The effect of maxillary protraction, with or without rapid palatal expansion, on airway dimensions: A systematic review and meta-analysis

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Abstract

Aim The use of maxillary protraction appliances (MPAs) and Facemask (FM), with or without a rapid maxillary expansion (RME), have become a routine orthopaedic treatment procedure for the treatment of Class III in growing individuals; several authors have suggested that maxillary protraction could have a positive impact on airway dimensions. The purpose of this systematic review and meta-analysis was to assess the efficacy of maxillary protraction appliances (MPAs), with or without a rapid maxillary expansion (RME), on airway dimensions in children in mixed or early permanent dentition.

Methods An electronic search was performed on PubMed, Medline, Scopus, The Cochrane Library, EMBASE and the System for Information on Grey Literature in Europe until November 30th, 2019. The Newcastle-Ottawa (NOS) scale was used to assess the studies' quality. Review Manager 5.3 (provided by the Cochrane Collaboration) was used to synthesize the effects on airway dimensions.

Results After full text assessment, 8 studies were included in the qualitative and quantitative synthesis. NOS scores ranged 6 to 9 indicating high quality. The effects of two therapeutic protocols were compared, treatment with MPAs only (113 subjects treated - 65 controls) and the treatment with MPAs + RME (137 subjects treated- 87 controls). The MPAs only treatment group displayed a significantly increase in nasopharyngeal airway dimension at PNS-AD1 (random: mean difference, 1.39 mm, 95% CI, 0.32 mm, 2.47 mm, p= 0.01) and at PNS-AD2 (random: mean difference, 1.70 mm, 95% CI, 1.14 mm, 2.26 mm, p= 0.00001). No statistically significant changes were found post treatment in MPAs + RME treatment groups at PNS-AD1 (P= 0.15), PNS-AD2 (P= 0.17), McNamara's upper pharynx (MPAs + RME P= 0.05, MPAs P= 0.99) and McNamara lower pharynx (MPAs + RME P= 0.25, MPAs P= 0.40).

Conclusion MPAs only treatment can increase the pharyngeal thickness after treatment both at PNS-A1 and PNS-AD2. MPA+ RME had no effect on sagittal widths compared with controls, but the effect on the transverse dimension could not be assessed.

Introduction

The treatment of a Class III malocclusion has always been a challenge for clinicians; nowadays the use of maxillary protraction appliances (MPAs) and Facemask (FM), with or without rapid maxillary expansion (RME), has become a routine orthopaedic treatment procedure for the treatment of Class III with maxillary retrusion in growing individuals [De Toffol et al., 2008]. The ultimate goal of the orthopaedic treatment with MPAs is to enhance the forward displacement of the maxilla. Some authors reported how this displacement can induce a change in the surrounding tissues and pointed out that this forward movement can have an effect on airway dimensions [Haas, 1965; Nanda, 1980]. In the last few years, there has been a growing interest in orthodontic literature on this topic [Adobes Martin et al., 2020]. An increasing number of studies suggested that MPAs could have a role in preventing the occurrence of sleep-disorders such as obstructive sleep apnoea syndrome (OSAS) in children [Conley, 2011; Camacho et al., 2017]. The interceptive dental and orthodontic treatment, possibly coupled with the referral to an otolaryngologist and body weight control, plays a key role in solving the respiratory issue and related clinical consequences [Paglia, 2019; Paglia et al., 2019].

OSAS is a common respiratory disorder that can have a dramatic impact on quality of life and requires treatment as soon as possible. However, the literature reports contrasting finding about the possible effects of MPAs on the oropharyngeal and nasopharyngeal dimensions. Kilinc et al. [2008], for instance, have reported significant changes on both dimensions, while Sayinsu et al. [2006] only on the nasopharyngeal whidth. This findings differ from the ones reported by Baccetti et al. [2010] and Mucedero et al. [2009], that concluded that no significant changes were produced by this type of treatment on airway dimensions.

The objective of this systematic review can be resumed by the following PICO question: (P) in Class III children in mixed or early permanent dentition (I) the orthopaedic traction of the maxilla (C) performed with or without rapid maxillary expansion (O) has an effect on the airway dimension?

In the last three years two clinical trials enrolling a large

number of patients have been published [Cretella Lombardo et al., 2020; Hwang et al., 2019] allowing a better data gathering compared to other reports on related topics [Ming et al., 2018]. This systematic review aimed to provide an update of knowledge about the changes that MPAs with or without RME produced on upper airway dimension compared with untreated control groups.

Methods

This systematic review and meta-analysis was performed in accordance with the statement of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Eligibility criteria
The inclusion and exclusion criteria were established according to the PICO question reported above.

The included studies were: Controlled Clinical Trial (CCTs); Randomised Clinical Trial (RCTs); Cohort studies both retrospective and prospective; published or in press; published in English and regarding the treatment of patients in mixed or early permanent dentition with Class III malocclusion treated with Maxillary protraction with or without rapid maxillary expansion; articles reporting the effect on airway dimensions assessed by linear changes on lateral cephalometric radiographs.

Exclusion criteria: Studies about patients with previous orthodontic treatment, systemic diseases, congenital cranio-facial anomalies, cleft palate, temporomandibular joint disorders, adenoid or tonsils hypertrophy or nasal obstruction problems. Reviews, case reports, case series, animal studies and clinical studies without control group.

Information sources
An electronic search was performed on the following databases: PubMed, Medline, Scopus, The Cochrane Library, EMBASE, System for Information on Grey Literature in Europe (SiGLE). The search was conducted until November 30, 2019. No restrictions were applied in time or language.

Search strategy
The search was performed on the advanced PubMed search tool with a combination of the following keywords, MeSH (Medical Subject Heading), non-indexed terms and the corresponding Boolean operators: (mixed dentition [MeSH] OR permanent dentition [MeSH] OR Children [MeSH]) AND (mandibular [MeSH] AND prognathism [MeSH]) OR (maxillary [MeSH] AND retrusion [MeSH]) OR Class III [MeSH] AND (face mask OR palatal expansion technique [MeSH] OR maxillary traction [MeSH] OR delaire OR extraoral traction appliance [MeSH]) AND (pharynx [MeSH] OR airway) OR (airway AND dimension) OR (airway AND flow). In all other databases, an advanced search was performed with the same combination of keywords, MESH terms and free search terms. The search was then implemented by a manual search on the references of the selected articles to locate further works that might have been missed in the initial search. If needed, the corresponding authors were contacted by e-mail to request missing information.

Study selection
Two authors (D.G. and E.L.) simultaneously and independently conducted the search process according to the criteria of the PRISMA Protocol. A first screening of the retrieved articles was performed on titles and abstracts, selecting any potentially eligible studies. Later, a second screening was conducted by the same researchers on the full text of the articles applying to the established inclusion and exclusion criteria. In case of any disagreement, a third reviewer was consulted.

Data collection process
The data of the selected articles were extracted by one reviewer and exported to an Excel datasheet (Microsoft Office for Mac 2011 package) organised according to the Cochrane Consumers and Communication Review Group's data extraction template. A second author checked the extracted data and disagreements were resolved by consensus. In this phase no author was contacted since all numerical data were provided in the published papers.

Data items
The following data were extracted:
a) Name of the authors;
b) year of publication;
c) study type;
d) sample size of the study group;
e) sample size of the control group;
f) gender of the participants;
g) average age;
h) treatment procedure;
i) treatment/observation time;
j) outcome variables analysed;
k) exclusion criteria;
l) control group;
m) results;
n) conclusions.
Unless the same parameters were originated from at least two of the selected studies, the relevant data could only be described but not synthesized. The following two-dimensional data measurements for airway changes obtained by cephalometric radiography were considered. Pharyngeal width measurements: McNamara's upper pharynx dimension (minimum distance in mm between the upper soft palate and the nearest point on the posterior pharynx wall); McNamara's lower pharynx dimension (the minimum distance in mm between the point where the posterior tongue contour crosses the mandible and the nearest point on the posterior pharynx wall) [McNamara]. Nasopharynx thickness measurements: PNS-AD1 lower airway thickness (distance in mm between PNS and the nearest adenoid tissue measured through the PNS-Ba line (AD1); PNS-AD2 upper airway thickness (distance between PNS and the nearest adenoid tissue measured through a perpendicular line to S-Ba from PNS (AD2) [Linder-Aronson and Henrikson, 1973].

Quality assessment
Independent quality assessment of the included studies was performed according to Newcastle-Ottawa Scale (NOS) [Stang, 2010] by three reviewers (D.G., M.A.M. and E.L.). Any disagreement was discussed and resolved by consensus when necessary. This scale was proposed by Wells et al. [2000] for assessing the quality of non-randomised studies which consists of 8 items distributed in 3 subgroups according to selection, comparability and outcome. A semi-quantitative evaluation of the quality of the studies is carried out using a star assignment system. A maximum of one star can be assigned to each item, with the exception of comparability, which allows for the

	Akin 2015	Baccetti 2010	Baloş 2015	Cretella 2019	Hwang 2018	Kilinç 2007	Mucedero 2009	Yagci 2011
Selection								
Representativeness of the exposed cohort (treated group)	*	*	*	*	*	*	*	*
Selection of the non-exposed cohort (control group)	*	*	*	*		*	*	*
Ascertainment of exposure	*	*	*	*	*	*	*	*
Outcome of interest was not present at start of study	*	*	*	*	*	*	*	*
Comparability								
Comparability of cohorts on the basis of the design or analysis	**	**	*	**	*	*	**	**
Exposure								
Assessment of outcome	*	*	*	*	*	*	*	*
Was follow-up long enough for outcomes to occur		*	*	*	*		*	*
Adequacy of follow up of cohorts		*		*	*			
Total Score	7	9	7	9	7	6	8	8

TABLE 1 Quality Assessment of the included studies according to the Ottawa-Newcastle scale. All the included studies can be considered of high quality presenting a Total score higher than 6.

Author (Year)	Study type	Characteristic of the included subjects	Interventions	N. of patients included	Female/male	Mean age	
Akin. M. et al. 2015	R	• Skeletal Class III malocclusion • Class III molar relationship • Edge-to-Edge or anterior crossbite relationship • Flat or mild concave facial profile • ANB angle of 0° or less	Gt: RME-FM Gc: Untreated	Gt: 25 Gc: 17	Gt: 10M\15F Gc: 8M\ 9F	Gt: 10.3 ± 1.5 Gc: 10.1±1.3	
Baccetti T. et al. 2010	P	• Skeletal Class III malocclusion • Class III molar relationship • Edge-to-Edge or anterior crossbite relationship • Wits appraisal of -2mm or less	Gt: FM-BB Gc: Untreated	Gt: 22 Gc: 14	Gt: 10M\12F Gc: 8M \6F	Gt: 8.9 ± 1.5 Gc: 7.6 ± 1.4	
Baloş T. B. et al 2015	R	• Skeletal Class III malocclusion • Class III molar relationship • Anterior crossbite relationship • Maxillary retrusion (SNA <82°) • Optimal or high mandibular plane angle (SN/GoGn: 26-38° or >38°) • ANB angle of 0° or less	Gt1: FM-ND Gt2: FM-HD Gc: Untreated	Gt1: 17 Gt2: 17 Gc: 11	Gt1: 9M\8F Gt2: 10M\7F Gc: 8M\3F	Gt1: 11.3 ± 0.98 Gt2: 11.5 ± 1.1 Gc: 9.1 ± 1.1	
Cretella L.E. et al. 2019	R	• Skeletal Class III malocclusion • Class III molar relationship • Edge-to-Edge or anterior crossbite relationship • Wits appraisal of -2mm or less	Gt: RME-FM Gc: Untreated	Gt: 47 Gc: 18	Gt: 25M\22F Gc: 9M\9F	Gt: 7.8 ± 1.5 Gc: 8.9 ± 0.8	
Hwang D-M. et al. 2018	P	• Skeletal Class III malocclusion • Class III molar relationship • Edge-to-Edge or anterior crossbite relationship • Maxillary hipoplasia • Wits appraisal of less than -3 mm	Gt: FM-BB Gc: Untreated	Gt: 30 Gc: 20	Gt: 13M\18F Gc: 9M\11F	Gt: 7.78 ± 1.17 Gc: 7.95 ± 1.17	
Kilinç A.S et al. 2007	R	• Skeletal Class III malocclusion • Class III molar relationship • Anterior crossbite relationship • Maxillary skeletal retrusion	Gt: RME-FM Gc: Untreated	Gt: 18 Gc: 17	Gt: 7M\11F Gc: 8M\9F	Gt: 10.5± 0.93 Gc: 10.9 ± 0.82	
Mucedero M. et al. 2009	P	• Skeletal Class III malocclusion • Class III molar relationship • Edge-to-Edge or anterior crossbite relationship • Wits appraisal of -2 or less	Gt1: FM-BB Gt2: RME-FM Gc: Untreated	Gt1: 22 Gt2: 17 Gc: 20	Gt1:10M\12F Gt2: 7M\10F Gc: 12M\ 8F	Gt1: 8.9±1.5 Gt2: 7.1±1.8 Gc: 8.1 ± 1.2	
Yagci A. et al. 2011	P	• Skeletal Class III malocclusion • Class III molar relationship • Edge-to-Edge or anterior crossbite relationship • Nasion perpendicular to A-point of 2 mm or less • ANB angle of 0° or less	Gt1: RME-FM Gt2: RME-MFM Gc: Untreated	Gt1: 15 Gt2: 15 Gc: 15	Gt1: 7M\8F Gt2: 8M\7F Gc: 8M\7F	Gt1: 9.6 ±1.3 Gt2: 9.5 ± 1.5 Gc: 9.8 ± 1.6	

R Retrospective study, P Prospective study

TABLE 2 Main characteristics of the included studies. GT, Treatment group; GC, control group; F, Female; M, Male; FM, Face-Mask;

assignment of two stars. NOS scores range from 0 to 9 stars. Scores 0 to 5 are regarded as indicator of a low quality while scores higher than 6 are considered good quality (Table 1).

Statistical analysis

The continuous data extracted from the included studied were analysed using Review Manager 5.3 (provided by the Cochrane Collaboration), according to the methods reported in the Cochrane Handbook for Systematic Reviews of Interventions. The forest plots of continuous data were constructed comparing the mean data difference at a 95% confidence interval (CI). The significance level was set at $p < .05$ and the Cochrane Q test was used to assess the heterogeneity between studies and Cochrane's test (statistic) to evaluate the magnitude of heterogeneity. If heterogeneity was low ($I2<50\%$), a fixed-effects model was used; in all the other cases a random-effect was adopted for the meta-analysis.

Results

The electronic search identified 152 published items, after removing duplicates 87 records were screened through their title and abstract. After this first screening 32 studies were assessed for eligibility screening the full-text. Out of these 32 studies, 24 studies were excluded after applying the inclusion and exclusion criteria. The flow-chart of the screening process according to the PRISMA statement is shown in Figure 1. Finally, eight studies were included in the qualitative and quantitative synthesis [Akin et al., 2015; Baccetti et al., 2010; Baloş Tuncer et al., 2015; Cretella Lombardo et al., 2020; Hwang et al., 2019; Kilinc et al., 2008; Mucedero et al., 2009; Yagci et al., 2011]. Four of the articles were prospective studies [Baccetti et al., 2010; Hwang et al., 2019; Mucedero et al., 2009; Yagci et al., 2011] and the other four were retrospective studies [Akin et al., 2015; Baloş Tuncer et al., 2015a; Cretella Lombardo et al., 2020; Kilinc et al., 2008]. They were published between 2008 and 2020. The key characteristics of the included studies are shown in Table 2.

Four of the retrieved studies included treatments performed by means of MPAs only [Baccetti et al., 2010; Baloş Tuncer et al., 2015b; Hwang et al., 2019; Mucedero et al., 2009]. A total of 113 treated growing subjects were compared with 65 controls properly matched for age and malocclusion except for the case of Hwang et al. [2019] whose control group was composed by skeletal Class I malocclusion subjects, due to

Type of appliance	T2-T1	Outcome
RME: maxillary acrylic expander FM: Dentarum, Pforzheim	N/A	The facemask group showed significant anteroposterior width increases of the pharynx (p<0.001), as well as significant area increases of the nasopharynx based on its anterior portion (p<0.001) and on its total area (p<0.001).
M-BB: lower arch Schwarz plate	1.6 ± 1.4 y	No significant short- or long-term changes in the sagittal oropharyngeal and nasopharyngeal airway dimensions were induced by maxillary protraction in subjects with a Class III malocclusion when compared with untreated controls.
FM: Delaire type facemask	10.15 ± 2 m	The airway dimensions at the adenoid side and soft palate were increased in the treatment groups compared to the control group (p < 0.05). The nasopharyngeal area demonstrated a significant difference in normodivergent and control subjects (p < 0.05). The effect of RH treatment on the sagittal airway dimensions revealed no significant difference between different vertical craniofacial features in the short term.
RME: banded or bonded BB:mandibular bite-block FM: Delaire type facemask	2 ± 1.7 y	A significant increase in airway size and a significant decrease in adenoid size were found in the treated group as well as an improvement in the pharynx dimension. During active treatment the treated group showed a significant improvement in lower airway size and in lower pharynx dimension. A significant decrease in adenoid size was also found.
FM: Petit type facemask	8.1 ±1.4 m	Immediately after maxillary protraction, the nasopharyngeal and superior oropharyngeal airway dimensions increased. No significant changes in the middle or inferior oropharyngeal airway dimensions or in the hyoid bone position were noted after treatment.
RME: banded Hyrax expanded appliance FM: Petit type facemask	6.94 ± 0.56 m	When the treatment and control groups were compared, the upper airway linear measurements (pns-ad1, pns-ad2, APW-PPW, APW'-PPW') and the nasopharyngeal area had increased in the treatment group.
RME: bondend acrylic splint	2.1 ± 1.8 y	The favorable skeletal maxillary and mandibular changes produced by maxillary protraction with or without RME were not associated with significant changes in the sagittal oropharygeal and nasopharyngeal airway dimensions
RME: bonded appliance CFM: Petit type facemask	1.18 ±0.36	Both treatment groups showed statistically significant changes in the sagittal (pitch) measurements of natural head position and upper pharynx, aerial, and total area of airway measurements during the treatment period. In the control group, the only statistically significant change was an increased upper pharynx measurement (P 0.020). The modified facemask group also showed significant changes in aerial (P 0.003) and total (P 0.001) areas of the airway measurements compared with the control group.

RME, Rapid Maxillary Expander; BB, Bite-Blocks; MFM, Modified Face-mask; y, year; m, month; N/A, not applicable.
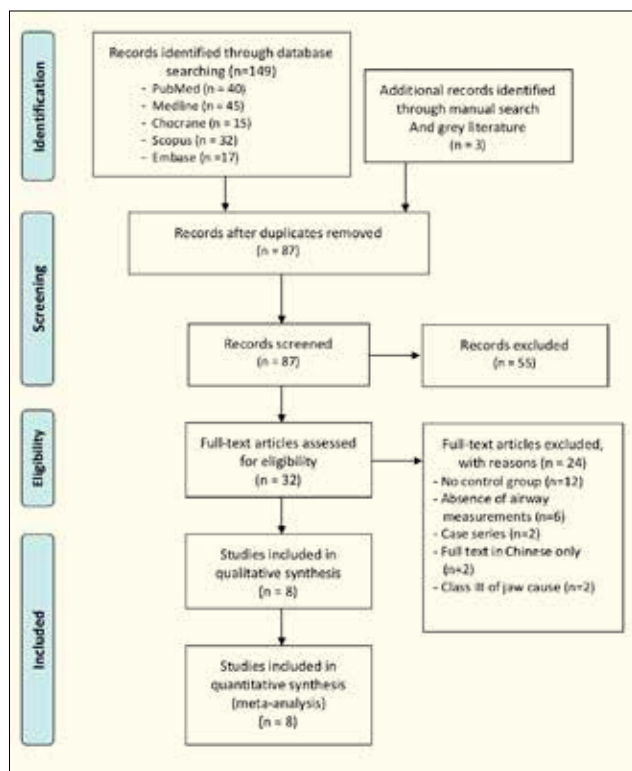
FIG. 1 Flow diagram of the performed search.

ethical concerns. Baccetti et al and Mucedero et al. [2010]. reported that patients were treated at least to a positive dental overjet before discontinuing treatment; most patients were overcorrected towards a Class II occlusion, the reported treatment time was in both cases of about 1.6 ± 1.4 years. Baloş [2015] reported a treatment time of 10.15 ± 2 months and all patients were treated at least to a positive dental overjet before discontinuing treatment. Hwang reported a treatment time of 8.1 ± 1.3 months and did not specify the occlusal goals set to stop the protraction phase [Hwang et al., 2019].

A total of 137 growing subjects were treated with MPAs plus RME and compared with 87 controls properly matched for age and malocclusion. Cretella reported a treatment time of 2 ± 1.7 years that included MPAs + RME treatment and 6–9 months of a mandibular retractor applied to the upper jaw, the treatment goal was to establish a positive overjet even if most of the patients were overcorrected towards a Class II relationship [Cretella Lombardo et al., 2020]. Mucedero established the same occlusal goals and reported a treatment time of 2.1 ± 0.28 years. Akin did not report the treatment duration that was continued until a Class II dental relationship was established [Akin et al., 2015]. Yagci reported a treatment time of 1.18 ± 0.36 years, treatment was continued till a positive overjet was achieved [Yagci et al., 2011]. Kilinç reported a treatment time of 6.94 ± 0.56 months without describing any specific occlusal goal [Kilinc et al., 2008].

Effect on pharyngeal width
Regarding the upper pharyngeal width measured according to McNamara (Fig. 2), four studies [Akin et al., 2015; Cretella Lombardo et al., 2020; Mucedero et al., 2009; Yagci et al., 2011] reported about MPAs + RME (119 subjects in the study group and 85 in the control group) reporting a non-significant difference at the end of treatment (random: mean difference, 1.00 mm, 95% CI, -0.01 mm- 2.00 mm, P= 0.05). The Random model was used because of the high heterogeneity (I2=51%). The increase in heterogeneity was especially due to the results of Akin [Akin et al., 2015] if this study was removed (Fig. 3) the heterogeneity dropped (I2=0) and a fixed effect could be used obtaining a similar result (fixed: mean difference, 0.59 mm, 95% CI, -0.19 mm 1.37 mm, P= 0.14). Two studies [Baccetti et al., 2010; Mucedero et al., 2009] reported the effect of a treatment based on MPAs only (44 subjects in the study group and 34 in the control group) reporting a non-significant difference at the end of treatment (random: mean difference, 0.01 mm, 95% CI , -1.45 mm 1.48 mm, P= 0.99). A meta-analyses with a low heterogeneity reported a non-significant improvement in this width in subjects treated with MPAs + RME protocols when compared to MPAs only treated groups (random: mean difference, 0.79 mm, 95% CI, -0.04 mm 1.61 mm, P= 0.006).

Regarding the lower pharyngeal width measured according to McNamara (Fig. 4) four studies [Akin et al., 2015; Cretella Lombardo et al., 2020; Mucedero et al., 2009; Yagci et al., 2011] reported about MPAs + RME treatment effect (111 subjects in the study group and 93 in the control group). A non-significant difference at the end of treatment was displayed when compared to control groups (random: mean difference, 0.83 mm, 95% CI, -0.59 mm, 2.26 mm, P= 0.25). Two studies [Baccetti et al., 2010; Mucedero et al., 2009] reported the effect of treatment based only on MPAs only (44 subjects in the study group and 34 in the control group) reporting a non-significant difference at the end of treatment (random: mean difference, -1.27 mm, 95% CI, -3.27 mm, 0.72 mm, P= 0.40). A meta-analysis with a high heterogeneity (I2=67%) reported a non-significant difference in this width in after treatment when both groups were compared (random: mean difference, 0.32 mm, 95% CI, -1.03mm, 1.68 mm, P= 0.64).

Effect on pharyngeal thickness
Regarding the distance PNS-AD1 (Fig. 5), three studies [Cretella Lombardo et al., 2020; Kilinc et al., 2008; Mucedero et al., 2009] reported about MPAs + RME treatment effect (82 subjects in the study group and 55 in the control group) reporting a non-significant difference at the end of treatment (random: mean difference, 1.75 mm, 95% CI , -0.63 mm, 4.14 mm, P= 0.15).

Four studies [Baccetti et al., 2010; Baloş Tuncer et al., 2015b; Hwang et al., 2019; Mucedero et al., 2009] reported the effect of treatment based on MPAs only (108 subjects in the study group and 76 in the control group) reporting a significant difference at the end of treatment (random: mean difference, 1.39 mm, 95% CI, 0.32 mm, 2.47 mm, P= 0.01). A meta-analysis with an acceptable heterogeneity (I2=39%) reported a significant difference in this width after treatment favouring the group treated with MPAs only (random: mean difference, 1.50 mm, 95% CI , 0.54 mm, 2.45 mm, P= 0.002).

Regarding the distance PNS-AD2 (Fig. 6), three studies [Cretella Lombardo et al., 2020; Kilinc et al., 2008; Mucedero et al., 2009] reported about MPAs + RME treatments (82 subjects in the study group and 55 in the control group) reporting a non-significant difference at the end of treatment (random: mean difference, 2.46 mm, 95% CI, -1.08 mm, 6.00 mm, P= 0.17). Four studies [Baccetti et al., 2010; Baloş Tuncer et al., 2015b; Hwang et al., 2019; Mucedero et al., 2009] reported the effect
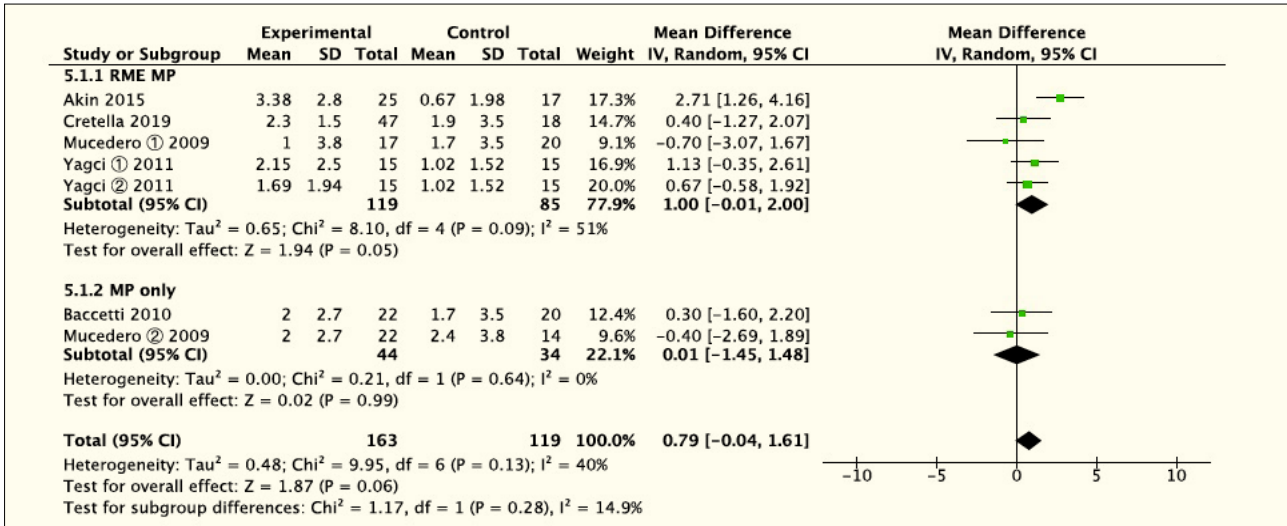
FIG. 2 Forest plot of the upper pharyngeal width measurements (McNamara's upper pharynx) change comparing MPAs groups and MPAs + RME groups with untreated controls.
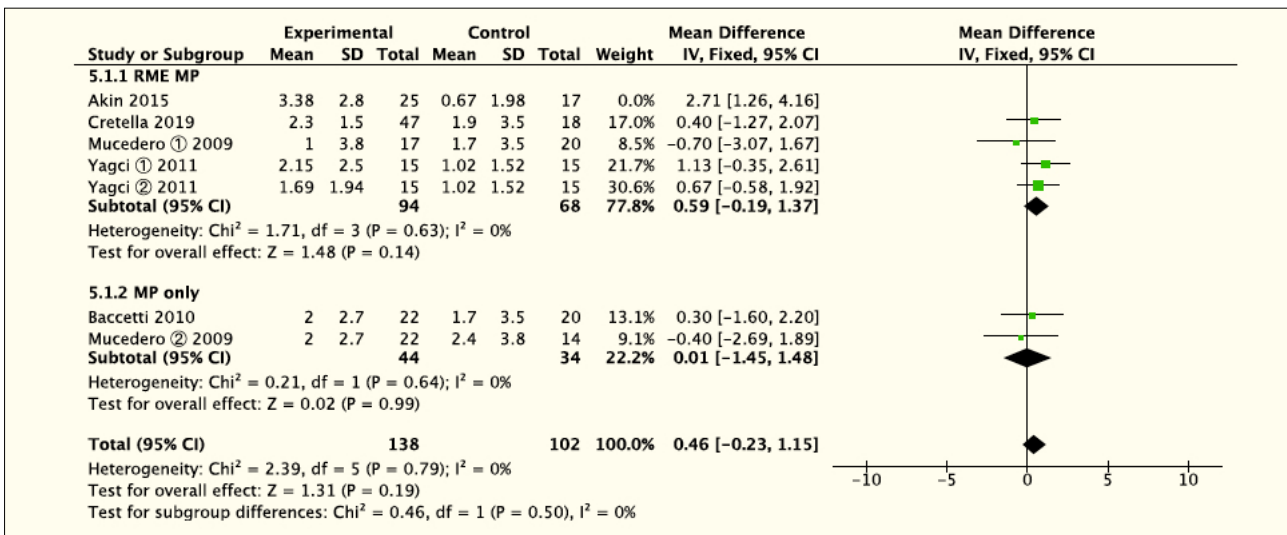

FIG 3 Forest plot of the upper pharyngeal width measurements (McNamara's upper pharynx) change comparing MPAs groups and MPAs + RME groups with untreated controls the study Akin is removed to lower the heterogeneity.
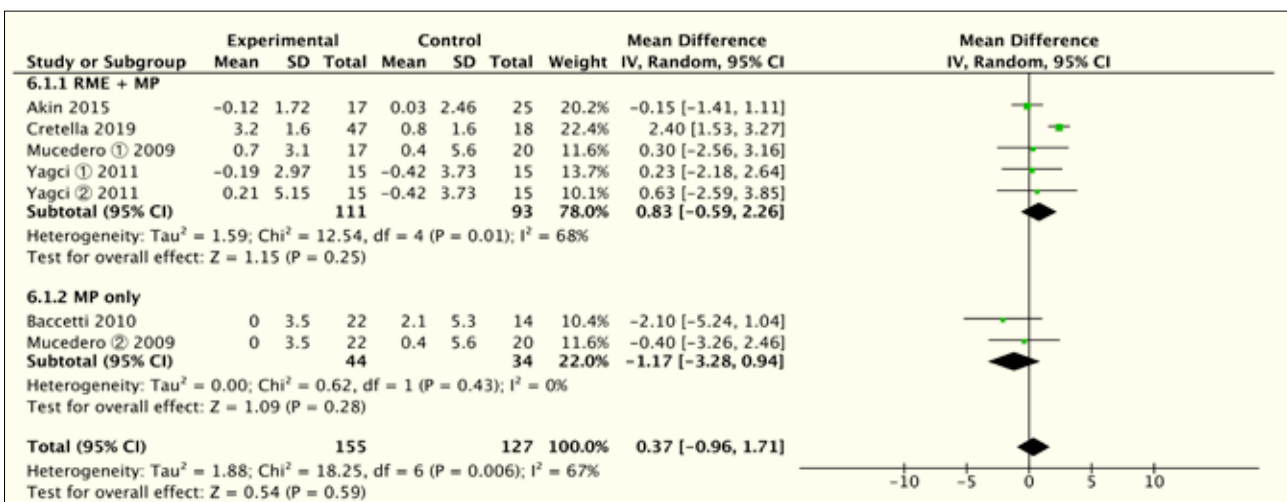

FIG 4 Forest plot of the lower pharyngeal width measurements (McNamara's lower pharynx) change comparing MPAs groups and MPAs + RME groups with untreated controls.
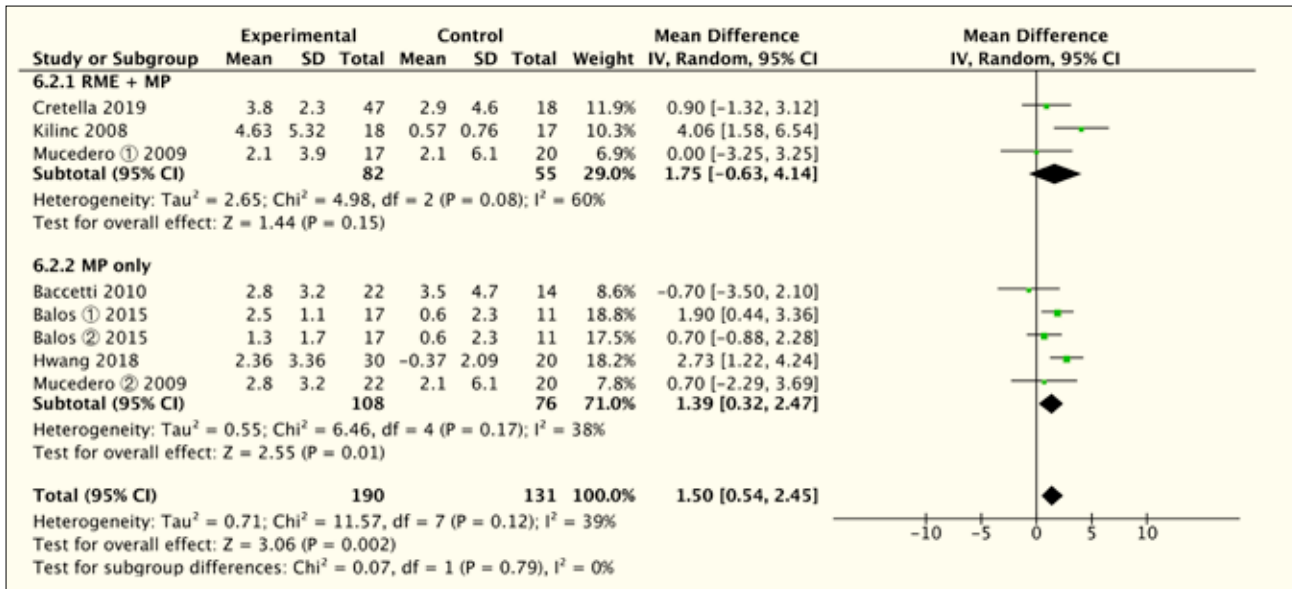
FIG. 5 Forest plot of the pharyngeal thickness (PNS-AD1) change comparing MPAs groups and MPAs + RME groups with untreated controls.
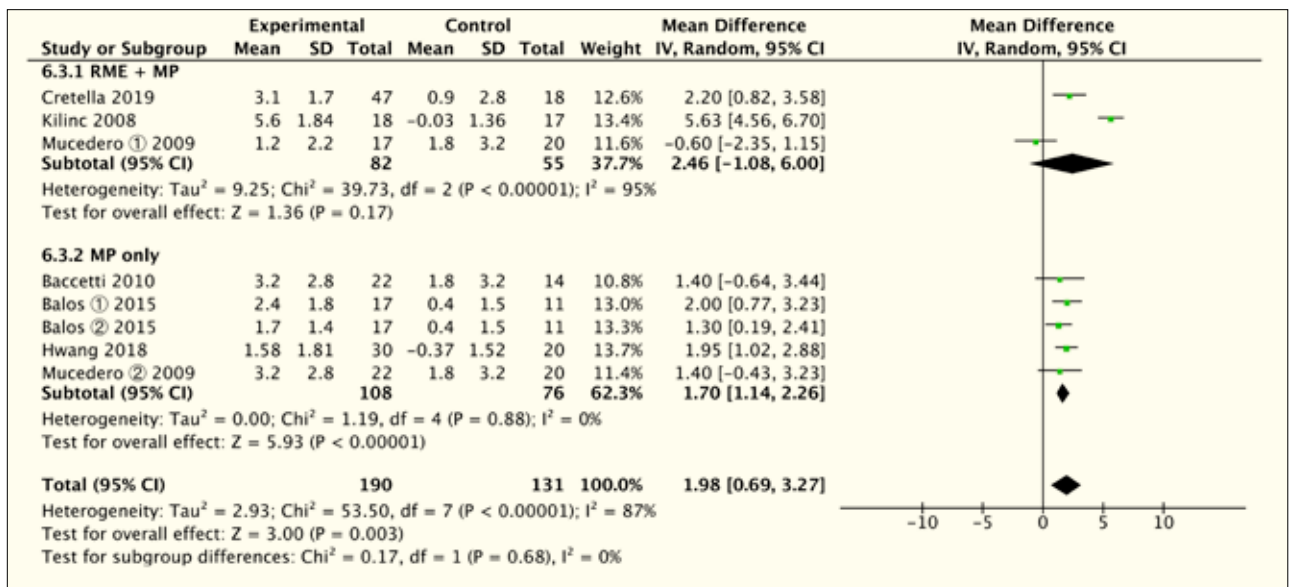

FIG. 6 Forest plot of the pharyngeal thickness (PNS-AD2) change comparing MPAs groups and MPAs + RME groups with untreated controls.

of a treatment based on MPAs only (108 subjects in the study group and 76 in the control group) a significant difference was assessed at the end of treatment (random: mean difference, 1.70 mm, 95% CI, 1.14 mm, 2.26 mm, P= 0.00001). A meta-analysis with high heterogeneity (I2=87%) reported a significant difference in this width after treatment favouring the group treated with MPAs only (random: mean difference, 1.50 mm, 95% CI, 0.54 mm, 2.45 mm, P= 0.003).

Discussion

In the last decade the interrelation between malocclusion, orthodontic therapy and airway function have received an increasing interest in literature [Alhammadi et al., 2019; Gong et al., 2018]. Maxillary protraction is one of the favourite approach to treat Class III malocclusion in growing individuals,

even in absence of maxillary retrusion. The rationale behind this approach is that this type of therapy can decrease the need of surgical correction once somatic growth is completed [Mandall et al., 2016]. Maxillary traction has demonstrated to produce a forward displacement of the entire maxillary complex in animal models [Jackson et al., 1979]. According to some authors a forward movement of the maxilla can have a positive effect on the respiratory function and may increase the nasopharyngeal airway dimension [Hiyama et al., 2002; Lee et al., 2011].

To our best knowledge this is the first systematic review in addressing the impact of MPAs only versus MPAs + RME treatment on the airway dimension. According to some authors, a maxillary traction performed after a rapid maxillary expansion could be more effective than the MP alone due to the disrupting effect of the RME on the circummaxillary sutures [Baccetti et al., 2000]. According to our meta-analyses treatments based on a RME + MPAs protocol are not superior to treatment

performed with MPAs only in increasing the upper airway width, according to McNamara upper pharyngeal width. At the end of treatment the mean difference in width is not significantly different from the one of the controls. The upper airway width, according to McNamara is measured between two soft-tissue landmarks, being the shortest distance from the soft palate to the nearest point on the posterior wall of the pharynx. According to Vaughn et al. [2005] in a randomized clinical trial about MPAs and MPAs + RME the mean maxillary advancement was 2.41-2.49 mm in the horizontal plane, Baccetti et al. [1998] reported a forward movement of between 1.7 and 2.0 mm, while MacDonald et al. [1999] observed a movement ranging from 1.61 and 2.20 mm. It could be argued how much of this advancement can be actually and effectively translated to the soft tissue and produce a significant increase in the pharyngeal width. In studies on the effect of maxillary advancement and mandibular setback on the linear airway dimensions most of the authors underlined the lack of a significant increase of the linear distance between the soft palate and the posterior wall of the pharynx [Chen et al., 2007; Jakobsone et al., 2010; Kilinc et al., 2008], even if the skeletal changes are larger in cases treated with a surgical and orthodontic approach. On the other hand, those of Mucedero [2009] and Baccetti [2010] are the only two studies using a control group comparing McNamara upper width before and after treatment and using a MPAs only treatment protocol. These authors were affiliated to the same research group and co-authored the two studies included in the meta-analyses. Their treatment group of bite-blocks and maxillary protraction included the same amount of patients and obtained the same results probably indicating that in the two studies this treatment sub-group was the same.

The effect of both treatment protocols on the lower airway width, according to McNamara, was not significant according to what reported also by other authors who did not discriminate about the two treatment sub-groups [Lee et al., 2018; Ming et al., 2018]. This result is somewhat expected since the face-mask exerts a posterior force directed on the mandible, halting its anterior growth displacement. The positive effect of mandibular advancement on the velo and oropharynx is a well-documented effect [Zhao et al., 2008] that cannot occur if the mandible is constricted posteriorly.

According to the change in pharyngeal thickness measured as the distance PNS-AD1 the effect was grater for the group treated only by MPAs while, the MPAs +RME group displayed a non-significant difference when compared to the control group. Due to the degree of heterogeneity (I2=60%) the meta-analysis was repeated removing the included studies one by one. The heterogeneity dropped (I2=0) when the study of Klinic was removed and a fixed effect could be used but the result did not change (fixed: mean difference, 0.17 mm, 95% CI, 0.25 mm, 0.58 mm, P= 0.43). Regarding the distance PNS-AD2 a similar result was obtained with a greater and significant effect in the MPAs only group. The heterogeneity of the MPAs + RME group could not be lowered even excluding the included studies one by one and displayed always a value higher than 93%. The result is somewhat surprising taking into account that the dentoalveolar and skeletal effect of both treatments is comparable according to most of the authors [Foersch et al., 2015; Kim et al., 1999] and the result is probably linked to the high heterogeneity of the studies included in this treatment sub-group. Moreover the RME is an appliance directed towards the transversal dimension of the malocclusion that is impossible to quantify on a 2D image.

Despite of the many studies reporting on airway dimensions change and MPAs treatment, we decided to include only studies where a control group was present due to the higher reliability of the results and the possibility of measuring the effect size. At present many authors report the ethical difficulties experienced in obtaining a control group [Celikoglu and Buyukcavus, 2017], other studies use Class I control group such as Hwang, but growth trends in Class III subjects may differ from Class I subjects [Hwang et al., 2019].

The current study presents some limitations. First, the sample size of the groups included in the quantitative synthesis for meta-analysis is relatively small, although the total sample size almost doubles the number of included cases if compared with previous meta-analyses on the global effect of MPAs treatment [Ming et al., 2018]. In some of the subgroups due to the high heterogeneity, it may be difficult to assess the relationship between the linear changes and MPAs + RME treatment protocols. Second, assessing the real pharyngeal airway changes relying on 2D cephalometric radiographs may not be ideal [Maspero et al., 2019]. 3D images are generally considered a better mean to assess volumetric changes. However, the number of studies performed on 3D images is very small, and the use of different landmarks and the absence of control groups made actually impossible to perform a meta-analysis based on the available evidence. According to various authors although 3D images are more reliable a positive correlation exists between the linear and volumetric findings [Aboudara et al., 2009], being the nasopharyngeal airway size on a head-film and its real volumetric size from a cone beam scan positively related in adolescents [Vizzotto et al., 2012]. During orthodontic treatment, lateral cephalograms are more routinely available than 3D images, which are usually requested for other diagnostic purposes and require a higher x-ray dose. Some authors estimated the radiation risk for dental CBCT imaging and concluded the need for justification and optimisation of CBCT exposure with a specific focus on children [Pauwels et al., 2014; Theodorakou et al., 2012]. The present systematic review included mostly observational studies, four retrospective and four prospective. There was no previous estimate of sample size and withdrawals (dropouts) were not declared in the included prospective studies. Moreover, due to the lack of randomisation and blinding, the quality of the evidence provided by these types of study designs is weak and it would be preferable to include a higher number of RCTs to improve the strength of the conclusions, decrease the risk of bias and the confounding factors. Unfortunately no RCTs based evidence could be found. Despite of the study design, the included research outputs presented a positive quality assessment according to the NOS assessment. The leave-one-out analyses were performed by repeating the meta-analysis excluding studies that caused an increase in heterogeneity and helped to perform a more reliable quantitative assessment. The comparison of the treatment effect involved only four out of the many linear measurements proposed to evaluate the airway morphology. We consider that an effort should be done to design a standardised set of measurement applicable to the future 3D and 2D records in order to increase the opportunity of comparing data from a higher number of studies in future meta-analyses.

Conclusions

Within the limitations of the current systematic review and meta-analysis, MPAs only treatment can widen the pharyngeal thickness after treatment both at PNS-A1 and PNS-A2, while

the effect of MPAs + RME treatment was not statistically different from the one of the control group. In the light of these findings MPAs + RME did prove to have a significant effect on the airway dimension when used to treat Class III growing individuals.

Both treatment approaches failed to demonstrate a significant effect on the lower pharynx width.

A larger standardised set of measurement and further RCTs are required to allow a better analyses of the effect of these treatment modalities on the airway.

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Registration

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