Pharyngeal airway changes following maxillary expansion or protraction: A meta-analysis

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Abstract
The aim of this meta-analysis was to investigate the changes in airway dimensions after rapid maxillary expansion (RME) and facemask (FM) protraction. Using PubMed, Medline, ScienceDirect and Web of Science, only controlled clinical trials, published up to November 2016, with RME and/or FM as keywords that had ≥6 months follow-up period were included in this meta-analysis. The changes in pharyngeal airway dimension in both two-dimensional and three-dimensional images were included in the analysis. Nine studies met the criteria. There are statically significant changes in upper airway and nasal passage airway in the intervention groups as compared to the control groups, assessed in two-dimensional and three-dimensional images. However, in the lower airway and the airway below the palatal plane, no statistically significant changes are seen in 2D and 3D images. RME/FM treatments might increase the upper airway space in children and young adolescents. However, more RCTs and long-term cohort studies are needed to further clarify the effects on pharyngeal airway changes.

KEYWORDS
expansion, meta-analysis, pharyngeal airway, protraction

1 | INTRODUCTION
Rapid maxillary expansion (RME) and facemask (FM) maxillary protraction therapy have been widely accepted in early orthodontic treatment for young patients with maxillary transverse and midface deficiency. RME and FM were further introduced as a treatment option for increasing the pharyngeal airway dimension and diversifying the paradigms of clinical orthodontic treatment. In addition, RME and FM were found to exert secondary treatment effects by increasing the pharyngeal airway dimension. However, several studies used only FM, some performed only RME, and other studies conducted FM in combination with RME.

The effects of RME or FM on the pharyngeal airway have been repeatedly investigated using various methods, such as cephalometric radiography, computed tomography (CT) and cone beam CT (CBCT), to measure the changes in airway dimensions. However, the study outcomes were inconsistent. Statistically significant dimensional changes in the pharyngeal or nasopharyngeal airway were observed after RME and/or FM treatment in some studies, whereas no significant or limited changes were observed in others. Among these studies, the major limitations included the lack of untreated controls and long-term observations, as well as the variation in definition of pharyngeal airways. This study was designed to evaluate changes in pharyngeal airway spaces following RME treatment and/or FM treatment in children or young adolescents compared to untreated controls through a meta-analysis.

2 | MATERIALS AND METHODS
2.1 | Search strategy
Studies that reported child/adolescent patients with transverse maxillary or midface deficiency who received maxillary expansion or protraction were included. In these studies, the pharyngeal airway changes after treatment were evaluated and compared with those of no expansion/protration.

This meta-analysis aimed to determine whether any pharyngeal airway changes exist in those who need maxillary expansion or protraction.
Four electronic databases, namely PubMed, Medline, ScienceDirect and Web of Science, were searched to identify studies. This search included "maxilla constriction" or "airway constriction" or "midfacial deficiency" or "Class III malocclusion" AND "airway" or "pharyngeal airway" or "pharynx" or "volume" or "area" or "CBCT" or "3 dimensional" or "2 dimensional" AND "RME" or "rapid maxillary expansion" or "maxilla expansion" or "maxillary protraction" or "facemask." References were also evaluated in the included papers to verify the inclusion of all related research.

2.2 | Inclusion and exclusion criteria

The included studies were controlled clinical trials with at least 6 months follow-up that were published from January 2000 to November 2016 without language restriction. Other inclusion criteria followed the PICO principle. For the type of participant, the patients chosen were those with transverse maxillary deficiency or midface deficiency from the period of early mixed dentition to early permanent dentition (age ranged from 6 to 16 years). Intervention was the selection of different treatment modalities of FM alone or RME alone or a combination of FM+RME. This study involved three comparisons between interventions, which were (i) FM/FM+RME vs control, (ii) FM/FM+RME or RME vs control and (iii) RME vs control. Two-dimensional (2D) and three-dimensional (3D) measurements for airway changes were obtained by cephalometric radiography (anteroposterior linear changes) and CBCT (volume changes), respectively. The linear changes in distances PNS-ad1 and PNS-ad2, the shortest distance in the upper airway and the shortest distance in the lower airway were included in 2D images as shown in Figure 1, whereas the changes in pharyngeal airway volumes were compared in 3D images. The articles that matched the inclusion criteria were retrieved and evaluated by the exclusion criteria: (i) letters, reviews, abstracts, case reports and case series; (ii) patients without upper first molars; and (iii) patients with history of systematic disease and craniofacial anomaly.

2.3 | Study selection

Two reviewers (WCL and RC) screened titles, abstracts and full-text articles independent of each other. Any disagreement was resolved by discussing with the senior author (EF) to achieve a final consensus.

2.4 | Data extraction

Among the included studies, the following variables were extracted and collected in a standardized form: publication year, author, study design, number of participants, patient classification, gender, mean age, duration of treatment and follow-up, measurement method and clinical results (e.g., dimensional changes in the pharyngeal airway). Data from all the included studies were assessed individually by WCL and RC. Any disagreement was overcome by discussion with the third reviewer (EF) to achieve the final determination.

2.5 | Quality assessment

The quality of each controlled clinical trial was assessed by three reviewers (WCL, RC and EF) according to the Newcastle-Ottawa Quality Assessment Scale. The quality assessments include the selection of cohorts, comparability of cohorts and assessment of outcome.

2.6 | Statistical analysis

In this meta-analysis, nine studies were included for analysis. Using Review Manager Version 5.3 software (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014), the mean difference and 95% confidence intervals (CI) were calculated. In each comparison, the first step was the analysis of the mean intragroup difference between initial and follow-up data.

Intragroup mean difference:

\[ \delta \text{Mean}_{\text{ctrl}} = (\text{Follow-up data of control group}) - (\text{Baseline data of control group}) \]

FIGURE 1 Two-dimensional cephalometric measurements for the analysis of airway dimensions. (1) PNS-ad1: Distance between the PNS and the nearest adenoid tissue measured through the PNS-Ba line (AD1). (2) PNS-ad2: Distance between the PNS and the nearest adenoid tissue measured through a perpendicular line to 5-Ba from PNS (AD2). (3) Upper airway (shortest distance): The minimum distance between the upper soft palate and the nearest point on the posterior pharyngeal wall. (4) Lower airway (shortest distance): The minimum distance between the point where the posterior tongue contour crosses the mandible and the nearest point on the posterior pharyngeal wall.
ΔMean = δMean_{tx} − δMean_{ctrl}

The variance of difference was analysed by:

Var = Var_{1}^2 + Var_{2}^2 − 2r·Var_{1}·Var_{2}

For weighted mean differences as the effect size, statistical significance was considered when \( P \leq .05 \). The \( I^2 \) measurement was used to assess heterogeneity. \( I^2 \) ranged from 0% to 100%. \( I^2 = 0\% \) indicated no heterogeneity, whereas \( \geq 5\% \) suggested high heterogeneity. In general, the fixed effect models are used when heterogeneity is low, whereas the random effects models are used when heterogeneity is high. We used leave-one-out analysis to assess the impact on the pooled summary estimates when significant heterogeneity was detected. The statistical analyses were performed using Comprehensive Meta-Analysis version 3.

3 | RESULT

The flow chart for the procedure of study collection is presented in Figure 2. According to the exclusion criteria, 269 publications were excluded, and only nine studies were included. As shown in Figure 3, four studies comprised of the RME group, whereas five studies were categorized into the FM group (FM or FM-plus-RME). The descriptions and quality assessment of the included studies are shown in Tables 1 and 2.

3.1 | Two-dimensional evaluation using lateral cephalometry

Changes in airway space, measured as the anteroposterior dimensional difference in the pre- and post-therapeutic phases, were compared between the groups with and without expansion/protrusion treatment (Figure 4). In the upper airway, the space changes were recorded by the length between two fixed landmarks or by the shortest distance. For the four studies, the lengths (including PNS-ad1 and PNS-ad2) between two fixed landmarks increased in the FM treatment groups more than in the non-treatment groups (random effect model, mean difference: 1.63 and 2.68, 95% CI = −0.14 to 3.39 and 0.37-5.00, \( P = .07 \) and .02 for PNS-ad1 and PNS-ad2, respectively). When the space changes were recorded by the shortest distance of the spaces, two subgroups were included based on the protocol of FM or RME. For the four studies, the random effects model with mean difference was 1.01 (95% CI = 0.49-1.53, \( P = .0002 \)).

In the lower airway, the space changes were recorded in four studies by merely the shortest distance, and the subgroups of FM or RME were also included. However, no statistical difference in space changes between the groups with and without treatment was noted (fixed effect model, mean difference: −0.27, 95% CI = −0.71 to 0.17, \( P = .23 \)).

3.2 | Three-dimensional evaluation using CBCT

A comparison of the RME and control groups was conducted (Figure 5). Using CBCT, the 3D volume changes in airway spaces, measured as the difference in the pre- and post-therapeutic phases, were compared between the groups with and without RME.

In the nasal passage airway volume, the volume changes between groups with and without treatment were statistically different (fixed effect model, mean difference: 0.89, 95% CI = 0.28-1.5, \( P = .004 \) for the nasal passage airway), but the analyses were performed in only one experiment collected. In the pharyngeal airway below the palatal plane, no difference in volume changes between the groups with and without treatment was noted (fixed effect model, mean difference: −0.27, 95% CI = −0.71 to 0.17, \( P = .23 \)).
3.3 | Leave-one-out analysis

The results from “the leave-one-out analysis” indicated the overall effects of the significant increased upper airway after treatment, in spite of any single study excluded. However, there was no significant difference in the lower airway via the leave-one-out analysis (Figure 6).

4 | DISCUSSION

This meta-analysis is the first to evaluate the changes in the pharyngeal airway following transverse maxillary expansion or FM maxillary protraction. In this meta-analysis, the nine selected studies revealed two major outcomes. Using 2D cephalometric radiography, two fixed landmarks (PNS-ad1 and PNS-ad2) and the shortest distance in the pharyngeal airway were measured, and a significant increase was found in the anteroposterior dimension changes in the upper airway in the treatment group compared with the non-treatment group. In this study, no significant difference was noted in the lower airway changes in A-P dimension between the two groups (Figure 3). Using 3D CBCT, the nasal passage airway volume increased significantly more in the RME group than in the non-RME group (Figure 1). However, in the airway below the palatal plane, no significant difference was observed.

<table>
<thead>
<tr>
<th>Study</th>
<th>Selection</th>
<th>Comparability</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aloufi 2012</td>
<td>☆☆☆☆</td>
<td>☆☆</td>
<td>☆☆</td>
</tr>
<tr>
<td>Mucedero 2009</td>
<td>☆☆☆☆</td>
<td>☆☆</td>
<td>☆☆☆</td>
</tr>
<tr>
<td>Baccetti 2010</td>
<td>☆☆☆☆</td>
<td>☆☆</td>
<td>☆☆</td>
</tr>
<tr>
<td>Baloş 2015</td>
<td>☆☆☆☆</td>
<td>☆☆</td>
<td>☆☆</td>
</tr>
<tr>
<td>Kilinç 2007</td>
<td>☆☆☆☆</td>
<td>☆☆</td>
<td>☆☆</td>
</tr>
<tr>
<td>Akin 2015</td>
<td>☆☆☆☆</td>
<td>☆☆</td>
<td>☆☆</td>
</tr>
<tr>
<td>Zhao 2010</td>
<td>☆☆☆☆</td>
<td>☆☆</td>
<td>☆☆</td>
</tr>
<tr>
<td>Iwasaki 2013</td>
<td>☆☆☆☆</td>
<td>☆☆</td>
<td>☆☆</td>
</tr>
<tr>
<td>EI 2014</td>
<td>☆☆☆☆</td>
<td>☆☆</td>
<td>☆☆</td>
</tr>
</tbody>
</table>

CCT, controlled clinical trial; RME, rapid maxillary expansion; T1, before treatment; T2, end of active treatment; T2−T1, end of active treatment- before treatment.
**UPPER AIRWAY: anteroposterior linear changes**

**A. By two fixed landmarks**

**A.1. PNS-ad1 (FM/FM + RME vs Control)**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baccetti (2010)</td>
<td>23.2</td>
<td>22</td>
<td>1.3</td>
<td>22</td>
<td>1.3</td>
<td>14</td>
<td>21.3%</td>
<td>-0.07</td>
<td>[-3.50, 3.10]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Busus (2015)</td>
<td>2.11</td>
<td>17</td>
<td>0.8</td>
<td>2.3</td>
<td>11</td>
<td>11</td>
<td>24.0%</td>
<td>1.90</td>
<td>[0.44, 3.36]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kilinc (2008)</td>
<td>6.83</td>
<td>4.22</td>
<td>1.57</td>
<td>16</td>
<td>1.76</td>
<td>17</td>
<td>24.0%</td>
<td>0.09</td>
<td>[0.46, 2.58]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucedero (2009)</td>
<td>23.8</td>
<td>22</td>
<td>1.8</td>
<td></td>
<td>14</td>
<td>14</td>
<td>19.6%</td>
<td>0.70</td>
<td>[-2.29, 3.69]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>23.2</td>
<td>22</td>
<td>1.3</td>
<td>22</td>
<td>1.3</td>
<td>14</td>
<td>21.3%</td>
<td>1.61</td>
<td>[-0.14, 3.36]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 1.77, Chi² = 6.77, df = 3; P = 0.08; I² = 66%

Test for overall effect: Z = 1.91 (P = 0.07)

**A.2 PNS-ad2 (FM/FM + RME vs Control)**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baccetti (2010)</td>
<td>23.2</td>
<td>22</td>
<td>1.3</td>
<td>22</td>
<td>1.3</td>
<td>14</td>
<td>21.3%</td>
<td>1.40</td>
<td>[-0.84, 3.44]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Busus (2015)</td>
<td>2.11</td>
<td>17</td>
<td>0.8</td>
<td>2.3</td>
<td>11</td>
<td>11</td>
<td>24.0%</td>
<td>2.00</td>
<td>[0.77, 3.23]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kilinc (2008)</td>
<td>6.83</td>
<td>4.22</td>
<td>1.57</td>
<td>16</td>
<td>1.76</td>
<td>17</td>
<td>24.0%</td>
<td>5.63</td>
<td>[4.56, 6.70]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucedero (2009)</td>
<td>23.8</td>
<td>22</td>
<td>1.8</td>
<td></td>
<td>14</td>
<td>14</td>
<td>19.6%</td>
<td>1.40</td>
<td>[-2.83, 3.63]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>23.2</td>
<td>22</td>
<td>1.3</td>
<td>22</td>
<td>1.3</td>
<td>14</td>
<td>21.3%</td>
<td>2.68</td>
<td>[0.37, 5.00]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 4.93, Chi² = 29.99, df = 3; P = 0.00001; I² = 80%

Test for overall effect: Z = 2.37 (P = 0.02)

**B. By shortest distance (FM/FM + RME or RME vs Control)**

**5.1.1 FM/FM+RME**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aloufi (2012)</td>
<td>1.3</td>
<td>1.10</td>
<td>30</td>
<td></td>
<td>0.5</td>
<td>30</td>
<td>74.0%</td>
<td>0.60</td>
<td>[0.19, 1.14]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>1.3</td>
<td>1.10</td>
<td>30</td>
<td></td>
<td>0.5</td>
<td>30</td>
<td>74.0%</td>
<td>0.60</td>
<td>[0.19, 1.14]</td>
</tr>
</tbody>
</table>

Heterogeneity: Not applicable

Test for overall effect: Z = 2.57 (P = 0.01)

Total (95% CI) 1.3 1.10 30 74.0% 0.60 [0.19, 1.14]

Heterogeneity: Chi² = 10.94, df = 3 (P = 0.01); I² = 73%

Test for overall effect: Z = 3.77 (P = 0.0002)

**5.1.2 RME**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aloufi (2012)</td>
<td>0.3</td>
<td>0.8</td>
<td>30</td>
<td></td>
<td>0.4</td>
<td>30</td>
<td>83.2%</td>
<td>0.20</td>
<td>-0.60, 0.20</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>0.3</td>
<td>0.8</td>
<td>30</td>
<td></td>
<td>0.4</td>
<td>30</td>
<td>83.2%</td>
<td>0.20</td>
<td>-0.60, 0.20</td>
</tr>
</tbody>
</table>

Heterogeneity: Not applicable

Test for overall effect: Z = 0.91 (P = 0.36)

Total (95% CI) 0.3 0.8 30 83.2% 0.20 [-0.60, 0.20]

Heterogeneity: Chi² = 2.80, df = 3 (P = 0.40); I² = 0%

Test for overall effect: Z = 1.20 (P = 0.22)

Test for subgroup differences: Chi² = 0.47, df = 1 (P = 0.50); I² = 0%

**LOWER AIRWAY: anteroposterior linear changes**

By shortest distance

**FM/FM + RME or RME vs Control**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
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<tr>
<td>Akim (2015)</td>
<td>0.12</td>
<td>2.50</td>
<td>22</td>
<td></td>
<td>2.0</td>
<td>22</td>
<td>11.3%</td>
<td>-0.15</td>
<td>-1.46, 1.16</td>
</tr>
<tr>
<td>Baccetti (2010)</td>
<td>0.35</td>
<td>22</td>
<td>2.4</td>
<td>3</td>
<td>3.8</td>
<td>14</td>
<td>3.2%</td>
<td>-2.40</td>
<td>-4.87, 0.07</td>
</tr>
<tr>
<td>Mucedero (2009)</td>
<td>0.35</td>
<td>22</td>
<td>2.4</td>
<td>3</td>
<td>3.8</td>
<td>14</td>
<td>3.2%</td>
<td>-2.40</td>
<td>-4.87, 0.07</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>0.35</td>
<td>22</td>
<td>2.4</td>
<td>3</td>
<td>3.8</td>
<td>14</td>
<td>3.2%</td>
<td>-2.40</td>
<td>-4.87, 0.07</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 2.51, df = 3 (P = 0.20); I² = 20%

Test for overall effect: Z = 1.11 (P = 0.24)

**5.2.2 RME**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aloufi (2012)</td>
<td>0.2</td>
<td>1.0</td>
<td>30</td>
<td></td>
<td>0.4</td>
<td>30</td>
<td>83.2%</td>
<td>-0.20</td>
<td>-0.60, 0.20</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>0.2</td>
<td>1.0</td>
<td>30</td>
<td></td>
<td>0.4</td>
<td>30</td>
<td>83.2%</td>
<td>-0.20</td>
<td>-0.60, 0.20</td>
</tr>
</tbody>
</table>

Heterogeneity: Not applicable

Test for overall effect: Z = 0.91 (P = 0.36)

Total (95% CI) 0.2 1.0 30 83.2% 0.20 [-0.60, 0.20]

Heterogeneity: Chi² = 2.80, df = 3 (P = 0.40); I² = 0%

Test for overall effect: Z = 1.20 (P = 0.22)

Test for subgroup differences: Chi² = 0.47, df = 1 (P = 0.50); I² = 0%

**FIGURE 4** Forest plots to evaluate the pharyngeal airway changes following rapid maxillary expansion (RME) or protraction with facemask (FM)/FM + RME measured on 2D lateral cephalograms
Airway above palatal plane

Nasal passage airway volume

![Forest plots to evaluate the pharyngeal airway changes following rapid maxillary expansion (RME) measured in 3D on cone beam CTs (CBCTs)](image)

in the volume of airway changes in the RME group compared with the control group.

In the present study, nine studies were included (Table 1); however, significant heterogeneity ($I^2 > 75\%$) was noted if the articles of Kilinç et al and Akin et al were included. The exact reason for this heterogeneity remains uncertain. One of the possibilities for the higher heterogeneity might be due to the duration of the initial and final records being less than 1 year (short-term follow-up), whereas other studies conducted long-term follow-up (longer than 1 year). Nevertheless, our final results were not affected when these two studies were excluded.

To the best of our knowledge, no meta-analysis has evaluated the pharyngeal airway space changes, either 2D or 3D, after RME and/or FM protraction treatment(s). Studies with 2D evaluation found that RME/FM is significantly related to the upper pharyngeal airway. Studies with 2D evaluation found that RME/FM is significantly related to the upper pharyngeal airway. In the present study, our results indicated that the patients who received RME/FM therapy were more likely to have an increased upper pharyngeal airway than those untreated in the control group (Figure 3). Several studies stated no significant change in the sagittal nasopharyngeal and oropharyngeal airway dimensions or volume changes following RME/FM; however, no untreated controls were involved in the studies. Additionally, the landmarks and measurements (eg 2D and 3D) used for recording the airway dimension changes were inconsistent. Therefore, information about the changes in nasopharyngeal and oropharyngeal airway dimensions is difficult to obtain.

![Table](image)
In previous studies with 3D evaluation, most were case series studies without control groups. A few studies reported a significant increase in pharyngeal airway volume. However, other studies demonstrated a limited increase in the pharyngeal airway. Based on these studies, the pharyngeal airway changes following RME/FM remain controversial. In addition, conclusive evidence about the relationship between such changes and RME/FM is lacking.

This study has three major limitations. First, the sample size in quantitative synthesis for meta-analysis is relatively small. The results may not show strong evidence to prove the relationships between the airway volume changes and RME and/or FM treatments. Second, quantifying the real pharyngeal airway changes using 2D cephalometric radiography may not be ideal. 3D CBCT images are generally believed to be a better choice of measure in volume assessment. However, given that the number of articles with 3D images is too small, we combined both 2D and 3D measurements to evaluate the difference and reveal the tendency of the pharyngeal airway changes. Third, the studies we included were observational studies rather than RCTs. Admittedly, RCTs can provide the strongest evidence for causality if the RCTs are blinded. In the present study, non-randomized studies were included. It has been shown that non-randomized studies have strong likelihood of bias and confounding, data are more likely to be incomplete and of poor quality, and outcomes are less likely to be validated. In particular circumstances, however, non-randomized studies may provide certain advantages, such as providing us long-term information on early treatment of Class III malocclusion or maxillary transverse deficiency. Moreover, observational studies may be more applicable in real-world settings than RCTs because of their broader range of participants included, large sample size and longer follow-up. In the present analysis, nevertheless, there is no RCT-based available evidence. Alternatively, the studies we included were positive for the quality assessment, and the leave-one-out analyses (Figure 6) were performed by repeating the meta-analysis excluding each individual study in turn. This assessment can point out which studies are most influential and evaluate how the individual study affects the overall estimate of the rest of the studies.

In conclusion, our meta-analysis showed that RME/FM treatments might increase the upper airway space changes in children or young adolescents. However, the relatively small sample size and real pharyngeal airway changes from 2D cephalometric radiography might not completely reflect the exact changes in the pharyngeal airway space. Further long-term 3D cohort studies are required for more comprehensive analyses.

FIGURE 6 Leave-one-out analysis: pooled summary estimates with each study removed at one time

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