Received: 16 October 2023 | Revised: 11 November 2023 | Accepted: 14 December 2023

DOI: 10.1111/ocr.12748

RESEARCH ARTICLE

Orthodontics & Craniofacial Research WILEY

Long-term effects produced by early treatment of Class III malocclusion with rapid maxillary expansion and facemask followed by fixed appliances: A multicentre retro-prospective controlled study

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Abstract

Objective: To assess the short- and long-term dentoskeletal effects of early Class III treatment with rapid maxillary expansion and facemask (RME/FM) followed by fixed appliances.

Materials and Methods: A total of 44 patients (27 females, 17 males) treated consecutively with RME/FM were included from the archives of 3 centres. Three lateral cephalograms were available: T0 (before the start of RME/FM therapy, mean age 8.1 ± 1.8 years), T1 (immediately after RME/FM, mean age 9.8 ± 1.6 years), and T2 (long-term observation, mean age 19.5 ± 1.6 years). A control group of 17 untreated Class III subjects (12 females and 5 males) also was selected. Between-group statistical comparisons were performed with ANCOVA.

Results: No statistically significant differences for any of the cephalometric variables were found at T0. In the short term, the treated group showed significant improvements in ANB (+2.9°), Wits appraisal (+2.7 mm), SNA (+1.8°) and SNB (−1.1°). A significant closure of CoGoMe angle (−1.3°) associated with smaller increments along Co-Gn (−2.4 mm) also was found together with a significant increase in intermaxillary divergence (+1.3°). In the long-term, significant improvements in ANB (+2.6°), Wits appraisal (+2.7 mm) and SNB (−1.7°) were recorded together with a significant closure of the CoGoMe angle (−2.9°). No significant long-term changes in vertical skeletal relationships were found.

Conclusions: RME/FM therapy was effective in improving Class III dentoskeletal relationships in the short term. These changes remained stable in the long-term due mainly to favourable mandibular changes.

KEYWORDS
angle Class III, cephalometry, growth, multicenter study, orthodontics

1 | INTRODUCTION

The long-term stability of early treatment of Class III malocclusion is one of the most controversial and complex issues in orthodontic clinical practice. In Class III patients, unpredictable mandibular overgrowth that is not accompanied by a corresponding maxillary advancement beyond the postpubertal stage can be a risk factor for reduced long-term stability.[1,2] The genetic component of this dentoskeletal disorder appears to play a significant role in its evolution, and the orthodontist has little control over this growth.[3]

Rapid maxillary expansion and facemask (RME/FM) are commonly used together for the orthopaedic treatment of growing Class III patients.[4,5] Systematic reviews on the short-[5–8] and medium-term (at a postpubertal stage of development)[5,8–10] effects produced by RME/FM indicated a good control of the Class III dentoskeletal imbalance. In the short term, a substantial improvement in the ANB angle of about 2.3–3.9° was demonstrated with an increase in the SNA angle (about 1.7–2.1°) and a reduction of the SNB angle (from −1.2 to −1.5°).[6–8,10] From these short-term meta-analyses, a downward and backward rotation of the mandible (1.4–1.6°) associated with an upward rotation of the palatal plane to the cranial base (−0.7 to −0.8°) was also found.[6–8]

Systematic reviews on the medium-term effects induced by RME/FM versus untreated Class III controls showed a significant increase in ANB (1.7°).[8] The SNA angle showed either a stability of its short-term improvement[9] or no significant differences between treated and untreated groups[8,10] in the medium term. A non-significant medium-term reduction in SNB (−0.7°) also was found.[8] No significant medium-term changes in vertical skeletal relationships were detected.[8] According to Kakali et al.,[9] relapse of the anteroposterior correction was due mainly to uncontrolled residual mandibular growth.

Few long-term studies on early treatment of Class III malocclusion are available in the literature.[2,11–14] In most of these long-term studies,[2,11,13] major limitations were the small sample size of the treated group and the lack of a control group of untreated Class III subjects. Masucci et al.[12] compared the treated group to a control group of untreated Class III subjects. For this study,[12] however, the sample size was limited for both the treated (22 patients) and control groups (13 subjects). Le et al[14] analysed the long-term efficacy of RME/FM by comparing a treatment group of 42 Class III patients with a control group of untreated Class III subjects. However, the two groups showed significantly different chronologic ages at baseline and at the long-term observation. Additionally, the long-term changes from initial to final observations in the treatment and control groups were not analysed or compared.

The aim of this multicentre study, therefore, was to evaluate the short- and long-term changes produced by early treatment of Class III malocclusion with RME/FM with respect to a control group of untreated Class III subjects.

2 | MATERIALS AND METHODS

2.1 | Study design

This was a retro-prospective, controlled, multicentre, long-term study. Data gathering relating to this study occurred from December 1989 to November 2022.

2.2 | Setting

The archives of three centres were screened to retrieve consecutively treated patients complying with the eligibility criteria of the study. The three centres were the University of "Tor Vergata", Italy (centre #1), the University of Florence, Italy (centre #2) and the Pontifical Catholic University of Minas Gerais, Belo Horizonte, Brazil (centre #3). Moreover, some of the patients for whom a long-term observation (at 17 years and older for females and at 20 years and older for males) was not available in the archives, were recalled prospectively from June 2020 to November 2022.

2.3 | Participants

The inclusion criteria for the treated group were:

- Caucasian patients with Class III malocclusion who had been treated with RME/FM.
- Prepubertal-to-pubertal stage of maturation at the start of treatment (cervical vertebral maturation, CVM, stages between CS1 and CS3).[15]
- Availability of a lateral cephalogram and panoramic radiograph before the RME/FM (T0).
- Presence of lateral cephalograms immediately after RME/FM (T1, from a minimum of 1 year to a maximum of 3 years after the start of therapy), and at a long-term follow-up (T2) taken at least at 17 years of age for females and 20 years of age for males.

As for patients who were recalled for the T2 record, patients with an age range between 17 and 25 years were considered.

The exclusion criteria were the following:

- Patients affected by cleft lip and/or cleft palate.
- Patients with craniofacial syndromes or with congenitally missing or supernumerary teeth.

For recalled patients, pregnant women were excluded.

The characteristics of the first and second phases of treatment for the three centres are reported in Table S1.

A control group of subjects with untreated Class III malocclusion was derived from a database described previously.[16] The inclusion criterion for the control sample was the availability of 3 longitudinal cephalograms taken at a prepubertal-to-pubertal stage of maturation (CVM stages between CS1 and CS3) (T0), after a minimum of 1 year to a maximum of 3 years from T0 (T1), and at a long-term follow-up (T2) at least 17 years of age for females and 20 years of age for males.

2.4 | Variables

The primary outcome variables were the ANB angle and the Wits appraisal.[17] The latter method involves constructing perpendiculars from Point A on the maxilla and Point B on the mandible onto the occlusal plane and measuring the distance between the 2 constructed perpendicular lines. The secondary outcome variables included all the other dentoskeletal cephalometric variables.

Digital cephalograms for both treated and control samples were available at 150 dpi. All cephalograms were digitized with a cephalometric software (Viewbox version 4.1.0.12, dHal Software), and they were standardized to 0% magnification (life size). The 15 cephalometric variables (10 angular, 5 linear) that were measured are illustrated in Figure 1 and described in Table S2. CVM stages[15] also were assessed in all cephalograms for both treated and control groups.

2.5 | Methods of collecting data

For all patients, the following data were gathered: gender, age at the three lateral cephalograms, and clinical history (time of facemask wear, type of retention after the first phase of treatment, second phase of treatment and duration, and type of retention after the second phase of treatment) (Table S1). For the control group, gender and age at the three lateral cephalograms were recorded. The long-term unsuccess rates for both treated patients and control subjects also were assessed following the method described by Souki et al.[18] that was based on the assessment of molar relationships, overjet and profile features.

2.6 | Intraobserver reproducibility

Twenty cephalograms were selected randomly from the total sample and digitized. The same cephalograms were re-digitized after a

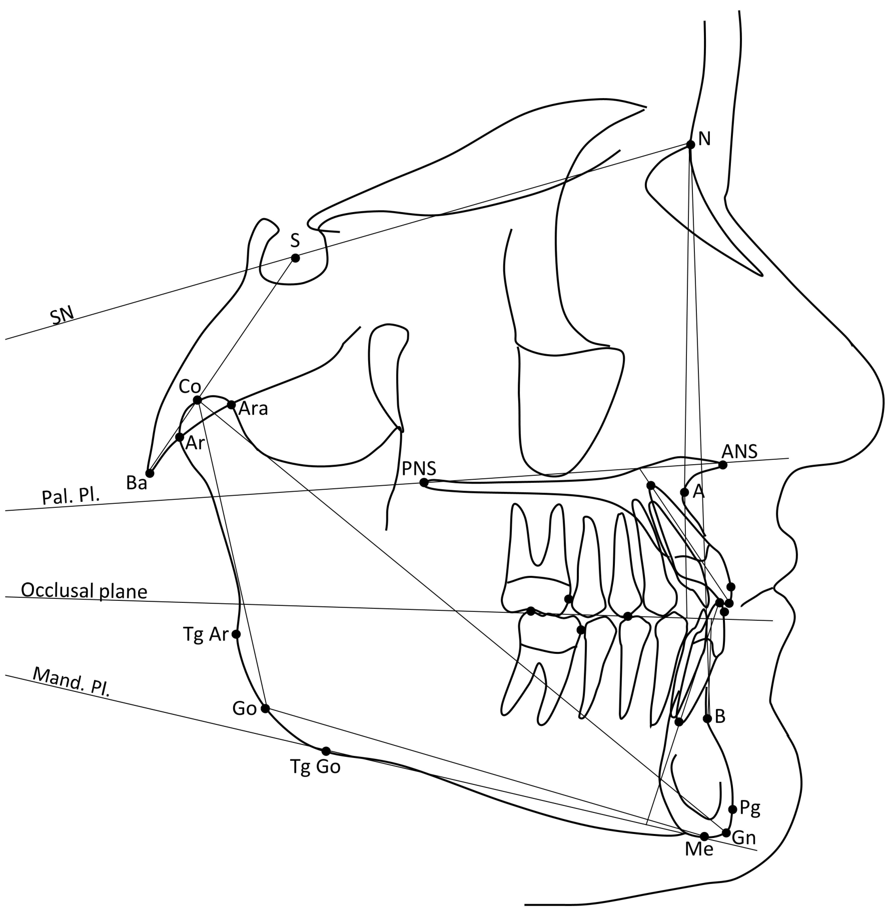

FIGURE 1 Cephalometric variables. SN line: line between Sella and Nasion points. Pal.Pl.: line passing through ANS and PNS points. Occlusal plane: line passing through a contact point on the first permanent molars and a contact point on the first permanent premolars. Mand.Pl.: line passing through point Menton and tangent to the lower border of the mandible in the gonial region.

wash-out period of 2 weeks by the same operator (V.R.) to check for intraobserver reproducibility for both the cephalometric variables and the CVM stages.

2.7 | Bias

Selection bias was reduced by including all patients treated consecutively in the period from December 1989 to November 2022 who complied with the inclusion criteria.

2.8 | Ethical permission

This research was approved by the Comitato Etico Regione Toscana Area Vasta Centro (number 16409_oss of 5-5-2020). The Ethics Committee verified the compliance of the study with the Good Clinical Practice of the European Union and the ethical principles expressed in the Helsinki Declaration. For recalled patients, all patients were first informed by phone of the characteristics of the study, and then written informed consent was obtained.

2.9 | Study size

To detect a clinically relevant difference in the Wits appraisal of 2 mm with a standard deviation of 2 mm,[12] an alpha of 0.05 and a power of 80%, a minimum sample size of 17 patients in each group was required (PS: Power and Sample Size Calculation, version 3.1.6, open-source, https://biostat.app.vumc.org/wiki/Main/PowerSampleSize). To reduce selection bias, all patients in the three centres who fulfilled the inclusion criteria were included in the study.

2.10 | Statistical methods

Intra-observer reproducibility for the cephalometric variables and for the CVM stages was performed with intraclass correlation coefficients and a weighted K-function, respectively. Descriptive statistics were performed using means and standard deviations for quantitative variables as well as the frequency and percentage for qualitative variables. Independent sample t-tests were performed for intergroup statistical comparisons for age and all cephalometric variables at baseline (T0) and for age at the long-term observation (T2). Statistical comparisons for the two dichotomous nominal variables (gender and CVM stage) were performed with a Fisher's Exact Test (FET). For the intergroup differences during the short-term (T0-T1), post-treatment (T1-T2) and long-term (T0-T2) intervals, an analysis of covariance (ANCOVA) was carried out with the values of the cephalometric variables at baseline as covariates. For the comparison of long-term unsuccess rate, the odds ratio was calculated. All statistical computations were performed with statistical software (JMP vers. 13.0.0; SAS Institute Inc, and MedCalc version 19.6.4, MedCalc Software Ltd.).

3 | RESULTS

The intraclass correlation coefficient (ICC) was excellent[19] for both the cephalometric variables (ranging from 0.92 for the Wits appraisal to 0.99 for the SNA angle) and the CVM stages (0.99).

3.1 | Participants

All patients who fulfilled eligibility criteria at the three centres were included in the study. The flow diagram for the assessment of the eligibility of patients was reported in Supplementary Figure S1.

A final sample of 44 patients (32% from centre #1, 27% from centre #2, 41% from centre #3), 27 females and 17 males, with a mean age at T0 of 8.1 ± 1.8 years, at T1 of 9.8 ± 1.6 years, and at T2 of 19.5 ± 1.6 years, was included. Of these patients, 3 patients in centre #1, 6 patients in centre #2, and 8 patients in centre #3 were re-called for long-term observation. Thirty-four out of the 44 patients of the present study were included also in a recent study.[20]

The control group consisted of 17 subjects (12 females and 5 males) with a mean age at T0 of 8.3 ± 2.4 years, at T1 of 10.2 ± 2.1 years, and at T2 of 18.8 ± 1.7 years.

3.2 | Descriptive data and main results

As for gender and CVM distribution, no significant differences were recorded for the two groups at baseline (Fisher exact probability test: females $p = .565$; CVM ≥ 3 $p = .191$) (Table 1). No significant differences between the two groups were found for chronological age at baseline (Table 1) or at T2 (Table 2). No significant between-group differences were found for any of the cephalometric variables at baseline (Table 1).

3.2.1 | Short-term changes (T1-T0)

As for the sagittal skeletal variables, both ANB and the Wits appraisal increased significantly in the treated group (ANB +2.9°, 95% CI from 1.9 to 3.9°, $p < .001$; Wits appraisal +2.7 mm, 95% CI from 1.4 to 4.1 mm, $p < .001$; Table 3). SNA increased significantly by 1.8° (95% CI from 0.9 to 2.7°, $p < .001$), while SNB decreased significantly by 1.1° in the treated group with respect to untreated controls (95% CI from −1.9 to −0.4°, $p = .002$).

As for the vertical skeletal relationships, the treated group showed a significant increase in intermaxillary divergence (Pal.Pl.-Mand.Pl.) (1.3°, 95% CI from 0.0 to 2.7°, $p = .048$), and a significant

TABLE 1 Descriptive statistics and between-group statistical comparisons at baseline (T0).

	Treated group N = 44 (SD)	Untreated group N = 17 (SD)	*p* Value
Females	27 (61%)	12 (71%)	.565 (FET)
Age	8.1 (1.8)	8.3 (2.4)	.679
Centre	1. 14 (32%)		
	2. 12 (27%)		
	3. 18 (41%)		
CVM ≥3	1 (2.3%)	2 (11.8%)	.191 (FET)
NSBa°	131.2 (4.6)	130.1 (4.5)	.373
SNA°	79.2 (4.0)	78.2 (4.2)	.425
SNB°	78.0 (3.8)	76.8 (4.5)	.295
ANB°	1.2 (2.0)	1.5 (1.8)	.631
Wits mm	−5.5 (2.8)	−5.5 (2.2)	.951
SN-Pal. Pl.°	9.5 (2.9)	10.3 (4.1)	.406
SN-Mand. Pl.°	37.3 (4.6)	38.8 (4.5)	.304
Pal. Pl.-Mand. Pl.°	27.8 (3.9)	28.6 (5.5)	.562
Co-Gn mm	97.8 (5.5)	95.9 (4.9)	.211
CoGoMe°	128.8 (4.8)	130.0 (5.4)	.415
OVJ mm	−0.9 (2.1)	0.2 (1.5)	.058
OVB mm	0.2 (2.0)	0.7 (1.4)	.370
Mol. Rel. mm	3.0 (1.9)	3.9 (2.0)	.107
Upper Inc.-Pal. Pl.°	108.4 (8.7)	108.8 (7.2)	.864
Lower Inc.-Mand. Pl.°	87.2 (7.2)	85.2 (8.2)	.340

Abbreviations: FET, Fisher's Exact Test; Inc., Incisor.; Mand., Mandibular; Mol., Molar; Pal., Palatal; Pl., Plane; Rel., Relationship; SD, Standard deviation.

TABLE 2 Descriptive statistics and between-group statistical comparison for chronologic age at T2.

	Treated group N = 44 (SD)	Control group N = 17 (SD)	*p* Value
Age	19.5 (1.6)	18.8 (1.7)	.149
NSBa°	131.5 (5.4)	130.6 (4.9)	
SNA°	80.7 (4.3)	78.8 (3.8)	
SNB°	79.6 (4.5)	80.2 (4.4)	
ANB°	1.1 (2.8)	−1.3 (1.6)	
Wits mm	−4.4 (2.7)	−7.2 (3.5)	
SN-Pal. Pl.°	9.6 (3.6)	11.0 (4.0)	
SN-Mand. Pl.°	34.8 (6.3)	37.2 (6.5)	
Pal. Pl.-Mand. Pl.°	25.2 (6.2)	26.2 (5.9)	
Co-Gn mm	117.0 (6.9)	118.8 (4.8)	
CoGoMe°	125.0 (6.4)	129.1 (6.8)	
OVJ mm	1.6 (1.1)	−0.5 (1.7)	
OVB mm	1.3 (1.3)	0.2 (1.2)	
Mol. Rel. mm	3.0 (1.9)	5.8 (2.1)	
Upper Inc.-Pal. Pl.°	117.1 (6.1)	118.6 (6.9)	
Lower Inc.-Mand. Pl.°	88.5 (7.6)	85.0 (9.9)	

Abbreviations: Inc., Incisor; Mand., Mandibular; Mol., Molar; Pal., Palatal; Pl., Plane; Rel., Relationship; SD, Standard deviation.

decrease in the inclination of the palatal plane to SN with respect to the control group (−0.9°, 95% CI from −1.8 to −0.1°, $p = .038$). A statistically significant decrease in the mandibular angle (CoGoMe) was also found in the treated group with respect to the untreated controls (−1.3°, 95% CI from −2.4 to −0.1°, $p = .031$). Total mandibular length showed a significantly smaller increase compared to controls (−2.4 mm, 95% CI from −3.8 to −1.1 mm, $p = .041$).

As for the dentoalveolar variables, overjet increased significantly (2.6 mm, 95% CI from 1.8 to 3.5 mm, $p < .001$), while molar relationship decreased significantly (−3.6 mm, 95% CI from −4.8 to −2.4 mm, $p < .001$) in the treated group with respect to the untreated controls.

3.2.2 | Post-treatment changes (T2-T1)

During the follow-up interval, no significant between-group changes were found for any of the sagittal or vertical skeletal variables (Table 4). As for the dentoalveolar variables, the treated group exhibited a significant increase in overjet (1.2 mm, 95% CI from 0.3 to 2.0 mm, $p = .008$) and overbite (1.2 mm, 95% CI from 0.5 to 1.9 mm, $p = .001$) and a significant decrease in molar relationship with respect to the control sample (−2.4 mm, 95% CI from −3.9 to −0.9 mm, $p = .002$). The mandibular incisors showed a significant increased proclination with respect to the mandibular plane in the treated group with respect to the control group (4.1°, 95% CI from 0.9 to 7.2, $p = .012$).

3.2.3 | Long-term changes (T2-T0)

Both ANB and Wits appraisal values increased significantly in the treated group with respect to the control group (2.6° for ANB angle, 95% CI from 1.5 to 3.7°, $p < .001$; 2.7 mm for the Wits appraisal, 95% CI from 1.1 to 4.4 mm, $p = .001$; Table 5). No significant between-group changes were found for SNA (1.0°, 95% CI from −0.1 to 2.1°, $p = .075$), while a significant decrease in the SNB angle was recorded in the treated group with respect to the control sample (−1.7°, 95% CI from −3.1 to −0.3°, $p = .021$). The mandibular angle (CoGoMe) decreased significantly in the treated group with respect to the untreated Class III controls (−2.9°, 95% CI from −4.9 to −0.9°, $p = .006$).

As for the dentoalveolar variables, overjet and overbite increased significantly (2.1 mm, 95% CI from 1.3 to 2.9 mm, $p < .001$ and 1.3 mm, 95% CI from 0.7 to 2.0 mm, $p < .001$, respectively), while the molar relationship decreased significantly in the treated group

TABLE 3 Descriptive statistics and statistical comparisons between treated and control groups for the T1-T0 changes.

	Treated group N = 44 (SD)	Control group N = 17 (SD)	Difference[a]	95% CI	*p* Value (ANCOVA)
Follow-up period	1.7 ± 0.4	1.9 ± 0.6	−0.2	−0.5; 0.0	.066
NSBa°	0.4 (1.9)	0.0 (1.8)	0.4	−0.7; 1.5	.448
SNA°	1.7 (1.6)	−0.1 (1.1)	1.8	0.9; 2.7	<.001
SNB°	−0.5 (1.3)	0.7 (1.3)	−1.1	−1.9; −0.4	.002
ANB°	2.2 (2.0)	−0.8 (1.1)	2.9	1.9; 3.9	<.001
Wits mm	2.0 (3.3)	−0.7 (2.4)	2.7	1.4; 4.1	<.001
SN-Pal. Pl.°	−1.0 (1.5)	−0.1 (1.5)	−0.9	−1.8; −0.1	.038
SN-Mand. Pl.°	0.5 (1.8)	0.1 (1.6)	0.4	−0.6; 1.4	.467
Pal. Pl.-Mand. Pl.°	1.4 (2.5)	0.2 (1.8)	1.3	0.0; 2.7	.048
Co-Gn mm	3.9 (2.6)	6.5 (1.6)	−2.4	−3.8; −1.1	.041
CoGoMe°	−1.2 (2.0)	0.1 (1.9)	−1.3	−2.4; −0.1	.031
OVJ mm	3.6 (2.3)	0.1 (1.5)	2.6	1.8; 3.5	<.001
OVB mm	0.2 (2.3)	−0.1 (1.4)	0.1	−1.1; 1.2	.887
Mol. Rel. mm	−2.6 (2.2)	0.4 (2.5)	−3.6	−4.8; −2.4	<.001
Upper Inc.-Pal. Pl.°	4.5 (6.8)	4.9 (9.5)	−0.6	−3.9; 2.6	.694
Lower Inc.-Mand. Pl.°	−0.4 (5.2)	2.3 (8.6)	−2.0	−5.3; 1.3	.227

Abbreviations: CI, Confidence interval; Inc., Incisor; Mand., Mandibular; Mol., Molar; Pal., Palatal; Pl., Plane; Rel., Relationship; SD, Standard deviation.
[a]Adjusted difference according to ANCOVA.

TABLE 4 Descriptive statistics and statistical comparisons between treated and control groups for the T2-T1 changes.

	Treated group N = 44 (SD)	Control group N = 17 (SD)	Difference[a]	95% CI	*p* Value (ANCOVA)
Follow-up period	9.7 (1.6)	8.6 (2.7)	0.8	−0.1; 1.7	.074
NSBa°	−0.1 (2.1)	0.5 (2.5)	−0.6	−1.9; 0.7	.372
SNA°	−0.2 (1.9)	0.7 (1.4)	−0.6	−1.6; 0.5	.276
SNB°	2.2 (1.9)	2.7 (2.1)	−0.5	−1.6; 0.7	.404
ANB°	−2.4 (1.9)	−2.0 (1.7)	0.1	−1.3; 1.1	.869
Wits mm	−1.0 (2.9)	−1.0 (2.8)	1.2	−0.5; 3.0	.154
SN-Pal. Pl.°	1.1 (2.0)	0.8 (1.9)	0.2	−1.0; 1.3	.752
SN-Mand. Pl.°	−3.0 (2.9)	−1.7 (3.3)	−1.2	−3.0; 0.5	.156
Pal. Pl.-Mand. Pl.°	−4.1 (3.3)	−2.6 (2.6)	−1.6	−3.4; 0.2	.089
Co-Gn mm	15.3 (6.0)	16.4 (7.3)	−1.5	−4.8; 1.9	.387
CoGoMe°	−2.7 (3.4)	−0.9 (3.5)	−1.6	−3.6; 0.4	.111
OVJ mm	−1.1 (1.5)	−0.7 (1.4)	1.2	0.3; 2.0	.008
OVBmm	0.9 (2.5)	−0.5 (1.4)	1.2	0.5; 1.9	.001
Mol. Rel. mm	2.6 (2.8)	1.5 (2.6)	−2.4	−3.9; −0.9	.002
Upper Inc.-Pal. Pl.°	4.2 (5.8)	4.9 (6.2)	−1.0	−4.0; 1.9	.484
Lower Inc.-Mand. Pl.°	1.7 (5.6)	−2.5 (5.5)	4.1	0.9; 7.2	.012

Abbreviations: CI, Confidence interval; Inc., Incisor; Mand., Mandibular; Mol., Molar; Pal., Palatal; Pl., Plane; Rel., Relationship; SD, Standard deviation.
[a]Adjusted difference according to ANCOVA.

with respect to the control group (−2.7 mm, 95% CI from −3.9 to −1.5 mm, $p < .001$).

The long-term unsuccess rate was significantly smaller in the treated group (25%, 11 out of 44 patients, 8 females, and 3 males) with respect to the control group (65%, 11 out of 17 patients, 8 females, and 3 males) (odds ratio 0.18, 95% CI from 0.05–0.61, $p = .007$).

4 | DISCUSSION

4.1 | Key results and interpretation

This study investigated the short- and long-term changes associated with early treatment of Class III malocclusion with RME/FM

TABLE 5 Descriptive statistics and statistical comparisons between treated and control groups for the T2-T0 changes.

	Treated group N = 44 (SD)	Control group N = 17 (SD)	Difference[a]	95% CI	p Value (ANCOVA)
Follow-up period	11.4 (1.7)	10.5 (2.9)	0.7	−0.1; 1.6	.098
Unsuccess	11 (25%)	11 (65%)	0.18 (Odds ratio)	0.05; 0.61	.007 (FET)
NSBa°	0.3 (2.5)	0.5 (2.2)	−0.2	−1.7; 1.2	.738
SNA°	1.5 (2.0)	0.6 (1.6)	1.0	−0.1; 2.1	.075
SNB°	1.7 (2.3)	3.4 (2.8)	−1.7	−3.1; −0.3	.021
ANB°	−0.2 (1.9)	−2.8 (2.1)	2.6	1.5; 3.7	<.001
Wits mm	1.0 (3.4)	−1.7 (3.4)	2.7	1.1; 4.4	.001
SN-Pal. Pl.°	0.1 (2.0)	0.7 (2.1)	−0.6	−1.8; 0.6	.299
SN-Mand. Pl.°	−2.5 (2.8)	−1.6 (4.3)	−0.8	−2.7; 1.1	.391
Pal. Pl.-Mand. Pl.°	−2.7 (3.4)	−2.3 (3.5)	−0.2	−2.1; 1.7	.831
Co-Gn mm	19.1 (6.2)	22.9 (7.4)	−2.7	−6.2; 0.7	.115
CoGoMe°	−3.9 (3.1)	−0.9 (4.4)	−2.9	−4.9; −0.9	.006
OVJ mm	2.5 (2.6)	−0.6 (1.2)	2.1	1.3; 2.9	<.001
OVB mm	1.1 (1.7)	−0.5 (1.5)	1.3	0.7; 2.0	<.001
Mol. Rel. mm	0.0 (2.7)	1.9 (2.6)	−2.7	−3.9; −1.5	<.001
Upper Inc.-Pal. Pl.°	8.7 (8.0)	9.8 (9.6)	−1.4	−4.8; 2.0	.418
Lower Inc.-Mand. Pl.°	1.3 (5.8)	−0.1 (8.6)	2.0	−1.7; 5.7	.285

Abbreviations: CI, Confidence interval; FET, Fisher's Exact Test; Inc., Incisor; Mand., Mandibular; Mol., Molar; Pal., Palatal; Pl., Plane; Rel., Relationship; SD, Standard deviation.
[a]Adjusted difference according to ANCOVA.

compared to growth variations in untreated Class III subjects. To our knowledge, this is the first controlled study that evaluated the long-term changes produced by early treatment with RME/FM in a relatively large sample of Class III patients with respect to growth in untreated Class III subjects. The evaluation of long-term outcomes of early Class III treatment is crucial because it has been shown that a relapse during the adolescent or post-adolescent periods may occur with an increase in the treatment failure rate.[2]

4.2 | Short-term changes (T1-T0)

Immediately after RME/FM therapy, the significant improvements in sagittal skeletal relationships, with an increase of almost 3° in ANB and of 2.7 mm in the Wits appraisal, had to be ascribed mainly to a significant maxillary protraction (SNA +1.8°) rather than to a significant, though not clinically relevant, mandibular retrusion (SNB −1.1°). These favourable sagittal skeletal changes agree with previous short-term systematic reviews[5–8,10] where a significant maxillary protraction (SNA from +1.7 to +2.1°) associated with a significant mandibular retrusion (SNB from −1.1 to −1.5°) leading to a significant increase in ANB (from +2.3 to +3.9°) was reported with respect to untreated Class III subjects.

As for vertical skeletal relationships, a significant increase in intermaxillary divergence was found in the present study, together with a significant counterclockwise rotation of the palatal plane (+1.3° Pal-Pl.-Mand. Pl.; −0.9° SN-Pal.Pl.). These changes, however, were not clinically relevant as they were smaller than 1.5 degrees. The 30° downward pull of the elastics relative to the occlusal plane may have contributed to controlling the vertical skeletal changes.[6]

When compared to untreated controls, a clockwise rotation of the mandibular plane and a counterclockwise rotation of the palatal plane have been reported in previous studies.[6–8] The clockwise rotation of the mandibular plane can improve the Class III sagittal skeletal relationship by increasing lower anterior facial height. This effect, however, could be detrimental to high-angle Class III patients.

In the present study, the significant closure of the mandibular angle (−1.3°) could have contributed to the significantly smaller increases in total mandibular length (−2.4 mm) with respect to untreated Class III controls. Previous controlled studies did not find any significant difference in the mandibular angle between the treated and control groups in the short-term.[1,12] The inclusion of only prepubertal patients (except one at CS 3) at T0 could explain the significant closure of the mandibular angle.[12]

As for the short-term dentoalveolar changes, there was a statistically significant improvement in both overjet (+2.6 mm) and molar relationship (−3.6 mm) that could be due to a maxillary molar mesialization rather than a mandibular distalization. The favourable change in overjet has been reported also in a previous systematic review.[8] Maxillary molar mesialization was reported extensively as a major side effect of dentally anchored maxillary expanders.[21,22] Bone-anchored facemasks have been shown to reduce or eliminate the mesialization of maxillary permanent molars.[23]

4.3 | Post-treatment changes (T2-T1)

During the follow-up interval, only significant dentoalveolar changes were observed, without significant sagittal or vertical skeletal changes between the two groups. Significant increases in both overjet (+1.2 mm) and overbite (+1.2 mm) were found, together with a significant improvement in the molar relationship (−2.4 mm). The short-term improvement in the overjet tended to decrease during the posttreatment period, though it maintained a positive value. A significant proclination of the mandibular incisors to the mandibular plane (+4.1°) also was detected; it could be ascribed, at least in part, to the effects produced by fixed appliance therapy. It should be noted that the amount of proclination of the lower incisors in the treated group was not clinically relevant (+1.7°). The relatively high value for the T2-T1 difference in the proclination of the mandibular incisors to the mandibular plane (+4.1°) has to be attributed mainly to the retroclination of the lower incisors in the control group as a result of dento-alveolar compensation to Class III occlusal relationships. These dentoalveolar findings also were reported in previous systematic reviews.[5,8,9]

4.4 | Long-term changes (T2-T0)

During the overall long-term observation period, a significant improvement in the sagittal intermaxillary relationship was found. ANB and Wits appraisal improvements that were achieved during the short-term period remained stable during the long-term interval (+2.6° and + 2.7 mm, respectively). These favourable sagittal skeletal modifications, however, must be attributed primarily to a significant control of mandibular sagittal position (SNB −1.7°) rather than to a non-significant maxillary advancement (SNA +1.0°). It should be noted that when looking at the long-term T2-T0 changes that occurred in SNA in the treated group, the value of +1.5° is similar to that shown during the short-term T1-T0 changes (+1.7°). The non-significant maxillary advancement (SNA +1.0°) during the long-term follow-up period (T2-T0) has to be ascribed mainly to the small amount of maxillary advancement that occurred in the control group (+0.6°). This observation is consistent with a previous long-term controlled study,[12] which reported a long-term decline in maxillary protraction gains in Class III patients compared to untreated controls. The long-term reduction of the maxillary protraction effect has been noted also in the medium-term, before the end of the mandibular growth.[8,10]

In the current study, the SNB angle decreased by approximately 2°. This finding is consistent with a previous long-term study[12] that identified an equivalent difference between Class III treated patients and untreated controls.

Vertical skeletal relationships did not increase during the overall interval. In both treated and control groups, intermaxillary divergence decreased by the same amount for the T2-T0 changes. The significant increase in intermaxillary divergence in the short-term tended to relapse during the post-treatment period. This outcome agrees with a previous study that did not report long-term differences in vertical skeletal relationships[12] and with two systematic reviews on the medium-term effects of RME/FM.[8,9]

The mandibular angle (CoGoMe) decreased significantly by almost 3° in the treated group with respect to the untreated Class III controls. This growth modification has been described as a mechanism that can be effective in controlling or dissipating excessive mandibular growth along Co-Gn.[24] The closure of the mandibular angle as a mechanism to control total mandibular length has been reported previously by Deguchi et al.[25] who analysed the long-term effects produced by the chincup. The Authors wrote: “Furthermore, a decrease (closing) in the gonial angle and a forward bending of the condylar neck induced by the chincup may contribute to shortening the effective mandibular lengths (Ar-Me, Gn-Co)”. Using a morphometric analysis (thin-plate spline), a long-term study on Class III patients treated with RME/FM[26] showed that both the mandibular rami and condyles grew in an upward and forward direction in the treated group, leading to a “shrinkage” of the mandible along Co-Gn. In the present study, the significant closure of the mandibular angle was associated with smaller increments, though not statistically significant, along total mandibular length in the treated group with respect to the untreated Class III controls (−2.7 mm). Similarly, Masucci et al.[12] reported nonsignificant long-term smaller increments along total mandibular length in the treated group versus untreated Class III controls (−3.9 mm), though not statistically significant.

As for the dentoalveolar variables, both the overjet and molar relationships improved significantly in the treated group in the long-term (+2.1 and −2.7 mm, respectively). Masucci et al.[12] found no significant long-term changes in overjet between the treated and untreated groups (+1.2 mm), while the improvement in molar relationship remained statistically significant in the treated sample (−3.2 mm).

In the current study, the long-term unsuccess rate was 25%, a percentage that was very similar to the value (27%) reported by Masucci et al.[12] Previous long-term studies reported an unsuccess rate percentage that varied from 0% to 45%.[2,11,13,14] The only RCT in the medium term (with a follow-up 6 years after the start of treatment) reported that 36% of the patients needed orthognathic surgery.[27]

4.5 | Strengths and limitations

To our knowledge, this controlled study includes the largest sample of Class III patients treated with RME/FM with a follow-up of at least 17 years of age in females and at least 20 years of age in males.

Long-term follow-up observations are important for all types of orthodontic treatment, but especially for Class III malocclusion, where active mandibular growth has been shown to continue long after the postpubertal phase.[16]

In this study, the treatment protocol was homogenous in the 3 participating centres regarding duration of treatment and modality of orthopaedic and orthodontic approach. Some heterogeneity was present for the types of appliances used (rapid maxillary expander, type of facemask, and type of retention).

Additionally, the relatively large attrition of the sample over time was due to the fact that patients declined to come back to the long-term follow-up visit because they had moved abroad for working reasons or they refused to perform a lateral cephalogram. We cannot exclude that some of the patients did not come back because he/she was not satisfied with treatment outcomes.

Another limitation of this study was the presence of a historical longitudinal control group with patients derived from Growth Study Centers in USA and Canada and from the University of Florence, Italy. Due to the low prevalence of Class III malocclusion and the unethical decision of leaving patients with a Class III malocclusion untreated, it became impossible to obtain a contemporary long-term control sample.

5 | CONCLUSIONS

- In the short term, RME/FM treatment significantly improved sagittal skeletal changes in comparison to untreated Class III patients. These favourable changes were due mainly to maxillary protraction rather than to mandibular retrusion. A significant closure of the mandibular angle was associated with significantly smaller increments along total mandibular length. Significant improvements in overjet and molar relationship were also observed.
- In the long term, Class III maxillomandibular relationship improvements remained stable, primarily due to favourable mandibular changes rather than to maxillary protraction. A significant closure of the CoGoMe angle was found in the treated group. This closure of the mandibular angle was associated with smaller increments, though not statistically significant, along total mandibular length in the treated group with respect to untreated Class III controls. Overjet, overbite, and molar relationship improved significantly in the treated group.
- The prevalence of long-term failure was substantially lower in the treated group (25%) than in the control group (65%).

AUTHOR CONTRIBUTIONS

VR selected patients of centre #2 and wrote the first draft of the manuscript. BQS treated patients of centre #3 and edited the manuscript. MN organized collected data, performed statistical analysis and edited the manuscript. ALFMC selected patients of centre #3. CP and PC treated and selected patients of centre #1. VG and JAMcJr reviewed the literature and edited the manuscript. LF designed the study and edited the manuscript. All authors read and approved the final manuscript.

FUNDING INFORMATION

No funding was received for this study.

CONFLICT OF INTEREST STATEMENT

All authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The authors make the data from this study accessible upon reasonable request.

ETHICS STATEMENT

This is a retro-prospective follow-up study with historical controls involving no drugs or medical devices. Full compliance with the principles of ethics and good clinical practice is declared. This research was approved by the Comitato Etico Regione Toscana Area Vasta Centro (number 16409_oss of 5-5-2020).

ACQUISITION OF INFORMED CONSENT AND DATA PROCESSING

The present study included data from archives. Every effort was made to obtain consent from patients. For the prospective part of this study, informed consent has been acquired.

PROTOCOL

The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines[28] were followed.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Rutili V, Souki BQ, Nieri M, et al. Long-term effects produced by early treatment of Class III malocclusion with rapid maxillary expansion and facemask followed by fixed appliances: A multicentre retro-prospective controlled study. *Orthod Craniofac Res*. 2024;27:429-438. doi:10.1111/ocr.12748