Clinical Oral Investigations (2018) 22:2639–2652
https://doi.org/10.1007/s00784-018-2363-8

ORIGINAL ARTICLE

Stability of maxillary protraction therapy in children with Class III malocclusion: a systematic review and meta-analysis

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Received: 22 December 2016 / Accepted: 24 January 2018 / Published online: 10 February 2018

Abstract

Objective The objective of this study was to evaluate the stability of treatment effects of maxillary protraction therapy in Class III children.

Materials and methods Multiple electronic databases were searched from 01/1996 to 10/2016. Randomized clinical trials, controlled clinical trials, and cohort studies with untreated Class III controls and a follow-up over 2 years were considered for inclusion. The methodological quality of the studies and publication bias were evaluated. Mean differences and 95% confidence intervals (CI) of six variables (SNA, SNB, ANB, mandibular plane angle, overjet, and lower incisor angle) were calculated.

Results Ten studies were included in the qualitative analysis, and four studies were included in the quantitative analysis. Compared with the control group, after treatment, the treated group showed significant changes: SNA +1.79° (95% CI: 1.23, 2.34), SNB −1.16° (95% CI −2.08, −0.24), ANB +2.92° (95% CI 2.40, 3.44), mandibular plane angle +1.41° (95% CI 0.63, 2.20), overjet +3.94 mm (95% CI 2.17, 5.71) and lower incisor angle −3.07° (95% CI −4.92, −1.22). During follow-up, the changes in five variables reflected significant relapse. Overall, the treated group showed significant changes only in ANB +1.66° (95% CI 0.97, 2.35) and overjet +2.41 mm (95% CI 1.60, 3.23).

Conclusions Maxillary protraction can be a short-term effective therapy and might improve sagittal skeletal and dental relationships in the medium term. But some skeletal and dental variables showed significant relapse during the follow-up period. Long-term studies are still required to further evaluate its skeletal benefits.

Clinical relevance The study evaluated the medium-term stability of skeletal and dental effects of maxillary protraction in Class III children and discussed whether the therapy can reduce the need for orthognathic surgery.

Keywords Maxillary protraction therapy · Class III children · Skeletal and dental changes · Medium-term stability · Systematic review and meta-analysis

Introduction

Treatment of Class III malocclusion in growing children is one of the most challenging problems in orthodontics. The unfavorable growth pattern in children with Class III discrepancy usually requires early orthopedic treatment. These treatments are usually focused on growth modification, including maxillary protraction, functional regulator, and chin cup [1–3]. According to previous studies, approximately two thirds of subjects with Class III skeletal relationship were due to either maxillary retrognathism or a combination of maxillary retrognathism and mandibular prognathism [4–6]. In view of the high frequency of maxillary retrusion, maxillary protraction using an orthopedic facemask has been widely applied as a major approach for Class III children. Its short-term effects include anterior movement of the maxilla, downward and backward rotation of the mandible, proclination of upper incisors, and retroclination of lower incisors [1, 7–9].

According to previous literature, the growth of the maxilla is slower than that of the mandible and ceases nearly 2 years before the mandible [10]. Due to the unpredictable growth patterns of Class III children and the propensity for relapse after orthodontic treatment, posttreatment changes in maxillary protraction should not be ignored. The relapse was attributed to unstable results of maxillary displacement, counterclockwise rotation of the mandible, unfavorable mandibular growth, and dental inclinations [11].

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In previous studies, positive overjet was a commonly used criterion for evaluating the long-term success of maxillary protraction. The results showed that 67–95% of treated subjects maintained a positive overjet after attaining post-pubertal skeletal maturation [11–19]. However, this assessment may not truly reflect the correction of skeletal discrepancy but rather the correction of dental relationships. As an early orthopedic treatment, the primary aim of maxillary protraction therapy is to maximally improve skeletal discrepancy while minimizing the compensatory effects of dental inclinations. It is difficult to argue whether the correction of overjet was due to skeletal improvements or to dental compensations.

So far, there has been no systematic review or meta-analysis evaluating the stability of skeletal and dental changes of maxillary protraction in Class III subjects. How much of the treatment effects could be maintained at the end of follow-up remained unclear.

The aim of this systematic review and meta-analysis was first to assess the short-term effects of maxillary protraction therapy for Class III children, second to evaluate whether the treatment changes would remain stable at the end of follow-up, and finally to discuss whether the therapy can reduce the need for orthognathic surgery.

Materials and methods

This systematic review and meta-analysis was based on the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines [20].

Eligibility criteria and literature search strategy

Inclusion and exclusion criteria were established prior to the search (Table 1).

Electronic searching was conducted using the following electronic databases: PubMed, Embase, Web of Science, and Cochrane Library, from 1 January 1996 to 29 October 2016, with no language restrictions. The gray literature was searched using the database SIGLE (System for Information on Grey Literature in Europe). The keywords were carefully selected and revised for each database. A detailed description of the search strategy applied to PubMed is provided in Table 2.

Selection of studies

The selection process was independently conducted by two researchers (Lin and Fu). Titles and abstracts were examined, and duplicate studies were eliminated. For articles where the abstracts did not present enough information, full texts were obtained and carefully inspected. Furthermore, three major orthodontic journals (*American Journal of Orthodontics and Dentofacial Orthopedics*, *Angle Orthodontist*, and *European Journal of Orthodontics*) from 01/1996 to 06/2016 and the reference lists of the selected articles were also hand searched.

Any inter-examiner disagreement was resolved by discussion with a third author (Li). The level of agreement between the two examiners was assessed using the Cohen kappa scores.

Quality assessment

The methodological quality of all included studies was independently assessed by two authors (Lin and Guo). The risk of bias of randomized clinical trials (RCT) was assessed using the Cochrane Collaboration's tool for assessing risk of bias [21]. Seven criteria were analyzed to grade the risk of bias inherent in the RCT: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective outcome reporting, and other potential sources of bias. The

Table 1 Eligibility criteria used for the study selection

Category	Inclusion criteria	Exclusion criteria
Study design	Randomized controlled trials	Case reports
	Controlled clinical trials	Commentaries
	Cohort studies	Systematic reviews or meta-analyses
Participants	Growing children with Class III malocclusion	Patients with cleft lip palate and/or craniofacial syndromes
		Patients with temporomandibular joint disorders
Comparison	Untreated Class III patients matched for age and gender	Studies without an untreated Class III control group
Intervention	Intra-oral bonded appliance, and maxillary protraction with an extra-oral facemask	Patients treated with other orthodontic or orthopedic appliances
Outcome	Skeletal and dentoalveolar variables measured by lateral cephalometric radiographs	Studies providing no cephalometric measurements
Average time of follow-up	Studies with an average follow-up at least 2 years after maxillary protraction therapy	Studies with an average follow-up less than 2 years

Table 2 Search strategy for PubMed

Literature search was conducted from 01/01/1996 to 29/10/2016		PubMed results
No. 1	Maxillary protraction OR facemask OR face mask OR facial mask OR reverse headgear	3995
No. 2	Class III OR Class 3	121,409
No. 3	Malocclusion, angle class III [Mesh]	2275
No. 4	No. 2 OR No. 3	121,409
No. 5	Long-term OR longterm OR long term OR follow-up OR follow up OR longitudinal	1,332,190
No. 6	Relapse OR recur* OR post-treatment OR posttreatment	752,075
No. 7	Stable OR stability OR instability OR retent* OR retain*	828,942
No. 8	No. 5 OR No. 6 OR No. 7	2,551,027
No. 9	No. 1 AND No. 4 AND No. 8	194

methodological quality of RCT was judged as low risk (low for all evaluated domains), high risk (high for one or more domains), and unclear risk (unclear for one or more domains). The quality of non-RCTs was assessed according to methodological items for non-randomized studies (MINORS) [22]. Agreement between the examiners concerning methodological quality was assessed by kappa statistics. Any disagreement on the quality assessment was resolved by discussion with a third author (Li).

Data extraction

Study characteristics were independently extracted by two authors (Lin and Guo) using pre-defined electronic sheets. Three time points were defined: T1 (before maxillary protraction therapy), T2 (after maxillary protraction therapy), and T3 (the end of follow-up). The outcomes include SNA, SNB, ANB, mandibular plane angle (MPA), overjet, and lower incisor/mandibular plane (L1/MP) angle, for which the changes during T1–T2 (treatment effects), T2–T3 (posttreatment changes), and T1–T3 (overall treatment effects) were recorded. The level of inter-examiner agreement of data extraction was measured using kappa statistics.

Statistical analysis

Clinical heterogeneity was gauged by assessing the treatment protocols, participants, treatment time, retention, and follow-up time. Meta-analyses were performed using Review Manager 5.1 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2011). For all the evaluated variables, weighted mean differences (WMD) with 95% confidence intervals (CI) were calculated.

Statistical heterogeneity was assessed by chi-square test and *I*-square index. If heterogeneity was not significant ($P > 0.10$, $I^2 < 50\%$), a fixed-effect model was adopted for analysis; otherwise, a random-effects model would be employed.

Moreover, Egger's test was used to quantify the small study effects or publication bias by Stata 14.0 (STATA Corp., College Station, TX, USA) [23]. If publication bias was detected, a fail-safe number (the number of unpublished negative studies that would be needed to nullify the result to non-significance) was calculated to assess the effect of such bias ($\alpha = 0.05$) [24]. A fail-safe number is often considered robust if it is greater than $5n + 10$, where n is the number of studies [25].

Results

Literature search

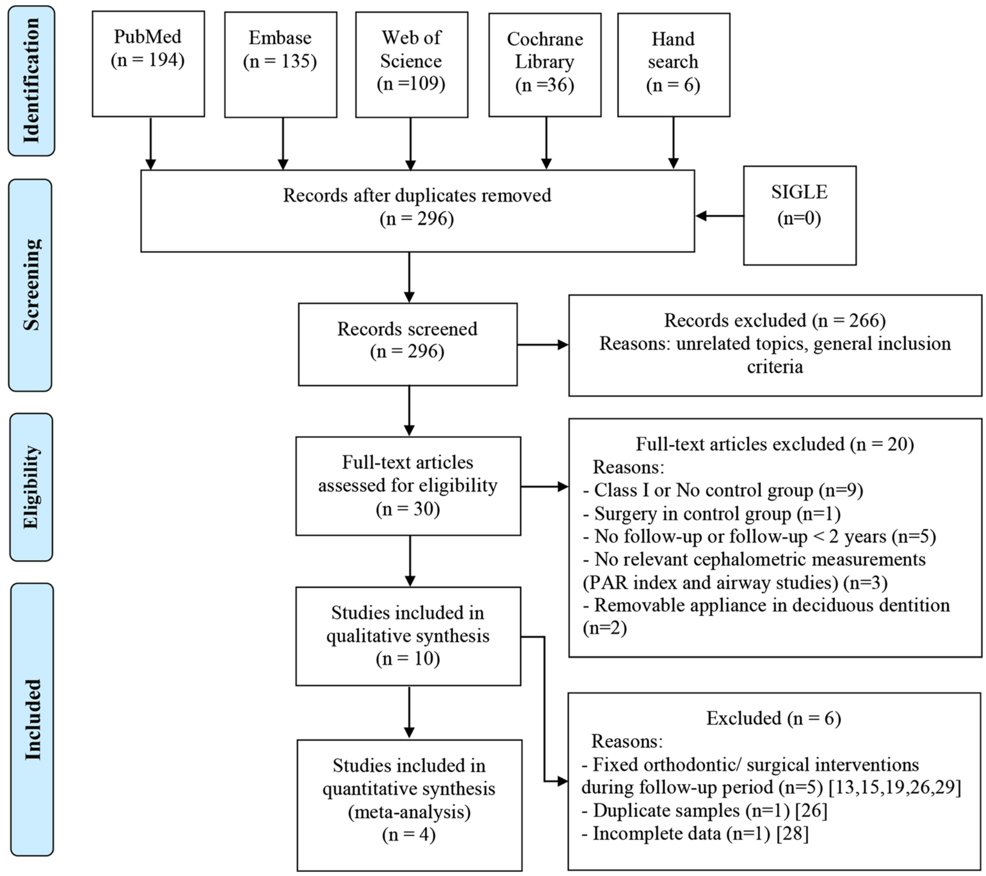
The PRISMA flow diagram of study selection is shown in Fig. 1. After reviewing titles and abstracts, 30 articles were obtained for full-text evaluation, and 20 were subsequently excluded due to various reasons described in the diagram. Ten studies met the eligibility criteria and were selected for quality evaluation. The kappa score for study selection was 0.979, indicating an excellent level of agreement.

Description of studies

Characteristics of the included studies are summarized in Table 3. The kappa scores ranged from 0.915 to 1.0 for the 13 characteristics of the included studies, indicating a high level of agreement.

Of the ten studies, seven [13, 16–19, 26, 27] are prospective (including four partially prospective), and three [15, 28, 29] are retrospective, and all studies included untreated Class III controls. Four studies [13, 16–18] are partially prospective, meaning that they present a retrospective control group (CG). It is not considered to be ethically justified to take radiographs without performing any active treatment, so it is rare that studies have prospective untreated CGs. Since the partially prospective studies have mentioned that the CG matched the treated group (TG) in age, sex, and type of malocclusion and

Fig. 1 PRISMA flow diagram



the two groups have similar cephalometric characteristics at baseline, we considered them acceptable as prospective studies.

After maxillary protraction therapy, all studies had an average follow-up of more than 2 years. During this period, four studies reported using mandibular retractor [13], Fränkel-III appliance [28], maxillary stabilization plate [15], and reverse activator [17] as retention devices. Fixed orthodontic appliance treatments were performed in five studies [13, 15, 19, 26, 28].

Notably, the studies of Mandall et al. [26] and Mandall et al. [27] appeared to be the same research with different follow-up times; therefore, only one of them was considered in the quantitative analysis.

Assessment of risk of bias

The risk of bias of the RCT [26, 27] was low for all domains, indicating an overall high methodological quality (Appendix Table 4). The MINORS's scores of the eight non-RCTs were between 13 and 17 (Appendix Table 5). The RCT [26, 27] reported details about random sequence generation and adequate allocation concealment. This study was single-blind, as the researchers measuring the radiographs and the statistician were blinded to the treatment/control allocation. Clinicians and patients were not blinded. However, this would be unlikely to affect the cephalometric outcomes. As such, the assessment could still be considered unbiased. Prospective calculation of sample size was performed in the RCT. Method error analysis was performed in all studies. The kappa scores ranged from 0.850 to 1.0 for the 12 items, indicating a high level of agreement.

Egger's test showed no publication bias in most measurements, except in T1–T2 ANB ($P = 0.008$) and T2–T3 SNB ($P = 0.039$) (Appendix Table 6). Therefore, the fail-safe number was calculated to estimate the number of potential missing studies needed to significantly change the result. The fail-safe number for T1–T2 ANB was 116 ($> 5n + 5 = 20$), indicating a robust result.

Quantitative synthesis of included studies

Conclusively, only four (one RCT [27] and three partly prospective [16–18]) studies with untreated Class III controls had no other active orthodontic and/or surgical interventions during the follow-up period, allowing for the pure effects of maxillary protraction to be evaluated. The other six studies [13, 15, 19, 26, 28, 29] were excluded from the quantitative analysis due to incomplete information and active orthodontic or surgical treatments during the follow-up period.

Table 3 Characteristics of the included studies

Study	Study design	Sample size (at T1)	Average age (years old)	Appliance	Force magnitude and angulation	Time of daily wearing (hours)	End point of treatment
Mandall et al. [26]	RCT	TG = 35 CG = 38	7–9	Bonded RME + FM	400 g 30°	14 h	Positive OJ and Class I relationship
Mandall et al. [27]	RCT	TG = 35 CG = 38	7–9	Bonded RME + FM	400 g 30°	14 h	Positive OJ and Class I relationship
Masucci et al. [13]	CCT (TG prospective, CG retrospective)	TG = 30 CG = 16/13	TG = 9.2 CG = 8.6/8.4	Bonded RME + FM	400–500 g	14 h	Positive OJ
Chen et al. [19]	CCT (prospective)	TG = 22 CG = 17	TG = 11.38 CG = 11.54	Bonded RME + FM	250–300 g 15–30°	9–10 h	Positive OJ
Cozza et al. [18]	CCT (TG prospective, CG retrospective)	TG = 22 CG = 12	TG = 8.9 CG = 7.6	Bonded molar bands + FM + bite-block	600 g 30°–40°	14 h	Positive OJ or Class II occlusal relationship
Pangrazio-Kulbersh et al. [28]	Cohort (retrospective)	TG = 17 CG = NM	8y7m	Bonded RME + FM	400–600 g 30°	14–16 h	OJ ≥ 5 mm
Westwood et al. [15]	Cohort (retrospective)	TG = 34 CG = 12 (T1–T2)/15 (T2–T3)/22 (T1–T3)	TG = 8y3m	Bonded RME + FM	300–500 g	14 h	Positive OJ
Macdonald et al. [29]	Cohort (retrospective)	TG = 24 CG = 24 (Class I)/ 27 (Class III)	TG = 7.4 CG = 7.2 (Class I)/ 8.7 (Class III)	Soldered jackscrew expansion appliance + FM	200–450 g 15–30°	18–22 h (3–4 months) then bed time	NM
Ngan et al. [17]	CCT (TG prospective, CG retrospective)	TG = 30 CG = 20	8.4	Bonded RME + FM	380 g 30°	12 h	Class I or Class II dental relationship
Chong et al. [16]	CCT (TG prospective, CG retrospective)	TG = 16 CG = 13	TG = 6.8 CG = 6.36	Bonded molar bands + FM (3 had ME)	230–285 g 30°–40°	12–16 h	Positive OJ and/or a flush post-lactal plane

Study	Average treatment time	Average follow-up time	Number of patients at follow-up	Retention	Fixed appliance (second phase)	Positive OJ in TG at the end of follow-up (%)
Mandall et al. [26]	8.6 months	6 years	TG = 33 CG = 32	No	Yes	68%
Mandall et al. [27]	< 15 months	3 years	TG = 30 CG = 33	No	No	70%
Masucci et al. [13]	1.1 years	9.4 years	TG = 22 CG = 16/13	Some used mandibular retractor	19	73% (16/22)
Chen et al. [19]	1.5 years	TG: 3 years CG: no follow-up	TG = 10 CG = 0	NM	8	90% (9/10) One end-to-end
Cozza et al. [18]	1.6 years	2.1 years	TG = 22 CG = 12	No	No	95% (21/22) One end-to-end
Pangrazio-Kulbersh et al. [28]	10 months	7 years 6 months	TG = 17 CG = NM	10 used Fränkel-III	7	NM
Westwood et al. [15]	10 months	5 years 7 months	TG = 34 CG = 12/15/22	Removable maxillary stabilization plate	34	76%
Macdonald et al. [29]	1 year	2.33 years	TG = 24 CG = 24 (Class I)/27 (Class III)	NM	No	100% (24/24)

Table 3 (continued)

Study	Average treatment time	Average follow-up time	Number of patients at follow-up	Retention	Fixed appliance (second phase)	Positive OJ in TG at the end of follow-up (%)
Ngan et al. [17]	8 ± 3 months	2 years	TG = 20 CG = 20	10 had reverse activator	No	90% (18/20)
Chong et al. [16]	0.61 year	3.57 years	TG = 16 CG = 13	No	No	69% (11/16) (OJ > 2 mm)

CG control group, *CCT* controlled clinical trial, *FM* facemask, *NM* not mentioned, *OJ* overjet, *RCT* randomized controlled trial, *RME* rapid maxillary expansion, *TG* treated group, *T1* before treatment, *T2* after treatment, *T3* end of follow-up

The changes in six variables (SNA, SNB, ANB, MPA, overjet, and L1/MP) during three time periods (T1–T2, T2–T3, and T1–T3) were compared between the TG and CG.

Short-term treatment effects (T1–T2, Fig. 2)

In the TG, the short-term treatment effects included significant increases in SNA (WMD 1.79; 95% CI 1.23, 2.34), ANB (WMD 2.92; 95% CI 2.40, 3.44), overjet (WMD 3.94; 95% CI 2.17, 5.71), and MPA (WMD 1.41; 95% CI 0.63, 2.20), while SNB (WMD −1.16; 95% CI −2.08, −0.24) and L1/MP angle (WMD −3.07; 95% CI −4.92, −1.22) had significant reductions.

Posttreatment changes (T2–T3, Fig. 3)

In the TG, SNA (WMD −0.75; 95% CI −1.38, −0.11), ANB (WMD −0.80; 95% CI −1.45, −0.15), overjet (WMD −0.69; 95% CI −1.28, −0.09), and MPA (WMD −0.89; 95% CI −1.68, −0.11) were significantly decreased, while L1/MP angle (WMD 3.31; 95% CI 1.49, 5.13) had a significant increase.

Medium-term effects (T1–T3, Fig. 4)

In the TG, the medium-term effects included significant increases in ANB (WMD 1.66; 95% CI 0.97, 2.35) and overjet (WMD 2.41; 95% CI 1.60, 3.23). No significant difference in SNA, SNB, MPA, and L1/MP angle was found between the TG and CG.

Discussion

According to previous reports, the average prevalence rate of Angle Class III malocclusion was 7.04% and varies in different populations, with those from Southeast Asian countries showing the highest rate of 15.80% [30]. For growing Class III children, maxillary protraction is widely used as a treatment approach. Although its short-term effects have been previously demonstrated, there is an uncertainty concerning its medium- to long-term stability. To the best of our knowledge, this is the first systematic review and meta-analysis that has reviewed the medium-term skeletal and dental effects of maxillary protraction therapy.

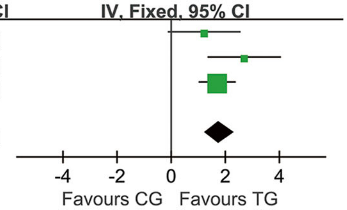
Short-term treatment effects (T1–T2)

The short-term skeletal modifications included forward displacement of the maxilla, backward displacement of the mandible, and clockwise rotation of the mandibular plane, which were similar to previous studies [1, 7–9]. The results indicated that maxillary protraction therapy not only affects the maxilla

2.1 T1-T2 SNA

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	0.91	1.04	16	-0.31	2.29	13	17.1%	1.22 [-0.13, 2.57]
Cozza 2010	2.1	2.8	22	-0.6	1.2	12	16.9%	2.70 [1.35, 4.05]
Ngan 1998	1.6	1.2	20	-0.1	1	20	66.0%	1.70 [1.02, 2.38]
Total (95% CI)			**58**			**45**	**100.0%**	**1.79 [1.23, 2.34]**

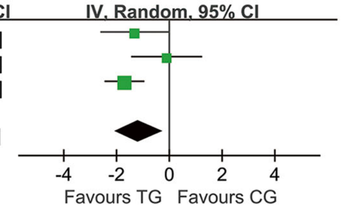
Heterogeneity: Chi² = 2.49, df = 2 (P = 0.29); I² = 20%
Test for overall effect: Z = 6.30 (P < 0.00001)



2.2 T1-T2 SNB

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Random, 95% CI
Chong, 1996	-1.13	1.1	16	0.19	2.16	13	28.3%	-1.32 [-2.61, -0.03]
Cozza 2010	-0.1	2.6	22	0	1.4	12	27.0%	-0.10 [-1.44, 1.24]
Ngan 1998	-1.5	1.4	20	0.2	1	20	44.7%	-1.70 [-2.45, -0.95]
Total (95% CI)			**58**			**45**	**100.0%**	**-1.16 [-2.08, -0.24]**

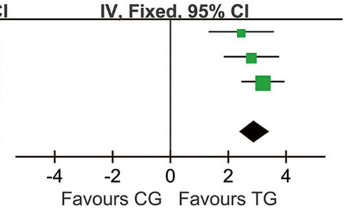
Heterogeneity: Tau² = 0.34; Chi² = 4.14, df = 2 (P = 0.13); I² = 52%
Test for overall effect: Z = 2.47 (P = 0.01)



2.3 T1-T2 ANB

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	2.03	1.62	16	-0.42	1.47	13	21.4%	2.45 [1.32, 3.58]
Cozza 2010	2.2	1.6	22	-0.6	1.2	12	29.8%	2.80 [1.85, 3.75]
Ngan 1998	3	1.5	20	-0.2	0.8	20	48.8%	3.20 [2.45, 3.95]
Total (95% CI)			**58**			**45**	**100.0%**	**2.92 [2.40, 3.44]**

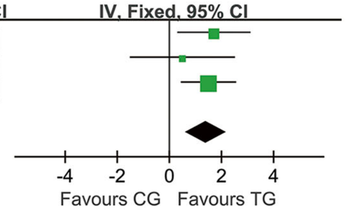
Heterogeneity: Chi² = 1.27, df = 2 (P = 0.53); I² = 0%
Test for overall effect: Z = 11.00 (P < 0.00001)



2.4 T1-T2 Mandibular plane angle

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	0.94	1.09	16	-0.77	2.39	13	30.9%	1.71 [0.31, 3.11]
Cozza 2010	0.9	3.3	22	0.4	2.6	12	15.0%	0.50 [-1.52, 2.52]
Ngan 1998	1.3	1.5	20	-0.2	1.9	20	54.1%	1.50 [0.44, 2.56]
Total (95% CI)			**58**			**45**	**100.0%**	**1.41 [0.63, 2.20]**

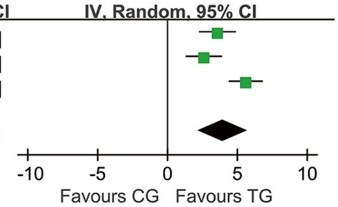
Heterogeneity: Chi² = 0.99, df = 2 (P = 0.61); I² = 0%
Test for overall effect: Z = 3.55 (P = 0.0004)



2.5 T1-T2 Overjet

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Random, 95% CI
Chong, 1996	4.76	1.96	16	1.19	1.67	13	33.0%	3.57 [2.25, 4.89]
Cozza 2010	3.1	2.1	22	0.5	1.7	12	33.1%	2.60 [1.30, 3.90]
Ngan 1998	5.5	2.11	20	-0.1	1.8	20	33.9%	5.60 [4.38, 6.82]
Total (95% CI)			**58**			**45**	**100.0%**	**3.94 [2.17, 5.71]**

Heterogeneity: Tau² = 2.02; Chi² = 11.50, df = 2 (P = 0.003); I² = 83%
Test for overall effect: Z = 4.36 (P < 0.0001)



2.6 T1-T2 L1/MP angle

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	-1.69	5.56	16	0.5	3.51	13	31.0%	-2.19 [-5.52, 1.14]
Cozza 2010	-0.4	6.2	22	0.7	4.7	12	24.9%	-1.10 [-4.81, 2.61]
Ngan 1998	-4.4	5.5	20	0.4	3.2	20	44.1%	-4.80 [-7.59, -2.01]
Total (95% CI)			**58**			**45**	**100.0%**	**-3.07 [-4.92, -1.22]**

Heterogeneity: Chi² = 2.83, df = 2 (P = 0.24); I² = 29%
Test for overall effect: Z = 3.25 (P = 0.001)

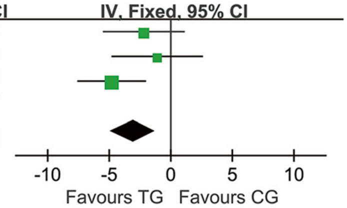
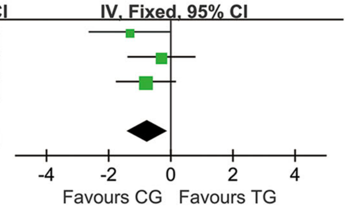


Fig. 2 Short-term treatment effects (T1–T2)

3.1 T2-T3 SNA

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	0	2.27	16	1.31	1.35	13	22.8%	-1.31 [-2.64, 0.02]
Cozza 2010	-0.2	1.8	22	0.1	1.4	12	33.9%	-0.30 [-1.39, 0.79]
Ngan 1998	-0.3	1.4	20	0.5	1.7	20	43.4%	-0.80 [-1.77, 0.17]
Total (95% CI)			**58**			**45**	**100.0%**	**-0.75 [-1.38, -0.11]**

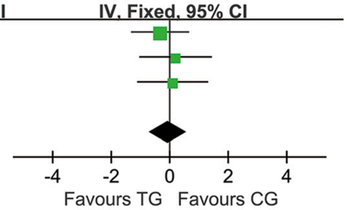
Heterogeneity: Chi² = 1.34, df = 2 (P = 0.51); I² = 0%
Test for overall effect: Z = 2.30 (P = 0.02)



3.2 T2-T3 SNB

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	1.63	1.22	16	1.96	1.46	13	43.2%	-0.33 [-1.32, 0.66]
Cozza 2010	0.8	1.7	22	0.6	1.8	12	27.7%	0.20 [-1.04, 1.44]
Ngan 1998	1.6	1.8	20	1.5	2.1	20	29.1%	0.10 [-1.11, 1.31]
Total (95% CI)			**58**			**45**	**100.0%**	**-0.06 [-0.71, 0.60]**

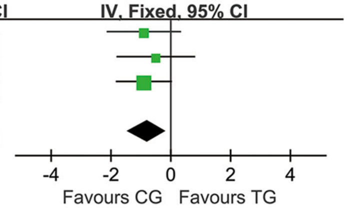
Heterogeneity: Chi² = 0.52, df = 2 (P = 0.77); I² = 0%
Test for overall effect: Z = 0.17 (P = 0.86)



3.3 T2-T3 ANB

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	-1.63	2.13	16	-0.73	1.24	13	27.4%	-0.90 [-2.14, 0.34]
Cozza 2010	-1	1.6	22	-0.5	2	12	24.5%	-0.50 [-1.81, 0.81]
Ngan 1998	-2	1.3	20	-1.1	1.7	20	48.1%	-0.90 [-1.84, 0.04]
Total (95% CI)			**58**			**45**	**100.0%**	**-0.80 [-1.45, -0.15]**

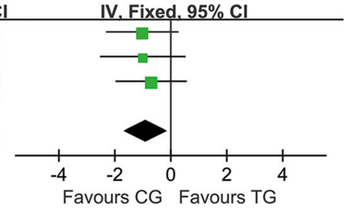
Heterogeneity: Chi² = 0.27, df = 2 (P = 0.87); I² = 0%
Test for overall effect: Z = 2.42 (P = 0.02)



3.4 T2-T3 Mandibular plane angle

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	-1.75	1.74	16	-0.73	1.79	13	36.4%	-1.02 [-2.31, 0.27]
Cozza 2010	-0.6	2.6	22	0.4	1.9	12	26.1%	-1.00 [-2.53, 0.53]
Ngan 1998	-1.2	1.9	20	-0.5	2.2	20	37.5%	-0.70 [-1.97, 0.57]
Total (95% CI)			**58**			**45**	**100.0%**	**-0.89 [-1.68, -0.11]**

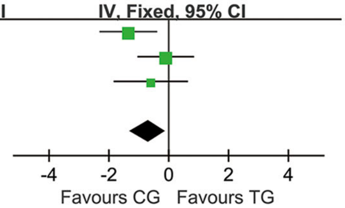
Heterogeneity: Chi² = 0.14, df = 2 (P = 0.93); I² = 0%
Test for overall effect: Z = 2.25 (P = 0.02)



3.5 T2-T3 Overjet

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	-1.19	1.73	16	0.16	0.85	13	37.8%	-1.35 [-2.32, -0.38]
Cozza 2010	-0.3	1	22	-0.2	1.5	12	39.4%	-0.10 [-1.05, 0.85]
Ngan 1998	-0.9	2.1	20	-0.3	1.9	20	22.9%	-0.60 [-1.84, 0.64]
Total (95% CI)			**58**			**45**	**100.0%**	**-0.69 [-1.28, -0.09]**

Heterogeneity: Chi² = 3.31, df = 2 (P = 0.19); I² = 40%
Test for overall effect: Z = 2.27 (P = 0.02)



3.6 T2-T3 L1/MP angle

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	3.34	6.22	16	-0.15	2.2	13	30.9%	3.49 [0.22, 6.76]
Cozza 2010	-0.9	5.4	22	-2.9	3.7	12	35.0%	2.00 [-1.08, 5.08]
Ngan 1998	3.3	5.5	20	-1.2	4.5	20	34.1%	4.50 [1.39, 7.61]
Total (95% CI)			**58**			**45**	**100.0%**	**3.31 [1.49, 5.13]**

Heterogeneity: Chi² = 1.27, df = 2 (P = 0.53); I² = 0%
Test for overall effect: Z = 3.57 (P = 0.0004)

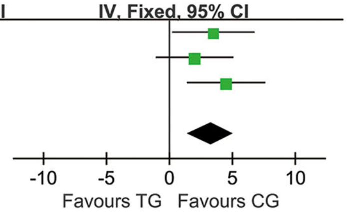
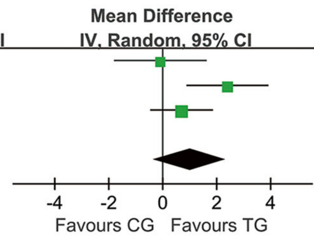


Fig. 3 Posttreatment changes (T2–T3)

4.1 T1-T3 SNA

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Random, 95% CI
Chong, 1996	0.91	1.93	16	1	2.64	13	28.8%	-0.09 [-1.81, 1.63]
Cozza 2010	1.9	3.1	22	-0.5	1.4	12	32.2%	2.40 [0.88, 3.92]
Mandall 2012	2.3	2.1	30	1.6	2.6	33	38.9%	0.70 [-0.46, 1.86]
Total (95% CI)			**68**			**58**	**100.0%**	**1.02 [-0.32, 2.36]**

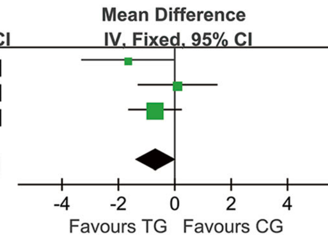
Heterogeneity: Tau² = 0.84; Chi² = 5.07, df = 2 (P = 0.08); I² = 61%
Test for overall effect: Z = 1.50 (P = 0.13)



4.2 T1-T3 SNB

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	0.5	1.47	16	2.15	2.77	13	18.3%	-1.65 [-3.32, 0.02]
Cozza 2010	0.7	2.6	22	0.6	1.6	12	25.4%	0.10 [-1.31, 1.51]
Mandall 2012	0.8	1.5	30	1.5	2.3	33	56.3%	-0.70 [-1.65, 0.25]
Total (95% CI)			**68**			**58**	**100.0%**	**-0.67 [-1.38, 0.04]**

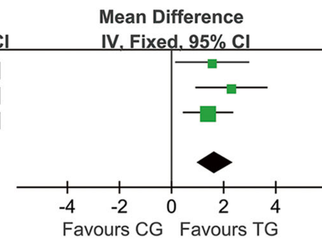
Heterogeneity: Chi² = 2.47, df = 2 (P = 0.29); I² = 19%
Test for overall effect: Z = 1.84 (P = 0.07)



4.3 T1-T3 ANB

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	0.41	1.51	16	-1.15	2.23	13	23.7%	1.56 [0.14, 2.98]
Cozza 2010	1.2	1.9	22	-1.1	2	12	25.0%	2.30 [0.92, 3.68]
Mandall 2012	1.5	2	30	0.1	1.9	33	51.3%	1.40 [0.43, 2.37]
Total (95% CI)			**68**			**58**	**100.0%**	**1.66 [0.97, 2.35]**

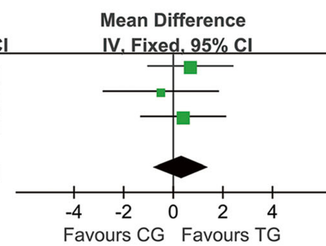
Heterogeneity: Chi² = 1.12, df = 2 (P = 0.57); I² = 0%
Test for overall effect: Z = 4.71 (P < 0.00001)



4.4 T1-T3 Mandibular plane angle

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	-0.81	1.8	16	-1.5	2.75	13	39.2%	0.69 [-1.05, 2.43]
Cozza 2010	0.3	3.2	22	0.8	3.4	12	21.5%	-0.50 [-2.84, 1.84]
Mandall 2012	1.2	3.1	30	0.8	3.9	33	39.3%	0.40 [-1.33, 2.13]
Total (95% CI)			**68**			**58**	**100.0%**	**0.32 [-0.77, 1.41]**

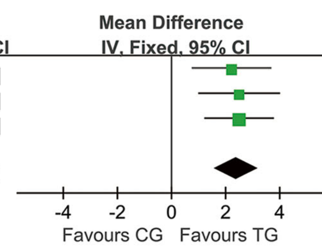
Heterogeneity: Chi² = 0.65, df = 2 (P = 0.72); I² = 0%
Test for overall effect: Z = 0.58 (P = 0.56)



4.5 T1-T3 Overjet

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	3.57	2.19	16	1.35	1.85	13	30.7%	2.22 [0.75, 3.69]
Cozza 2010	2.8	2.4	22	0.3	2	12	29.1%	2.50 [0.99, 4.01]
Mandall 2012	3.6	2.6	30	1.1	2.6	33	40.2%	2.50 [1.21, 3.79]
Total (95% CI)			**68**			**58**	**100.0%**	**2.41 [1.60, 3.23]**

Heterogeneity: Chi² = 0.10, df = 2 (P = 0.95); I² = 0%
Test for overall effect: Z = 5.80 (P < 0.00001)



4.6 T1-T3 L1/MP angle

Study or Subgroup	TG Mean	TG SD	TG Total	CG Mean	CG SD	CG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chong, 1996	1.66	4.48	16	0.35	3.7	13	27.0%	1.31 [-1.67, 4.29]
Cozza 2010	-1.3	5.4	22	-2.2	6.1	12	14.1%	0.90 [-3.22, 5.02]
Mandall 2012	-1.5	3.4	30	-0.7	4.7	33	59.0%	-0.80 [-2.81, 1.21]
Total (95% CI)			**68**			**58**	**100.0%**	**0.01 [-1.54, 1.55]**

Heterogeneity: Chi² = 1.53, df = 2 (P = 0.46); I² = 0%
Test for overall effect: Z = 0.01 (P = 0.99)

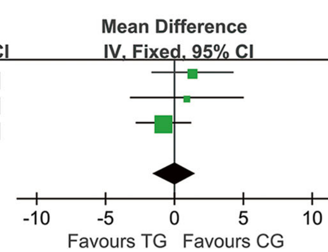


Fig. 4 Medium-term effects (T1–T3)

but also restricts the mandible by rotating it clockwise. Patients with Class III malocclusion present a unique growth pattern, which tends to worsen as growth proceeds [31]. To maximize treatment effects, orthopedic protraction treatment should be conducted in accordance with the timing of maxillary growth. In the current study, the average ages of the four included studies are 6.8 years [16], 8.4 years [17], 8.9 years [18], and 7–9 years [27], respectively. It is accepted that the patients were at suitable ages for maxillary protraction therapy.

Posttreatment changes (T2–T3)

During the follow-up period, the changes of five variables (SNA, ANB, MPA, overjet, and L1/MP) reflect significant relapse.

Although each individual study reported insignificant SNA and ANB decreases, the combined results showed that both had significant reductions ($P = 0.02$ for both SNA and ANB). The reason for this is that by combining several individual studies, meta-analysis can have a higher chance of detecting an effect [21]. The results reflected significant relapse of anterior maxillary position and intermaxillary relationship during the follow-up period. Regarding the mandible, the SNB had a slight increase in both groups with no significant intergroup difference ($P = 0.77$). The result agreed with previous findings that a Class III craniofacial growth pattern is reestablished after active orthopedic treatment and was generally similar with patients who were untreated [15, 32].

As for dental changes, the significant decrease in overjet ($P = 0.02$) could be attributed to a combination of skeletal and dental relapse. Chong et al. [16] and Wisth et al. [33] suggested that the relapse in overjet was mainly due to proclination of lower incisors caused by the removal of restricting forces from the chin cup, which was consistent with the increased L1/MP angle ($P < 0.01$) in the current study. These results indicated that overcorrection might be needed to counteract the relapse during the post-protraction period [15, 16, 29, 34].

In contrast to the TG, the lower incisors in the CG retroclined during the follow-up period. Mandall et al. [26] suggested that this marginally more dentoalveolar compensation in CG may be due to the biological attempts to maintain a positive overjet, despite the underlying Class III skeletal pattern.

Medium-term effects (T1–T3)

In previous studies on maxillary protraction, 67–95% of treated patients maintained a positive overjet after attaining postpubertal skeletal maturation [11–19]. A positive overjet may be an important concern for Class III patients; however, its reasonable indication is the correction of the anterior dental relationship rather than the correction of a skeletal discrepancy. Whether there is any improvement in skeletal deformity remains unclear. In the current study, the stability of skeletal and dental changes was evaluated.

Regarding the overall effects, the SNA had a relative increase of 1.02° ($P = 0.13$), and the SNB had a relative decrease of 0.67° ($P = 0.07$), while the intergroup differences were not significant. These results agreed with the newly published RCT with 6-year follow-up [26]. However, a 1.66° increase of ANB ($P < 0.01$) was found in our study, which indicated a significant improvement in sagittal intermaxillary relationship.

With regard to the MPA, there was no significant difference in medium-term changes between the TG and CG. Based on current results, the mandible indeed rotated clockwise during treatment; however, this clockwise rotation was not stable and did significantly relapse in the follow-up period. With a similar chin cup component of the facemask, the current results were consistent with previous studies on chin cup, in which the application of chin cup force could hardly alter the mandibular growth pattern, and initial changes might not be well-maintained after discontinuation of chin cup therapy [35, 36]. These results indicated that the mandibular growth tends to return to its original pattern, which may have been predetermined morphogenetically. Therefore, it may be inferred that if the improvement of intermaxillary relationship was achieved more by clockwise rotation of the mandible than by forward growth and/or displacement of the maxilla, the relapse would have a higher possibility of occurrence. Similarly, some studies concluded that maintaining the stability of mandibular plane and gonial angle is favorable for Class III treatment outcomes [15, 32, 37]. Wells et al. [11] suggested that downward-backward rotation of the mandible during treatment increases the chance of long-term failure. Moreover, Cozza et al. [18] advocated using bite-block in preventing the clockwise rotation of mandible.

Regarding the dental changes, compared with that in the CG, the overjet in the TG had a significant increase of 2.41 mm ($P < 0.01$). However, no significant difference in L1/MP angle was found. Based on the results, it could be inferred that the increase in overjet resulted from the improvement in sagittal intermaxillary relationship. Moreover, maxillary protraction could cause inevitable proclination of upper incisors because of mesial dental movement. Therefore, it is assumed that the proclination of upper incisors after protraction may also contribute to the increase in overjet. However, the measurements used in evaluating the angulation of upper incisors are highly variable, and thus, no analysis is conducted with respect to the assumption. This assumption needs to be further explored in future studies.

In contrast to our results, Mandall et al. [26] and Masucci et al. [13] reported no significant difference in overjet between the TG and CG group at the end of follow-up. The reason might be that some patients in the above two studies received fixed appliance treatment during their follow-up period, whereas we analyzed the pure effects of maxillary protraction.

The need for orthognathic surgery

It has long been debated whether maxillary protraction therapy can reduce the need for surgical correction after growth is completed. In reviewing articles, only a few prospective studies answered this question.

Recently, Mandall et al. [26] reported that maxillary protraction therapy can significantly reduce the need for orthognathic surgery (odds ratio = 3.34; 95% CI 1.21–9.24). At the end of the 6-year follow-up, 36% of treated patients in TG needed orthognathic surgery, compared with 66% of the CG. Although the cephalometric variables of SNA, SNB, and ANB did not show significant differences on their own, between the TG and the CG, the accumulation of multiple effects together shift the clinical decision away from surgery. However, the author mentioned that since the patients had remaining growth potential (average 15 years old), these rates may be underestimates. Hagg et al. [38] reported that 7 of 21 treated patients had negative overjet on an average 8-year recall, and at least six (29%) were considered to need surgery. Pangrazio-Kulbersh et al. [28] suggested that early orthopedic treatment might reduce the need for orthognathic surgery, and can increase stability, if surgery is necessary. However, due to the variability of facial growth and different individual response to orthopedic treatments, it is difficult to precisely predict the need for orthognathic surgery in Class III children [39].

Limitations

This systematic review and meta-analysis might be considered a first step in addressing the stability of skeletal and dental effects of maxillary protraction therapy. Although this study provides an overview of the topic, there are several limitations.

One main limitation was the shortage of large and high-quality RCTs. The numbers of relevant research articles and patients included in the meta-analysis were not sufficiently large. Moreover, clinical heterogeneity existed in individual studies. In the quantitative analysis, two studies [17, 27] adopted RME and facemask protocols, while the other two studies [16, 18] used only facemask. As previous studies reported, there is no significant difference in treatment outcomes between RME/non-RME maxillary protraction, except for reduced upper incisor angulation when RME is carried out [1, 7, 40]. Therefore, in the current analysis, data were synthesized in the TG and CG without discriminating the different protocols. In addition, the six cephalometric variables (SNA, SNB, ANB, MPA, overjet, and L1/MP) included in the quantitative analysis may not accurately and completely reflect real skeletal and dental changes. However, the measurements reported by each study are highly variable, which limits our analysis.

Additionally, the duration of follow-up in the studies may not truly reflect prognosis. We intended to include as many prospective controlled trials as possible, which had long-term follow-ups and no active treatment being rendered during follow-up periods. However, due to ethical reasons, the number of studies is limited. Therefore, we selected those studies that had a medium-term follow-up of more than 2 years. As expected, the treatment effects of maxillary protraction may diminish over time as a result of a continued Class III growth pattern. Therefore, future research is required to follow up patients until completion of growth and to determine whether maxillary protraction therapy in Class III children can reduce the need for orthognathic surgery.

Last but not least, some studies proposed that maxillary protractions using skeletal anchorage can produce more favorable treatment changes and fewer side effects [41, 42]; however, whether their treatment effects can be stable remains unclear. Attention should also be paid to the stability of treatment effects of maxillary protractions using skeletal anchorage.

Conclusions

1. Maxillary protraction therapy can produce favorable effects on a short-term basis.
2. During the follow-up period, the posttreatment changes in most variables reflected significant relapse, including backward retrusion of the maxilla, diminution of improvement in the intermaxillary relationship, and a decrease in overjet.
3. Regarding the overall effects, in comparison with those who were untreated, the overjet and sagittal intermaxillary relationship improved in the treated subjects. However, there was no significant difference in the anterior positions of maxilla and mandible between the two groups.
4. In summary, maxillary protraction therapy can be effective in the short term and might improve the sagittal intermaxillary skeletal and dental relationship in the medium term. But some skeletal and dental variables showed significant relapse during the follow-up period. More long-term studies are still required to further evaluate its skeletal benefits and whether this therapeutic approach can reduce the need for orthognathic surgery.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this type of study, formal consent is not required.

Appendix

Table 4 Assessment of risk of bias for the RCT using Cochrane's risk of bias tool

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Mandall et al. [26, 27]	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

Table 5 Quality assessment for non-randomized studies using MINORS

Study	A	B	C	D	E	F	G	H	I	J	K	L	Total
Chen et al. [19]	2	2	2	2	0	2	1	0	1	1	2	2	17
Masucci et al. [13]	2	1	1	2	0	2	1	1	1	1	2	2	16
Cozza et al. [18]	2	1	1	2	0	2	2	0	1	1	2	2	16
Chong et al. [16]	2	1	1	2	0	1	2	0	1	1	2	2	15
Pangrazio-Kulbersh et al. [28]	2	1	1	2	0	2	1	0	0	1	2	2	14
Westwood et al. [15]	2	1	1	2	0	2	1	0	1	0	2	2	14
Ngan et al. [17]	2	1	1	2	0	1	1	0	1	1	2	2	14
Macdonald et al. [29]	2	1	1	2	0	1	1	0	1	0	2	2	13

The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). The full score being 24 for comparative studies

MINORS methodological items for non-randomized studies, *A* a clearly stated aim, *B* inclusion of consecutive patients, *C* prospective collection of data, *D* endpoints appropriate to the aim of the study, *E* unbiased assessment of the study endpoint, *F* follow-up period appropriate to the aim of the study, *G* loss to follow-up less than 5%, *H* prospective calculation of the study size, *I* an adequate control group, *J* contemporary groups, *K* baseline equivalence of groups, *L* adequate statistical analyses

Table 6 Egger's test for the analysis of small study effects or publication bias

	SNA	SNB	ANB	MPA	Overjet	L1/MP
T1–T2	0.821	0.396	0.008*	0.454	0.301	0.082
T2–T3	0.650	0.039*	0.534	0.678	0.991	0.812
T1–T3	0.986	0.856	0.524	0.189	0.732	0.388

*$P < 0.05$

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