

Upper Airway Changes in Diverse Orthodontic Looms: A Systematic Review and Meta-Analysis

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Abstract: Upper airway assessment is particularly important in the daily work of orthodontists, because of its close connection with the development of craniofacial structures and with other pathologies such as Obstructive Sleep Apnea Syndrome (OSAS). Three-dimensional cone-beam computed tomography images provide a more reliable and comprehensive tool for airway assessment and volumetric measurements. However, the association between upper airway dimensions and skeletal malocclusion is unclear. Therefore, the current systematic review evaluates the effects of different surgical movements on the upper airway. **Materials and Methods:** Medline (PubMed, OVID Medline, and EBSCO), Cochrane Library (Cochrane Review and Trails), Web of Knowledge (social science, and conference abstracts), Embase (European studies, pharmacological literature, and conference abstracts), CINAHL (nursing and allied health), PsycInfo (psychology and psychiatry), SCOPUS (conference abstracts, and scientific web pages), and ERIC (education) databases were searched. Two authors independently performed the literature search, selection, quality assessment, and data extraction. Inclusion criteria encompassed computed tomography evaluations of the upper airway spaces with retrospective, prospective, and randomised clinical trial study designs. To grade the methodological quality of the included studies a GRADE risk of bias tool was used. **Results and conclusion:** In total, 29 studies were included. Among these, 17 studies had a low risk of bias, whereas 10 studies had a moderate risk of bias. A meta-analysis was performed with the mean differences using a fixed-effects model. Heterogeneity was assessed with the Q-test and the I^2 index. The meta-analysis revealed significant ($p \leq 0.001$, 95% confidence interval) increases in upper airway volume after rapid maxillary expansion and surgical advancement for the correction of Class II.

Keywords: airway; orthodontics; extraction; expansion; protraction; surgery



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1. Introduction

The human upper airway could be defined as the airway space extending from the nose's nares and the mouth's stoma down to the cricoid cartilage in the larynx. The nasal and oral cavities merge in the area known as the pharynx, which is divided anatomically into three sections: the nasopharynx, oropharynx, and hypopharynx.

The shape and dimensions of the upper airway passages influence the volume of air passing through them. The close anatomical relationship between the upper airway and the

craniofacial and dental structures dictates their influence on each other. The normal growth and development of craniofacial structures depend on a patent airway and nasal breathing.

Orthodontists have long been interested in airway analysis because of the airway's potential importance to the normal development of the craniofacial region as well as its involvement in the diagnosis and treatment of mouth breathing and sleep disorders. Clinicians need to evaluate the upper airway objectively and identify the normal and abnormal anatomical boundaries and dimensions. Although two-dimensional lateral cephalograms have been used for decades to evaluate the airway's shape, size, position, and relationship with other anatomical structures, they lack the information to illustrate the anatomically complex airway structure in three dimensions. Lateral cephalograms could be used as an initial screening method for airway evaluation, but three-dimensional cone-beam computed tomography (CBCT) images provide a more reliable and comprehensive tool for airway assessment and volumetric measurements. The findings of snoring and interrupted sleep together with diagnostic images obtained during the dental examination can provide indications of possible airway disorders and support the need for referral to a medical specialist referral.

Nasal obstruction and its inseparable companion, "mouth breathing," have been assumed to affect dentofacial growth in the current literature. Although some researchers have found no association between the adequacy of the airway and dentofacial morphology [1]. It seems to be a consensus that the oropharyngeal (OP) and nasopharyngeal structures play roles in the development of the dentofacial complex [2].

The etiology of malocclusions is believed to be multifactorial, and it could be considered erroneous to associate malocclusions with only breathing mode. Because the airway is assumed to play a role in dentofacial development, several studies have attempted to correlate patients with normal naso-respiratory functions with different malocclusions and airway dimensions.

Despite this, the relationship between upper airway dimensions and skeletal malocclusion remains controversial. Some studies have shown no effect on the airway after orthodontic treatment [3], whereas others have reported a change in the airway [4]. The controversy regarding these outcomes might be related to the heterogeneity in the included articles, types of malocclusions, and imaging methods.

In addition, there has been no meta-analysis published in the literature that has compared changes in the airway dimensions resulting from different types of orthodontic treatment by using cone-beam computed tomography (CBCT), a 3D imaging technique, and only one single meta-analysis that included a small number of studies [5]. Previous systematic reviews [5–8] have investigated this subject based on data from only two-dimensional images.

Therefore, the present meta-analysis focused only on studies that used computed tomography (CT) for airway evaluation, particularly CBCT. Through a meta-analysis, this study aims to assemble scientific evidence related to the effects of orthodontic treatment modalities on airway space.

2. Materials and Methods

The systematic review is constructed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses standards of quality for the planning, conducting, and reporting of systematic reviews and meta-analyses [9]. A search protocol was specified in advance and registered at PROSPERO (International Prospective Register of Systematic Reviews ID CRD42020180936).

Participants, Interventions, Control and Outcomes (PICO) question.

To better outline the study, the participants, interventions, control and outcomes (PICO) format was followed (Table A1).

2.1. Search Strategy for the Identification of Studies

We performed a database search that included Medline (PubMed, OVID Medline, and EBSCO), Cochrane Library (Cochrane Review, Trails), Web of Knowledge (social science, and conference abstracts), Embase (European studies, pharmacological literature, and conference abstracts), CINAHL (nursing and allied health), PsycInfo (psychology and psychiatry), SCOPUS (conference abstracts, and scientific web pages), and ERIC (education). We used a specific search strategy with the following focused key terms: (airway OR oropharyngeal OR pharyngeal) AND ((orthodontic AND extraction) OR (Orthodontic AND Expansion)) OR ((Orthodontic AND ORTHOGNATHIC SURGERY)) OR ((Orthodontic AND Non-Extraction)) OR ((Orthodontic AND Distalization)) OR ((Orthodontic AND Expansion)) OR ((Orthodontic AND Cleft)) OR ((Orthodontic AND Functional Appliance)) OR ((Orthodontic AND Headgear)) OR ((Orthodontic AND Surgery)) OR (Orthodontic AND functionalization) OR (Orthodontic AND instrumentation) OR (Orthodontic AND surgical procedures) OR (Orthodontic AND oropharynx).

A gray literature search was performed using the following databases: Google Scholar, National Library of Medicine, and Social Science Research for Thesis. In addition, we searched four key orthodontic journals (Angle Orthodontics, American Journal of Orthodontics and Dentofacial Orthopedics, Journal of Clinical Orthodontics, and European Journal of Orthodontics) using their table of contents for relevant articles. The article search was performed up to November 2021.

2.2. Study Selection Procedure

Two authors independently reviewed all studies. Titles and abstracts were first screened to exclude irrelevant articles. Full texts of the remaining studies were further evaluated on the basis of preset selection criteria. Discrepancies between the two reviewers were addressed by a discussion with a third author. Final decisions were made after a consensus was reached. The selection of articles for inclusion in this review was based on the following criteria: human clinical trials with a prospective or retrospective design children or adult patients submitted to orthodontic treatment measurement of OP airway via CT before and after treatment and articles in English. The exclusion criteria were case reports, review articles, editorials, or opinions, and patients with a syndromic cleft.

2.3. Data Extraction

Data were extracted independently by two reviewers, using a specially designed data extraction form. The following data were extracted: author, year of publication, country, age, sample size, study design, type of orthodontic intervention, methodology, mean results, and outcome.

2.4. Risk of Bias Assessment

The risk of bias assessment of the included studies was performed using the GRADE tool [10]. We developed a checklist for evaluating meta-analyses of RCTs for the purpose of informing a GRADE assessment. The checklist covers the main determinants for each of the five factors (risk of bias, inconsistency, indirectness, imprecision, and publication bias) that can lead to a downgrading of quality in the GRADE system. Table A2 summarised the domains used to determine the risk of bias using standardized criteria, the included studies were further classified for each domain as low risk, moderate risk, serious risk, and critical risk of bias. The experiments were comparable to well-performed randomised controlled trials, and the domain in question was considered to have a low risk of bias. The experiments that could not be compared with well-performed randomised studies but were sound within the domain of a nonrandomized trial were considered to have a moderate bias. Studies containing certain significant problems were classified as being at serious risk of bias. A critical risk of bias was classified as studies that were too problematic to provide any useful evidence on the effect of the intervention or that did not provide any

information on the basis of the included of the 29 studies, 9 studies had a low risk of bias, 2 studies had a high risk of bias, and 18 studies had a moderate risk of bias.

2.5. Meta-Analysis

RevMan 5.3 analysis software (<http://ims.cochrane.org/revman> (accessed on 11 January 2022)) was used for conducting the meta-analysis (Cochrane Collaboration, Copenhagen, Denmark). Data related to the Mean Difference (MD) from various studies were estimated using the inverse-variance method. Two-sided 95% confidence intervals (95% CIs) were computed by using the fixed-effect model. The proportion of variability that attributes for heterogeneity was assessed via Cochran's Q-statistic and I^2 statistics. A fixed-effects model was used when heterogeneity was low ($I^2 < 50\%$) and, when I^2 was $>50\%$, a random-effects model was used. Funnel plots were employed for the detection of publication bias, and bias is revealed if the plots are asymmetrical. A value of $p < 0.05$ was considered statistically significant. Sensitivity analysis was performed to evaluate the robustness of the meta-analysis by removing outliers from the analyses with publication bias.

3. Results

After screening the titles and abstracts of 102 unique papers, 66 potentially eligible articles were selected. Two researchers independently reviewed each title and abstract, and the obtained information was compared. Inter-examiner disagreements were resolved in a consensus meeting. Of the 66 potentially eligible articles, 37 were excluded. These articles were excluded for the following reasons: non-3D ($n = 27$) and systematic review and review articles ($n = 15$) (Figure 1).

3.1. Included Studies

A total of 29 articles were identified for inclusion in this review (Table A3). This systematic review was based on prospective and retrospective cross-sectional studies and controlled clinical trials.

3.2. Study Characteristics

Of the 29 included studies, 10 studies were performed in the United States, 5 were performed in China, 2 studies were published in each Australia, Brazil, Italy, and Turkey. Other studies were performed in Egypt, Korea, Minneapolis, Singapore, South Korea, and India. Among the included 29 studies in this review, 20 studies were retrospective studies, 6 studies were prospective studies and the remaining studies were controlled clinical studies, longitudinal study and Quasi-experimental study.

3.3. Clinical Characteristics

A total of 1012 patients were included in the study, with sample sizes ranging from 8 to 83. Female patients were dominant in this review. The majority of the included studies demonstrated the Class III malocclusion type of malocclusion ($n = 9$) followed by Class II malocclusion ($n = 7$) and Class I malocclusion ($n = 9$). Out of 29 studies included in this review, 27 studies were used CBCT for the assessment of airways.

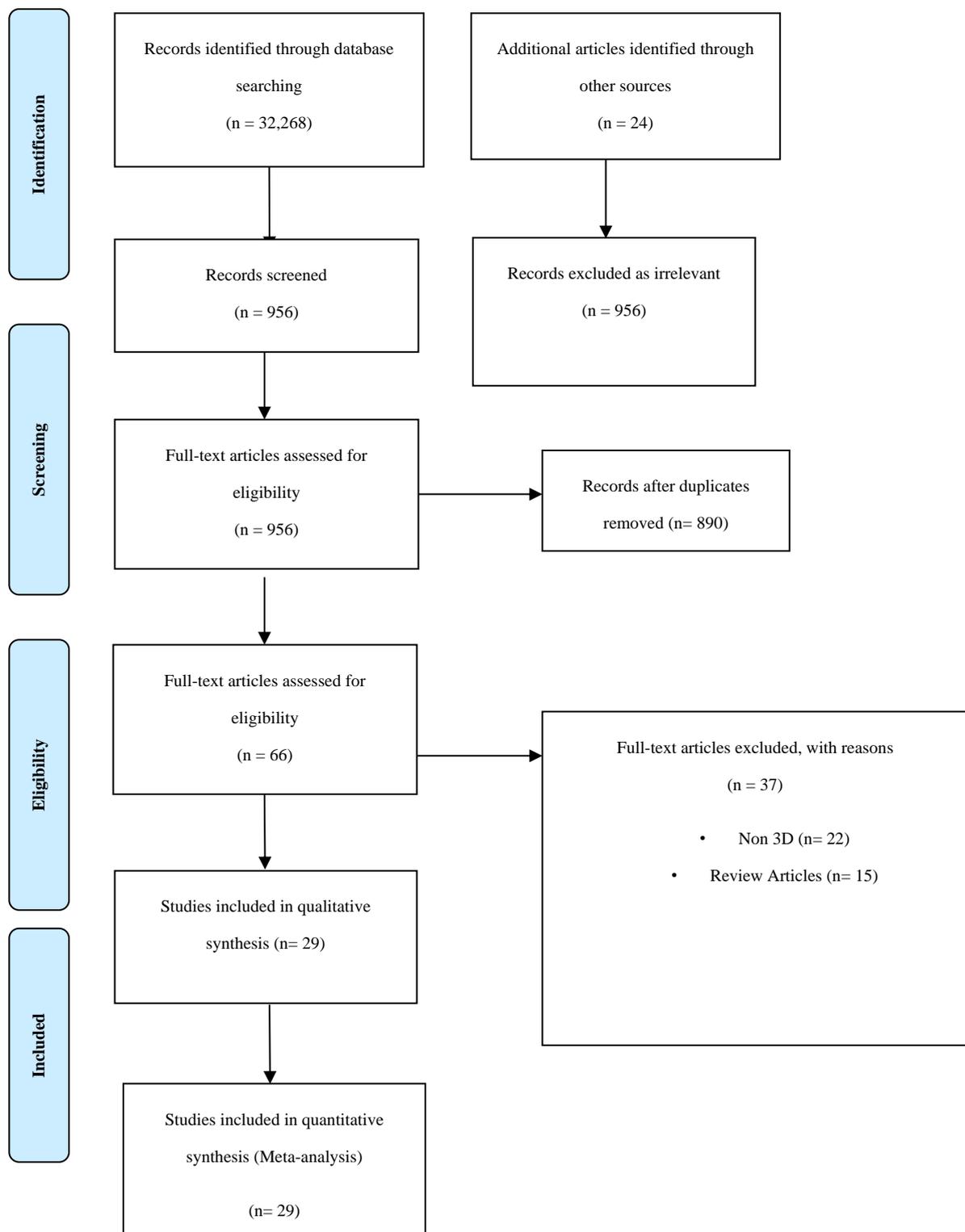


Figure 1. PRISMA flow diagram.

3.4. Change in Airway Space

3.4.1. Expansion with Protraction

Five studies report the Meta analysis for expansion with protraction between the experimental and control group. The pooled analysis showed a significant effect on expansion with protraction between the experiment and control group (MD = 0.78, CI-0.29,1.28;

$\text{Chi}^2 = 9.01$; $I^2 = 56\%$, $p = 0.002 < 0.05$). Heterogeneity between the five studies is medium ($I^2 = 56\%$). Test for overall effect: $Z = 3.12$ ($p = 0.002$) (Figures 2 and 3).

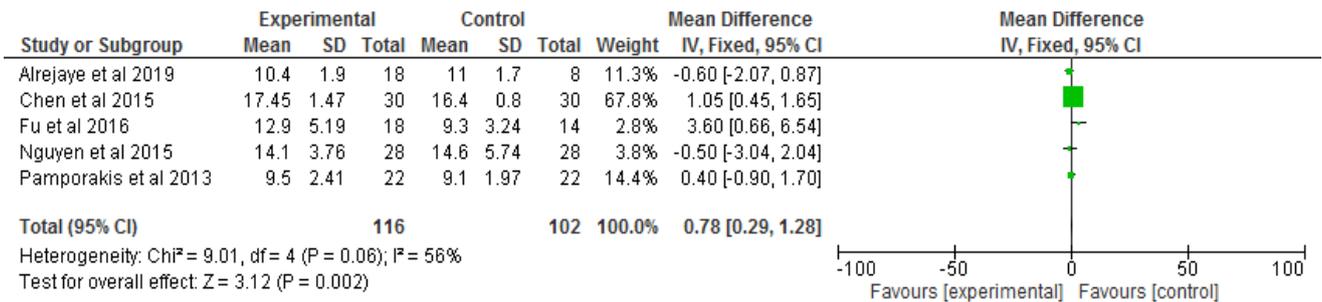


Figure 2. Forest plot for expansion with protraction between experiment and control.

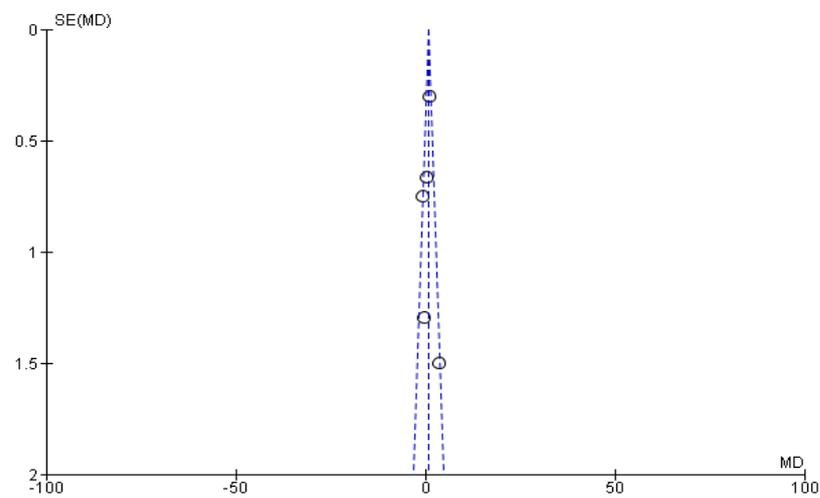


Figure 3. Funnel plot for expansion with protraction between experiment and control.

3.4.2. Clean Aligner

Two studies reported the Meta analysis for clear aligners between before and after treatment. The pooled analysis showed no effect on the clear aligner between before and after treatment ($MD = 1.57$, $CI -0.56, 3.71$; $\text{Chi}^2 = 0.05$; $I^2 = 0\%$, $p = 0.15 > 0.05$). Heterogeneity between the two studies is low ($I^2 = 0\%$). Test for overall effect: $Z = 1.44$ ($p = 0.15$) (Figures 4 and 5).

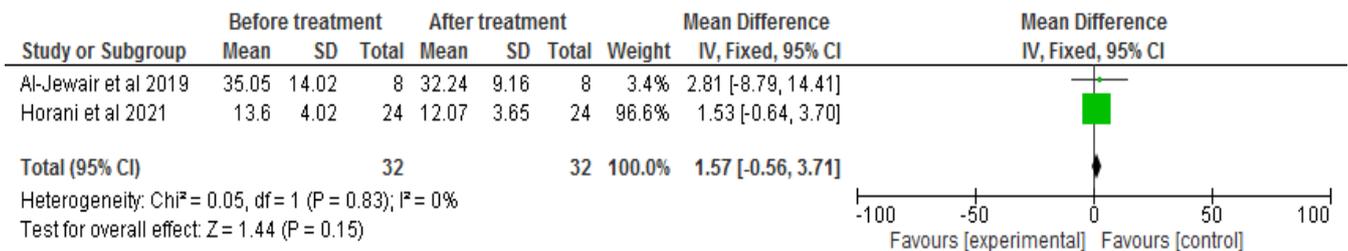


Figure 4. Forest plot for clear aligner between before and after treatment.

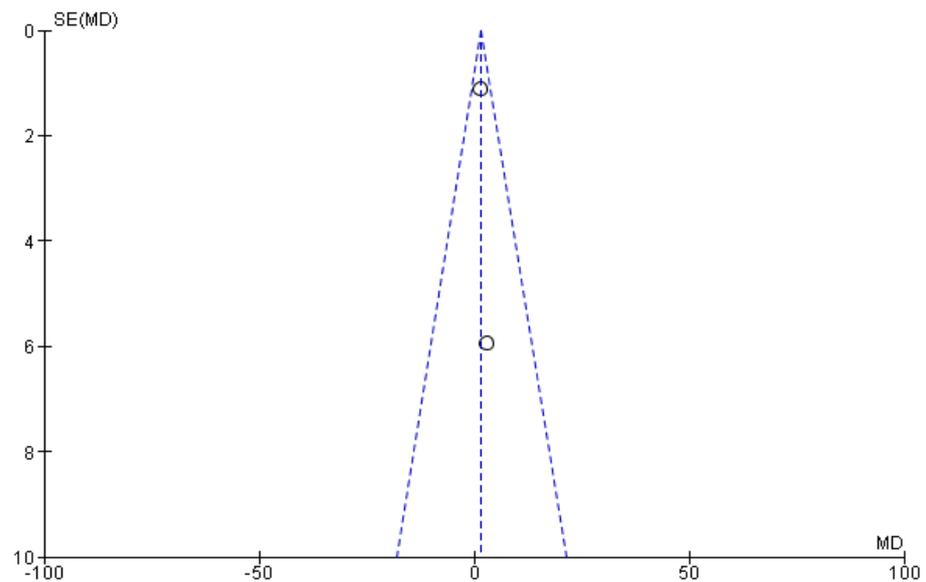


Figure 5. Funnel plot for clear aligner between before and after treatment.

3.4.3. Extraction and Non-Extraction

Five studies report the Meta analysis between extraction and non-extraction. The pooled analysis showed no effect on extraction and non-extraction (MD = 0.37, CI −1.11,1.85; $\text{Chi}^2 = 62.54$; $I^2 = 94\%$, $p = 0.62 > 0.05$). Heterogeneity between the five studies is high ($I^2 = 94\%$). Test for overall effect: $Z = 0.49$ ($p = 0.62$) (Figures 6 and 7).

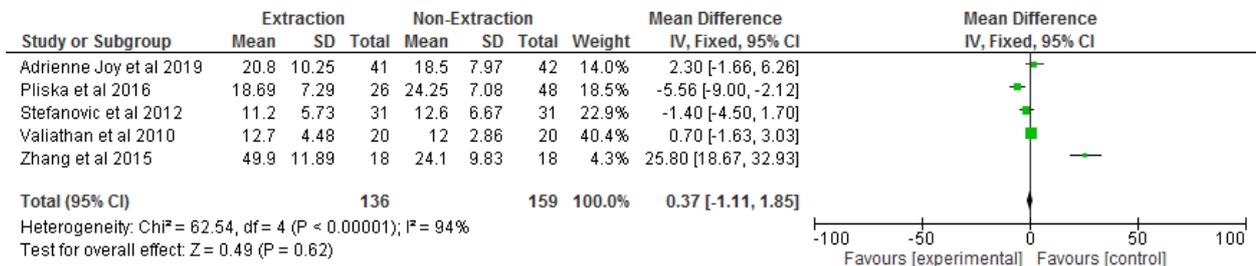


Figure 6. Forest plot for extraction and non-extraction.

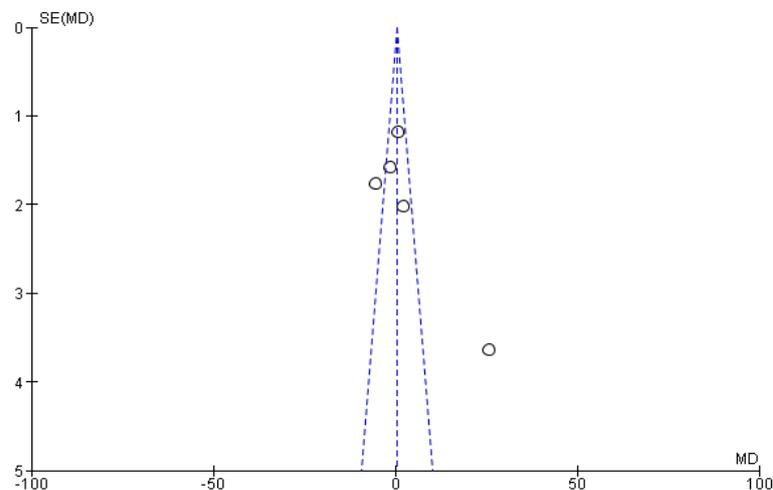


Figure 7. Funnel plot for extraction and non-extraction.

3.4.4. Functional Appliance

Three studies report the Meta analysis for functional appliance between the experiment and control group. The pooled analysis showed a significant effect on functional appliance between the experiment and the control group (MD = 2.54, CI 1.17,3.90; $\text{Chi}^2 = 10.27$; $I^2 = 81\%$, $p = 0.0003$). Heterogeneity between the three studies is high ($I^2 = 81\%$). Test for overall effect: $Z = 3.64$ ($p = 0.0003$) (Figures 8 and 9).

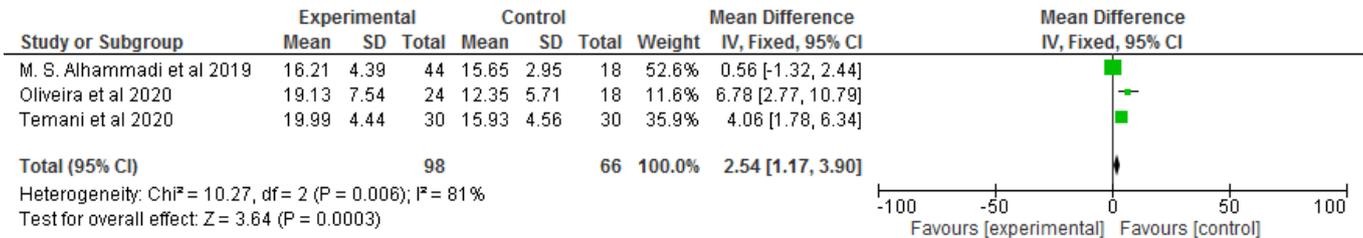


Figure 8. Forest plot for functional appliance between experiment and control.

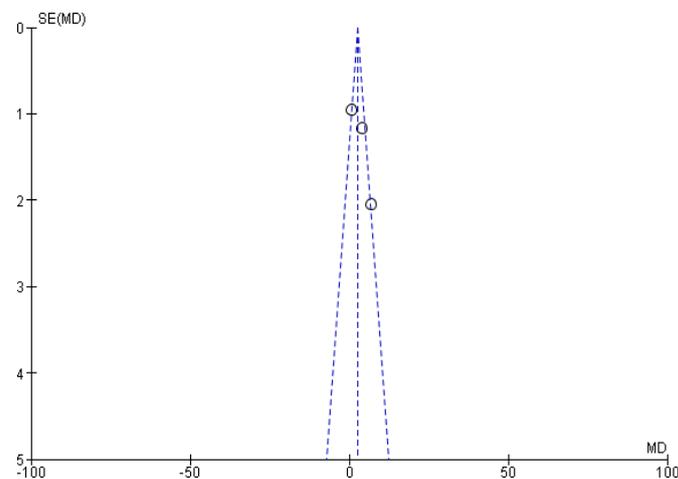


Figure 9. Funnel plot for functional appliance between experiment and control.

3.4.5. Maxillary Expansion

Eight studies report the Meta analysis for maxillary expansion between the experiment and control group. The pooled analysis showed a significant effect on maxillary expansion between the experiment and control group (MD = -1.94, CI -2.44, -1.43; $\text{Chi}^2 = 588.08$; $I^2 = 99\%$, $p < 0.0001$). Heterogeneity between the eight studies is high ($I^2 = 99\%$). Test for overall effect: $Z = 7.47$ ($p = 0.0001$) (Figures 10 and 11).

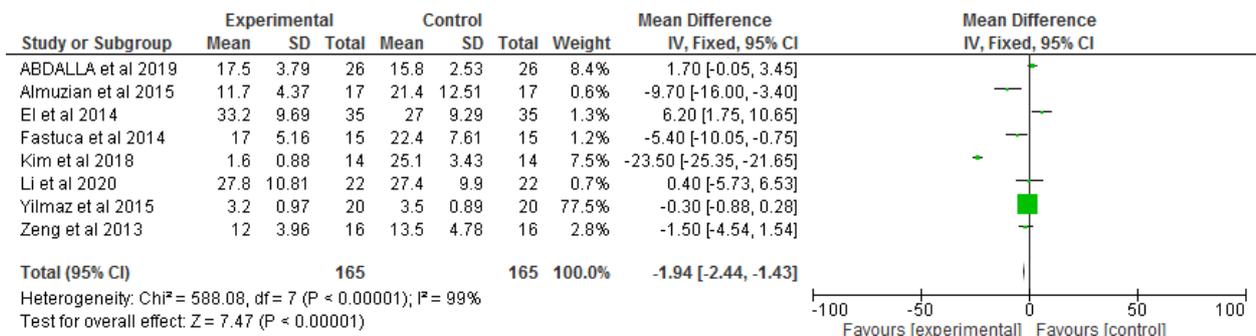


Figure 10. Forest plot for maxillary expansion between experiment and control.

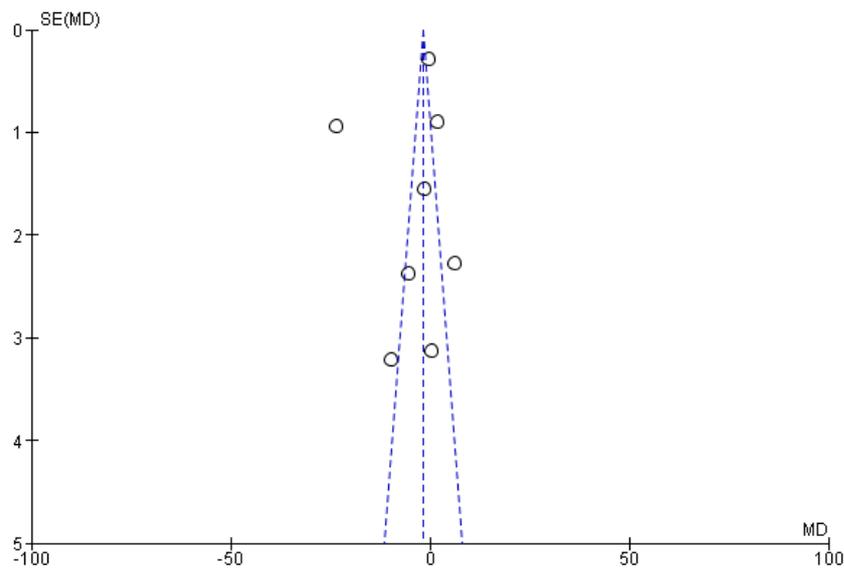


Figure 11. Funnel plot for maxillary expansion between experiment and control.

3.4.6. Surgery Class III

Three studies report the Meta analysis for surgery class III between the pre- and post-surgical group. The pooled analysis showed a significant effect on surgery class III between the pre- and post-surgical group (MD = 3.45, CI 2.54, 4.35; $\text{Chi}^2 = 7.60$; $I^2 = 74\%$, $p < 0.0001$). Heterogeneity between the three studies is high ($I^2 = 74\%$). Test for overall effect: $Z = 7.48$ ($p = 0.0001$) (Figures 12 and 13).

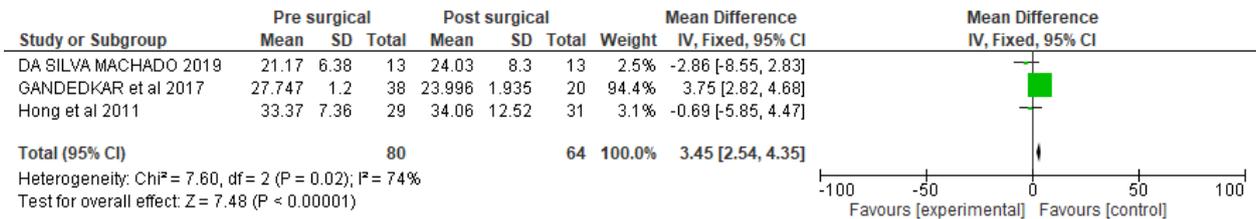


Figure 12. Forest plot for Surgery class III between pre and post surgery.

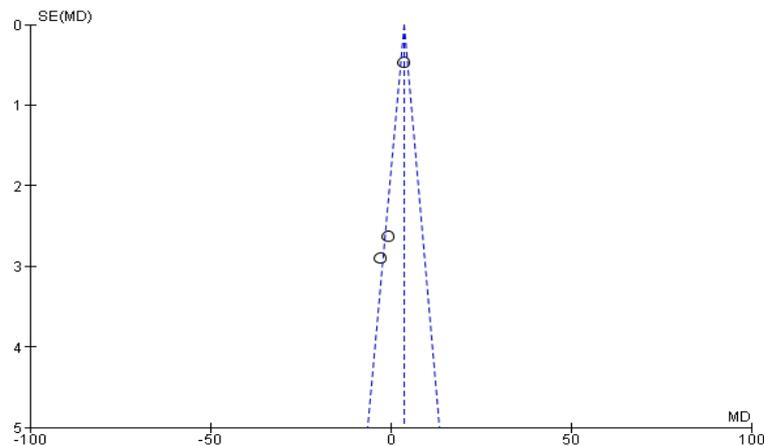


Figure 13. Funnel plot for Surgery class III between pre and post surgery.

3.5. Sensitivity Analysis

3.5.1. Extraction and Non-Extraction

Two studies [11,12] lies outside the funnel, so removing the studies and rerunning the analysis we get three studies that report the Meta analysis between extraction and

non-extraction. The pooled analysis showed no effect on extraction and non-extraction (MD = 0.37, CI -1.32, 2.05; $\text{Chi}^2 = 2.25$; $I^2 = 11\%$, $p = 0.67 > 0.05$). Heterogeneity between the five studies is low ($I^2 = 11\%$). Test for overall effect: $Z = 0.43$ ($p = 0.67$) (Figures 14 and 15).

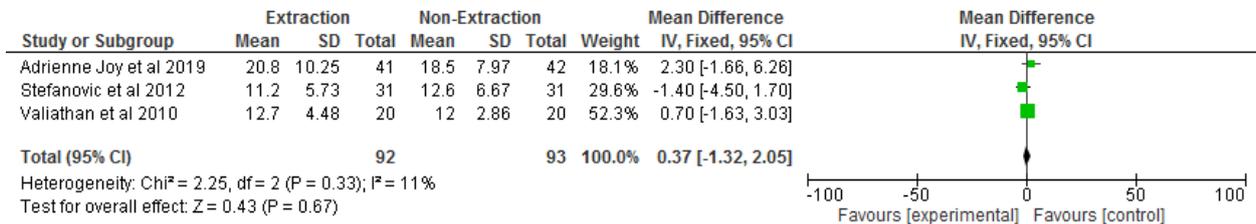


Figure 14. Forest plot for extraction and non-extraction after removing the studies lies outside the funnel.

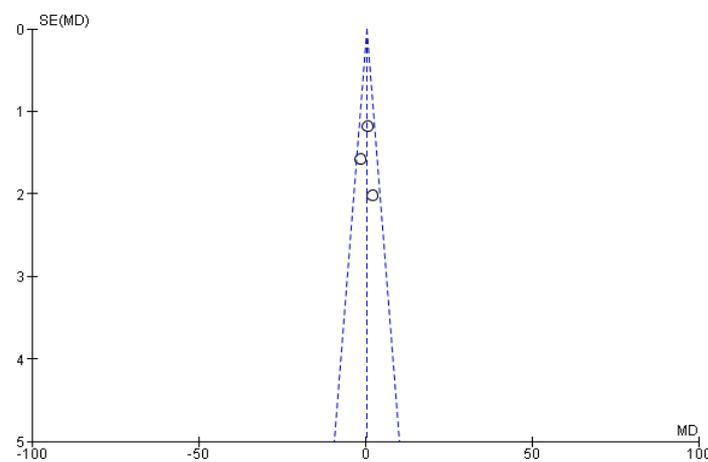


Figure 15. Funnel plot for extraction and non-extraction after removing the studies lies outside the funnel.

3.5.2. Maxillary Expansion

Four studies [4,13–15] lie outside the funnel, so removing the studies and rerunning the analysis we get four studies that report the Meta analysis for maxillary expansion between experiment and control group. The pooled analysis showed no effect on maxillary expansion between experiment and control group (MD = -0.14, CI -0.68,0.39; $\text{Chi}^2 = 5.33$; $I^2 = 44\%$, $p = 0.60 > 0.05$). Heterogeneity between the four studies is low ($I^2 = 44\%$). Test for overall effect: $Z = 0.53$ ($p = 0.60$) (Figures 16 and 17).

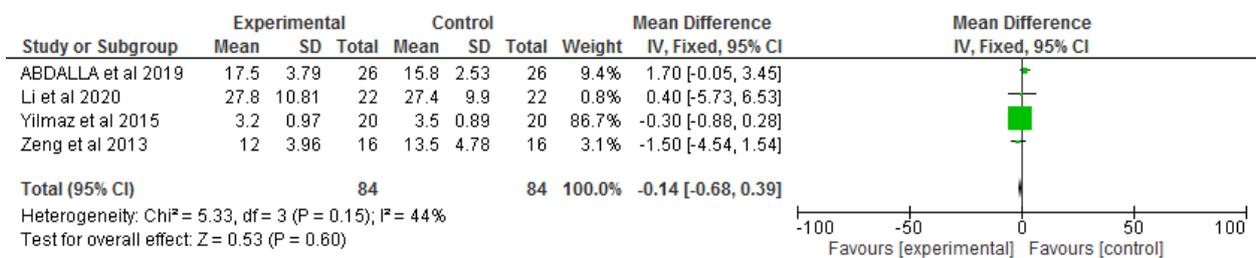


Figure 16. Forest plot for maxillary expansion between experiment and control after removing the studies lies outside the funnel.

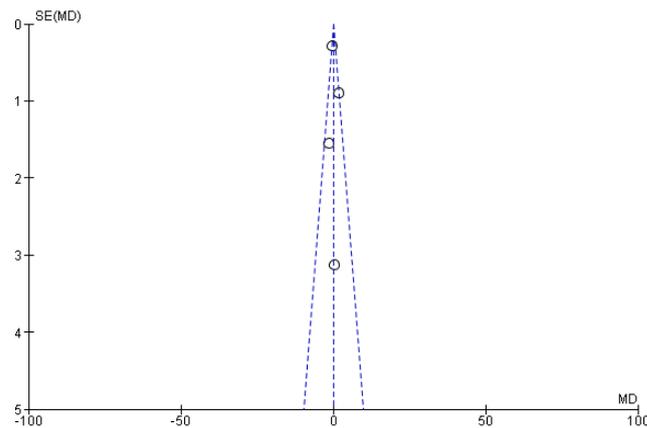


Figure 17. Funnel plot for maxillary expansion between experiment and control after removing the studies lies outside the funnel.

4. Discussion

Respiratory function has a considerable influence on the development of the cranio-facial complex, and the upper airway assessment has been an important concern for the orthodontist while performing different modalities of the management of dental and skeletal malocclusion [2]. Controversies exist regarding the influence of orthodontic treatment on the upper airway; hence we undertook this systematic review. Twenty-seven studies were found to be appropriate for inclusion in this review, and the methodological quality of most of the studies was acceptable which permitted quantitative synthesis. The effects on the airway were assessed with orthopaedic protraction, rapid maxillary expansion, myofunctional appliances, fixed orthodontic therapy with extraction, and orthognathic surgery for correction of skeletal Class II and Class III malocclusion.

Randomised controlled trials provide the highest level of evidence. However, well-conducted observational studies also contribute meaningful evidence to the existing scientific knowledge, especially when randomised clinical trials are unethical or unfeasible [16]. Because there were not enough randomised studies that evaluated the airway after different modalities of orthodontic treatment, prospective, and retrospective observational studies were also included in this review.

Airway dimensions are assessed by various means including lateral cephalograms, and CBCT. Although the pharyngeal airway is a 3-D structure. Conventional lateral cephalography provides only the sagittal and vertical dimensions and thus has limited value for an accurate assessment. The transverse dimension of the airway has been found to be variable for a similar area of the nasopharyngeal airway, which raises concerns over the conclusions drawn from the lateral head film [17]. Thus, it would be more accurate to provide a 3-D analysis of the airway assessment and this review included studies evaluating the 3-D volume of the airway after the use of various orthodontic treatment approaches.

Rapid maxillary expansion, introduced in the 19th century, is routinely performed for the correction of posterior crossbite and the creation of space to relieve crowding. This technique is now believed to be helpful for additional purposes, such as reduction of nocturnal enuresis [18], improvement of impaired nasal respiration [19], and relief from obstructive sleep apnoea [20]. This review identified eight studies that assessed the impact of rapid palatal expansion on the airway where all of them were found to have significant improvements except for the study by El et al. [4] and Abdalla et al. [21]. The combined analysis showed a significant improvement in the upper airway, which is similar to the findings reported by Buck et al. [22] in their 2017 systematic review. The mean age of the patient was higher in the studies by Kim et al. [15] and Li et al. [23] and those authors used implant-supported maxillary expansion in contrast to other studies in which tooth-supported expanders were used in adolescents.

For managing skeletal class III malocclusion, retrognathic maxilla expansion in combination with protraction is indicated for growth modulation. This modality has recently

received increased attention as several studies have suggested improvement in the airway dimension facilitating the management of obstructive sleep apnoea [15,20,24]. Separation of the midpalatal suture decreases the resistance of the circummaxillary sutures and subsequent protraction initiates the cellular response resulting in the forward and downward movement of the maxillary complex [25]. This review included five observational studies that assessed the effect of maxillary expansion and protraction on the airway. All of the studies were retrospective except the study by Fu et al. [26] which had a prospective study design. Fu et al. [26] and Alrejaye et al. [3] enrolled cleft patients, whereas noncleft subjects were evaluated in the other studies. The pharyngeal anatomy of cleft patients was found to be different from the noncleft children and there was a varying effect of skeletal protraction among the cleft patients as compared with non-cleft patients [27]. Only the study by Fu et al. [26] showed a significant increase in the pharyngeal airway volume after expansion and protraction, however, this difference was insignificant when combined with the data from other studies. In contrast, the systematic review by Lee et al. [5] found a significant increase in the upper airway after rapid maxillary expansion and protraction with nonsignificant changes in the lower airway when assessed on two-dimensional lateral cephalogram.

The extraction of one or more teeth is frequently indicated in contemporary orthodontics for the management of various dentoskeletal problems. Premolars are most often extracted for crowding correction and retraction of anteriors which can result in a considerable number of changes in the hard and soft tissues of the dentofacial region [28]. Distal movement of the incisors could lead to the encroachment of space with posterior displacement of the tongue narrowing the upper airway. In this review, we identified five observational studies that assessed the upper airway after the extraction of premolars and the retraction of anteriors. All the studies were retrospective and compared airway changes after orthodontic treatment in patients with and without extraction of at least two premolars. Studies by Stefanovic et al. [29] and Valiathan et al. [30] included adolescent patients, whereas the other three studies included adult patients (>18 years). During the period of active craniofacial growth (i.e., 8 to 18 years of age), the length and volume of the airways increase. Thus, in adolescents' treatment effect, if any, can be compensated by the growth of tissues surrounding the airway in adolescents [31]. In this review, none of the included studies reported a significant volumetric change in the upper airway, and the results of the pooled analysis were inconclusive. The hyoid bone was displaced backward and downward with a large incisor retraction [32] and the evidence varies on its effect on the airway [33,34]. Only the study by Zhang et al. [12] reported a change in the position of the hyoid bone in which the displacement was not statistically significant.

A posteriorly positioned mandible is commonly associated with obstructive sleep apnoea [35] and its advancement is believed to facilitate an increase in the upper airway volume which mitigates the apnoea [36]. Functional appliances enhance the growth of the mandible by repositioning it anteriorly, however, recent evidence suggests that the advancement consists of dentoalveolar changes with only minimal skeletal changes [37,38]. We identified three studies measuring the volumetric changes in the airway after functional appliances in growing Class II patients with mandibular retrusion. Among all the studies, airway volume immediately after the treatment was compared with the pretreatment values, we conclude the effects on long-term changes could not explore the effect on long-term changes. The studies varied in the type of appliances used: Oliveira et al. [39] used Herbst appliance, Temani et al. [40] studied on Forsus, and Alhammadi et al. [41] compared removable twin block and Forsus with the control group. All studies reported a significant improvement in the upper airway except for the Forsus group in the study by Alhammadi et al. [41] in which insignificant changes were noticed. The pooled analysis revealed an insignificant increase in the airway volume which is in contrast with the result of the meta-analysis by Xiang et al. [42], who found a significant increase in the airway dimension at the OP region as measured with a cephalogram. In the systematic review by Kannan et al. [43] in which most of the included studies used lateral cephalogram, the use

of twin block induced significant changes in the airway volume at the nasopharynx, and hypopharynx, however, no such improvement was observed with the Herbst.

A retrognathic maxilla and mandible can compromise the upper airway volume and are associated with obstructive sleep apnoea [35,44,45]. Orthognathic surgery involves the manipulation of the jawbones in which their position is changed from the surrounding craniofacial structures. This may cause morphological alteration of the airway resulting in further respiratory complications such as obstructive sleep apnea. However, there is conflicting evidence on the effects of this surgery on the airway [46,47]. This review identified six studies, three each for skeletal Class II and Class III malocclusion treated by means of orthognathic surgery. Da Silva Machado et al. [48] found an overall increase in the upper airway after bimaxillary surgery in Class III which contradicts the findings by Gandedkar et al. [49] who noticed a decrease in the oropharynx volume without any change in the STOP-BANG score. The pooled analysis showed a significant decrease in the upper airway after orthognathic surgery for skeletal Class III malocclusion. All included studies for surgical Class II correction found a significant increase in the airway volume. Similarly, in their systematic reviews, Christovam et al. [50] Hernando et al. [51] found significant improvement in the airway dimensions after maxillomandibular advancement.

This systematic review differs from the past reviews in which two-dimensional cephalography was used to assess 3-D airways. In addition, CBCT measures the transverse dimension and evaluates the volume rather than the area. However, there are also some technical issues with the CBCT with regard to quantifying the airway volume. Most of the included studies captured the CBCT images in an upright position with the Frankfort Horizontal (FH) plane parallel to the ground [13,21,22] or the head in the natural head position [4,12,22]. Only the study by Li et al. [23] considered CBCT in a supine position with the FH plane perpendicular to the ground. The dimension of the upper airway is sensitive to the body position [52], and the volume at the supine position is important because obstructive sleep apnoea occurs only during sleep. Although CBCT provides a clear picture of the hard and soft tissues at a single point in time, it does not provide any information on the muscle tone or susceptibility of collapse. Hence, the use of CBCT alone is not valuable for the diagnosis of obstructive sleep apnoea [10].

Most of the studies in this review consisted of adolescent participants. It is well known that the pharyngeal airway continues its growth along with the other craniofacial structures until 18 years of age, and future growth of the airway can compensate for any change resulting from the treatment. Furthermore, a shorter duration of follow-up cannot give a clear picture of the result in the long term which is most important for the patient and clinician. In addition, assessment of the respiratory functions and sleep quality would have more clinical applicability. The inclusion of randomised trials with large samples and a longer duration of follow-up would yield a better quality of evidence.

5. Conclusions

There is considerable heterogeneity in the available literature with regard to the methodology of the assessment of the airway after different orthodontic therapies. Within the limitations of this study, we conclude that rapid maxillary expansion and surgical advancement for the correction of Class II patients are associated with significant improvement in the upper airway, whereas maxillary protraction, extraction therapy, orthognathic surgery for Class III, and the use of a functional appliance have no significant impact.

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Data Availability Statement: The data used to support the findings of this study are included in the article.

Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

List of Tables

Table A1. PICO details.

Participants (<i>p</i>)	Studies on Human Participants of Any Gender or Malocclusion Undergo Orthodontic Treatment
Intervention (I)	Orthodontic treatment
Control (C)	The baseline-airway dimensions prior to orthodontic intervention
Outcome (O)	Effect on airway spaces volume assessed with CBCT

Table A2. Risk of bias assessment of the included studies.

S.NO	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
Risk of Bias	Oliveira et al.	Alhammadi et al., 2019	Adrienne Joy et al., 2019	Alrejayee et al., 2019	Da Silva Machado et al. 2019	Abdalla et al., 2019	Kim et al., 2018	Yuen et al., 2018	Pliska et al., 2016	Fu et al., 2016	Temani et al., 2020	Almuzian et al., 2015	Zhang et al. 2015	Chen et al., 2015	Nguyen et al., 2015	Yilmaz et al., 2015	Pamprakis et al., 2013	Zeng et al., 2013	El et al., 2014	Stefanovic et al., 2013	Hong et al., 2011	Valiathan et al., 2010	Li et al., 2020	De Sousa Miranda et al. 2015	Raffaini et al., 2013	Gandedkar et al., 2017	Fastuca et al., 2015	Al-Jewair et al., 2019	Horani et al., 2021
Was random sequence generation used (i.e., no potential for selection bias)?	L	M	L	H	H	L	M	L	M	M	M	L	L	L	M	M	M	L	H	H	H	H	L	L	H	L	H	L	L
Was allocation concealment used (i.e., no potential for selection bias)?	L	L	M	L	M	L	M	L	M	M	H	H	M	M	H	H	H	M	M	H	L	L	L	M	M	M	M	L	M
Was there blinding of participants and personnel (i.e., no potential for performance bias)?	M	H	H	M	M	H	L	L	M	H	M	H	H	L	H	L	H	L	M	H	M	H	M	H	M	M	L	H	H
Was there blinding of outcome assessment (i.e., no potential for detection bias)?	M	M	H	M	M	H	L	M	L	L	M	L	L	M	L	M	M	M	L	M	L	M	L	L	M	L	H	H	H
Was an objective outcome used?	M	L	M	M	M	M	L	M	M	M	M	M	L	L	L	M	M	L	L	M	L	L	M	L	L	M	L	L	L
Were more than (80%) a of participants enrolled in trials included in the analysis? (i.e., no potential attrition bias)	M	L	M	M	M	H	M	M	M	M	L	H	H	H	L	M	L	M	L	M	L	M	L	L	H	L	H	M	M
Were data reported consistently for the outcome of interest (i.e., no potential selective reporting)? (no potential reporting bias)	H	L	H	H	H	H	L	M	M	L	M	L	H	H	M	H	M	H	M	L	M	L	L	M	H	M	M	L	L
No other biases reported? (no potential of other bias)	L	H	M	H	H	M	M	M	M	M	M	L	M	L	M	L	H	M	H	M	H	M	M	H	M	H	H	H	H
Did the trials end as scheduled (i.e., not stopped early)?	M	H	H	L	L	M	M	M	L	M	L	L	L	L	M	H	M	H	H	L	L	L	M	H	L	H	L	M	M
Inconsistency																													
Point estimates did not vary widely? (i.e., no clinical meaningful inconsistency)	M	L	L	M	M	M	M	M	M	M	M	M	L	M	H	H	M	H	H	M	L	M	L	H	M	H	L	L	L
To what extent do confidence intervals overlap?	M	M	L	M	M	L	L	M	H	H	L	L	H	H	H	M	L	M	M	H	H	L	L	M	L	L	M	M	L
Was the direction of effect consistent?	H	H	L	L	H	L	L	M	M	M	H	H	L	H	L	M	M	M	L	H	L	H	H	L	H	H	H	L	M

Table A2. Cont.

S.NO	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
Risk of Bias	Oliveira et al.	Alhammadi et al., 2019	Adrienne Joy et al., 2019	Alrejaye et al., 2019	Da Silva Machado et al. 2019	Abdalla et al., 2019	Kim et al., 2018	Yuen et al., 2018	Pliska et al., 2016	Fu et al., 2016	Temani et al., 2020	Almuzian et al., 2015	Zhang et al. 2015	Chen et al., 2015	Nguyen et al., 2015	Yilmaz et al., 2015	Pamporakis et al., 2013	Zeng et al., 2013	Ei et al., 2014	Stefanovic et al., 2013	Hong et al., 2011	Valiathan et al., 2010	Li et al., 2020	De Sousa Miranda et al. 2015	Raffaini et al., 2013	Gandedkar et al., 2017	Fastuca et al., 2015	Al-Jewair et al., 2019	Horani et al., 2021
What was the magnitude of statistical heterogeneity (as measured by I^2)?	H	M	L	M	H	L	L	L	L	M	M	L	M	L	M	L	M	L	L	M	L	M	L	H	L	H	L	H	L
Was the test for heterogeneity statistically significant ($p < 0.1$)?	L	M	M	M	L	M	M	L	L	M	L	M	L	M	L	M	L	M	L	M	L	M	L	H	L	H	L	H	L
Indirectness																													
Were the populations in included studies applicable to the target population?	L	M	M	M	M	L	M	L	L	H	H	H	H	M	L	L	M	M	L	M	M	L	M	L	H	L	H	L	H
Were the interventions in included studies applicable to target intervention?	L	L	H	H	H	H	M	L	L	M	L	L	M	L	M	L	L	M	L	M	M	M	M	L	H	L	H	L	H
Was the included outcome not a surrogate outcome?	H	L	M	H	H	M	L	L	H	M	H	H	M	H	H	L	H	L	H	H	L	H	L	H	L	H	L	L	H
Was the outcome timeframe sufficient?	M	M	M	H	L	L	L	H	L	M	L	L	M	L	L	M	M	L	L	M	L	M	L	L	L	M	L	M	L
Were the conclusions based on direct comparisons?	H	H	M	M	L	H	H	H	H	M	H	M	H	H	M	H	M	H	L	M	L	H	H	H	M	M	L	H	L
Imprecision																													
Was the confidence interval for the pooled estimate not consistent with benefit and harm?	L	L	L	L	L	H	H	H	M	M	L	M	H	L	H	L	H	L	H	L	H	L	H	L	H	L	L	H	L
What was the magnitude of the median sample size?	L	L	L	L	L	H	M	H	M	L	M	M	L	M	L	M	L	M	L	H	L	H	L	H	L	H	H	L	L

Table A2. Cont.

S.NO	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29
Risk of Bias	Oliveira et al.	Alhammadi et al., 2019	Adrienne Joy et al., 2019	Alrejaye et al., 2019	Da Silva Machado et al. 2019	Abdalla et al., 2019	Kim et al., 2018	Yuen et al., 2018	Pliska et al., 2016	Fu et al., 2016	Temani et al., 2020	Almuzian et al., 2015	Zhang et al. 2015	Chen et al., 2015	Nguyen et al., 2015	Yilmaz et al., 2015	Pamporakis et al., 2013	Zeng et al., 2013	Ei et al., 2014	Stefanovic et al., 2013	Hong et al., 2011	Valiathan et al., 2010	Li et al., 2020	De Sousa Miranda et al. 2015	Raffaini et al., 2013	Gandedkar et al., 2017	Fastuca et al., 2015	Al-Jewair et al., 2019	Horani et al., 2021
What was the magnitude of the number of included studies?	L	M	M	M	M	M	L	L	L	M	L	M	L	M	L	M	L	M	L	M	L	M	L	H	L	H	H	L	H
Was the outcome a common event? (e.g., occurs more than 1/100) a	M	L	M	H	M	L	M	L	H	H	H	H	L	H	L	L	L	M	L	M	L	M	L	M	L	L	M	M	M
Was there no evidence of serious harm associated with treatment?	M	L	M	H	L	L	L	L	L	M	L	M	L	M	M	M	M	L	M	H	H	L	H	L	H	H	H	L	H
Publication bias Did the authors conduct a comprehensive search?	L	M	H	M	M	L	M	L	M	L	M	L	M	L	M	L	M	L	L	M	L	M	L	M	L	M	L	M	M
Did the authors search for grey literature?	M	M	H	L	L	M	H	L	M	L	M	L	L	M	L	M	L	L	H	L	H	L	L	L	H	L	H	L	H
Authors did not apply restrictions to study selection on the basis of language?	L	H	L	L	L	M	H	M	L	M	L	M	M	L	M	L	M	L	L	M	L	L	H	H	H	L	H	L	H
There was no industry influence on studies included in the review?	L	H	L	L	L	H	M	M	M	L	M	L	L	L	L	M	L	M	H	M	H	M	H	M	M	L	M	L	M
There was no evidence of funnel plot asymmetry?	L	L	M	M	M	H	M	M	M	L	M	M	L	M	M	L	M	M	L	M	L	M	L	M	L	M	L	M	M
There was no discrepancy in findings between published and unpublished trials?	M	M	M	L	M	H	M	L	M	L	M	L	M	L	M	M	L	H	L	H	H	L	H	M	M	H	L	L	M
Overall score	M	M	H	M	M	H	M	L	M	M	M	M	L	M	L	L	M	M	L	M	L	M	L	M	M	L	M	L	M

Table A3. Study characteristics.

S.No	Author & Year	Country	Study Design	Sample Size	Gender	Age (Years) Range/Mean/Median	Orthodontic	Type of Malocclusion	Method Used to Assess the Airway	Specific Airway Space That Was Assessed	Variables	Actual Baseline	Follow up Duration	p-Values	Outcome
1	Oliveira et al. [39]	USA	Retrospective	42	25/M & 17/F	Mean-13.8 ± 1.2	Functional appliance (HERBST)	Class II malocclusion	CBCT	The upper airway was divided into 3 regions: nasal cavity, nasopharynx, and oropharynx	Functional appliance: Experiment: Mean:28.5, SD: 10.8, Control: Mean: 20.6, SD: 9.4	Class II malocclusion with an ANB angle >4°	NR	Nasal cavity-HAG-0.144 and CG-0.046; Nasopharynx-HAG-0.071 and CG-0.211; Oropharynx-HAG-0.003 and CG-0.666	Increased the volume of the oropharynx, but no volumetric modifications in the nasal cavity and nasopharynx.
2	Alhammadi et al. [41]	Egypt	Controlled clinical study	62	62/F	Mean-11.27 ± 1.19	Functional appliance (Twinblock & Forsus Fatigue Resistance Device)	Class II malocclusion	Pre- and post-treatment/observational cone beam computed tomography	Pharyngeal airway	Functional appliance: Experiment: Mean:16.8, SD: 3.26, Control: Mean: 20.1, SD: 2.7	NR	Every 4 weeks	TWB (p < 0.001)	Twin block functional appliance induced significant pharyngeal airway changes than Forsus
3	Adrienne Joy et al. [53]	USA	Retrospective study	83	42/M & 41/F	Mean-26.1 ± 7.1	Extraction	NR	CBCT	Various airway measures in the nasopharynx, retropalatal, or retroglossal regions.	Extraction: Mean-20.8, SD-10.3, Non-extraction: Mean-18.5, SD-8.0	baseline MCA was less than 100 mm ² or greater than 200 mm ² .	NR	p < 0.001.	No effect
4	Alrejaye et al. [3]	USA	Retrospective study	26	14/M & 12/F	Mean-8.4 ± 1.7	Maxillary expansion with protraction	NR	CBCT	Oropharyngeal airway	Experimental: Mean-10.3, SD-, Control: Mean-8.7, SD-Surgery Class III	NR	NR	p-value: < 0.0001	No effect
5	Da Silva Machado et al. [48]	Brazil	Quasi-experimental study	13	NR	NR	Class III surgery	Class III malocclusion	multislice computed tomography	Pharyngeal airway	Experimental: Mean- 21.2, SD-6.4 Control: Mean- 24.0, SD- 8.3	NR	NR	p < 0.05	Increase airway space

Table A3. Cont.

S.No	Author & Year	Country	Study Design	Sample Size	Gender	Age (Years) Range/Mean/Median	Orthodontic	Type of Malocclusion	Method Used to Assess the Airway	Specific Airway Space That Was Assessed	Variables	Actual Baseline	Follow up Duration	p-Values	Outcome	
6	Abdalla et al. [21]	Australia	Retrospective study	26	14/F & 12/M	Mean-12 years, 4 months \pm 2 years, 4 months	Rapid maxillary expansion	Minor malocclusions	CBCT	Pharyngeal airway	Experimental: Mean-17.5 SD-, Control: Mean-15.8, SD- Maxillary Expansion	NR	NR	$p < 0.001$	No effect	
7	Kim et al. [15]	South Korea	Retrospective study	14	10/F & 4/M	Mean-22.7 \pm 3.3	Rapid maxillary expansion	NR	CBCT	Nasal airway	Experimental: Mean-1.6, SD-0.9 Control: Mean- 25.1, SD-3.4	NR	12-year	$p < 0.05$	Increase	
8	Yuen et al. [54]	USA	Retrospective study	137	126/F & 11/M	NR	Class II surgery	NR	CBCT	Pharyngeal airway	Pre-surgical: Mean-9.0, SD-4.1, Post-surgical: Mean-12.0, SD-5.3 Extraction non extraction	NR	1-year after surgery	p -value: < 0.0001	Increase	
9	Pliska et al. [11]	Minneapolis	Retrospective study	74	25/M & 49/F	Mean-31.9 \pm 12.0	Extraction	NR	CBCT	Orthodontic upper airway	Experimental: Mean-20.0564, SD-6.8488 Control: Mean-25.9513, SD-8.1603 Expansion with Protraction	Class II (ANB angle $> 4^\circ$)	NR	NR	NR	No change
10	Fu et al. [26]	China	Longitudinal study	18	13/M & 5/F	Mean-9.6 \pm 1.7	Rapid maxillary expansion with protraction	Class III malocclusion	CBCT	Pharyngeal airway	Experimental: Mean-9.2481, SD-3.237 Control: Mean-12.9176, SD-5.193 Functional appliance:	NR	NR	$p < 0.001$	Increase	
11	Temani et al. [40]	India	Prospective study	30	NR	NR	Functional appliance	Class II malocclusion	CBCT	Pharyngeal airway	Experiment: Mean:20.0, SD: 4.4, Control: Mean: 15.9, SD: 4.6	NR	Longer period of follow-up	$p < 0.001$	Increase	

Table A3. Cont.

S.No	Author & Year	Country	Study Design	Sample Size	Gender	Age (Years) Range/Mean/Median	Orthodontic	Type of Malocclusion	Method Used to Assess the Airway	Specific Airway Space That Was Assessed	Variables	Actual Baseline	Follow up Duration	p-Values	Outcome
12	Almuzian et al. [13]	Australia	Prospective study	17	8/M & 9/F	Mean-12.6 ± 1.8	Rapid maxillary expansion	NR	CBCT	Nasopharyngeal airway	Experimental: Mean-17.45, SD-1.47, Control: Mean-16.4, SD-0.8	NR	Longer term follow-up	$p < 0.05$	Increase
13	Zhang et al. [12]	China	Retrospective study	18	5/M & 13/F	Mean-24.1 ± 3.8	Extraction	Class II malocclusion	CBCT	The upper airway was divided into nasopharynx, velopharynx, and hypopharynx	Extraction: Mean-49.8, SD-, Non-extraction: Mean-241, SD-	NR	Greater length of follow-up	$p < 0.01$	Decrease
14	Chen et al. [55]	China	Retrospective study	60	28/F & 32/M	Mean-7 ± 1.21	Rapid maxillary expansion with protraction	Class III malocclusion	CBCT	Upper airway of nasopharynx, velopharynx	Experimental: Mean-11.7 SD-4.4, Control: Mean-21.3, SD-12.5 Expansion with Protraction	NR	NR	$p < 0.05$	Increase
15	Nguyen et al. [56]	North Carolina	Prospective study	28	14/F & 14/M	NR	Rapid maxillary expansion with protraction	Class III malocclusion	CBCT	Nasopharyngeal, oropharynx airway	Experimental: Mean-14.14, SD-3.76173 Control: Mean-14.56, SD-5.74	NR	NR	$p < 0.05$	No effect
16	Yilmaz et al. [57]	Turkey	Prospective study	20	10/F & 10/M	Mean-9	Rapid maxillary expansion	Class III malocclusion	CBCT	The airway was divided into three parts; pharyngeal, nasal, and anterior nasal compartments	Maxillary Expansion Experimental: Mean-3.1967, SD-0.967 Control: Mean-3.51, SD-0.9	NR	9 weeks	$p < 0.05$	Increase
17	Pamporakis et al. [58]	Turkey	Retrospective study	22	14/F & 8/M	Mean-10	Protraction	Class III malocclusion	CBCT	Pharyngeal airway	Expansion with Protraction Experimental: Mean-9.1, SD-2.0 Control: Mean-9.5, SD-2.4	NR	NR	$p < 0.05$	Increase

Table A3. Cont.

S.No	Author & Year	Country	Study Design	Sample Size	Gender	Age (Years) Range/Mean/Median	Orthodontic	Type of Malocclusion	Method Used to Assess the Airway	Specific Airway Space That Was Assessed	Variables	Actual Baseline	Follow up Duration	p-Values	Outcome
18	Zeng et al. [22]	China	Prospective study	16	6/F & 10/M	Mean-12.73 ± 1.73	Rapid maxillary expansion	NR	CBCT	Nasopharyngeal airway	Experimental: Mean-12, SD-4 Control: Mean-13.5, SD-4.8	NR	5 years	$p < 0.0033$	Limited effect
19	El et al. [4]	USA	Retrospective study	35	15/M & 20/F	Mean-14.02 ± 1.46	Rapid maxillary expansion	Class I malocclusion	CBCT	Oropharyngeal airway	Experimental: Mean-33.2, SD-9.7 Control: Mean-27.0, SD-9.3 Extraction: Mean-11.2, SD-5.7, Non-extraction: Mean-12.6, SD-6.7	NR	NR	$p < 0.001$	No change
20	Stefanovic et al. [29]	USA	Retrospective study	31	15/M & 16/F	Mean-12.97 ± 1.15	Extraction	NR	CBCT	Pharyngeal airway	Surgery Class III Experimental: Mean-33.36815, SD-7.3556 Control: Mean-34.0623, SD-12.51731 Extraction non extraction	NR	NR	$p \leq 0.05$	No change
21	Hong et al. [59]	Korea	Retrospective study	60	30/M & 30/F	Mean- 26.0 ± 4.5	Class III surgery	Class III malocclusion	CBCT	Pharyngeal airway	Experimental: Mean-33.36815, SD-7.3556 Control: Mean-34.0623, SD-12.51731 Extraction non extraction	NR	NR	$p \leq 0.05$	Increase
22	Valiathan et al. [30]	USA	Retrospective study	20	10/M & 10/F	Mean-13.8 ± 1.3	Extraction	Class I malocclusion	CBCT	Oropharyngeal airway	Experimental: Mean-12.7, SD-4.5 Control: Mean-12.0, SD- 2.9	NR	NR	$p \leq 0.05$	No change
23	Li et al. [23]	China	Retrospective study	22	4/M & 18/F	Mean-22.6 ± 4.5	Rapid maxillary expansion	NR	CBCT	Upper airway of nasal cavity, nasopharyngeal, retropalatal, retroglossal and hypopharyngeal airway	Experimental: Mean-27.8, SD-10.8 Control: Mean-27.4, SD-10	NR	NR	$p \leq 0.05$	Increase

Table A3. Cont.

S.No	Author & Year	Country	Study Design	Sample Size	Gender	Age (Years) Range/Mean/Median	Orthodontic	Type of Malocclusion	Method Used to Assess the Airway	Specific Airway Space That Was Assessed	Variables	Actual Baseline	Follow up Duration	p-Values	Outcome
24	De Sousa Miranda et al. [60]	Brazil	Retrospective study	23	8/M & 15/F	Mean-33	Class II surgery	Class II malocclusion	CBCT	Oropharyngeal airway	Surgery Class II Experimental: Mean-20.4767 Control: Mean-30.5952 Pre-surgical: Mean-15.3, SD-, Post-surgical: Mean-22.6, SD- Pre-surgical: Mean-27.7, SD-1.2, Post-surgical: Mean-23.9, SD-1.4 Maxillary Expansion Experimental: Mean-17.0 Control: Mean- 2.4	NR	23 patients be followed-up at a later date	$p \leq 0.05$	Increase
25	Raffaini et al. [61]	Italy	Retrospective study	10	10/F	NR	Class II surgery	Class II malocclusion	CBCT	Pharyngeal airway	Pre-surgical: Mean-15.3, SD-, Post-surgical: Mean-22.6, SD- Pre-surgical: Mean-27.7, SD-1.2, Post-surgical: Mean-23.9, SD-1.4 Maxillary Expansion Experimental: Mean-17.0 Control: Mean- 2.4	NR	6 to 12 months after surgery	$p \leq 0.05$	Increase
26	Gandedkar et al. [49]	Singapore	Retrospective study	58	32/F & 26/M	Mean-13.4 \pm 0.5	Class III surgery	Class III malocclusion	CBCT	Pharyngeal airway	Pre-surgical: Mean-15.3, SD-, Post-surgical: Mean-22.6, SD- Pre-surgical: Mean-27.7, SD-1.2, Post-surgical: Mean-23.9, SD-1.4 Maxillary Expansion Experimental: Mean-17.0 Control: Mean- 2.4	NR	NR	$p \leq 0.05$	Decrease
27	Fastuca et al. [14]	Italy	Retrospective study	15	11/F & 4/M	Mean-7.5 \pm 0.3	Rapid maxillary expansion	NR	CBCT	Nasal airway	Pre-surgical: Mean-15.3, SD-, Post-surgical: Mean-22.6, SD- Pre-surgical: Mean-27.7, SD-1.2, Post-surgical: Mean-23.9, SD-1.4 Maxillary Expansion Experimental: Mean-17.0 Control: Mean- 2.4	NR	Long term follow-up	$p < 0.001$	No change
28	Al-Jewair et al. [62]	USA	Prospective study	8	5/F & 3/M	Mean-44.6	Clear aligner	Class II malocclusion	CBCT	The upper airway was divided into three regions: the nasopharynx (NP), oropharynx (OP), and hypopharynx (HP).	Clear aligner Before Treatment: Mean-35.05, SD-14.02 After Treatment: Mean-32.24, SD-9.16	NR	NR	$p = 0.250$	Increase
29	Al-Jewair et al. [62]	USA	Retrospective study	24	16/F & 8/M	Mean-35.33 \pm 11.14	Clear aligner	Class III malocclusion	CBCT	Pharyngeal airway	Before: Mean-13.6, SD-4.02, After: Mean-12.07, SD-3.65	NR	NR	$p \leq 0.05$	Decrease

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