ± 1.46 (−4.52 to 1.16)
	U6 point	5.79 ± 1.56 (3.17 to 8.75)
	ANS point	−2.62 ± 2.12 (−5.84 to 0.60)
	PNS point	3.97 ± 1.11 (2.4 to 5.97)
	B point	7.57 ± 4.12 (1.8 to 15.88)
	L1 point	3.4 ± 3.8 (−1.33 to 11.62)
	L6 point	9.3 ± 2.78 (6.00 to 16.55)
	Pogonion point	12.47 ± 4.77 (7.53 to 21.28)
	Menton point	13.80 ± 4.83 (8.09 to 22.62)
	Mental foramen point	10.43 ± 3.40 (7.26 to 19.38)
Degree	SNA	−1.12 ± 1.38 (−3.41 to 1.38)
	SNB	4.31 ± 2.17 (1.26 to 8.79)
	ANB	−5.13 ± 2.10 (−8.29 to −1.60)
	OP-SN	−0.37 ± 4.32 (−9.06 to 6.69)

SNA, Sella turcica-Nasion-Point A Angle; SNB, Sella turcica-Nasion-Point B Angle; ANB, Point A-Nasion-Point B Angle; OP-SN, Occlusal Plane to SN Plane.

Discussion

OSA is a very common disorder among adults. Globally, an estimated 936 million adults aged 30–69 years are affected by mild to severe obstructive sleep apnea, while 425 million within the same age range have moderate to severe obstructive sleep apnea (14). High BMI, increasing age, and male gender are regarded as risk factors for the incidence and severity of OSA (3). In our study, potential confounding variables, including sex, age, and BMI, were excluded to minimize their influence on the results.

The aim of OSA treatment is to restore adequate ventilatory function and maintain blood oxygen saturation during sleep (15). Therapeutic options can be categorized into four types: lifestyle modification, mandibular advancement devices (MADs), CPAP, and surgical interventions (4, 16). Lifestyle modifications, such as sleeping in a side-lying position and weight management, are effective for patients with mild OSA. Although CPAP remains the gold standard treatment for OSA, not all patients can tolerate lifelong CPAP use. MADs are becoming increasingly popular due to their effectiveness, convenience, and non-invasiveness; however, their use is limited by potential complications such as temporomandibular joint (TMJ) and periodontal damage. Surgical interventions are considered the last option when the non-invasive treatments fail. The aim of surgical intervention is to increase the upper airway patency at specific anatomical levels, including uvulopalatopharyngoplasty, hyoid suspension, epiglottoplasty, implantable neurostimulation devices, and orthognathic surgery (14). Since craniofacial disharmony is recognized as a predisposing risk factor for OSA, orthognathic surgery is considered the best choice to improve both ventilatory function and facial appearance (6–11).

The OSA patients in our study commonly presented with a normal or protruded maxilla combined with mandibular

TABLE 5 3D morphological characteristics of the upper airway.

Morphological characteristics of the upper airway		Preoperative		Postoperative		*p*-value
		Mean	Standard deviation	Mean	Standard deviation	
Volume (mm^3)	Postpalatal	3,276.99	643.44	6,481.44	1,883.33	<0.001[a]
	Retrolingual	3,439.56	1,246.94	4,709.84	1,173.91	0.011[a]
	Total	6,716.55	1,357.73	11,191.28	2,563.79	<0.001[a]
Surface area (mm^2)	Postpalatal	1,537.04	308.42	2,338.70	674.76	0.001[a]
	Retrolingual	1,393.73	425.56	1,606.31	462.22	0.072[a]
	Total	2,930.77	685.22	3,945.02	971.25	<0.001[a]
Length (mm)	Postpalatal	32.05	4.51	31.78	4.60	0.748[a]
	Retrolingual	25.92	5.91	23.48	5.65	0.033[b]
	Total	57.98	8.87	55.26	7.32	0.104[a]
Cross-sectional area (mm^2)	PNS	284.17	84.18	432.43	147.40	0.002[a]
	Uvula	116.65	30.30	230.40	96.88	0.001[b]
	Epiglottic	180.34	89.91	237.53	95.35	0.005[a]
	Narrowest point	61.38	25.67	113.23	37.86	<0.001[a]
Mean cross-sectional area (mm^2)	Postpalatal	103.32	21.92	202.76	48.75	<0.001[a]
	Retrolingual	136.52	47.39	206.90	54.09	0.001[a]
	Total	117.38	24.25	201.58	35.76	<0.001[a]

[a]Paired sample *t*-test.
[b]Wilcoxon rank-sum test.

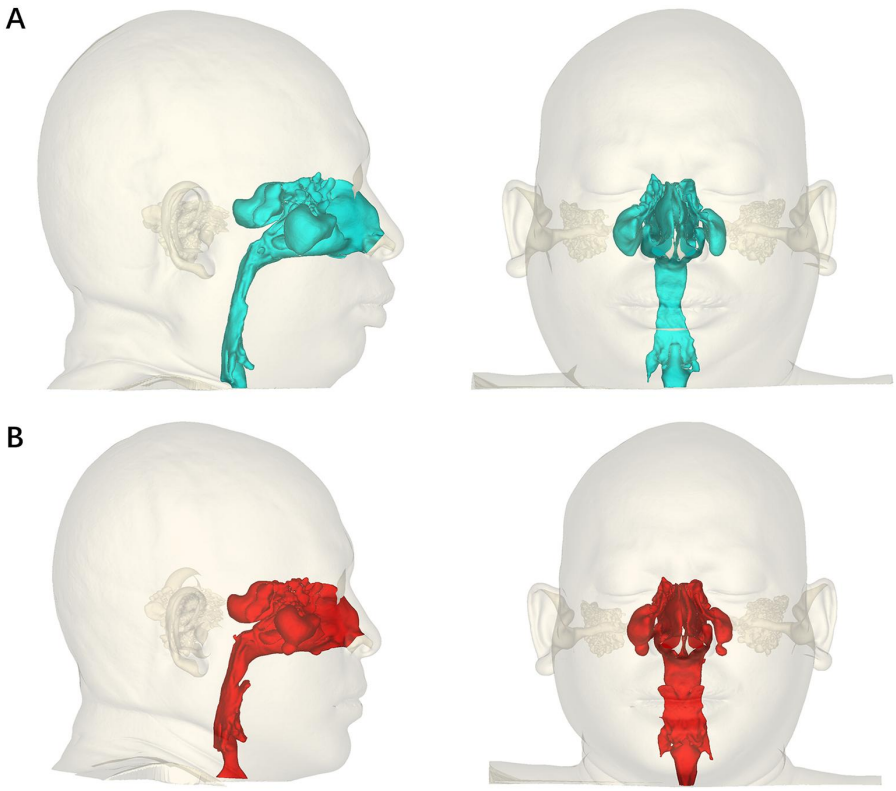

FIGURE 4
Pre-orthognathic (A) and post-orthognathic (B) three-dimensional reconstruction of the upper airway.

TABLE 6 Patient upper airway aerodynamic characteristics.

Aerodynamic characteristics of the upper airway		Preoperative		Postoperative		*p*-value
		Mean	Standard deviation	Mean	Standard deviation	
Pressure drop (Pa)	Total	35.54	9.22	25.79	6.53	<0.001[a]
	Nasal part	19.48	8.19	14.16	6.49	<0.001[a]
	Postpalatal part	13.7	3.21	9.22	2.07	<0.001[a]
	Retrolingual part	3.43	2.85	2.10	2.20	0.001[b]
	Postpalatal and retrolingual parts	14.45	4.54	9.70	2.85	<0.001[a]
Gas velocity (m/s)	Boundary of the nasal cavity and nasopharynx	3.41	0.78	2.72	0.71	<0.001[a]
	Soft palate	6.21	1.89	4.25	1.4	<0.001[a]
	Epiglottis	6.05	1.68	3.92	1.13	<0.001[a]
	Narrowest level	7.02	1.86	4.9	1.73	<0.001[a]
Resistance (Pa·s/m^3)	Total	1,77,721	46,086.53	1,28,926.1	32,642.06	<0.001[a]
	Nasal part	96,130.83	39,955.22	70,776.17	32,457.93	<0.001[a]
	Postpalatal part	68,485.26	16,049.58	46,116.26	10,347.14	<0.001[a]
	Retrolingual part	17,139.98	14,271.91	10,487.14	10,997.86	0.001[b]
	Postpalatal and retrolingual parts	72,260.12	22,683	48,477.27	14,252.12	<0.001[a]

[a]Paired sample *t*-test.
[b]Wilcoxon rank-sum test.

retraction, which is not rare in East Asia. Traditional MMA has become an effective, safe, and long-term stable treatment option for OSA (17–19). However, for these patients, the MMA is unsuitable because it may result in esthetic dissatisfaction due to postoperative bimaxillary protrusion. To avoid this problem, a balance between esthetic improvement and therapeutic efficacy for OSA could be achieved using a modified MMA technique, taking advantage of the existing edentulous spaces created after the extraction of premolars. Benito Anguita et al. reported that with traditional MMA, the mean preoperative AHI decreased significantly from 48.8 to 12.4, while ESS scores improved from 14.5 to 7.8 (17). In a meta-analysis, the mean reduction in AHI

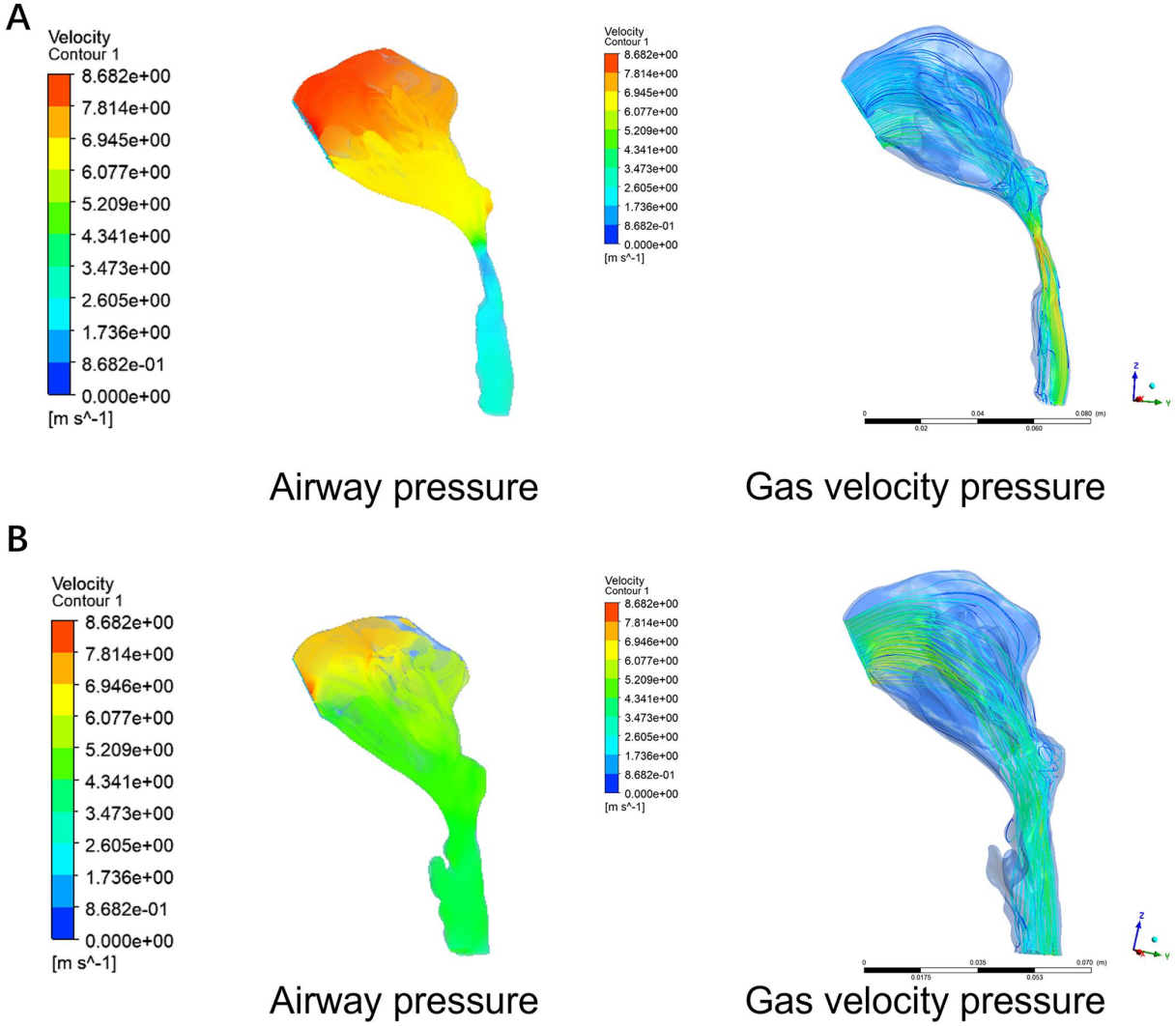

FIGURE 5
Computational Fluid Dynamics (CFD) of pre-orthognathic (A) and post-orthognathic (B) upper airway. Simulation of upper airway pressure is on the left and simulation of upper airway gas velocity is on the right.

was 39.6 among Caucasians and 42.7 among other populations (18). Previous studies using modified MMA (9–11) reported successful therapeutic outcomes in all cases, with a significant decrease in AHI and marked recovery of OSA symptoms. Meanwhile, all patients reported satisfaction with their postoperative appearance. Furthermore, the surgery-first or early approach significantly shortens the lengthy process of preoperative orthodontic decompensation and prevents worsening of OSA symptoms (20), which may result from decreased oral cavity volume (12). Taken together, modified MMA is a better therapeutic option for Eastern Asian patients with skeletal class II dentomaxillofacial deformity and OSA.

Anatomically, abnormalities in craniofacial skeletal and soft tissue structures contribute to partial or complete obstruction of the upper airway in OSA patients. Neelapu et al. showed strong evidence of reduced pharyngeal airway space, inferiorly positioned hyoid bone, and increased anterior facial height in adult OSA patients compared with control subjects (2). Another study reported that upper airway collapsibility is closely associated with hyoid position, tongue volume, pharyngeal length, and waist circumference (21). A study showed that patients with a higher hyoid position responded better to MMA (19). In our study, modified MMA significantly elevated the hyoid bone and increased upper airway volume, consistent with previous reports. The increase in airway volume was closely associated with the forward movement of the hyoid bone, suggesting that OSA patients might benefit from additional hyoid suspension during modified MMA (22). Notably, movement of the hyoid bone is primarily driven by significant advancement of the mandible. Furthermore, the anterior segment of the mandible, rather than the posterior segment,

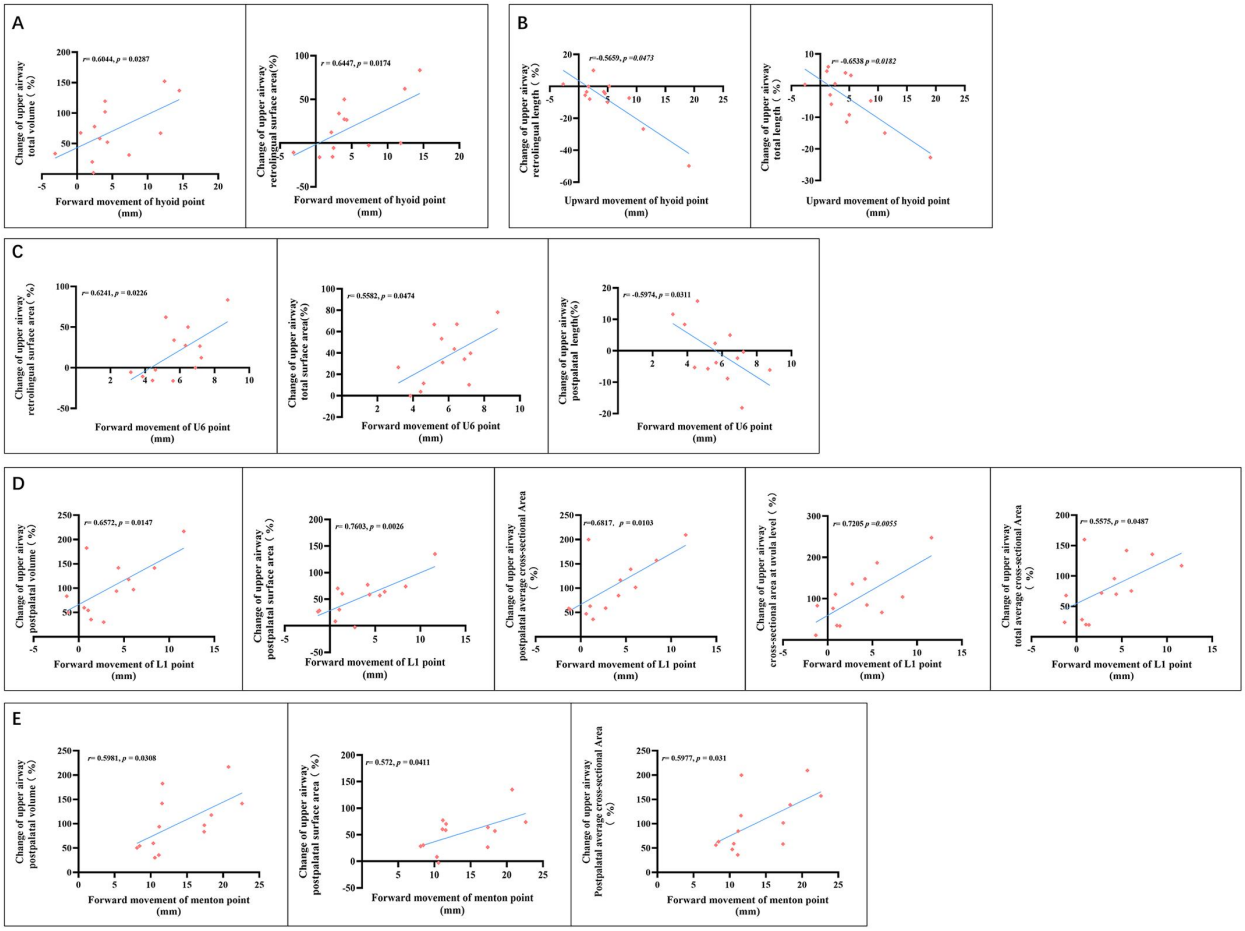

FIGURE 6
Correlation analysis between change of airway morphological characteristics and forward movement of the hyoid bone (A), upward movement of the hyoid bone (B), posterior maxillary segment (C), anterior mandible segment (D), posterior mandible segment (E).

demonstrates greater predictability in improving airway morphology. This finding implies that the airway enlargement achieved through maxillomandibular advancement may be counteracted if the anterior section of the mandible is set back. While the movement of the anterior maxillary section shows no significant influence on airway morphology, advancement of the posterior maxillary segment contributes to airway improvement to some extent.

Aerodynamically, airflow accelerates in narrowed regions. According to the Bernoulli effect, intraluminal pressure decreases as airflow increases. If the intra-airway pressure is lower than the external pressure, airway collapse occurs, which leads to apnea (23, 24). CFD provides an engineering modeling approach using the Navier–Stokes equation to study airway dynamics. CFD simulations showed that decreasing the airway pressure resulting from MMA decreases the breathing workload (25). It is reported that MMA increases airway volume, with a decrease in airway velocity. Significant correlations have been reported between improvements in apnea–hypopnea index values and both the increase in airway volume and the decrease in maximum airway velocity (26). Our study suggested that after removal of the airway narrow structure through modified MMA, the pressure drop, gas velocity, and resistance in the upper airway were significantly decreased.

Conclusion and limitations

Due to the limitation of sample size, our study provides only a preliminary evaluation of the efficacy of modified MMA in treating moderate to severe OSA. Based on our existing data, modified MMA appears to be an excellent therapeutic method for the Eastern Asian population with skeletal class II dentomaxillofacial deformity suffering from moderate to severe OSA, achieving a balance between esthetic improvement and therapeutic efficacy for OSA both anatomically and aerodynamically. Further studies with larger sample sizes and comparisons with other therapeutic methods are warranted.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the Hospital of Stomatology, Guanghua School of Stomatology, Sun Yat-sen University. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

KL: Methodology, Conceptualization, Software, Writing – original draft, Funding acquisition, Formal analysis. TZ: Software, Writing – original draft, Investigation, Formal analysis. YL: Writing – original draft, Investigation, Methodology. YC: Conceptualization, Supervision, Project administration, Funding acquisition, Data curation, Writing – review & editing, Validation. XL: Writing – review & editing, Methodology. SG: Writing – review & editing, Formal analysis. WS: Writing – review & editing, Investigation. TW: Writing – review & editing, Investigation. LZ: Writing – review & editing, Methodology. ZF: Writing – review & editing, Supervision, Formal analysis, Data curation, Resources. GZ: Validation, Conceptualization, Resources, Writing – original draft, Project administration, Writing – review & editing, Supervision, Methodology, Visualization, Formal analysis, Data curation, Software.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/froh.2025.1598511/full#supplementary-material

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Application of drug-induced sleep endoscopy in infants with dynamic upper airway collapse

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Objective: The study aimed to evaluate the utility and safety of drug-induced sleep endoscopy (DISE) in infants with suspected dynamic upper airway collapse.

Methods: Infants with suspected dynamic upper airway collapse were enrolled in the study. All subjects developed clinical symptoms within the first year of life. Each subject underwent both awake endoscopy (AE) and DISE. Endoscopic findings and sedation strategies for DISE were recorded. The diagnostic rate of dynamic upper airway collapse was compared between the DISE and AE. Adverse events during DISE were also recorded.

Results: (1) A total of 21 cases were included. The median age at the time of bronchoscopy was 4.0 months. (2) For the cases beyond neonatal age ($n = 18$), 16 (88.9%) received midazolam only, and 2 (11.1%) received midazolam combined with dexmedetomidine. For the neonates ($n = 3$), two (66.7%) received 10% chloral hydrate only, and one (33.3%) received 10% chloral hydrate combined with phenobarbital. (3) Six cases (28.6%) were diagnosed under both AE and DISE, whereas 15 cases (71.4%) were diagnosed under DISE only. The diagnostic rate was significantly higher under DISE than that under AE (100.0% vs. 28.6%, $P < 0.01$) in the cases with dynamic upper airway collapse. Of the cases with laryngomalacia, 3 cases (18.7%) were diagnosed under both AE and DISE, whereas 13 cases (81.3%) were diagnosed under DISE only. The diagnostic rate was significantly higher under DISE than that under AE (100.0% vs. 18.7%, $P < 0.01$) in the cases with laryngomalacia. Of the cases with tongue base collapse, all (100.0%) were diagnosed under both AE and DISE. Of the cases with retropalatal and hypopharynx collapse, all (100.0%) were diagnosed under DISE only. (4) One case (4.8%) developed a hypoxic episode during DISE, which was resolved by the pressurized facial mask-assisted ventilation.

Conclusions: DISE was found to be a feasible and safe procedure in infants with suspected dynamic upper airway collapse. Compared with AE, DISE significantly improved the diagnostic rate of laryngomalacia and appeared to be a more reliable method to diagnose pharyngeal airway collapse, especially retropalatal and hypopharynx collapse.

KEYWORDS

drug-induced sleep endoscopy, infant, dynamic upper airway collapse, laryngomalacia, pharyngeal airway collapse, midazolam

Introduction

Drug-induced sleep endoscopy (DISE) is a medical procedure used to identify sites of upper airway obstruction and collapse in patients with sleep-related respiratory issues, such as obstructive sleep apnea (OSA) syndrome (1). When an endoscopy is performed during pharmacologically induced sleep, upper airway blockages and collapse can be detected, and their types, levels, and patterns can be determined (1). DISE was first described by Croft and Pringle in 1991. It has been widely adopted and is frequently utilized to evaluate adults with OSA, which can help make the treatment decision and predict surgical outcomes (2). In children, especially in infants, DISE is still in the exploratory stage, and the indications, sedation regimen, endoscopy protocol, and the interpretation of DISE findings remain controversial (2, 3). In this study, we conducted DISE in infants with suspected dynamic upper airway collapse to evaluate the utility and safety of DISE in infants.

Subjects and methods

Subjects

All subjects were enrolled from the Department of Pediatrics at the First Affiliated Hospital of Guangxi Medical University from August 2023 to April 2025.

Children with a suspected diagnosis of dynamic upper airway collapse who underwent bronchoscopy during the first year of life were enrolled. Children who developed clinical signs of dynamic upper airway collapse during the first year of life but underwent bronchoscopy later were enrolled. A suspected diagnosis of dynamic upper airway collapse was made in infants with clinical manifestations of stridor, noisy breathing, snoring, and suprasternal retraction (4, 5). A definitive diagnosis of dynamic upper airway collapse was confirmed by endoscopy.

The exclusion criteria were as follows: (1) subjects requiring non-invasive or invasive mechanical ventilation; (2) subjects with choanal atresia or significant nasal cavity stenosis that prevented passage of a flexible bronchoscope (outer diameter 2.8 mm); and (3) subjects with tracheobronchial anomalies resulting in excessive airway stenosis or severe pneumonia.

Methods

Procedure of DISE

Informed consent was obtained from the legal guardians of the subjects. The infants underwent a pre-operative fasting period of 2 h for liquids and 6 h for solids. Routinely, 4 mL of 2% lidocaine inhalation and 0.01–0.02 mg/kg of atropine were administered subcutaneously 30 min before bronchoscopy. In the operating room, the infants were placed in the supine position, and heart rate (HR), oxygen saturation (SpO_2), and blood pressure (BP) were monitored. Bronchoscopy was performed under spontaneous breathing with unilateral nasal catheter oxygen inhalation. Firstly, bronchoscopy was performed in an awake state without the use of any sedative or anesthetic drugs. Local anesthesia was induced by spraying 2% lidocaine hydrochloride solution over the nasal cavity, avoiding the nasopharynx, oropharynx, hypopharynx, or larynx. In addition, tetracaine (tetracaine 1% SDU Faure; Novartis, Basel, Switzerland) was applied to the surface of the bronchoscope as a local anesthetic. The flexible bronchoscope (BF-XP290; Olympus, or QG-3320; SeeSheen) was inserted through the nasal cavity. Endoscopic findings of the palate/velum, lateral oropharyngeal wall, tongue base, and supraglottic larynx were recorded in the awake state. If obstruction was present, the site, pattern or shape, and severity of obstruction were recorded. Next, the infants were given adequate sedation. For the cases beyond neonatal age, sedation strategies included 3–4 μg/kg of intranasal dexmedetomidine and/or 0.1 mg/kg of midazolam (not exceeding 0.3 mg/kg) or 2–3 mg/kg of propofol via intravenous push (2, 6, 7). For the neonates, sedation strategies included 0.5–1.0 mL /kg of 10% chloral hydrate enema either alone or combined with 5 mg/kg of phenobarbital via intravenous push (6). The level of sedation allowed for flexible endoscopy without patient reactivity or awakening (2). A thin bronchoscope with an outer diameter of 2.8 mm was used in all cases. Endoscopic findings, as mentioned above, were recorded under adequate sedation. Finally, the flexible bronchoscope was passed through the glottis to the lungs for routine examination of the trachea and bronchi. Topical anesthesia with 1 mL of 2% lidocaine was administered in the glottis, trachea, and the main bronchus. During the procedure, when SpO_2 dropped below 85%, bronchoscopy was terminated, and oxygen flow was increased, or pressurized mask ventilation was applied. When SpO_2 returned above 95%, bronchoscopy was resumed.

Diagnostic criteria for pharyngeal airway collapse, laryngomalacia, and dynamic upper airway collapse under the endoscopy

Pharyngeal airway collapse (PAC) was defined as a reduction of more than 50% in the pharyngeal internal diameter during inspiration, causing airway obstruction (8). Based on the collapse region, PAC was classified as retropalatal collapse, hypopharynx collapse, or tongue base collapse (1, 9). Multilevel collapse was defined as the presence of two or more collapse regions simultaneously. Laryngomalacia was defined as an inward collapse of the supraglottic structures into the glottis during inspiration, causing airway obstruction (10). Laryngomalacia was classified as type I (redundant arytenoid mucosa), type II (short aryepiglottic fold with curled epiglottis), type III (epiglottic collapse), and mixed type with the presence of two or more types simultaneously (10). Dynamic upper airway collapse was defined as the presence of PAC and/or laryngomalacia. The diagnosis was made after the deliberation of two endoscopists.

Data collection

Clinical data were recorded by collecting data on medical history, including the age of onset and clinical manifestations during wakefulness and sleep. Endoscopic findings in the awake

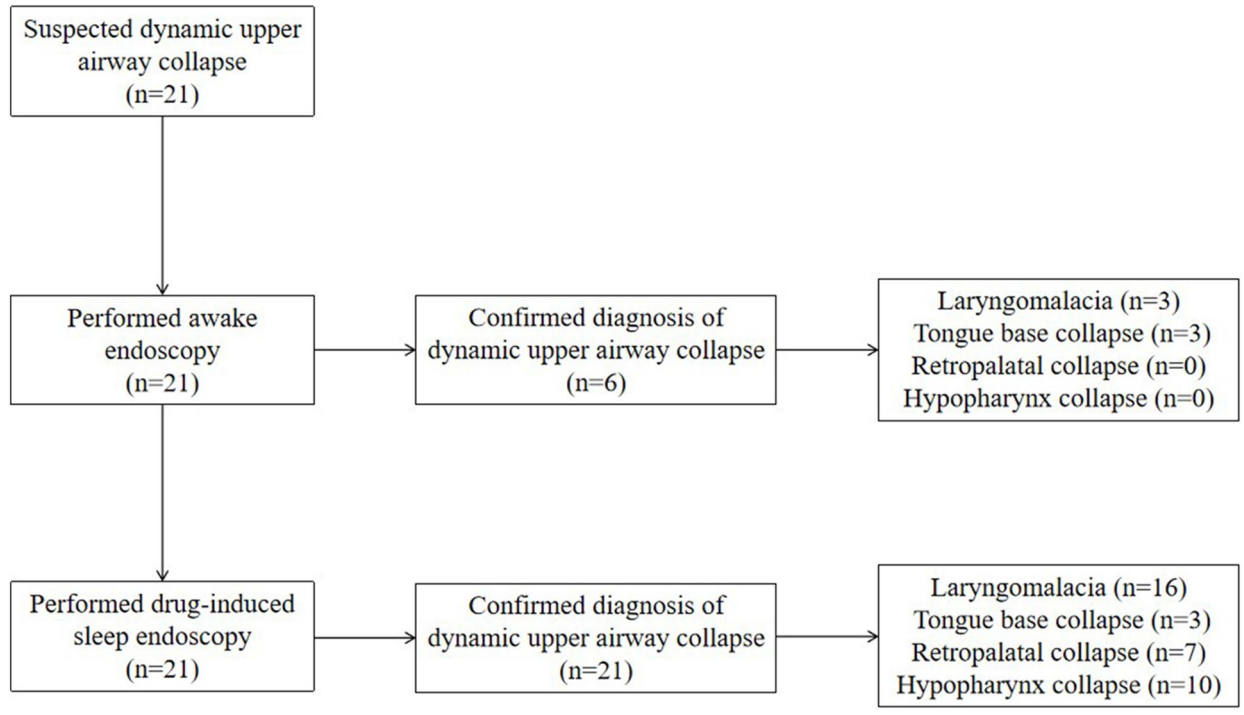

FIGURE 1
The study flow diagram and endoscopic findings.

state and under adequate sedation were recorded as mentioned above. The sedation protocol and sedation-related complications were also recorded.

Statistical analysis

Statistical analysis was performed using SPSS 20.0 software. Measurement data are expressed as medians (25th–75th percentile). Counting data are expressed as count or percentage. For the categorical variables, between-group comparisons were performed using the χ^2 test or Fisher's exact test. A two-sided *P*-value of <0.05 was considered statistically significant.

Results

General information

A total of 21 cases (male $n = 17$, female $n = 4$) were included. All 21 cases were initially suspected of having dynamic upper airway collapse based on clinical manifestations and were definitively diagnosed by endoscopy. The study flow diagram is shown in Figure 1. The cohort included 3 neonates and 18 cases beyond neonatal age. Six cases were born preterm, and 15 cases were born full term. At the time of bronchoscopy, the median age was 4.0 (2.0–9.0) months, and the median weight was 5.5 (4.2–7.4) kg. In terms of clinical manifestations, noisy breathing was observed in 12 cases, suprasternal retraction in 8 cases, and snoring in 7 cases (Table 1).

Sedation strategies during DISE

For the cases beyond neonatal age ($n = 18$), 16 (88.9%) received midazolam only, and 2 (11.1%) received midazolam combined with dexmedetomidine. For the neonates ($n = 3$), two (66.7%) received 10% chloral hydrate only, and one (33.3%) received 10% chloral hydrate combined with phenobarbital. No cases received propofol. All cases successfully completed DISE (Table 1).

Endoscopic findings

Laryngomalacia was diagnosed in 16 cases (76.2%), and PAC was diagnosed in 15 cases (71.4%). Ten cases (47.6%) concurrently had laryngomalacia and PAC. Of the cases with laryngomalacia, 5 (31.3%) had a single type of laryngomalacia, and 11 (68.7%) had a mixed type. Of the cases with PAC, 3 (20.0%) had tongue base collapse, 7 (46.7%) had retropalatal collapse, and 10 (66.7%) had hypopharynx collapse, whereas 4 (26.7%) had multilevel collapse (Figure 1 and Table 1).

Comparisons between AE and DISE

Of the cases with dynamic upper airway collapse, 6 (28.6%) were diagnosed under both awake endoscopy (AE) and DISE, whereas 15 (71.4%) were diagnosed under DISE only. The diagnostic rate was significantly higher under DISE than that

TABLE 1 Clinical data and endoscopy of the cases with dynamic upper airway collapse.

No.	Gender	Sedation strategy	Age at the time of endoscopy	Weight at the time of endoscopy	Clinical manifestations	Endoscopy during AE	Clinical manifestations during DISE	Endoscopy during DISE
1	M	Dexmedetomidine 4 μg/kg, midazolam 0.2 mg/kg	10 months	5.4 kg	Suprasternal retraction	Normal	Stridor, exacerbation of suprasternal retraction	PAC (lateral hypopharynx collapse), laryngomalacia (type I + II + III)
2	F	Midazolam 0.2 mg/kg	13 months[a]	8.4 kg	Noisy breathing during activity and sleep	Normal	Noisy breathing, suprasternal retraction	PAC (lateral retropalatal collapse + lateral hypopharynx collapse)
3	M	Midazolam 0.2 mg/kg	8 months	6.8 kg	Noisy breathing during activity	Normal	Suprasternal retraction	Laryngomalacia (type II + III)
4[d]	M	10% chloral hydrate 0.5 mL/kg	Neonate	3.4 kg	Suprasternal retraction	Normal	Exacerbation of suprasternal retraction	PAC (lateral hypopharynx collapse), laryngomalacia (type III)
5[d]	M	Midazolam 0.3 mg/kg	13 months[a]	9.2 kg	Noisy breathing during activity	Normal	Noisy breathing, suprasternal retraction	PAC (lateral hypopharynx collapse), laryngomalacia (type II + III)
6	M	Midazolam 0.1 mg/kg	8 months	5.7 kg	Noisy breathing during activity and sleep	Normal	Noisy breathing, suprasternal retraction	Laryngomalacia (type I + II)
7	M	Midazolam 0.2 mg/kg	2 months	5.5 kg	Snoring	Normal	Snoring, suprasternal retraction	PAC (lateral retropalatal collapse)
8[d]	M	Midazolam 0.1 mg/kg	4 months	6.0 kg	Noisy breathing	Laryngomalacia (type II + III)	Noisy breathing, suprasternal retraction	Laryngomalacia (type II + III)
9[d]	M	Midazolam 0.1 mg/kg	5 months	5.4 kg	Stridor, suprasternal retraction	Laryngomalacia (type I + II + III)	Exacerbation of stridor and suprasternal retraction	Laryngomalacia (type I + II + III)
10	M	Midazolam 0.2 mg/kg	5 months	7.4 kg	Snoring	Normal	Snoring, suprasternal retraction	PAC (lateral retropalatal collapse)
11	M	10% chloral hydrate 0.5 mL/kg, phenobarbital 5 mg/kg	Neonate	3.5 kg	Snoring, suprasternal retraction	Normal	Snoring, exacerbation of suprasternal retraction	PAC (lateral hypopharynx collapse)
12[d]	M	Midazolam 0.2 mg/kg	2 months	4.0 kg	Noisy breathing, snoring	PAC (tongue base collapse)	Snoring, suprasternal retraction	PAC (lateral hypopharynx collapse + tongue base collapse)[c], laryngomalacia (type I)
13	M	Midazolam 0.2 mg/kg	4 months	7.4 kg	Noisy breathing during activity, snoring	Normal	Stridor, suprasternal retraction	PAC (lateral hypopharynx collapse), laryngomalacia (type I + II)
14	M	Dexmedetomidine 4 μg/kg, midazolam 0.3 mg/kg	11 months	8.2 kg	Noisy breathing	Normal	Noisy breathing, suprasternal retraction	PAC (anteroposterior retropalatal collapse + lateral hypopharynx collapse)
15	F	Midazolam 0.2 mg/kg	4 months	4.2 kg	Stridor, suprasternal retraction	Laryngomalacia (type I + II + III)	Stridor, suprasternal retraction	Laryngomalacia (type I + II + III)
16	M	10% chloral hydrate 0.5 mL /kg	Neonate	4.1 kg	Noisy breathing, suprasternal retraction	PAC (tongue base collapse)	Exacerbation of suprasternal retraction	PAC (tongue base collapse), laryngomalacia (type III)
17[d]	M	Midazolam 0.2 mg/kg	10 months	5.0 kg	Suprasternal retraction	Normal	Exacerbation of suprasternal retraction	Laryngomalacia (type I)
18[b]	F	Midazolam 0.2 mg/kg	1 months	4.0 kg	Noisy breathing, snoring, suprasternal retraction	PAC (tongue base collapse)	Stridor, exacerbation of suprasternal retraction	PAC (lateral retropalatal collapse + lateral hypopharynx collapse + tongue base collapse)[c], laryngomalacia (type I + II)
19	M	Midazolam 0.1 mg/kg	3 months	5.0 kg	Noisy breathing during activity	Normal	Stridor, suprasternal retraction	PAC (lateral retropalatal collapse), laryngomalacia (type I + II + III)
20	M	Midazolam 0.2 mg/kg	4 months	7.3 kg	Snoring	Normal	Stridor, suprasternal retraction	PAC (lateral hypopharynx collapse), laryngomalacia (type I + II)
21	F	Midazolam 0.3 mg/kg	5 months	6.4 kg	Noisy breathing during activity	Normal	Suprasternal retraction	PAC (lateral retropalatal collapse), laryngomalacia (type III)

M, male; F, female; PAC, pharyngeal airway collapse.

[a]Cases with clinical manifestations of dynamic upper airway collapse at 1-year-old.

[b]Cases that developed a hypoxic episode during DISE, which was resolved by pressurized facial mask-assisted ventilation.

[c]Exacerbation of tongue base collapse was found in the cases during the inspiratory period under DISE compared with AE.

[d]Cases born preterm, and the rest born full term.

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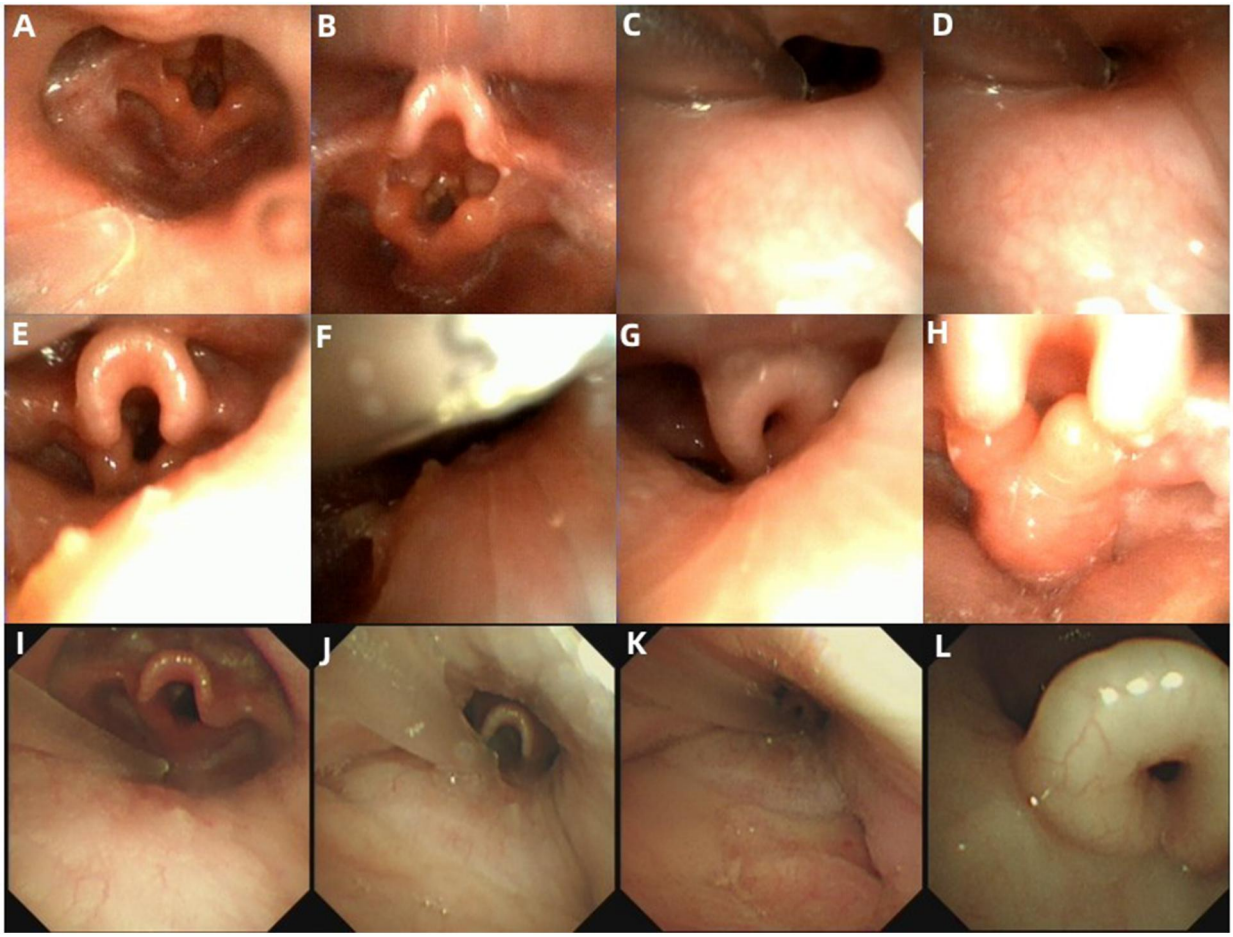

FIGURE 2
Endoscopic presentations in the cases with dynamic upper airway collapse. **(A–H)** Endoscopic findings in Case 18. **(A)** Normal appearance of the retropalatal cavity during the inspiratory period under AE. **(B)** Tongue base collapse during the inspiratory period under AE. **(C)** Retropalatal cavity during the expiratory period under DISE. **(D)** A significant reduction of retropalatal internal diameter during the inspiratory period under DISE. **(E)** Hypopharyngeal cavity during the expiratory period under DISE. **(F)** A significant reduction of the hypopharyngeal internal diameter during the inspiratory period under DISE. **(G)** Epiglottis curling and exacerbation of tongue base collapse during the inspiratory period under DISE. **(H)** Inward collapse of the redundant arytenoid mucosa and cartilages during the inspiratory period under DISE. **(I–L)** Endoscopic findings in Case 5. **(I)** Normal appearance of the hypopharyngeal cavity during the inspiratory period under AE. **(J)** Hypopharyngeal cavity during the expiratory period under DISE. **(K)** A significant reduction of the hypopharyngeal internal diameter during the inspiratory period under DISE. **(L)** Epiglottis curling during the inspiratory period under DISE.

under AE (100.0% vs. 28.6%, $P < 0.01$). Of the cases with laryngomalacia, 3 (18.7%) were diagnosed under both AE and DISE, whereas 13 cases (81.3%) were diagnosed under DISE only. The diagnostic rate was significantly higher under DISE than that under AE (100.0% vs. 18.7%, $P < 0.01$). Of the cases with tongue base collapse, all (100.0%) were diagnosed under both AE and DISE, whereas two (66.7%) presented exacerbation of the collapse under DISE compared with AE. Of the cases with retropalatal collapse and hypopharynx collapse, all (100.0%) were diagnosed under DISE only (Figure 2 and Table 1).

Adverse events during DISE

One case (4.8%) developed a hypoxic episode during DISE, which was resolved by pressurized facial mask-assisted ventilation (Table 1).

Discussion

Dynamic upper airway collapse is a group of diseases characterized by narrowing of the upper airway lumen and airflow limitation during inspiration. In adults, it typically presents as snoring and OSA (11). Since abnormal performance mainly occurs during sleep, DISE is widely used in adults to evaluate the dynamic upper airway collapse, which can help make the treatment decision and predict surgical outcomes. However, the presentation differs in children especially in infants. In addition to snoring and OSA during sleep, infants with dynamic upper airway collapse usually present with stridor or noisy breathing during wakefulness (4). This suggests that AE, rather than DISE, might also display the abnormal performance and help diagnose dynamic upper airway collapse in infants. Moreover, sedative or anesthetic drugs used during

DISE might worsen airway obstruction in infants with dynamic upper airway collapse (12). Therefore, the role of DISE in the diagnosis of dynamic upper airway collapse in infants remains controversial. In view of this, we conducted this study to evaluate the utility and safety of DISE in infants with suspected dynamic upper airway collapse.

In this study, dynamic upper airway collapse was defined as the presence of PAC and/or laryngomalacia. In infants, PAC is often missed during endoscopic evaluation (13). This is partly due to a lack of awareness of the condition (4). Another reason may be poor compliance in infants. Thus far, few studies have reported an endoscopic diagnostic method for PAC in infants. During AE, infants usually fuss and cry, and when they do this, the pharyngeal isthmus closes due to soft palate elevation, making it difficult to assess retropalatal collapse (3, 14). DISE can eliminate the fussing and crying during endoscopy, allowing better diagnosis of retropalatal collapse. In this study, all cases with retropalatal collapse were diagnosed under DISE only. It was noteworthy that all cases with hypopharynx collapse were also diagnosed under DISE only, demonstrating that the hypopharyngeal cavity may maintain patency during wakefulness. Therefore, identification of hypopharynx collapse may also rely on DISE. Moreover, laryngomalacia in infants may be sleep-dependent (15), requiring DISE to make a diagnosis. In this study, 14 cases with laryngomalacia were confirmed, 11 of which were sleep-dependent. In view of the above reasons, DISE appeared to improve the diagnostic rate for dynamic upper airway collapse in infants compared with AE. The results of this study support this viewpoint. In this study, the majority of the cases (68.4%) with dynamic upper airway collapse revealed abnormal under DISE only but revealed normal under AE. Furthermore, the diagnostic rate was significantly higher under DISE than that under AE in cases with dynamic upper airway collapse.

The choice of sedative or anesthetic drugs for pediatric DISE is still controversial. The ideal sedative or anesthetic drugs for pediatric DISE are those that can mimic natural sleep with a wide safety margin (2). In this study, we chose dexmedetomidine and/or midazolam for DISE in cases beyond neonatal age, and all cases had completed DISE successfully. At present, midazolam and dexmedetomidine, either alone or in combination, are considered optimal sedation or anesthetic agents for pediatric DISE (2). In fact, propofol is also considered suitable for DISE (2). However, the major concerns included its potential for dose-dependent airway collapse and the need for target-controlled infusion, as rapid infusion can cause central sleep apnea (16). In view of this, propofol was not used in this study. In addition, ketamine is also avoided in pediatric DISE as it can increase muscle tone, which can stiffen the airway and mask a true obstructive breathing pattern (2). Inhalational agents are also not suitable for pediatric DISE, as they can cause upper airway obstruction in a dose-dependent manner (2). In this study, neither ketamine nor an inhalational agent was used for DISE. It is worth noting that there have been no reports of DISE performed in neonates until now. Therefore, the choice of sedative or anesthetic drugs for neonatal DISE is typically inexperienced. Due to safety concerns, we used 10% chloral hydrate—combined with phenobarbital or not—for neonates, all of whom also completed DISE successfully.

The safety of DISE in infants with dynamic upper airway collapse warrants focused attention. Some infants with dynamic upper airway collapse may develop hypoxic episodes due to upper airway obstruction (4). It is well known that sedative or anesthetic drugs can induce sleep and reduce the pharyngeal muscle tension, which can aggravate upper airway obstruction (12). In this study, one case (4.8%) developed a hypoxic episode during DISE, which was resolved by pressurized facial mask-assisted ventilation. Therefore, application of DISE in infants with dynamic upper airway collapse is safe and feasible. However, the emergency planning for hypoxic episodes during DISE should be well prepared.

This study has some limitations. First, it was a single-center study with a small sample size. Second, this study had a certain bias in case selection. All cases in this study were examined using a thin bronchoscope with an outer diameter of 2.8 mm. However, in very small infants, particularly preterm neonates, this size may still be relatively large for the airway. Moreover, the cases that were unable to tolerate the sedative or anesthetic drugs were excluded. These factors may influence both the safety and diagnostic accuracy of dynamic airway collapse assessment. Third, this was a self-control study without a control group of infants without dynamic upper airway collapse, limiting the ability to further identify potential misdiagnosis by DISE. Multicenter studies with larger sample sizes should be performed in the future.

Conclusions

DISE was found to be feasible and safe in infants with suspected dynamic upper airway collapse. Compared with AE, DISE improved the diagnostic rate of laryngomalacia and appeared to be a more reliable method for diagnosing PAC, especially retropalatal and hypopharynx collapse.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding authors.

Ethics statement

The studies involving humans were approved by the Medical Ethics Committee of The First Affiliated Hospital of Guangxi Medical University. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin. Written informed consent was obtained from the individual(s), and minor(s)' legal guardian/next of kin, for the publication of any potentially identifiable images or data included in this article.

Author contributions

QW: Methodology, Writing – original draft, Software, Formal analysis, Data curation, Resources, Project administration, Conceptualization, Investigation. RY: Software, Writing – original draft, Methodology, Investigation, Data curation, Resources, Conceptualization, Formal analysis, Project administration. XC: Validation, Conceptualization, Methodology, Visualization, Writing – review & editing, Investigation, Supervision. XY: Supervision, Methodology, Software, Visualization, Validation, Writing – review & editing. JL: Writing – review & editing, Investigation, Supervision, Conceptualization, Funding acquisition, Visualization, Data curation, Formal analysis, Validation, Methodology. YL: Data curation, Conceptualization, Visualization, Methodology, Validation, Investigation, Supervision, Funding acquisition, Writing – review & editing, Formal analysis.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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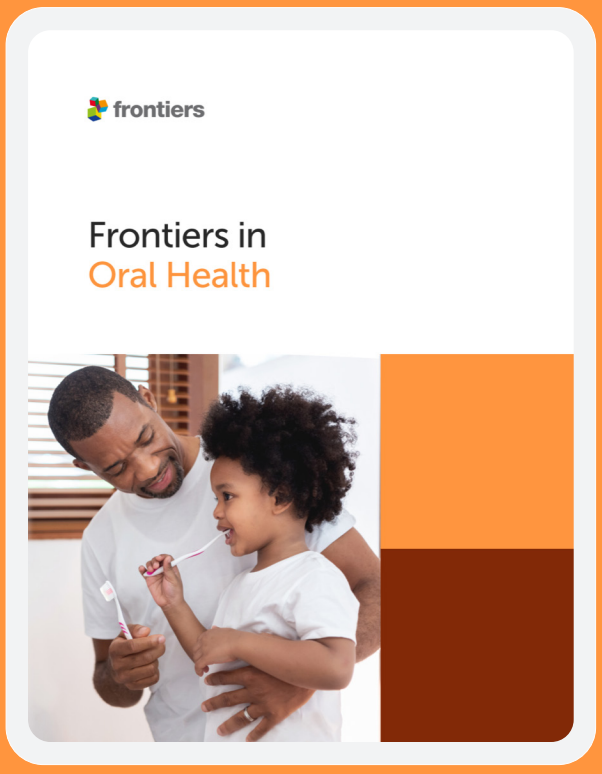

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