



## Original Article

# Rapid maxillary expansion outcomes in treatment of obstructive sleep apnea in children



Maria Pia Villa <sup>a,\*</sup>, Alessandra Rizzoli <sup>a</sup>, Jole Rabasco <sup>a</sup>, Ottavio Vitelli <sup>a</sup>,  
Nicoletta Pietropaoli <sup>a</sup>, Manuela Cecili <sup>a</sup>, Alessandra Marino <sup>b</sup>, Caterina Malagola <sup>b</sup>

<sup>a</sup> Neuroscience, Mental Health and Sense Organs Department, Paediatric Sleep Disorder Centre, Sant'Andrea Hospital, Faculty of Medicine and Psychology, "Sapienza" University, Rome, Italy

<sup>b</sup> Orthodontic Clinic Sant'Andrea Hospital, Faculty of Medicine and Psychology, "Sapienza" University, Rome, Italy

## ARTICLE INFO

## Article history:

Received 1 August 2014

Received in revised form 19 November 2014

Accepted 23 November 2014

Available online 16 March 2015

## Keywords:

Rapid maxillary expansion

Pediatric OSA

Orthodontic treatment

Residual OSA

## ABSTRACT

**Objectives:** The objectives of this study were to confirm the efficacy of rapid maxillary expansion in children with moderate adenotonsillar hypertrophy in a larger sample and to evaluate retrospectively its long-term benefits in a group of children who underwent orthodontic treatment 10 years ago.

**Methods:** After general clinical examination and overnight polysomnography, all eligible children underwent cephalometric evaluation and started 12 months of therapy with rapid maxillary expansion. A new polysomnography was performed at the end of treatment (T1). Fourteen children underwent clinical evaluation and Brouillette questionnaire, 10 years after the end of treatment (T2).

**Results:** Forty patients were eligible for recruitment. At T1, 34/40 (85%) patients showed a decrease of apnea–hypopnea index (AHI) greater than 20% ( $\Delta$ AHI  $67.45\% \pm 25.73\%$ ) and were defined responders. Only 6/40 (15%) showed a decrease  $<20\%$  of AHI at T1 and were defined as non-responders ( $\Delta$ AHI  $-53.47\% \pm 61.57\%$ ). Moreover, 57.5% of patients presented residual OSA (AHI  $> 1$  ev/h) after treatment. Disease duration was significantly lower ( $2.5 \pm 1.4$  years vs  $4.8 \pm 1.9$  years,  $p < 0.005$ ) and age at disease onset was higher in responder patients compared to non-responders ( $3.8 \pm 1.5$  years vs  $2.3 \pm 1.9$  years,  $p < 0.05$ ). Cephalometric variables showed an increase of cranial base angle in non-responder patients ( $p < 0.05$ ).

Fourteen children (mean age  $17.0 \pm 1.9$  years) who ended orthodontic treatment 10 years previously showed improvement of Brouillette score.

**Conclusion:** Starting an orthodontic treatment as early as symptoms appear is important in order to increase the efficacy of treatment. An integrated therapy is needed.

© 2014 Elsevier B.V. All rights reserved.

## 1. Introduction

Obstructive sleep apnea (OSA) is a sleep disordered breathing characterized by prolonged partial and/or intermittent collapse of the airway during sleep, that interrupts normal ventilation and normal sleep patterns, with a prevalence of 1% to 5.7% in children [1–3].

OSA is a multifactorial disease where different risk factors such as craniofacial anomalies, adenotonsillar hypertrophy, obesity, alterations in upper airway neuromotor tone and airway inflammation can co-exist. These lead to a decrease in nasopharyngeal airway dimensions that promotes a wide spectrum of symptoms ranging from primary snoring, to upper airway resistance syndrome, to frank OSA [4,5].

Among all the causative factors, adenotonsillar hypertrophy is the most common cause of childhood OSA [6,7]. Since it is a surgical therapy, adenotonsillectomy (AT) is limited by surgical risks and, although it leads to significant improvements in respiratory indices, residual disease is present in a large proportion of children, especially if aged  $>7$  years, where obesity, severe OSA before surgery and asthma are present [8]. Moreover, Guilleminault et al. reported in a recent study the recurrence of sleep respiratory symptoms on a cohort of OSA patients during adolescence, not depending on the standard therapies [9].

In addition to large tonsils and adenoids, children with OSA may present narrow upper airways deriving from narrow and long faces, maxillary constriction and/or high arched palates and/or some degree of mandibular retrusion [10–12]. However these orthodontic and craniofacial abnormalities in children with OSA have been widely ignored even if, in the last decades, correction of mandibular or maxillomandibular anomalies has been shown to improve OSA [13–18].

Rapid maxillary expansion (RME) is a dentofacial orthopedic treatment procedure commonly adopted in young patients for the

\* Corresponding author. Sleep Disorder Centre, Sant'Andrea Hospital, Via di Grottarossa 1035-1039, 00189 Rome, Italy. Tel.: +39 0633775855; fax +39 0633775941.

E-mail address: [mariapia.villa@uniroma1.it](mailto:mariapia.villa@uniroma1.it) (M.P. Villa).

treatment of constricted maxillary arches. Several studies have shown the short-term efficacy of orthodontic treatment with rapid maxillary expander with evidence of a significant improvement of OSA even in children with adenotonsillar hypertrophy [14,15,18].

Pirelli et al. [16] demonstrated that all 31 children studied, with upper jaw contraction, oral breathing, nocturnal snoring, and OSA, achieved a normal anterior rhinometry and an apnea–hypopnea index (AHI) < 1 event per hour after four months of treatment with RME. Our group has previously demonstrated in 14 children with dental malocclusion, a body mass index (BMI) <85 percentile, and OSA confirmed by polysomnography (PSG) a significant decrease in the AHI, hypopnea obstructive index and arousal index after 12 months of RME therapy [17]. Moreover questionnaires on daytime and night-time, fulfilled before and after treatment, showed significant decreases in the severity of symptoms.

Only few studies have investigated the long-term effects of orthodontic treatment in OSA by considering the growing and the skeletal changes occurring through the years [18]. Ten of the 14 children who completed our 12-month therapeutic trial using RME (see above) performed 24 months follow-up after the end of the RME orthodontic treatment. No significant changes in the AHI or in other variables were observed.

Previous papers regarding orthodontic treatment, associated or not with AT, studied small-size samples. For this reason, the primary aim of this prospective study was to confirm our previous findings [17] on the efficacy of RME in children with moderate adenotonsillar hypertrophy, with a larger sample. The second aim was to retrospectively evaluate any long-term benefit after onset of puberty in a group of children who underwent orthodontic treatment with RME 10 years ago.

## 2. Methods

Children between 4 and 10 years of age who had been referred to our Paediatric Sleep Center (Sant'Andrea Hospital, Rome, Italy) and satisfied the following inclusion criteria were included: clinical signs of malocclusion (high, narrow palate associated with deep bite, retrusive bite or crossbite); tonsillar grading I–III [19], signs and symptoms of OSA (including habitual snoring, apnea and restless sleep as witnessed by parents), AHI > 1 as defined by a laboratory PSG recording. All the participants' parents provided written informed consent to the study. The study procedures were approved by the hospital ethics committee.

We excluded patients with a history of previous treatment for OSA (including tonsillectomy, adenoidectomy and AT), severe tonsillar hypertrophy (grade IV), obesity (BMI value  $\geq$ 95th centile [20]), genetic disorders, cerebral palsy, neuromuscular diseases, cardiac disease, renal disease any systemic diseases or chronic cardiorespiratory or neuromuscular diseases, dysmorphism, major craniofacial abnormalities or associated chromosomal syndrome.

### 2.1. Study design

The study design is shown in Fig. 1. After recruitment, all participants underwent a detailed personal and family history and general clinical examination and had an ear, nose and throat (ENT) and orthodontic assessment before overnight PSG (T0). Parents were asked when their child started to present daytime and night-time symptoms.

All children who met inclusion criteria underwent cephalometric evaluation and started 12 months of therapy with RME and performed a new polysomnographic assessment (T1). Disease duration was defined as the time between onset of symptoms and the beginning of the treatment. Parents fulfilled a questionnaire at T0 and T1.

Presence of daytime and night-time symptoms in children who had completed the 12-month therapeutic trial with RME [17] was investigated through a questionnaire and clinical evaluation, 10 years after the end of treatment (T2).

### 2.2. Questionnaire data

The participants' parents completed the previously validated Brouillette questionnaire [21], at T0, T1 and T2. The questionnaire elicited information on daytime symptoms of OSA (including sleepiness, irritability, headache, school problems, tiredness and oral breathing) and night-time symptoms (including habitual snoring, apneas, restless sleep, and nightmares).

### 2.3. Polysomnography

Standard overnight PSG recordings were obtained at baseline, before starting orthodontic treatment (T0) and after 12 months of treatment (T1) using a Grass heritage polygraph. The variables recorded included an electroencephalogram (EEG) with at least six channels (bilateral frontal, central temporal, and occipital monopolar

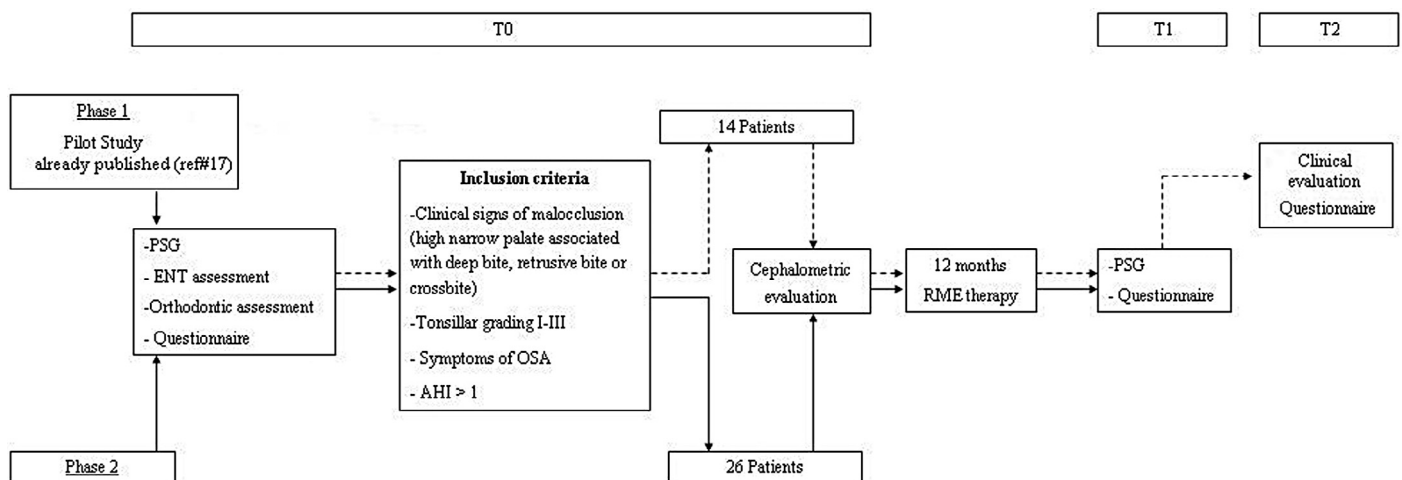


Fig. 1. Study design graph. ---->, pilot study ( $N = 14$ ); -->, new sample enrolment ( $N = 26$ ). AHI, apnea–hypopnea index; ENT, ear, nose and throat; OSA, obstructive sleep apnea syndrome; PSG, polysomnography; RME, rapid maxillary expansion.

montages referred to the contralateral mastoid), an electro-oculogram (electrodes placed 1 cm above the right outer cantus and 1 cm below the left outer cantus and referred to A1), a submental electromyogram, and an electrocardiogram (ECG) (1 derivation). Sleep was subdivided into 30-s epochs, and sleep stages were scored according to the standard criteria of the American Academy of Sleep Medicine (AASM) [22]. The following conventional sleep parameters were measured: total sleep time, defined as the time from sleep onset to the end of the final sleep stage; sleep efficiency, defined as the percentage ratio between total sleep time and total recording time (from lights-out clock time to lights-on clock time). The percentage of total sleep time in each stage was measured as follows: percentage of stage N1, stage N2, stage N3, and stage R (REM sleep). Arousals were detected visually according to the criteria reported in the recent annual for the scoring of sleep and associated events by the AASM [22].

Central, obstructive, and mixed apnea events were counted according to the criteria established by the AASM [23]. Chest and abdomen movements were measured by strain gauges. Oronasal airflow was recorded by means of an oronasal thermocouple and nasal pressure. Arterial oxygen saturation (SpO<sub>2</sub>) was monitored with a pulse oximeter. The AHI was defined as the average number of apneas and hypopneas per hour of sleep. All recordings started at the patients' usual bedtime and continued until spontaneous awakening. All recordings were scored visually by one of the investigators, who was blinded to the subjects' group, age, and sex. Residual OSA after treatment was defined as the presence of AHI >1/h [8].

#### 2.4. Ear, nose and throat assessment

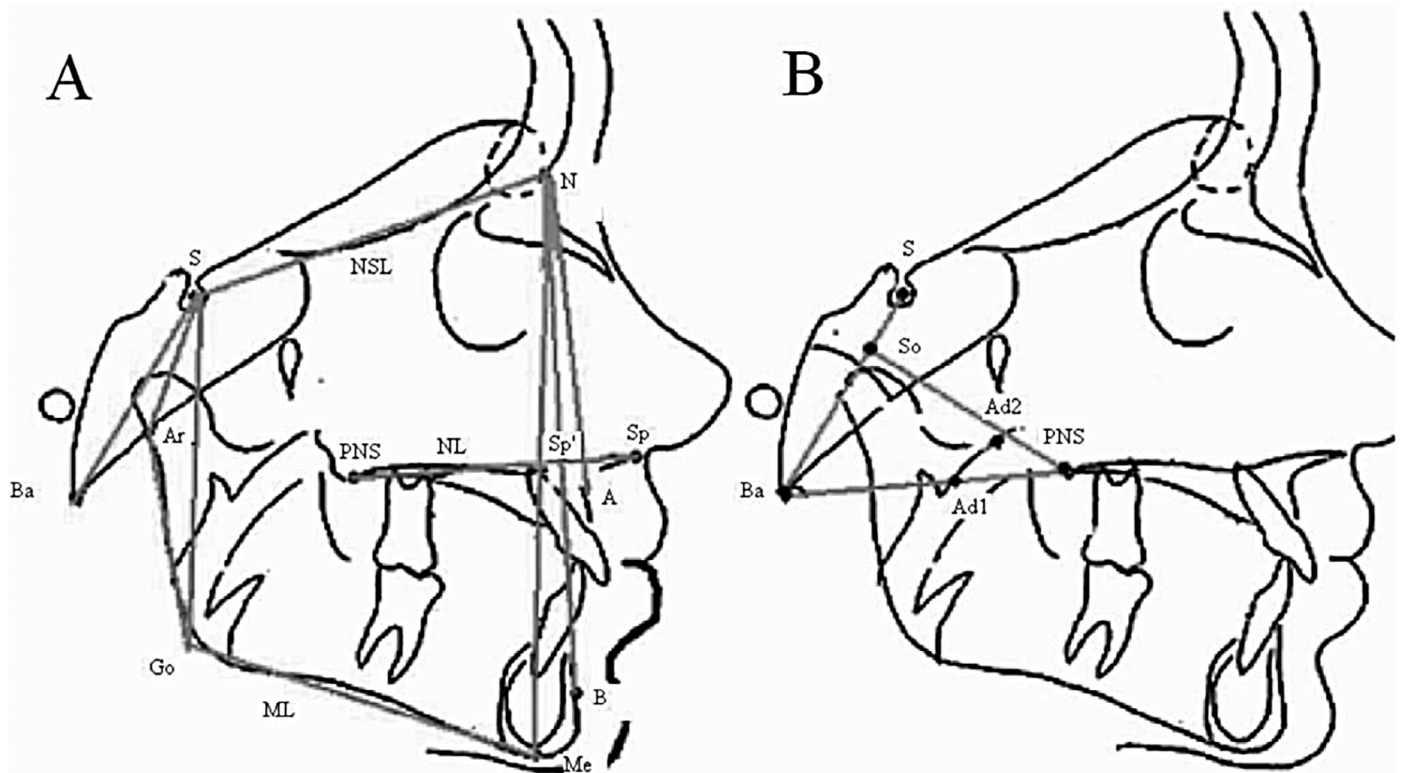
Before orthodontic assessment children underwent an ENT examination to grade tonsillar hypertrophy according to a standardized scale ranging from 1 to 4 [20].

#### 2.5. Orthodontic assessment and orthopedic therapy

The orthodontic evaluation detected the presence of malocclusion. The malocclusion was classified according to Angle's criteria [24]. Lateral cephalometric films were obtained before the orthodontic treatment (T0). All the radiographs were taken using a standardized technique, with teeth in occlusion and lip relaxed. The head was adjusted so that the Frankfurt horizontal plane was parallel to the floor. All of the lateral cephalograms were traced and the measurements recorded by the same operator (M.C.). The method error was determined by repeating the measurement process for 15 randomly selected radiographs again. Mean values from the first and second tracings were used to determine the method error through Dahlberg's formula. The paired samples *t*-test showed no significant mean differences between the two series of records [25].

Cephalometric measurements are illustrated in Fig. 2.

At the end of evaluation a Rapid Maxillary Expander (RME) was applied. RME is a fixed device with an expansion screw and two bands (Leone Sesto Fiorentino, Florence) cemented to the second deciduous molars of the upper jaw because the first permanent molar in many subjects was not completely erupted. The screw was



**Fig. 2.** Cephalometric measurements. SNA, maxillary prognathism; SNB, mandibular prognathism; ANB, difference between SNA and SNB; NSBa, cranial base angle; ML-NSL, mandibular inclination in relation to the anterior cranial base; NL-NSL, maxillary inclination in relation to the anterior cranial base; ML-NL, mandibular inclination in relation to the maxillary inclination; NSAr, sella angle; SarGo, articular angle; ArGoMe, gonial angle; S Go/NMe, total facial index; NANS/ANSMe, anterior facial index; PNSAd<sup>1</sup>, linear distance between PNS and the nearest point of adenoids along the PNSBa line; PNSBa, distance between PNS and Ba; PNSAd<sup>2</sup>, linear distance between PNS and the nearest point of adenoids along the line passing in PNS and perpendicular to the SBa line; PNSSo, perpendicular from PNS to the SBa line in point So (point of intersection of line from PNS perpendicular to SBa line); Ad<sup>2</sup>So, linear distance between So and the outmost point of adenoids along the PNSSo line; Ad<sup>1</sup>Ba, linear distance between Ba and the outmost point of adenoids along the PNSBa line; PNSAd<sup>1</sup>/PNSBa, superior nasopharyngeal adenoids gradient; PNSAd<sup>2</sup>/PNSSo, superior nasopharyngeal airway gradient; PNSAd<sup>2</sup>/PNSSo, inferior nasopharyngeal adenoids gradient; Ad<sup>1</sup>Ba/PNSBa, inferior nasopharyngeal airway gradient.

turned two consecutive turns once a day for several days ( $10.9 \pm 1.2$  days) until the palatal cusp of the upper molars came into contact with the buccal cusp of the lower molars. Finally the screw was fixed with a steel ligature wire and acrylic in order to keep the achieved maxillary expansion. The device was removed after 12 months.

### 2.6. Statistical analysis

Paired *t*-test or Wilcoxon test and the non-parametric test ANOVA (Friedman test) were used to compare two or more repeated measurements. Unpaired *t*-test or Mann–Whitney and non-parametric ANOVA test (Kruskal–Wallis) with post hoc Bonferroni were used to compare two or more groups. Contingency tables ( $\chi^2$  test) with Fisher's correction were used for comparison of proportions. Pearson correlations and multiple regression analysis were used to assess the relation between the dependent variables and potentially explanatory variables.

The variance of AHI ( $\Delta$ AHI) before and after the orthodontic therapy (AHI T1 – AHI T0/AHI T0  $\times$  100) was used to define the impact of treatment. Differences and correlations were considered to achieve statistical significance when the *p*-value was  $<0.05$ . A statistical software package (SPSS 13, Chicago, Ill) was used for calculations.

### 3. Results

The previous 12 months' follow-up study protocol [17] was continued for the following four years. Thirty out of 64 eligible patients for the orthodontic treatment agreed to start the therapy in the orthodontic department of our hospital. Four of them refused to repeat PSG. Twenty-six patients completed the follow up and this allowed us to increase the sample size up to 40 patients (mean age  $6.3 \pm 1.6$  years, range 4.3–10.5; 23 boys). At baseline orthodontic evaluation all children presented with narrow palate, associated in 29 cases (72.5%) to malocclusion: 8/29 subjects (20%) had crossbite, 13/29 subjects (32.5%) deep, and 5/29 subjects (12.5%) open bite. A retrusive bite was present in 10/29 subjects (25%). Moreover 10 patients (25%) had moderate tonsillar hypertrophy (grade III) (Table 1). A questionnaire showed that snoring and apneas were the most common symptoms reported. However most of the daytime and night-time symptoms improved significantly after the treatment (Table 1).

The AHI decreased significantly from T0 to T1 ( $4.7 \pm 4.4$  ev/h vs  $1.6 \pm 1.4$  ev/h,  $p < 0.001$ ) as well as the arousal index ( $16.3 \pm 7.9$  n/h vs  $13.2 \pm 6.7$  n/h,  $p < 0.05$ ), whereas total sleep time ( $402.1 \pm 50.3$  min vs  $433.4 \pm 67.2$  min,  $p < 0.05$ ) and mean overnight oxygen saturation ( $96.8 \pm 1.5\%$  vs  $97.5 \pm 1.8\%$ ,  $p < 0.05$ ) increased significantly. BMI centile did not increase significantly from T0 to T1 (Table 1).

$\Delta$ AHI (mean  $49.31\% \pm 54.39\%$ ) was significantly related to disease duration ( $p < 0.05$ ) (Fig. 3), and there was no difference according to type of malocclusion and presence of severe tonsillar hypertrophy. Stepwise linear multiple-regression analysis identified disease duration as the only variable that was significantly correlated with  $\Delta$ AHI ( $p = 0.006$ ;  $r^2 = 0.18$ ; standardized  $\beta$  coefficient =  $-0.431$ ). We defined responders patients as children who showed a decrease of AHI greater than 20% at T1 and as non-responders children who showed a decreasing  $<20\%$  of AHI at T1.

The present data showed that in 6/40 patients (15%) AHI did not respond to the treatment ( $2.1 \pm 1.3$  ev/h vs  $2.9 \pm 1.3$  ev/h,  $\Delta$ AHI  $-53.47\% \pm 61.57\%$ ). In 34/40 patients (85%) AHI decrease was greater than 20% from T0 to T1 ( $5.2 \pm 4.7$  ev/h vs  $1.4 \pm 1.3$  ev/h,  $\Delta$ AHI  $67.45\% \pm 25.73\%$ ) (Fig. 4).

No differences for gender, malocclusion, tonsillar hypertrophy, BMI centile, and atopy emerged between the two groups. Disease duration was significantly lower ( $2.5 \pm 1.4$  years vs  $4.8 \pm 1.9$  years,  $p < 0.005$ ) and age at disease onset was higher in responder patients compared to non-responders ( $3.8 \pm 1.5$  years vs  $2.3 \pm 1.9$  years,  $p < 0.05$ ) (Table 2). By examining baseline values of cephalometric variables it is possible

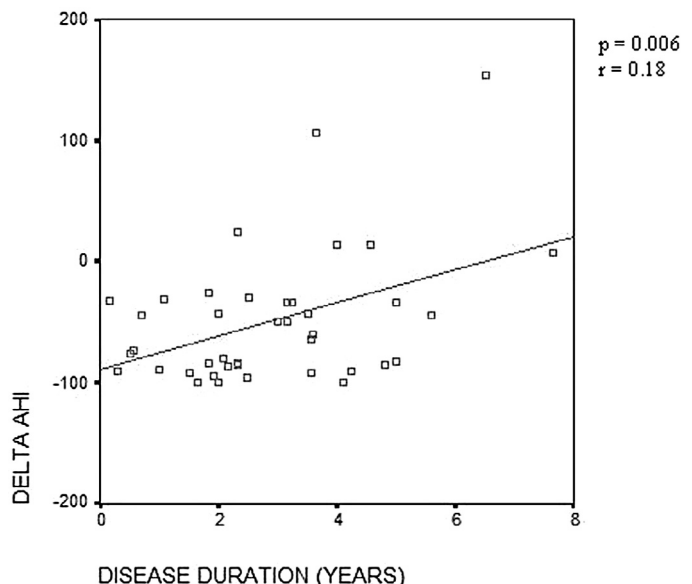
**Table 1**

Clinical, anthropometric and polysomnographic parameters in children at baseline (T0) and 1 year after treatment (T1).

	Baseline (T0) N = 40	One year after treatment (T1)N = 40	<i>p</i>
	Mean $\pm$ SD	Mean $\pm$ SD	
<i>Anthropometric parameters</i>			
Age (years)	$6.3 \pm 1.6$	$7.6 \pm 1.5$	$<0.001$
BMI ( $\text{kg}/\text{m}^2$ )	$17.7 \pm 3.3$	$18.2 \pm 3.7$	$<0.05$
BMI centile	$66.2 \pm 26.3$	$71 \pm 15$	NS
<i>Questionnaire</i>			
Brouillette score	$-0.03 \pm 1.8$	$-3.0 \pm 1.1$	$<0.001$
	N (%)	N (%)	
<i>Daytime symptoms</i>			
Oral breathing	25.8%	25%	NS
Bruxism	27.6%	17.9%	NS
Daily sleepiness	48.3%	14.8%	0.004
Halitosis	65.5%	39.3%	0.04
<i>Night-time symptoms</i>			
Snoring	96.8%	17.9%	0.000
Apneas	80.6%	10.7%	0.000
Respiratory effort	74.2%	11%	0.000
Night-time sweating	37.9%	32.1%	NS
Restless sleep	63.3%	25%	0.002
	Mean $\pm$ SD	Mean $\pm$ SD	
<i>Polysomnographic parameters</i>			
AHI (events/h)	$4.7 \pm 4.4$	$1.6 \pm 1.4$	$<0.001$
SpO <sub>2</sub> 4	$96.8 \pm 1.5$	$97.5 \pm 1.8$	$<0.05$
TST (min)	$402.1 \pm 50.3$	$433.4 \pm 67.2$	$<0.05$
SE (TST/time in bed) (%)	$86.1 \pm 9.7$	$86.5 \pm 10.1$	NS
Arousal index (number of events/hour of sleep)	$16.3 \pm 7.9$	$13.2 \pm 6.7$	$<0.05$
S1 (%)	$5.9 \pm 4.6$	$8.3 \pm 14.1$	NS
S2 (%)	$43.4 \pm 10.1$	$44.3 \pm 11.9$	NS
SWS (%)	$32.3 \pm 10$	$29.3 \pm 9.1$	NS
REM (%)	$17.8 \pm 6.2$	$20.2 \pm 7.2$	NS

AHI apnea–hypopnea index; BMI, body mass index; S1, sleep stage 1; S2, sleep stage 2; SE, sleep efficiency; SWS, slow-wave sleep; SpO<sub>2</sub>%, average overnight arterial oxygen saturation; TST, total sleep time.

to note that the parameter NSBa (cranial base angle) is significantly higher in the non-responder group ( $p = 0.03$ ). Despite a tendency for difference ( $p = 0.06$ ) the anterior total facial ratio SGo/NMe was not smaller in the responder group. This result is confirmed by the higher angle, in the vertical plane, of the parameter ML-NSL (mandibular inclination in relation to the anteriorcranial base) even though not



**Fig. 3.** Correlation between  $\Delta$ AHI and disease duration. AHI, apnea–hypopnea index.

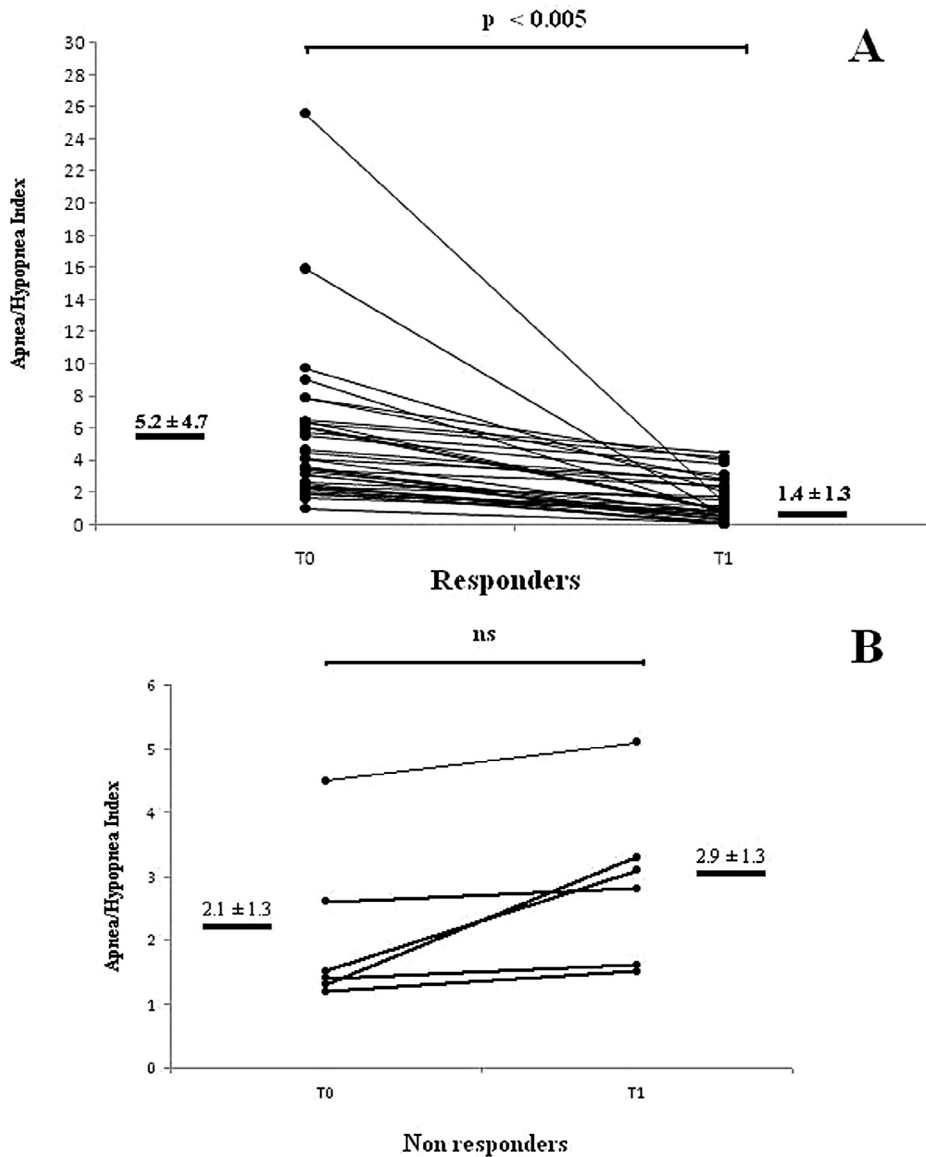


Fig. 4. AHI changes from baseline (T0) to 1 year after treatment (T1) in group 1 and group 2. AHI, apnea-hypopnea index.

**Table 2**  
Clinical and polysomnographic parameters in responder and non-responder patients.

	Responders N = 34	Non-responders N = 6	
	Mean $\pm$ SD	Mean $\pm$ SD	<b>p</b>
Age (years)	6.3 $\pm$ 1.4	7.1 $\pm$ 2.7	NS
Age at onset (years)	3.8 $\pm$ 1.5	2.3 $\pm$ 1.9	<0.05
Disease duration (years)	2.5 $\pm$ 1.4	4.8 $\pm$ 1.9	<0.005
	N (%)	N (%)	<b>p</b>
Gender (males)	15 (44.1%)	2 (33.3%)	NS
Malocclusion	25 (73.5%)	4 (66.7%)	NS
Tonsillar hypertrophy (grade III)	9 (26.4%)	1 (16.6%)	NS
	Mean $\pm$ SD	Mean $\pm$ SD	<b>p</b>
AHI T0	5.2 $\pm$ 4.7	2.1 $\pm$ 1.3	<0.005
SpO <sub>2</sub> % T0	96.7 $\pm$ 1.6	97.3 $\pm$ 1.4	NS
AHI T1	1.4 $\pm$ 1.3	2.9 $\pm$ 1.3	<0.05
SpO <sub>2</sub> % T1	97.4 $\pm$ 1.9	98.0 $\pm$ 1.7	NS

AHI, apnea-hypopnea index (events/h); BMI, body mass index; NS, not significant; SpO<sub>2</sub>%, average overnight arterial oxygen saturation.

statistically significant in the same group. No other variables differed between the two groups of patients (Table 3).

Looking at the complete efficacy of treatment, defined as AHI < 1, 23/40 patients (57.5%) presented residual OSA since they had AHI > 1. No significantly clinical anthropometric and cephalometric differences were noted in children with residual OSA and children without (Table 4).

No patient was treated again with RME after the initial treatment. Patients were followed-up by the orthodontists every year for five years (they are still ongoing follow-up). Considering the second aim of our study, Brouillette score was administered to 14 children (mean age of these children was 17.0  $\pm$  1.9 years, 10 males) who ended the orthodontic treatment 10 years previously, to evaluate the recurrence of night-time and daytime symptoms, through the years. The mean age of these children was 17.0  $\pm$  1.9 years, 10 males (62.5%). Night-time and daytime symptoms were decreased compared to T0 but they were not modified by the end of the treatment through the following 10 years. After 10 years (T2), the Brouillette score improved compared to baseline (Table 5).

**Table 3**  
Cephalometric variables in responder and non-responder patients.

	Responders	Non-responders	p
	N = 34	N = 6	
	Mean ± SD	Mean ± SD	
<i>Skeletal</i>			
SNA (°)	79.61 ± 3.32	77.30 ± 2.90	NS
SNB (°)	75.10 ± 3.40	73.76 ± 1.73	NS
ANB (°)	4.33 ± 1.80	3.30 ± 1.62	NS
NSBa (°)	132.05 ± 4.85	138.01 ± 6.49	0.03
ML-NSL (°)	37.96 ± 5.14	39.66 ± 3.93	NS
NL-NSL (°)	6.57 ± 2.87	9.05 ± 4.16	NS
ML-NL (°)	30.69 ± 5.42	31.11 ± 3.25	NS
NSAr (°)	123.36 ± 4.98	127.08 ± 4.60	NS
SarGo (°)	147.44 ± 6.75	144.98 ± 4.70	NS
ArGoMe (°)	129.52 ± 6.67	129.73 ± 3.38	NS
SOMMAT (°)	400.30 ± 5.16	401.80 ± 4.34	NS
S Go/Nme ratio (%)	61.63 ± 3.49	59.33 ± 1.96	0.06
NANS/ANSMe ratio (%)	76.31 ± 4.89	80.33 ± 5.24	NS
<i>Nasopharynx</i>			
PNSAd <sup>1</sup> /PNSBa (mm)	31.42 ± 22.36	32.80 ± 9.73	NS
Ad <sup>2</sup> So/PNSSo (mm)	73.47 ± 7.13	70.80 ± 8.28	NS
Ad <sup>1</sup> Ba/PNSBa (mm)	25.57 ± 7.19	28.60 ± 8.26	NS
PNSAd <sup>2</sup> /PNSSo (mm)	71.61 ± 11.05	69.75 ± 7.54	NS

SNA, maxillary prognathism; SNB, mandibular prognathism; ANB, difference between SNA and SNB; NSBa, cranial base angle; ML-NSL, mandibular inclination in relation to the anterior cranial base; NL-NSL, maxillary inclination in relation to the anterior cranial base; ML-NL, mandibular inclination in relation to the maxillary inclination; NSAr, sella angle; SarGo, articular angle; ArGoMe, gonial angle; S Go/Nme, total facial index; NANS/ANSMe, anterior facial index; PNSAd<sup>1</sup>, linear distance between PNS and the nearest point of adenoids along the PNSBa line; PNSBa, distance between PNS and Ba; PNSAd<sup>2</sup>, linear distance between PNS and the nearest point of adenoids along the line passing in PNS and perpendicular to the SBa line; PNSSo, perpendicular from PNS to the SBa line in point So (point of intersection of line from PNS perpendicular to SBa line); Ad<sup>2</sup>So, linear distance between So and the outmost point of adenoids along the PNSSo line; Ad<sup>1</sup>Ba, linear distance between Ba and the outmost point of adenoids along the PNSBa line; PNSAd<sup>1</sup>/PNSBa, superior nasopharyngeal adenoids gradient; Ad<sup>2</sup>So/PNSSo, superior nasopharyngeal airway gradient; PNSAd<sup>2</sup>/PNSSo, inferior nasopharyngeal adenoids gradient; Ad<sup>1</sup>Ba/PNSBa, inferior nasopharyngeal airway gradient.

#### 4. Discussion

Our data support the usefulness and the efficacy of orthodontic treatment in children with OSA and support previous findings [13–18].

A larger sample size highlights that the best results are achieved when an early orthodontic/orthopedic treatment is undertaken in late deciduous dentition and early mixed dentition. Moreover it is known that early recognition and early treatment of OSA could prevent its complications such as neurocognitive and behavioral disturbances, systemic inflammation, and cardiovascular and metabolic dysfunction [26–31].

Although sleep respiratory parameters improved after 12 months of treatment, our results highlighted that oral breathing is still reported suggesting that a precocious re-education intervention is

**Table 5**  
Anthropometric parameters and questionnaire results of treated subjects at baseline (T0), 1 year after treatment (T1) and 10 years after the end of treatment (T2).

	Baseline (T0)	1 year after treatment (T1)	10 years after the end of treatment (T2)	1 vs 2 vs 3	p		
	N = 14	N = 14	N = 14		1 vs 2	1 vs 3	2 vs 3
	Mean ± SD	Mean ± SD	Mean ± SD				
<i>Clinical and anthropometric parameters</i>							
Age (years)	5.9 ± 1.7	7.3 ± 1.7	17.0 ± 1.9				
Percentile of BMI	77.4 ± 34	82.5 ± 11.9	69.4 ± 22.6	NS			
Brouillette score	0.8 ± 1.4	-2.9 ± 1.2	-2.4 ± 1.1	<0.005	<0.005	<0.005	NS
<i>Clinical symptoms</i>							
Snoring	14 (100%)	6 (42.8%)	10 (71.4%)	<0.005	<0.005	NS	NS
Oral breathing	13 (92.8%)	10 (71.4%)	8 (57.1%)	NS	NS	NS	NS
Bruxism	5 (35.7%)	4 (28.5%)	3 (21.4%)	NS	NS	NS	NS
Daily sleepiness	10 (71.4%)	3 (21.4%)	1 (7.1%)	<0.005	<0.005	<0.005	NS
Halitosis	9 (64.3%)	7 (50%)	11 (78.6%)	NS	NS	NS	NS

**Table 4**  
Cephalometric variables in children with residual OSA (AHI >1 ev/h) and in children with complete resolution of OSA (AHI <1 ev/h) after treatment.

	Residual OSAS	No residual OSAS	p
	N = 23	N = 17	
	Mean ± SD	Mean ± SD	
<i>Skeletal</i>			
SNA (°)	79.31 ± 2.52	79.19 ± 4.06	NS
SNB (°)	74.33 ± 2.84	75.46 ± 3.56	NS
ANB (°)	4.80 ± 2.01	3.41 ± 1.09	NS
NSBa (°)	132.42 ± 4.39	133.81 ± 6.58	NS
ML-NSL (°)	38.65 ± 5.33	37.95 ± 4.56	NS
NL-NSL (°)	6.36 ± 2.67	7.65 ± 3.63	NS
ML-NL (°)	31.33 ± 5.35	30.18 ± 4.71	NS
NSAr (°)	122.44 ± 4.39	125.93 ± 5.27	NS
SArGo (°)	148.60 ± 7.13	145.15 ± 5.15	NS
ArGoMe (°)	129.26 ± 7.02	129.88 ± 5.14	NS
SOMMAT (°)	400.38 ± 5.33	400.86 ± 4.73	NS
S Go/Nme (ratio%)	61.16 ± 3.78	61.14 ± 2.93	NS
NANS/ANSMe (ratio%)	76.26 ± 5.24	78.23 ± 5.03	NS
<i>Nasopharynx</i>			
PNSAd <sup>1</sup> /PNSBa (mm)	32.76 ± 28.23	30.61 ± 8.15	NS
Ad <sup>2</sup> So/PNSSo (mm)	75.15 ± 7.31	70.76 ± 6.79	NS
Ad <sup>1</sup> Ba/PNSBa (mm)	23.92 ± 7.43	28.38 ± 6.78	NS
PNSAd <sup>2</sup> /PNSSo (mm)	72.76 ± 12.96	69.75 ± 7.07	NS

SNA, maxillary prognathism; SNB, mandibular prognathism; ANB, difference between SNA and SNB; NSBa, cranial base angle; ML-NSL, mandibular inclination in relation to the anterior cranial base; NL-NSL, maxillary inclination in relation to the anterior cranial base; ML-NL, mandibular inclination in relation to the maxillary inclination; NSAr, sella angle; SarGo, articular angle; ArGoMe, gonial angle; S Go/Nme, total facial index; NANS/ANSMe, anterior facial index; PNSAd<sup>1</sup>, linear distance between PNS and the nearest point of adenoids along the PNSBa line; PNSBa, distance between PNS and Ba; PNSAd<sup>2</sup>, linear distance between PNS and the nearest point of adenoids along the line passing in PNS and perpendicular to the SBa line; PNSSo, perpendicular from PNS to the SBa line in point So (point of intersection of line from PNS perpendicular to SBa line); Ad<sup>2</sup>So, linear distance between So and the outmost point of adenoids along the PNSSo line; Ad<sup>1</sup>Ba, linear distance between Ba and the outmost point of adenoids along the PNSBa line; PNSAd<sup>1</sup>/PNSBa, superior nasopharyngeal adenoids gradient; Ad<sup>2</sup>So/PNSSo, superior nasopharyngeal airway gradient; PNSAd<sup>2</sup>/PNSSo, inferior nasopharyngeal adenoids gradient; Ad<sup>1</sup>Ba/PNSBa, inferior nasopharyngeal airway gradient.

needed in addition to standard therapy as reported by several authors [32–35]. Several considerations could have been studied in the non-responder patients. Our interest was to evaluate whether patients who do not benefit at all from treatment had specific craniofacial characteristics. Looking at baseline cephalometric evaluation, it is possible to note that the parameter NSBa (cranial base angle) is significantly higher in the non-responder group ( $p = 0.03$ ), indicating that non-responder patients showed a more retrognathic facial type. Moreover the vertical parameter, SGo/Nme, was lower in the non-responder group indicating an increase in the anterior total face height, even if not statistically significant ( $p = 0.06$ ) (Table 3).

According to Jarabot classification [36], facial height ratio (FHR) or Jarabot quotient is 59–63% in the neutral growth pattern. If we compare the non-responder group with the responder group they

show a lower value and they are closer to the hyperdivergent growth pattern (FHR < 59%). This result is confirmed by the greater amplitude in the vertical plane of the angle ML-NSL even though not statistically significant. It is well documented, indeed, that mouth-breathing, presented in children with OSA, induced the development of longer faces [37–41]. The switch from a nasal to an oronasal (mouth and nose combined) breathing pattern, in fact, induces functional adaptations that include an increase in total anterior face height and vertical development of the lower anterior face. Moreover, it is important to bear in mind that in this group, disease duration was significantly higher and age at disease onset was lower compared to responders, suggesting that the earlier the oral breathing occurs, the more serious skeletal alterations typical of snoring and OSA become, the more difficult it will be to achieve OSA resolution. This is the reason why the patients should be treated as early as symptoms appear in order to interrupt the vicious circle. Maybe a new treatment with RME or with a different orthodontic device should be performed.

Although it is well known that a successful outcome is achieved in both AT and orthodontic treatment, our goal was to highlight the role of RME in OSA children with malocclusion and without significant tonsillar hypertrophy. Although only 42.5% of patients achieved an AHI < 1 as determined by the post-RME PSG, most children had evidence of residual OSA after RME treatment. It is important to underline that residual OSA was present also in responder children (AHI T1  $2.44 \pm 1.2$  ev/h  $\Delta$ AHI  $48.59 \pm 20.78\%$ ). The occurrence of residual OSA is supported by different studies underlying that a single treatment is often not enough to obtain a complete resolution of the disease even if a significant  $\Delta$ AHI after treatment is present and that a multidisciplinary approach could be successful [8,14,42–46]. Moreover since the AHI < 1 may not be appropriate and an agreement of AHI cut-off value for residual OSAS is currently unavailable, cut-off value could influence the evaluation of treatment efficacy. It is easy to understand that considering a higher cut-off to define residual OSAS, the percentage of patients who showed a resolution of the disease consequently increases. There are very important open questions on the definition of residual OSA that will clearly be the focus of further studies in the next years.

The ideal treatment should be able to eradicate the disease, as suggested by the normalization of AHI independently from the decreasing rate of it, so we evaluated the cephalometric parameters in order to understand whether there were structural issues that can predict the treatment efficacy or characteristics that might suggest alternative or integrated orthodontic treatments.

No differences in cephalometric measurements were present comparing the group of patients with residual OSA with the patients who achieved complete resolution. However it is possible to note that the patients with residual OSA showed a higher value of the cephalometric parameter ANB (difference between maxillary prognathism and mandibular prognathism) angle, even if it was not statistically significant.

Guilleminault et al. showed that recurrence of symptoms during teenage years in a group of adolescents with OSA, previously treated with AT and orthodontia at a mean age of 7.5 years, may be due to hormonal status changes [9].

Our data on follow-up evaluation of 14 patients after 10 years showed that orthodontic treatment has long-lasting benefits on symptoms and prevents, after the onset of puberty, the recurrence of baseline conditions (Table 5). It is important to underline that symptoms such as snoring and oral breathing persist after the onset of puberty or are present again after 10 years from the end of treatment showing that RME is not the definitive treatment and that a closer follow-up is needed.

Once again we could suppose that myofunctional re-education could help subjects to acquire physiological breathing and to correct

oral breathing, both of which are involved in airway muscle function and upper airway patency in order to ameliorate symptoms after 10 years. As suggested by data from the literature, best results are achieved with a combination of oropharyngeal exercises and other therapeutic options [32–35,44]. It is therefore clear that rehabilitation should follow or integrate treatments for sleep disorders to prevent future complications.

This study presents several limitations such as the lack of polysomnographic data in the 10 years follow-up group. Since they refused to undergo a new PSG, only the questionnaire could be administered. Moreover the age of onset of symptoms was parentally reported and this could have also influenced the assessment of disease duration.

We administered Brouillette questionnaire to evaluate the recurrence of symptoms in adolescent patients 10 years after the end of orthodontic treatment in order to compare it with the questionnaire previously administered, although Brouillette questionnaire was originally validated for children until the age of 10 years. On the other hand the questions of Brouillette questionnaire used for the score are about snoring, apneas and restless sleep and there should be no difference in asking the questions of a child or of a teenager. Further studies with larger samples are needed to assess the predictive role of cephalometric analysis in the choice of treatment and its efficacy.

## 5. Conclusions

In conclusion, our results confirm our previous findings and data by other authors. Starting orthodontic treatment as early as symptoms appears to be, once again, an important message to transmit in order to increase the efficacy of treatment. Non-responder patients, in fact, have a longer duration of disease and a lower age of onset. Moreover, it could be suggested that, in the presence of some structural characteristics, the orthodontic treatment should be personalized based on the patient's phenotype. An early myofunctional rehabilitation may be useful.

## Conflict of interest

The authors confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support that could have influenced its outcome.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: <http://dx.doi.org/10.1016/j.sleep.2014.11.019>.

## References

- [1] Marcus CL, Brook LJ, Davidson Ward S, et al. Diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics* 2012;130:e714.
- [2] Katz ES, D'Ambrosio CM. Pathophysiology of pediatric obstructive sleep apnea. *Proc Am Thorac Soc* 2008;5(2):253–62.
- [3] Alabi BS, Abdulkarim AA, Musa IO, et al. Prevalence of snoring and symptoms of sleep disordered breathing among primary school pupils in Ilorin, Nigeria. *Int J Pediatr Otorhinolaryngol* 2012;76(5):646–8.
- [4] Guilleminault C, Li KK, Khamstov A, et al. Sleep disordered breathing: surgical outcomes in prepubertal children. *Laryngoscope* 2004;114(1):132–7.
- [5] Zonato AI, Martinho FL, Bittencourt LR, et al. Head and neck physical examination: comparison between nonapneic and obstructive sleep apnea patients. *Laryngoscope* 2005;115(6):1030–4.
- [6] Marcus CL. Sleep-disordered breathing in children. *Am J Respir Crit Care Med* 2001;164:16–30.
- [7] Arens R, McDonough JM, Costantino AT, et al. Magnetic resonance imaging of the upper airway structure of children with obstructive sleep apnea syndrome. *Am J Respir Crit Care Med* 2001;164(4):698–703.
- [8] Bhattacharjee R, Kheirandish-Gozal L, Spruyt K, et al. Adenotonsillectomy outcomes in treatment of obstructive sleep apnea in children: a multicenter retrospective study. *Am J Respir Crit Care Med* 2010;182(5):676–8.
- [9] Guilleminault C, Huang YS, Quo S, et al. Teenage sleep-disordered breathing: recurrence of syndrome. *Sleep Med* 2013;14(9):927–8.

- [10] Guilleminault C, Li KK, Khrantsov A, et al. Sleep disordered breathing: surgical outcomes in prepubertal children. *Laryngoscope* 2004;114:132–7.
- [11] Tasker C, Crosby JH, Stradling JR. Evidence for persistence of upper airway narrowing during sleep, 12 years after adenotonsillectomy. *Arch Dis Child* 2002;86:34–7.
- [12] Souki BQ, Pimenta GB, Souki MQ, et al. Prevalence of malocclusion among mouth breathing children: do expectations meet reality? *Int J Pediatr Otorhinolaryngol* 2009;73:767–73.
- [13] Villa MP, Bernkopf E, Pagani J, et al. Randomized controlled study of an oral jaw positioning appliance for the treatment of obstructive sleep apnea in children with malocclusion. *Am J Respir Crit Care Med* 2002;165:123–7.
- [14] Villa MP, Castaldo R, Miano S, et al. Adenotonsillectomy and orthodontic therapy in pediatric obstructive sleep apnea. *Sleep Breath* 2014;18:533–9.
- [15] Villa MP, Miano S, Rizzoli A. Mandibular advancement devices are an alternative and valid treatment for pediatric obstructive sleep apnea syndrome. *Sleep Breath* 2012;16(4):971–6.
- [16] Pirelli P, Saponara M, Guilleminault C. Rapid maxillary expansion in children with obstructive sleep apnea syndrome. *Sleep* 2004;27(4):761–6.
- [17] Villa MP, Malagola C, Pagani J, et al. Rapid maxillary expansion in children with obstructive sleep apnea syndrome: 12-month follow-up. *Sleep Med* 2007;8:128–34.
- [18] Villa MP, Rizzoli A, Miano S, Malagola C. Efficacy of rapid maxillary expansion in children with obstructive sleep apnea syndrome: 36 months of follow-up. *Sleep Breath* 2011;15:179–84.
- [19] Friedman M, Ibrahim H, Joseph NJ. Staging of obstructive sleep apnea/hypopnea syndrome: a guide to appropriate treatment. *Laryngoscope* 2004;114(3):454–9.
- [20] Cole TJ, Bellizzi MC, Flegal KM, et al. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* 2000;320(7244):1240–3.
- [21] Brouillette R, Hanson D, David R, et al. A diagnostic approach to suspected obstructive sleep apnea in children. *J Pediatr* 1984;105:10–14.
- [22] Iber C, Ancoli-Israel S, Chesson A, et al. for the American Academy of Sleep Medicine. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications. 1st ed. Westchester, IL: American Academy of Sleep Medicine; 2007.
- [23] Berry RB, Budhiraja R, Gottlieb DJ, et al. for the American Academy of Sleep Medicine. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. *J Clin Sleep Med* 2012;8(5):597–619.
- [24] Angle EH. Treatment of malocclusion of the teeth: Angle's system. Philadelphia: SS White Dental Manufacturing Co; 1907.
- [25] Houston WJ. The analysis of errors in orthodontic measurements. *Am J Orthod* 1983;83(5):382–90.
- [26] Bhattacharjee R, Kim J, Kheirandish-Gozal L, et al. Obesity and obstructive sleep apnea syndrome in children: a tale of inflammatory cascades. *Pediatr Pulmonol* 2011;46(4):313–23.
- [27] Gozal D, Kheirandish-Gozal L, Bhattacharjee R, et al. C-reactive protein and obstructive sleep apnea syndrome in children. *Front Biosci (Elite Ed)* 2012;4:2410–22.
- [28] James AL, Runciman M, Burton MJ, et al. Investigation of cardiac function in children with suspected obstructive sleep apnea. *J Otolaryngol* 2003;32(3):151–4.
- [29] Gozal D, Capdevila OS, Kheirandish-Gozal L. Metabolic alterations and systemic inflammation in obstructive sleep apnea among nonobese and obese prepubertal children. *Am J Respir Crit Care Med* 2008;177(10):1142–9.
- [30] Chervin RD, Dillon JE, Bassetti C, et al. Symptoms of sleep disorders, inattention, and hyperactivity in children. *Sleep* 1997;20(12):1185–92.
- [31] Beebe DW, Gozal D. Obstructive sleep apnea and the prefrontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits. *J Sleep Res* 2002;11(1):1–16.
- [32] Villa MP, Brasili L, Ferretti A, et al. Oropharyngeal exercises to reduce symptoms of OSA after AT. *Sleep Breath* 2015;19:281–9.
- [33] Guimarães KC, Drager LF, Genta PR, et al. Effects of oropharyngeal exercises on patients with moderate obstructive sleep apnea syndrome. *Am J Respir Crit Care Med* 2009;179(10):962–6.
- [34] Guilleminault C, Huang YS, Monteyrol PJ, et al. Critical role of myofascial re-education in pediatric sleep-disordered breathing. *Sleep Med* 2013;14(6):518–25.
- [35] Moeller J, Paskay LC, Gelb ML. Myofunctional therapy: a novel treatment of pediatric sleep-disordered breathing. *Sleep Med Clin* 2014;9(2):235–43.
- [36] Siritwat PP, Jarabat J. Malocclusion and facial morphology. Is there a relationship? *Angle Orthod* 1985;55(2):127–36.
- [37] Flores-Mir C, Korayem M, Heo G, et al. Craniofacial morphological characteristics in children with obstructive sleep apnea syndrome: a systematic review and meta-analysis. *J Am Dent Assoc* 2013;144(3):269–77, Review.
- [38] Vieira BB, Itikawa CE, de Almeida LA, et al. Cephalometric evaluation of facial pattern and hyoid bone position in children with obstructive sleep apnea syndrome. *Int J Pediatr Otorhinolaryngol* 2011;75(3):383–6.
- [39] Arens R, Marcus CL. Pathophysiology of upper airway obstruction: a developmental perspective. *Sleep* 2004;27(5):997–1019.
- [40] Marino A, Ranieri R, Chiarotti F, et al. Rapid maxillary expansion in children with Obstructive Sleep Apnoea Syndrome (OSA). *Eur J Paediatr Dent* 2012;13(1):57–63.
- [41] Souki BQ, Lopes PB, Pereira TBJ, et al. Mouth breathing children and cephalometric pattern: does the stage of dental development matter? *Int J Pediatr Otorhinolaryngol* 2012;76:837–41.
- [42] Tauman R, Gulliver TE, Krishna J, et al. Persistence of obstructive sleep apnea syndrome in children after adenotonsillectomy. *J Pediatr* 2006;149(6):803–8.
- [43] Guilleminault C, Monteyrol PJ, Huynh NT, et al. Adeno-tonsillectomy and rapid maxillary distraction in pre-pubertal children, a pilot study. *Sleep Breath* 2011;15(2):173–7.
- [44] Huang YS, Guilleminault C. Pediatric obstructive sleep apnea and the critical role of oral-facial growth: evidences. *Front Neurol* 2013;3:1–7.
- [45] Guilleminault C, Partinen M, Praud JP, et al. Morphometric facial changes and obstructive sleep apnea in adolescents. *J Pediatr* 1989;114:997–9.
- [46] Tasker C, Crosby JH, Stradling JR, et al. Evidence for persistence of upper airway narrowing during sleep, to 12 years after adenotonsillectomy. *Arch Dis Child* 2002;86:34–7.