Submitted: 23 March, 2024 Accepted: 20 June, 2024 Published: 03 March, 2025 DOI:10.22514/jocpd.2025.037

ORIGINAL RESEARCH

Journal of Clinical Pediatric Dentistry

Long-term recurrence-free survival of orthodontic treatments for Class II malocclusion as the important supplement protocol to adenotonsillectomy in children with obstructive sleep apnea syndrome: a case-control retrospective study

Tian Xia[1], Ruqian Luo[1], Mengxing Wan[1,*]

[1]Department of Stomatology, Children's Hospital affiliated to Capital Institute of Pediatrics, 100020 Beijing, China

***Correspondence**
summer861202@163.com
(Mengxing Wan)

Abstract

Background: To estimate the long-term recurrence-free-survival of three orthodontic treatments in the management of residual obstructive sleep apnea syndrome (OSAS) after adenotonsillectomy in children combined with Class II malocclusion taking conventional positive airway pressure (PAP) as control. **Methods**: A retrospective case-control cohort study, enrolled pediatric OSAS with Class II after adenotonsillectomy. The records of the patients were divided into a rapid maxillary expansion (RME), mandibular advancement appliances (MAA) and myofunctional therapy (MFT) group based on the therapy they received. Control group comprised patients used PAP at the same admission time. The primary endpoint was a long-term recurrence-free-survival. Secondary outcomes measures included the immediate post-operative success rate, improvements in the Epworth Sleepiness Scale (ESS) scores, craniofacial changes, s-electromyogram (s-EMG) changes of masticatory muscle and long-term OSAS sequelae. **Results**: A total of 1217 cases were analyzed. The estimated 1-, 3- and 5-year recurrence-free rate was 81.9%, 70.8% and 56.4% in PAP *vs.* 86.2%, 81.0% and 77.5% in RME *vs.* 85.5%, 78.0% and 74.7% in MAA *vs.* 83.0%, 74.9% and 58.3% in MFT, respectively. Significantly greater median of recurrence-free-survival was observed in RME, MAA and MFT group as opposed to PAP-control group (122.04 $\pm$ 3.04 (95% CI (confidence interval): 116.08, 127.99), 20.04 $\pm$ 4.21 (95% CI: 111.79, 128.28), 68.96 $\pm$ 4.95 (95% CI: 59.24, 78.68) *vs.* 54.96 $\pm$ 2.51 (95% CI: 50.05, 59.87)). The post-treatment ESS scores, craniofacial variables, s-EMG parameters greatly improved at post-treatment from the baseline value and sustained during long-term follow-up. No severe complications were observed. **Conclusions**: As opposed to conventional PAP, a better long-term RFS (recurrence free survival) was associated with the therapeutic trial using RME and MAAs, which provided a reasonable alternative for residual OSAS after adenotonsillectomy in children combined with Class II malocclusion. Their benefits appeared especially in children due to poor compliance to conventional PAP.

Keywords

Residual obstructive sleep apnea syndrome; Class II malocclusion; Positive airway pressure; Rapid maxillary expansion; Mandibular advancement appliances; Myofunctional therapy

1. Introduction

Obstructive sleep apnea syndrome (OSAS) is the most serious pediatric disease with sleep disorder. It is characterized by episodes of hypopnea or obstructive apnea during sleep, resulting in abnormal ventilation and sleep pattern [1]. The prevalence ranges from 1% to 5% in children, with a peak incidence between 2 and 6 years of age [2]. If not treated in an early time point, it can lead to severe complications such as growth retardation, learning deficits, neurocognitive impairments, pulmonary hypertension and cardiovascular consequences, that persist into adulthood [3]. Analysis of large-scale in Chinese children verified that unlike the cases in adults, tonsillar hypertrophy and adenoid hypertrophy were identified as the primary factors associated with the development of pediatric OSAS [4, 5]. Given that the adenotonsillectomy (AT) is reported as the first-line surgical treatment and cures airway obstruction in 75% to 100% of the cases. However, resid-

ual OSAS may persist in a substantial proportion of children even after AT, which indicates that in addition to large tonsils and adenoids, other comorbidities are present. Children with OSAS often present the underlying craniofacial abnormalities such as narrow upper airway as a result of having mandibular retrusion, small mandible and Class II malocclusion, which influence the presence and/or the severity of OSAS [6, 7]. The constant use of continuous positive airway pressure (PAP) is usually considered as the gold standard treatment for residual OSAS despite AT. Nevertheless, adherence to PAP in youth is generally very poor, and might be limited due to the risk of developing craniofacial sequels over time [8, 9]. Based on the existing findings, OSAS patients may benefit from orthodontic treatment options, such as rapid maxillary expansion (RME), mandibular advancement appliances (MAA) and myofunctional therapy (MFT), depending on repositioning the mandible in a forward and downward position to relieve upper airway obstructions during sleep. As tied together with conventional AT as the multidisciplinary treatment, it is more effective rather than separately to treat by AT alone [10, 11].

To our knowledge, there are systemic reviews and meta-analyses, supported mainly by uncontrolled clinical trials or limited in terms of small sample sizes, reporting the effectiveness of different types of orthodontic and functional treatments for pediatric OSAS, but very few studies compared these modalities together with long-term rather than short-term follow-up, or even had conflicting results. We therefore firstly conducted a 10-year retrospective case-control study, the aim of which was to estimate the long-term recurrence-free survival (RFS) of the three common orthodontic treatments for residual OSAS after AT in growing children, taking PAP as control.

2. Methods

2.1 Study design and participant recruitment

From 01 January 2012 to 29 February 2023, the electronic medical records (EMRs) of children affected by mild to moderate OSAS, with Class II malocclusion patterns, and treated by orthodontic treatments were screened in our stomatology department following the the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [12]. Inclusion criteria were as follow: (1) patient diagnosed with OSAS based on the polysomnography (PSG) examination in compliance with the standard criteria of the American Academy of Sleep Medicine (AASM) international classification of sleep disorders [13], or the inclusion (or not) of excessive daytime sleepiness as a necessary diagnostic criterion [14]; (2) an obstructive apnea-hypopnea index (AHI) score between 1 and 9 [13]; (3) age between 5–10 years; (4) history of AT surgery before orthodontic treatments; (5) cephalometric standards of Class II malocclusion with overjet $\geq$5.0 mm and ANB (AB plane angle) angle $>4°$; (6) body mass index (BMI) <24 kg/m^2; (7) complete medical data; (8) at least 1 years of follow-up. Patients were excluded if they had other sleep disorders rather than OSAS, *i.e.*, asthma, craniofacial anomalies related to certain syndromes such as Down, Pierre Robin Syndromes, *etc.*, or other concomitant anatomical factors including severe temporomandibular disorders, nasal stenosis, macroglossia, rhinosinusitis and cleft palate.

Subjects were separated into one of the following three case groups or control group according to their therapeutic modalities (Fig. 1). RME, MAA and MFT group respectively consisted of patients receiving RME, MAAs and MFT therapy for residual OSAS following AT surgery. The control group were selected in patients who did not undergo any orthodontic procedure after AT surgery, whereas, used positive airway pressure therapy (PAP) at the same admission time. They were individually matched to cases by same sex, similar age and hospital admission date.

2.2 PAP therapy

All patients were prescribed continuous PAP used a ResMed AirSense 10 AutoSet machine (ResMed, San Diego, CA, USA) with the ability to auto-titrate positive airway pressure mode based on a proprietary algorithm. After initial inpatient-education and mask fitting program, patients underwent a nocturnal polysomnography with PAP titration. The minimal PAP pressure able to improve the AHI to <5 episodes/h and without desaturation $<90\%$ including supine rapid eye movement (REM) sleep was used for the therapeutic PAP pressure. Participants were instructed to wear the PAP $\geq$4 hours a night over a 1-year period after trial and fitting. Adherence data including the PAP usage time, 95th percentile air pressure, AHI and mask leak were automatically upload to ResMed AirView™ 10 (ResMed, San Diego, CA, USA) for review.

2.3 Orthodontic therapy

All treatments were conducted by the same skilled clinicians who had expertise in techniques for children with class II malocclusion in our department.

2.3.1 RME procedures

Patients in this group were treated with the Hyrax expander, using fixed devices to anchor in the second deciduous molars and weld to an expander screw in the palatal surfaces. All patients were treated based on the same expansion protocol. The device was active after cementation. The spiral expander was rotated every 1/4 rotation (90°), and the rapid expansion involved 2 to 4 times per day for a total of 15 days. Therefore, the maxillary arch would be expanded by 0.4 mm a day and 4 mm in 10 days. Patients were reviewed at intervals of two weeks. Subsequently, the device was kept in the mouth as a retainer for an average duration of 12 months after the active expansion period.

2.3.2 MMA (mandibular advancement appliances) procedures

The Twin-Block appliance was used for all patients in this group, which was custom-made from dental impressions. It comprised the upper and lower bite blocks with inclined planes, which are designed to fit together so that the mandible adopted an anterior position. All patients were treated based on the standard titration protocol, in which the titration was set at 50% of the maximal mandibular protrusion at baseline.

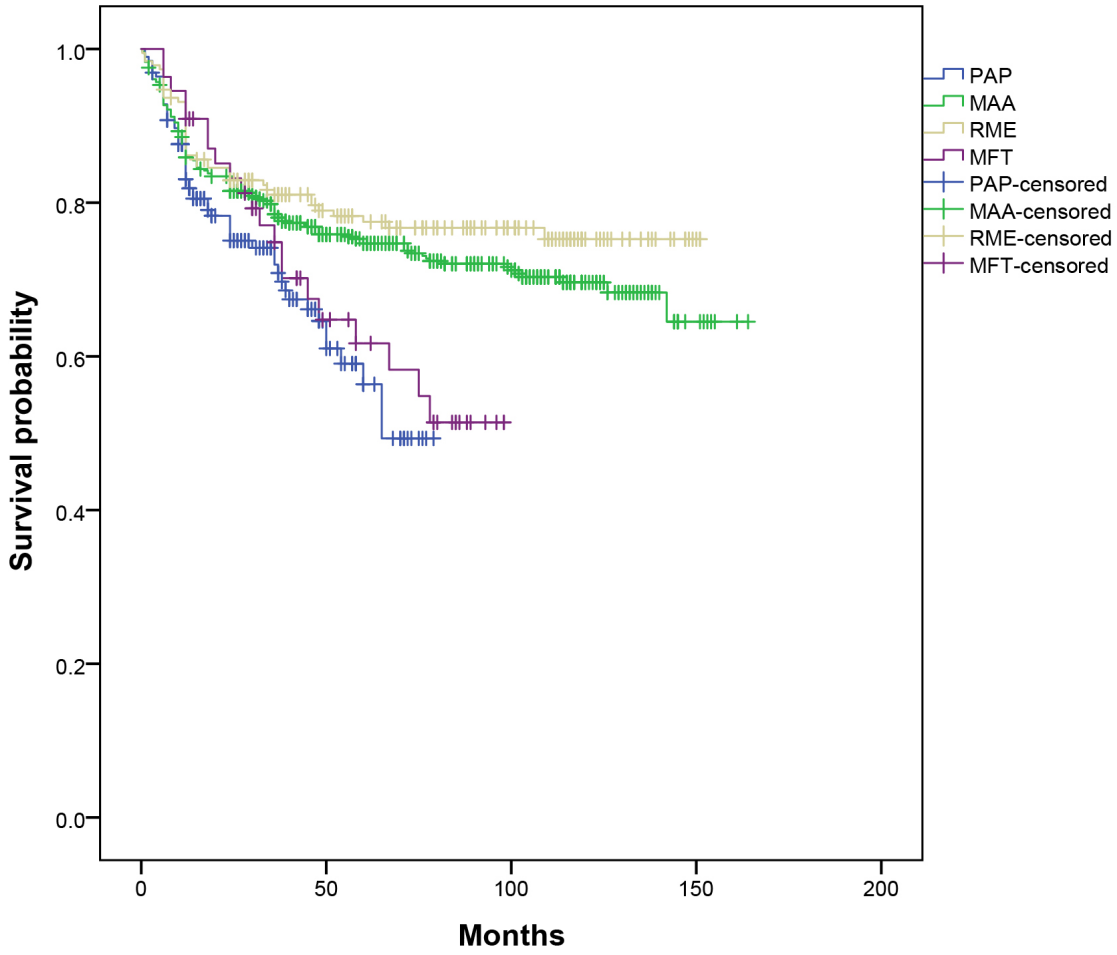


FIGURE 1. Recurrence-free survival (RFS) curves for PAP, RME, MAA, MFT group over a 10-year follow-up period. According to Log-rank test, significant higher long-term RFS was observed in RME group as compared to PAP ($p < 0.001$) and MFT group ($p = 0.016$), while comparable to MAA group ($p = 0.217$). PAP: positive airway pressure; MAA: mandibular advancement appliances; RME: rapid maxillary expansion; MFT: myofunctional therapy.

Next, patients were evaluated and advanced in steps of 0.5 mm per week at each clinic visit until the maximum comfortable mandibular advancement. The duo-block device should be worn for a period of about 12 months.

2.3.3 MFT procedures

Each subject in this group were treated by the speech pathologists of the same rank according to oropharyngeal exercise protocol including both isotonic and isometric exercises to strengthen mouth and pharynx muscles, which were mainly working on functions such as breathing, blowing, sucking, speaking, chewing and swallowing. The MFT training included (1) soft palate: oral vowel sound pronunciation; (2) tongue: brushing it along the superior and lateral teeth surfaces, placing its tip against the hard palate and sliding it backward, pressing entirely the tongue against the hard palate and sucking upward against the palate, forcing its back against the floor of the mouth and keeping its tip in contact with the inferior incisive teeth; (3) face: alternated contraction and relaxation of orbicular muscle movements and lateral movements of buccinators and mandible muscles; (4) stomatognathic functions: inhaling nasally and exhaling orally, in conjunction with specific chewing training exercise using the tongue in the palate closed teeth without perioral contraction [15]. Two-hour exercises should be guaranteed every day, and persisted for a total of 12 months.

2.4 Outcome measurement

Demographic details and clinical information were taken from the EMRs. Follow-up data were collected as part of routine contact tracing through clinic visits at intervals of 6 months for at least two years after initiation of treatments, and thereafter every 12 months on schedule through telephone interviews by the specially trained investigators for the long-term follow-up visits. All data were documented in our prospective database.

Daytime sleepiness was estimated by the Epworth Sleepiness Scale (ESS), which is an 8-item questionnaire scored on a scale of 0–3 with a maximum score of 24. Higher scores indicated a higher likelihood of falling asleep [16]. The severity of OSAS was clinically evaluated by AHI, defined as the number of apneas or hypopneas recorded during per

hour of sleep using polysomnogram. Therefore, a successful responder was pre-defined as a reduction of AHI >50% from the initial AHI value was achieved. Recurrence was considered as the recurrence of clinical sleep-related symptoms or AHI by repeat polysomnogram in patients, who were treated by AT followed by orthodontic treatments. Consequently, RFS was defined as the interval of maintaining clinical remission from the complete of treatments to the date when OSAS was recurrent. Cephalometric variables were estimated by the lateral cephalograms.

The primary endpoint was a long-term success rate after treatment. The secondary outcomes measures included the immediate post-operative success rate, improvements in ESS scores, the craniofacial changes, s-EMG changes of masticatory muscle and long-term OSAS sequelae.

2.5 Sample size calculation

PASS software, version 22 (NCSS, LLC. Kaysville, UT, USA) was used to calculate sample size. Our hypothesis was that the RME or MAA treatment for OASA children with Class II malocclusion were superior to the conventional PAP therapy with regard to long-tern RFS. Based on the previous publications, we estimated that the probability of observing a recurrence of OASA was 0.5 to 0.7 in the conventional PAP group and 0.4 to 0.6 in the RME or MAA group [17, 18]. The margin of clinical superiority was set at 0.9 with actual Hazard Ratio at 0.4 to 0.6 by 0.1. Assuming a power of 90% and type I error of 5% in a two-sided test, we determined to include at least 161 patients in each group.

2.6 Statistical analysis

Statistics were performed with SPSS software, version 22.0 (SPSS Inc, Chicago, IL, USA). Statistical significance was set at the 5% level with 2-tailed test.

Normal distribution (age, BMI, OAHI (obstructive apnea hypopnea index), ESS scores) and categorical variables (gender, OSAHS (obstructive sleep apnea hypopnea syndrome) severity, successful responders, compliance rate, adverse events) were shown as mean ± standard deviation (SD) and proportion. Statistic differences among groups were determined using analysis of variance (ANOVA) and Chi-square test, respectively. The probability of RFS was evaluated by the Kaplan-Meier method, with differences among groups assessed by log-rank analysis with 95% confidence interval (CI). The censored point was defined as remission at the last clinical contact or the last follow-up assessment. Patients lost during follow-up were censored at the time of the last follow-up. Analysis of cephalometric changes and s-EMG changes was performed using ANOVA and Bonferroni *post-hoc* test.

3. Results

3.1 Patients' recruitment and baseline characteristics

A total of 1367 children were assessed for eligibility from 2005 to 2022. Of these, 10.9% of cases were excluded following data review, including 86 cases not meeting the inclusion criteria, 27 meeting the exclusion criteria and 37 with missing data. Therefore, a total of 1217 cases were involved. Demographic data and clinical characteristic of subjects before orthodontic treatments were illustrated in Table 1. No significant differences were observed among the four groups.

3.2 Short-term outcomes

Among the involved cohort, 81.1% of patients achieved immediate success after MAAs therapy with a ≥50% AHI reduction, which is similar to that after 12 months of RME treatment (85.0%). Whereas, it is greater compared with PAP-control (71.1%) and MFT treatment (67.1%). According to

TABLE 1. Baseline demographics and clinical characteristics for two groups.

Parameter	PAP (n = 274)	RME (n = 628)	MAA (n = 233)	MFT (n = 82)	F/χ^2 value	p
Age (yr)	6.69 ± 1.73	6.59 ± 1.70	6.61 ± 1.91	6.67 ± 1.69	0.065	0.978
Female, sex, n (%)	144/274 (52.6%)	292/628 (46.5%)	113/233 (48.5%)	44/82 (53.7%)	3.660	0.301
BMI, kg/m^2	21.21 ± 1.84	21.94 ± 3.33	21.53 ± 2.65	21.16 ± 3.29	0.377	0.770
OAHI (times/h)	5.87 ± 0.74	6.21 ± 1.28	5.95 ± 1.00	6.28 ± 1.08	0.850	0.470
min SaO_2 (%)	87.45 ± 6.34	86.86 ± 6.68	87.66 ± 8.78	87.84 ± 6.23	0.136	0.938
OSAHS severity						
Mild (1 ≤ AHI < 5 time/h)	127 (46.4%)	307 (48.9%)	112 (48.1%)	38 (46.3%)	0.587	0.899
Moderate (5 ≤ AHI < 10 time/h)	147 (53.6%)	321 (51.1%)	121 (51.9%)	44 (53.7%)		
Adherence rate, n (%)	222 (81.0%)	577 (91.9%)	221 (94.8%)	72 (87.8%)	32.648	<0.001
Successful responders (%)	195/274 (71.2%)	534/628 (85.0%)	189/233 (81.1%)	55/82 (67.1%)	31.981	<0.001

PAP: positive airway pressure; MAA: mandibular advancement appliances; RME: rapid maxillary expansion; MFT: myofunctional therapy; BMI: body mass index; SaO_2: arterial oxygen saturation; OSAHS: obstructive sleep apnea hypopnea syndrome; AHI: obstructive apnea-hypopnea index.

ANOVA analysis, the post-treatment ESS scores (mean ± SD) decreased greatly from the baseline value of 21.33 ± 3.67 in PAP, 22.50 ± 1.64 in RME, 22.56 ± 3.04 in MAA and 23.09 ± 2.59 in MFT.

The cephalometric analysis was revealed in Table 2 using ANOVA analysis with Bonferroni *post-hoc* test. The maxillary incisor angle between the upper incisor line and maxillary plane significantly decreased as results of RME, MAA and MFT treatment, when comparing to PAP control group, indicating a maxillary incisor retroclination. Mandibular measurements showed that the SNB (sella-nasion-B point) angle presenting the sagittal position of the mandible significantly increased, and the mandibular incisor angle between the lower incisor line and the mandibular plane significantly increased after three orthodontic treatments. In which, it indicated a proclination of the mandibular incisors. Additionally, an increased mandibular base was also observed. Regarding the intermaxillary relationships, there was a significant increase in the ANB-angle. Ultimately, the overjet and overbite had significantly decreased. Table 3 showed the s-EMG findings. Significant improvements were achieved in the AsI (asymmetry index) of TA and MM (masseter muscles) after three orthodontic interventions. In addition to the benefits of balanced occlusion, the mV (millivolt) of TA and MM also showed significant increases. The control group did not show any significant changes.

3.3 Long-term outcomes

The median duration of follow-up was 105.00 months (IQR (inter-quartile range): 32, 178) (range: 24, 162) in PAP group, 96.50 (IQR: 30.5, 162.5) (range: 24, 178) in RME, 95.00 (IQR: 27, 163) (range: 24, 159) in MAA and 99 (IQR: 27, 171) (range: 24, 145) in MFT, respectively. No differences were observed with $p = 0.842$. Fig. 2 showed the RFS curves. A total of 29.7%, 26.6%, 22.2% and 38.2% of patients in PAP, RME, MAA and MFT experienced an event of OSAS recurrence during the long-term follow-up period. According to the Kaplan-Meier analysis, the rate of RFS was achieved as 81.9% *vs.* 86.2% *vs.* 85.5% *vs.* 83.0% in PAP, RME, MAA and MFT group, of 1 year, which were significantly higher than that in the matched-control group. The estimated 3-year recurrence-free of PAP, RME, MAA and MFT was 70.8%, 81.0%, 78.0% and 74.9%, respectively. Compared to those in control group, patients had a significantly higher rate of long-term remission of OSAS. As expected, this difference remained highly significant on the estimated 5-year in REM, MMA and MFT as opposed to control group (77.5% *vs.* 74.7% *vs.* 58.3% *vs.* 56.4%). As a matter of fact, the median of RFS was significantly longer in patients involved in RME (122.04 ± 3.04 (95% CI: 116.08, 127.99)), MAA group (120.04 ± 4.21 (95% CI: 111.79, 128.28)) than those in PAP-control (54.96 ± 2.51 (95% CI: 50.05, 59.87)) and MFT group (68.96 ± 4.95 (95% CI: 59.24, 78.68)) (RME *vs.* PAP, $p = 0.001$; MAA *vs.* PAP, $p = 0.002$; RME *vs.* MFT, $p = 0.016$; MAA *vs.* MFT, $p = 0.048$). But it did not differ between RME and MAA ($p = 0.217$), and between PAP and MFT ($p = 0.408$).

As far as the long-term cephalometric variables were concerned, significant differences were found among RME, MMA and MFT in respect to ANB angle, mandibular base, overjet and overbite during the long-term follow-up based on the ANOVA analysis and Bonferroni *post-hoc* test. Subjects in PAP-control group showed a negative change in SNA (sella-nasion-A point) and maxillary base in response to the development of retrusion in midface (Table 2). Additionally, the results of long-term follow-up also confirmed the improved s-EMG parameters of masticatory muscles. However, significantly decreased AsI of TA and MM occurred after long-term of MFT treatment as compared to RME and MAA (Table 3).

3.4 Adverse events

There were no major complications observed in any of the orthodontic groups. The minor side-effects were reported in 52.1% of the patients receiving RME and MAA, with temporomandibular joint pain (10.3%), myofascial pain, mouth dryness, excessive drooling, gingiva irritation (18.6%), discomfort and tenderness of the teeth being the most frequent (23.2%). But these symptoms were transient and resolved in a few months post-treatment. Facial flattening and maxillary retrusion were observed in 65.3% and 34.3% of cases in the PAP group. Other side effects including nasal congestion, oronasal dryness, epistaxis, eye irritation from air leak, facial pain and skin abrasion affected 23.1% of the patients.

4. Discussion

To the best of our knowledge, the present study was firstly presented a 10-year longitudinal comparison of RFS of the common orthodontic modalities as a part of comprehensive treatment in a large group of pediatric patients with residual OSAS following AT. Our main result indicated that the use of RME and MMA as an adjuvant therapy for craniofacial alterations in persist OSAS after AT, resulted in significantly longer RFS than MFT and conventional PAP, with fewer new adverse events identified.

According to preliminary studies, many adolescences or adults begin snoring and experience OSAS in childhood, therefore, the importance of early diagnosis and measurement to prevent long-term behavioral and emotional problems in adult life should be stressed [19]. AT surgery is a well-established treatment option for pediatric OSAS. However, pediatric OSAS presents a multifactorial etiology leading to residual apnea when AT was only submitted. Interestingly, radiological study proved that craniofacial morphological factors were associated with a narrow upper airway and sleep-disordered breathing [20]. Epidemiological literature pointed out that the prevalence of craniofacial abnormalities in children with OSAS was 89.9% as compared to a healthy pediatric population [21], and various in persistent OSAS despite AT surgery [22]. Although PAP therapy is an effective treatment modality in this setting, effectiveness is limited by poor adherence [23]. If the etiology of residual OSAS is retrognathia or maxillary constriction, nowadays, there are orthodontic treatment options, such as RME, MAAs and MFT, suggested to complete correction of the malocclusion and to gain long-term stability during growth [24].

TABLE 2. Comparative cephalometric changes between trial group and control group.

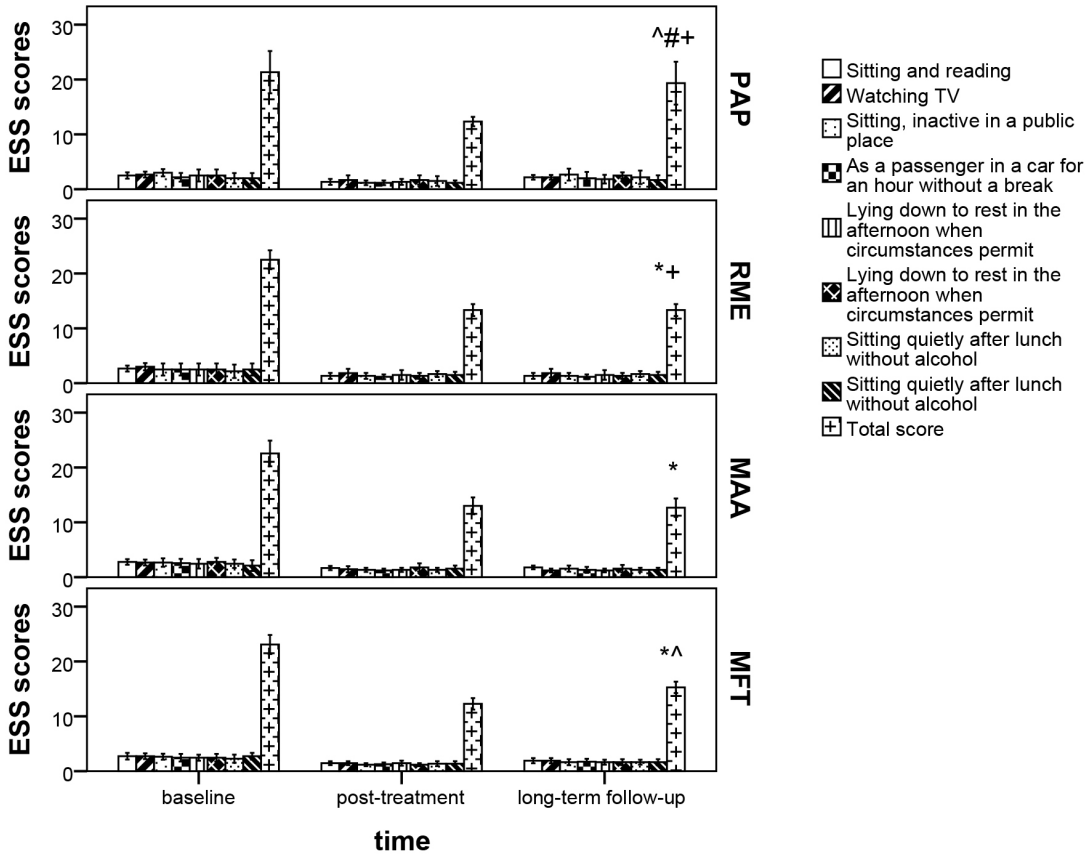
Parameters	PAP (n = 195)			RME (n = 534)			MAA (n = 189)			MFT (n = 55)		
	T0	T1	T2	T0	T1	T2	T0	T1	T2	T0	T1	T2
						Angular (°)						
SNA	80.93 ± 1.35	77.21 ± 1.48*	78.35 ± 1.36*	80.44 ± 1.37	80.65 ± 1.36	81.42 ± 1.17	79.50 ± 1.29	80.25 ± 1.16	80.89 ± 1.25	79.75 ± 1.25	80.00 ± 1.41	80.75 ± 1.01
SNB	74.24 ± 1.52	74.53 ± 1.64^#■	74.58 ± 1.33^#■	74.35 ± 1.16	76.65 ± 1.26*•	77.00 ± 2.04*•	74.51 ± 1.29	76.75 ± 1.28*•	76.93 ± 1.94*•	73.50 ± 0.99	75.75 ± 0.96*•	75.13 ± 1.79*
ANB	5.71 ± 1.14	5.53 ± 1.21^#■	5.43 ± 1.02^#■	5.76 ± 1.19	3.04 ± 1.06*•	3.12 ± 1.04*•	5.80 ± 1.24	3.01 ± 1.31*•	3.10 ± 1.05*•■	5.70 ± 1.06	3.40 ± 0.89*•	3.56 ± 2.04*•^#
Maxillary incisor angle Is-as/Max	102.71 ± 1.64	102.36 ± 1.40^#■	102.12 ± 1.23^#■	101.65 ± 1.39	96.02 ± 2.91*•	95.26 ± 2.26*•	101.80 ± 1.92	95.81 ± 2.68*•	95.38 ± 2.63*•	101.81 ± 1.52	97.81 ± 1.47*•	96.44 ± 1.70*•
Mandibular incisor angle ii-ai/Man	90.22 ± 1.07	90.92 ± 1.35^#■	92.80 ± 1.63^#■	90.50 ± 1.19	97.44 ± 1.70*•	97.12 ± 1.47*•	90.40 ± 1.14	97.82 ± 1.30*•	97.63 ± 1.52*•	90.80 ± 1.10	95.38 ± 1.22*•	96.04 ± 1.49*•
						Linear (mm)						
Maxillary base Art-A	86.06 ± 4.05	84.12 ± 4.84*^#■	83.01 ± 5.20*^#■	86.72 ± 4.74	88.81 ± 4.64*•	89.01 ± 4.66*•	87.11 ± 4.55	88.94 ± 4.59*•	88.92 ± 3.83*•	86.80 ± 4.44	88.80 ± 4.28*•	88.17 ± 3.69*
Mandibular base Art-Pog	68.12 ± 3.25	69.34 ± 3.33^#■	68.27 ± 3.63^#■	67.05 ± 3.24	73.14 ± 3.70*•	73.81 ± 3.94*•	66.83 ± 3.03	73.21 ± 3.70*•	73.63 ± 3.83*•■	68.11 ± 3.63	71.87 ± 3.33*•	70.18 ± 3.58*•^#
Overjet	7.35 ± 1.48	7.38 ± 1.54^#■	7.44 ± 1.55^#■	7.39 ± 1.66	3.38 ± 1.17*•	3.12 ± 1.44*•	7.40 ± 1.89	3.44 ± 1.71*•	3.20 ± 1.65*•■	7.33 ± 1.75	3.58 ± 1.86*•	3.65 ± 1.49*•^#
Overbite	6.26 ± 1.26	6.19 ± 1.56^#■	6.63 ± 1.41^#■	6.17 ± 1.05	3.68 ± 1.59*•	3.70 ± 1.96*•	6.10 ± 1.58	3.63 ± 1.51*•	3.78 ± 2.09*•	6.25 ± 1.66	3.61 ± 1.14*•	4.03 ± 1.25*•^#

*SNA: sella-nasion-A point; SNB: sella-nasion-B point; ANB: AB plane angle; PAP: positive airway pressure; RME: rapid maxillary expansion; MAA: mandibular advancement appliances; MFT: myofunctional therapy. *$p < 0.05$ compared with T0, ^$p < 0.05$ compared with RME group, #$p < 0.05$ compared with MAA group, ■$p < 0.05$ compared MFT group, •$p < 0.05$ compared with PAP group.*

TABLE 3. Comparative mean values of s-EMG (surface electromyography) changes between three orthodontic groups and control group.

Variables	PAP (n = 274)			RME (n = 628)			MAA (n = 233)			MFT (n = 82)		
	T0	T1	T2	T0	T1	T2	T0	T1	T2	T0	T1	T2
mV of MM	85.93 ± 13.51	81.21 ± 14.80^#■	81.35 ± 13.69^#■	84.65 ± 13.74	113.91 ± 14.84*•	111.42 ± 11.71*•	88.60 ± 10.48	109.64 ± 21.64*•	110.89 ± 11.25*•	86.75 ± 14.25	108.00 ± 12.41*•	109.75 ± 10.01*•
mV of TA	64.24 ± 15.23	74.53 ± 16.49^#■	74.58 ± 1.33^#■	65.63 ± 15.75	89.91 ± 17.14*•	90.00 ± 18.61*•	66.98 ± 14.88	88.55 ± 19.96*•	89.93 ± 16.94*•	63.50 ± 14.99	85.75 ± 15.41*•	84.13 ± 11.79*•
AsI of MM	79.90 ± 5.17	81.97 ± 7.20^#■	80.65 ± 7.66^#■	78.94 ± 5.85	91.18 ± 4.85*•	90.88 ± 4.33*•■	77.59 ± 4.02	92.03 ± 3.54*•	91.00 ± 4.64*•■	78.34 ± 5.67	88.23 ± 4.57*•	86.09 ± 3.57*•^#
AsI of TA	76.26 ± 4.97	78.33 ± 3.74^#■	76.63 ± 3.41^#■	76.95 ± 5.11	90.49 ± 4.22*•	93.70 ± 4.96*•■	78.08 ± 4.90	91.63 ± 4.03*•	91.78 ± 4.09*•■	77.25 ± 5.66	90.42 ± 5.14*•	83.83 ± 5.25*•^#

*s-EMG: surface electromyography; TA: anterior temporalis; MM: masseter muscles; mV: maximum voltage; AsI: asymmetry index; PAP: positive airway pressure; RME: rapid maxillary expansion; MAA: mandibular advancement appliances; MFT: myofunctional therapy. *$p < 0.05$ compared with T0, ^$p < 0.05$ compared with RME group, #$p < 0.05$ compared with MAA group, ■$p < 0.05$ compared MFT group, •$p < 0.05$ compared with PAP group.*



F I G U R E 2. ANOVA analysis showed that PAP, RME, MAA and MFT treatment were associated with significant greater decreases in the mean of ESS scores at post-treatment and long-term follow-up. Significant lower ESS scores were observed in three orthodontic groups as opposed to PAP-control group. $*p < 0.05$ compared with PAP, $^{\wedge}p < 0.05$ compared with RME, $^{\#}p < 0.05$ compared with MAA, $+p < 0.05$ compared with MFT. PAP: positive airway pressure; MAA: mandibular advancement appliances; RME: rapid maxillary expansion; MFT: myofunctional therapy; TV: television; ESS: Epworth Sleepiness Scale.

RME correction was first proposed as an orthodontic treatment in young patients. Recently, it was widely adopted in clinical practice to correct a narrow upper jaw since it first successfully linked to SDB (sleep-disordered breathing). It could reduce the risk of obstruction by decreasing nasal resistance and allowing tongue repositioning, which contributed to OSAS. As a consequence, the meta-analysis confirmed the short-term efficacy of RME with the evidence of a significant improvement in the AHI in children with slight or moderate OSAS as early as symptoms appear [18, 25]. The functional MAAs aiming to correct mandibular retrognathia through redirecting and stimulating of anterior mandibular growth has been used as an efficient therapy for mild-to-moderate pediatric OSAS with a reduction of at least 50% in the AHI [26]. MFT proposals is a multi-component treatment including several combinations of isotonic and isometric exercises, which involves several combinations of oropharyngeal muscles. The primary mechanism of action of MFT is to improve the function of upper airway dilator muscles that are essential to maintain pharyngeal patency, while muscular endurance exercises aim to improve the mobility of oropharyngeal muscles to reduce airway closures during sleep. Based on previous findings, it probably reduces AHI by 62% in children, daytime sleepiness and snoring in the short-term as opposed to sham therapy or no treatment [15]. Consistent with previous literatures, 85.0%, 81.1% and 67.1% of child patients achieved a 50% reduction in AHI immediately after RME, MAA and MFT for the treatment of residual OSAS following AT. In addition, we found that the ESS cores were significantly reduced from the baseline value in all the three orthodontic groups. Furthermore, RME, MAA and MFT were significantly associated with good adherence as compared to the conventional PAP, which was consistent to previous study [27]. Nowadays, elastodontic appliances or clear aligners have sustained their upward trend of being utilized more frequently as technology advances, which also showed good adherences [28]. However, their effects on OSAS patients are highly debatable with very limit evidences.

In the present study, at the end of orthodontic treatments, subjects showed a corrected positive overjet and overbite with better s-EMG results, which reflected the improvement in facial profile and occlusion. To have a better explanation of these results, some authors reported that after the mid-palatal suture opening using RME, not only transversal, but also vertical and anteroposterior changes occurred [29]. Previous study also revealed evidence that orofacial muscle training protocols on the correction of myofunctional and musculoskeletal problems in developing dentition, particular facilitating anterior open bite

correction, which resulted in a positive overjet and overbite [30].

To our knowledge, only a few studies, even with small-size samples, have evaluated the long-term effects of these orthodontic treatments in pediatric OSAS, and their results were disappointing, as they did not address the etiological causes. To investigate the long-term stability, this study estimated the long-term effect of orthodontic treatments as adjunctive therapies to AT in children with Class II Malocclusion during a 10-year follow-up. According to our results, after a median of 90 months (IQR: 20, 160) follow-up, a 122.04 (95% CI: 116.07, 127.99), 120.04 (95% CI: 111.79, 128.28) and 68.96 (95% CI: 59.24, 78.68) months of RFS was observed in RME, MAA and MFT group, respectively, as opposed to 54.95 (95% CI: 50.05, 59.87) in PAP-control group. The estimated 3-year and 5-year recurrence-free of PAP, REM, MMA was 70.8% *vs.* 81.0% *vs.* 78.0% *vs.* 74.9% and 56.4% *vs.* 77.5% *vs.* 74.7%% *vs.* 58.3%, respectively. This was comparable to previous data reporting that the AHI decline maintained as indicated by follow-up tests ranging from 3 months to 14 years following RME [18]. The AHI significantly decreased at the long-term of 6.6 $\pm$ 2.8 years evaluation after MAA with 46.7% of patients obtaining an AHI $<$5 and 83.4% of patients attaining an AHI $\leq$15 events [31]. A longitudinal follow-up study taken from a randomized control trial containing 103 patients with OSAS revealed that both PAP and MAA therapy demonstrated good and stable treatment effects after a 1-, 2- and 10-year follow-up. PAP was better in terms of lowering AHI values after a decade of treatment, when both therapies are compared. However, it was limited in high rate of dropout due to nonadherence, died or lost to follow-up [17]. Conversely, this study found that patients had a significantly higher rate of long-term remission of OSAS as compared to PAP-control, for the correction of craniofacial abnormalities. Significant changes of overjet and overbite were found not only in short-term after a 12-month use of orthodontic appliances but also during the 10-year long-term follow-up. This results again mirrored findings by a meta-analysis of 12 studies revealing a significant improvement of the function or morphology of the craniofacial surface occurred over time with at least one year use of orthodontic appliances or MFT, and the impact becomes more pronounced as the duration of the intervention lengthens [31]. To the best of our knowledge, we firstly found that significant improvements about s-EGM factors illustrating balanced occlusion were achieved after long-term of three orthodontic interventions as opposed to control group, that did not show any significant changes.

With regard to long-term sequelae, this study showed that patients in three orthodontic groups did not experience a significant number of adverse events. Only a few minor post-treatment side effects occurred, which gradually resolved in a few months after therapy and not resulted in any significant long-term complications. Whereas, subjects in PAP control group experienced significant midfacial retrusion as opposed to other groups in our findings, which was consistent with previous evidence that nasal mask pressure inhibited midface growth or actively pushed midfacial structure backward during the growth phase [32].

The present study had several limitations. First, there might be the undetected confounders and probable bias due to the nature of retrospective analysis with observational data. Second, investigators who reviewed data were unable to be blinded to patients' cohort. Thirdly, only a few cases were recruited for MFT group, this limited our ability to detect effects of long-term RFS. Future large-scale, long-term randomized studies were needed to validate our findings.

5. Conclusions

In conclusion, therapeutic trial using RME and MAAs showed a better long-term RFS as opposed to conventional PAP, based on our Kaplan-Meier analysis, and provided a reasonable alternative for residual OSAS after AT in children combined with Class II malocclusion. Their benefits appeared especially in children due to poor compliance to conventional PAP.

ABBREVIATIONS

RFS, recurrence-free survival; OSAS, obstructive sleep apnea syndrome; AT, adenotonsillectomy; PAP, positive airway pressure; RME, rapid maxillary expansion; MAA, mandibular advancement appliances; MFT, myofunctional therapy; ESS, Epworth Sleepiness Scale; EMG, electromyogram; STROBE, Observational Studies in Epidemiology; EMRs, electronic medical records; PSG, polysomnography; AASM, American Academy of Sleep Medicine; AHI, apnea-hypopnea index; BMI, body mass index; SD, standard deviation; IQR, interquartile range; CI, confidence interval; ANOVA, analysis of variance; OAHI, obstructive apnea hypopnea index; OSAHS, obstructive sleep apnea hypopnea syndrome; AsI, asymmetry index; MM, masseter muscles; mV, millivolt.

AVAILABILITY OF DATA AND MATERIALS

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author (Mengxing Wang) on reasonable request.

AUTHOR CONTRIBUTIONS

MXW—was involved in the conception and design, analysis and interpretation of the data; the drafting of the paper, revising it critically for intellectual content; and the final approval of the version to be published. TX, RQL—was involved in the conception and design, analysis and interpretation of the data; the drafting of the paper, revising it critically for intellectual content. And all authors agreed to be accountable for all aspects of the work.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The ethics was approved by the Ethics Examining Committee of Human Research of Children's Hospital affiliated to Capital Institute of Pediatrics (approval number 2023-012-17). Written informed consent was obtained from all participants.

ACKNOWLEDGMENT

Not applicable.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Perez C. Obstructive sleep apnea syndrome in children. General Dentistry. 2018; 66: 46–50.

[2] Savini S, Ciorba A, Bianchini C, Stomeo F, Corazzi V, Vicini C, *et al.* Assessment of obstructive sleep apnoea (OSA) in children: an update. ACTA Otorhinolaryngologica Italica. 2019; 39: 289–297.

[3] Chan KC, Au CT, Hui LL, Wing YK, Li AM. Childhood OSA is an independent determinant of blood pressure in adulthood: longitudinal follow-up study. Thorax. 2020; 75: 422–431.

[4] Xiao L, Su S, Liang J, Jiang Y, Shu Y, Ding L. Analysis of the risk factors associated with obstructive sleep apnea syndrome in Chinese children. Frontiers in Pediatrics. 2022; 10: 900216.

[5] Gulotta G, Iannella G, Vicini C, Polimeni A, Greco A, de Vincentiis M, *et al.* Risk factors for obstructive sleep apnea syndrome in children: state of the art. International Journal of Environmental Research and Public Health. 2019; 16: 3235.

[6] Xu Q, Wang X, Li N, Wang Y, Xu X, Guo J. Craniofacial and upper airway morphological characteristics associated with the presence and severity of obstructive sleep apnea in Chinese children. Frontiers in Pediatrics. 2023; 11: 1124610.

[7] Garg RK, Afifi AM, Garland CB, Sanchez R, Mount DL. Pediatric obstructive sleep apnea: consensus, controversy, and craniofacial considerations. Plastic and Reconstructive Surgery. 2017; 140: 987–997.

[8] Ramar K, Dort LC, Katz SG, Lettieri CJ, Harrod CG, Thomas SM, *et al.* Clinical practice guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy: an update for 2015. Journal of Clinical Sleep Medicine. 2015; 11: 773–827.

[9] Bariani R, Guimaraes TM, Cappellette MJ, Moreira G, Fujita RR. The impact of positive airway pressure on midface growth: a literature review. Brazilian Journal of Otorhinolaryngology. 2020; 86: 647–653.

[10] Templier L, Rossi C, Miguez M, Perez JC, Curto A, Albaladejo A, *et al.* Combined surgical and orthodontic treatments in children with OSA: a systematic review. Journal of Clinical Medicine. 2020; 9: 2387.

[11] Yu M, Ma Y, Xu Y, Bai J, Lu Y, Han F, *et al.* Orthodontic appliances for the treatment of pediatric obstructive sleep apnea: a systematic review and network meta-analysis. Sleep Medicine Reviews. 2023; 72: 101855.

[12] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. International Journal of Surgery. 2014; 12: 1495–1499.

[13] Section on Pediatric Pulmonology, Subcommittee on Obstructive Sleep Apnea Syndrome. American Academy of Pediatrics. Clinical practice guideline: diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics. 2002; 109: 704–712.

[14] Patinkin ZW, Feinn R, Santos M. Metabolic consequences of obstructive sleep apnea in adolescents with obesity: a systematic literature review and meta-analysis. Child Obesity. 2017; 13: 102–110.

[15] Rueda JR, Mugueta-Aguinaga I, Vilaro J, Rueda-Etxebarria M. Myofunctional therapy (oropharyngeal exercises) for obstructive sleep apnoea. Cochrane Database of Systematic Reviews. 2020; 11: CD013449.

[16] Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991; 14: 540–545.

[17] Uniken VJ, Doff M, Joffe-Sokolova D, Wijkstra PJ, van der Hoeven JH, Stegenga B, *et al.* Long-term obstructive sleep apnea therapy: a 10-year follow-up of mandibular advancement device and continuous positive airway pressure. Journal of Clinical Sleep Medicine. 2020; 16: 353–359.

[18] Camacho M, Chang ET, Song SA, Abdullatif J, Zaghi S, Pirelli P, *et al.* Rapid maxillary expansion for pediatric obstructive sleep apnea: a systematic review and meta-analysis. The Laryngoscope. 2017; 127: 1712–1719.

[19] Pirelli P, Saponara M, De Rosa C, Fanucci E. Orthodontics and obstructive sleep apnea in children. Medical Clinics of North America. 2010; 94: 517–529.

[20] Tsuda H, Fastlicht S, Almeida FR, Lowe AA. The correlation between craniofacial morphology and sleep-disordered breathing in children in an undergraduate orthodontic clinic. Sleep and Breathing. 2011; 15: 163–171.

[21] Galeotti A, Festa P, Viarani V, D'Anto V, Sitzia E, Piga S, *et al.* Prevalence of malocclusion in children with obstructive sleep apnoea. Orthodontics & Craniofacial Research. 2018; 21: 242–247.

[22] Cohen-Levy J, Quintal MC, Rompre P, Almeida F, Huynh N. Prevalence of malocclusions and oral dysfunctions in children with persistent sleep-disordered breathing after adenotonsillectomy in the long term. Journal of Clinical Sleep Medicine. 2020; 16: 1357–1368.

[23] Uong EC, Epperson M, Bathon SA, Jeffe DB. Adherence to nasal positive airway pressure therapy among school-aged children and adolescents with obstructive sleep apnea syndrome. Pediatrics. 2007; 120: e1203–e1211.

[24] Giuca MR, Carli E, Lardani L, Pasini M, Miceli M, Fambrini E. Pediatric obstructive sleep apnea syndrome: emerging evidence and treatment approach. The Scientific World Journal. 2021; 2021: 5591251.

[25] Sanchez-Sucar AM, Sanchez-Sucar FB, Almerich-Silla JM, Paredes-Gallardo V, Montiel-Company JM, Garcia-Sanz V, *et al.* Effect of rapid maxillary expansion on sleep apnea-hypopnea syndrome in growing patients. A meta-analysis. Journal of Clinical and Experimental Dentistry. 2019; 11: e759–e767.

[26] Yanyan M, Min Y, Xuemei G. Mandibular advancement appliances for the treatment of obstructive sleep apnea in children: a systematic review and meta-analysis. Sleep Medicine. 2019; 60: 145–151.

[27] Gambino F, Zammuto MM, Virzi A, Conti G, Bonsignore MR. Treatment options in obstructive sleep apnea. Internal and Emergency Medicine. 2022; 17: 971–978.

[28] Koletsi D, Makou M, Pandis N. Effect of orthodontic management and orofacial muscle training protocols on the correction of myofunctional and myoskeletal problems in developing dentition. A systematic review and meta-analysis. Orthodontics & Craniofacial Research. 2018; 21: 202–215.

[29] Farronato G, Giannini L, Galbiati G, Maspero C. Sagittal and vertical effects of rapid maxillary expansion in Class I, II, and III occlusions. The Angle Orthodontist. 2011; 81: 298–303.

[30] Boyd SB, Walters AS, Waite P, Harding SM, Song Y. Long-term effectiveness and safety of maxillomandibular advancement for treatment of obstructive sleep apnea. Journal of Clinical Sleep Medicine. 2015; 11: 699–708.

[31] Araie T, Okuno K, Ono MH, Sakai T. Dental and skeletal changes associated with long-term oral appliance use for obstructive sleep apnea: a systematic review and meta-analysis. Sleep Medicine Reviews. 2018; 41: 161–172.

[32] Bjork A, Skieller V. Growth of the maxilla in three dimensions as revealed radiographically by the implant method. British Journal of Orthodontics. 1977; 4: 53–64.

How to cite this article: Tian Xia, Ruqian Luo, Mengxing Wan. Long-term recurrence-free survival of orthodontic treatments for Class II malocclusion as the important supplement protocol to adenotonsillectomy in children with obstructive sleep apnea syndrome: a case-control retrospective study. Journal of Clinical Pediatric Dentistry. 2025; 49(2): 178-187. doi: 10.22514/jocpd.2025.037.