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TURKISH JOURNAL OF
ORTHODONTICS

Original Article

Assessment of Maxillary Molar Tooth Changes Caused by Class III Elastics in Hybrid Hyrax-Mentoplate Treatments: A Pilot Study

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Main Points

- Dental extrusion occurs in the molar teeth, even with the use of skeletal anchorage.
- The transversal width is more at apical level than coronal due to elastic usage.
- Due to mesial tipping, the molar teeth move mesially despite the skeletal anchorage.

ABSTRACT

Objective: This study aimed to investigate the positional changes of maxillary first molars in patients treated with the hybrid hyrax-mentoplate and Cl III elastics combination using cone-beam computed tomography (CBCT).

Methods: Ten patients (7 females-3 males, mean age: 11.66±0.83 years) treated with hybrid hyrax-mentoplate at Marmara University Department of Orthodontics were included. Angular and linear measurements were taken from pre-treatment and post-treatment CBCT images, and changes in maxillary first molar teeth were examined using 3D SLICER version 5.0.2 (www.slicer.org). Statistical significance was set at p≤0.05.

Results: Significant increases were observed in all distance measurements except C16p-C26p in the coronal plane, and significant decreases were observed in angular measurements only at 16mb and 26mb (p≤0.05). All measurements in the sagittal plane significantly increased compared to the vertical and horizontal reference lines (p≤0.001). Angular measurements relative to the palatal reference line significantly increased only in P-16p, P-26mb, and P-26p (p≤0.05). In skeletal measurements, significant changes were observed only in V-A, V-ANS, H-PNS, and V-PNS measurements (p≤0.05). The expansion at the apical level was significantly higher than that at the coronal level (p≤0.05). Compared to the V line, more mesial movement was observed at the coronal level than at the apical level (p≤0.001).

Conclusion: The use of Class III elastics causes greater expansion at the apical level than the coronal. Molar teeth exhibit a mesial movement, but there could be multiple contributing factors. In molars connected to Class III elastics, extrusion occurs. When vertical control is important, appropriate safety measures are advised.

Keywords: Angle Class III, orthodontic appliances, orthodontic anchorage procedures

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INTRODUCTION

Different techniques are used during the different growth and development period for the orthopedic treatment of Class III malocclusions. While the facemask appliance, whose effectiveness has been proven, is utilized in conjunction with appliances supported by maxillary teeth, orthopedic therapy procedures utilizing various intra-oral anchorage units have also gained prominence due to technological advancements.[1,2] Appliances placed on the maxilla for anchorage can be tooth-borne, bone-borne, or tooth-bone-borne.[3-5] Particularly, tooth-borne appliances cause mesial movement in the maxillary dentition with the effect of orthopedic forces.[2] However, when bone-borne anchorage units are used, this effect is very minimal or non-existent.[6,7]

Maxillary expansion is a common method to increase the effectiveness of orthopedic forces.[2,8] The hybrid hyrax appliance can be used as a maxillary anchorage unit in Class III orthopedic treatments since it can expand and become a unit of anchorage.[1] Among publications in which hybrid hyrax was used as a maxillary anchorage unit in the orthopedic treatment of Class III malocclusions, only four publications investigating maxillary molar movements were found. These studies were not only specific to upper molar movements but also examined the general effects of the technique, and while some reported significant changes in the upper molars the orhers reported insignificant changes.[1,2,4,8] Three of the studies were conducted on lateral cephalometric X-rays.[2,4,8] Two-dimensional (2D) imaging has some disadvantages such as distortion in anatomical structures and inability to mark points accurately due to overlaps in images.[9] Moreover, in the another study that uses the intraoral models for examination, the movement of the roots in three-dimensional (3D) planes was neglected.[1] However, the movements of the maxillary molar teeth in 3 planes (coronal, sagittal, and horizontal) are important for both dental and skeletal effects that may occur during orthopedic treatment and also for the dental development that will continue afterward. To the best of our knowledge, there is no study in the literature examining the movements of maxillary molars in all three planes in which a hybrid hyrax appliance was used as a skeletal anchorage unit in the maxilla in the orthopedic treatment of Class III malocclusions. Therefore, the aim of this study was to examine the movements of the maxillary molars of patients treated with the hybrid hyrax-mentoplate and Class III elastic combination in 3D using cone-beam computed tomography (CBCT) data.

METHODS

Ethical Approval and Patient Selection

This retrospective study was approved by the Marmara University Faculty of Medicine Non-Drug and Medical Device Research Ethics Committee (approval no.: 09.2024.623, date: 08.07.2024). The inclusion criteria were as follows:

- Patients treated with hybrid hyrax-mentoplate for the orthopedic correction of Class III skeletal malocclusions,
- A concave profile,
- Dental Class III molar or canine relationship,
- Overjet ≤0,
- ANB angle ≤0,
- No skeletal unit failure during treatment,

The exclusion criteria were as follows:

- Craniofacial deformity, growth disorder, or hormonal disorder,
- Missing files, routine records, or CBCT data,
- Non-cooperative patients.

Considering these criteria, the data of 10 patients (7 females and 3 males, mean age: 11.66±0.83 years) were retrieved from the archive of Marmara University Faculty of Dentistry, Department of Orthodontics and included in the study. All included patients have an informed consent form in their files.

Treatment Protocol

Based on data gathered from patient files, two miniscrews with a diameter of 1.7 mm and a length of 8 mm (OrthoEasy® Pal Forestadent®, Bernhard Foerster GmbH, Pforzheim, Germany) were placed on both sides of the midpalatal suture, near the level of the third rugae.[10] To create a hybrid hyrax appliance, an alginate impression (Alginate, Tropicalgin, Zhermack, Rovigo, Italy) was taken following the insertion of two orthodontic bands for maxillary first molars and abutments for palatal screws. Two fixation screws were used to secure the hybrid hyrax appliance in the mouth. A mucoperiosteal flap was elevated to place the mentoplates (ANCOR Orthodontics, Ankara, Türkiye). The same surgeon positioned the mentoplates at the anterior symphysis while administering a local anesthetic and fastened them with three screws.

The parents or the legal guardians of the patients performed a week of rapid maxillary expansion (RME) using the hybrid hyrax appliance, turning the screws 0.5 mm each day (1/4 turn in the morning and 1/4 turn in the evening). After RME, bilateral intermaxillary Class III elastics with 200-250 grams on each side between the hooks of the mentoplates and the molar bands of the hybrid hyrax were used to obtain an orthopedic response. When a dental Class II canine relationship was achieved, positive overjet was gained, and the desired change in the profile was obtained, the active treatment was terminated (8.2±1.7 months on average) (Figure 1).

Data Collection and Method of Measurements

Lateral cephalograms were taken both before (T0) and after therapy (T1), based on the data obtained from the patient files. All lateral cephalograms were traced using the NemoStudio

Figure 1. Intraoral photos of one of the patients included in this study were taken from the archive. A) Initial right side. B) Initial frontal side. C) Initial left side. D) Final right side. E) Final frontal side. F) Final left side

NX-Pro software v.10.4.2 (Nemotec, Madrid, Spain) in order to assess the effectiveness of the treatment. With reference to each patient's Sella-Nasion length, the calibration of lateral cephalograms at the two time points was further established.

CBCT scans were performed both before the miniscrew and Mentoplate placement (T0) and after (T1) the active treatment by using an Imtec Iluma Imaging Machine (3M, Ardmore, OK, USA; X-ray tube voltage: 120 kV; X-ray tube current: 1-4 mA; scanning time: 40 seconds maximum and 7.8 seconds minimum; field of view: 14.2×21.1 cm; voxel size: 0.0936 mm; grayscale: 14 bit). During both imaging times, the patients were seated in an upright position with the Frankfurt horizontal plane parallel to the floor. The 3D SLICER version 5.0.2 program was used to examine skeletal and dental alterations (www.slicer.org).[11] All CBCT images were reoriented by arranging midsagittal, Frankfort horizontal, and transporionic planes to match with sagittal, axial, and coronal planes which were embedded in the software, respectively.[12] After head reorientation, 3D models were constructed, and on the CBCT slices and 3D models, bony and dental points were marked and verified (Table 1, Figure 2). The "Slicer CMF" extension was used to create midpoints and perform measurements, and the "Volume Rendering" tool was used to mark intraosseous landmarks.

Statistical Analysis

The IBM SPSS Statistics (version 23, IBM Corp, Armonk, NY) software was used for statistical analyses. To evaluate the overall power of the study, a post-hoc power analysis was carried out. The conformity of the parameters to normal distribution was determined using the Shapiro-Wilk test. The normally distributed data and the non-normally distributed data were compared between time points using paired samples t-tests and Wilcoxon signed-rank tests, respectively. To compare the mean values of two different measurement groups, Independent Samples t-test was used. Intra-examiner reliability was assessed based on the intraclass correlation coefficient (ICC). Statistical significance was set at $p<0.05$.

Table 1. Definition of landmarks and measurements

Abbreviation	Definition
	Reference Lines
H	Horizontal Reference Line: The line passing through the midpoint of Porions and midpoint of Orbitales
V	Vertical Reference Line: The line passing through the midpoint of Porions and bone projection on the superoinferior coordinate line according to the coordinate data of the midpoint of Porions
T	Transverse Reference Line: The line passing through the right and left Porions
P	Palatal Reference Line: The line passing through the ANS and PNS
	Dental Points
C	Coronal Points
A	Apical Points
C16db	Top of the distobuccal cusp of the maxillary right first molar
C16mb	Top of the mesiobuccal cusp of the maxillary right first molar
C16p	The projection of the midpoint of palatal cusps at palatal groove of the maxillary right first molar
A16db	Apex of distobuccal root of maxillary right first molar
A16mb	Apex of mesiobuccal root of maxillary right first molar
A16p	Apex of palatal root of maxillary right first molar
C26db	Top of the distobuccal cusp of the maxillary left first molar
C26mb	Top of the mesiobuccal cusp of the maxillary left first molar
C26p	The projection of the midpoint of palatal cusps at palatal groove of the maxillary left first molar
A26mb	Apex of mesiobuccal root of maxillary left first molar
A26db	Apex of distobuccal root of maxillary left first molar
A26p	Apex of palatal root of maxillary left first molar
	Measurements
C16db-C26db (mm)	3D distance between C16db and C26db
C16mb-C26mb (mm)	3D distance between C16mb and C26mb
C16p-C26p (mm)	3D distance between C16p and C26p
A16db-A26db (mm)	3D distance between A16db and C26db
A16mb-A26mb (mm)	3D distance between A16mb and C26mb
A16p-A26p (mm)	3D distance between A16p and C26p
16db (°)	The roll angle between the line that connects the A16db and C16db and the line and T line
16mb (°)	The roll angle between the line that connects the A16mb and C16mb and T line
16p (°)	The roll angle between the line that connects the A16p and C16p and T line
26db (°)	The roll angle between the line that connects theA26db and C26db and T line
26mb (°)	The roll angle between the line that connects theA26mb and C26mb and T line
26p (°)	The roll angle between the line that connects theA26p and C26p and T line
V-C16db (mm)	The anteroposterior component of the distance from the C16db to the V line
V-C16mb (mm)	The anteroposterior component of the distance from the C16mb to the V line
V-C16p (mm)	The anteroposterior component of the distance from the C16p to the V line
V-A16db (mm)	The anteroposterior component of the distance from the A16db to the V line
V-A16mb (mm)	The anteroposterior component of the distance from the A16mb to the V line
V-A16p (mm)	The anteroposterior component of the distance from the A16p to the V line
V-C26db (mm)	The anteroposterior component of the distance from the C26db to the V line
V-C26mb (mm)	The anteroposterior component of the distance from the C26mb to the V line
V-C26p (mm)	The anteroposterior component of the distance from the C26p to the V line
V-A26db (mm)	The anteroposterior component of the distance from the A26db to the V line
V-A26mb (mm)	The anteroposterior component of the distance from the C26mb to the V line

Table 1. Continued

Abbreviation	Definition
	Measurements
V-A26p (mm)	The anteroposterior component of the distance from the C26p to the V line
V-16db (°)	The pitch angle between the V line and the line that connects the A16db and C16db
V-16mb (°)	The pitch angle between the V line and the line that connects the A16mb and C16mb
V-16p (°)	The pitch angle between the V line and the line that connects the A16p and C16p
V-26db (°)	The pitch angle between the V line and the line that connects the A26db and C26db
V-26mb (°)	The pitch angle between the V line and the line that connects the A26mb and C26mb
V-26p (°)	The pitch angle between the V line and the line that connects the A26p and C26p
H-C16db (mm)	The superoinferior component of the distance from the C16db to the H line
H-C16mb (mm)	The superoinferior component of the distance from the C16mb to the H line
H-C16p (mm)	The superoinferior component of the distance from the C16p to the H line
H-A16db (mm)	The superoinferior component of the distance from the A16db to the H line
H-A16mb (mm)	The superoinferior component of the distance from the A16mb to the H line
H-A16p (mm)	The superoinferior component of the distance from the A16p to the H line
H-C26db (mm)	The superoinferior component of the distance from the C26db to the H line
H-C26mb (mm)	The superoinferior component of the distance from the C26mb to the H line
H-C26p (mm)	The superoinferior component of the distance from the C26p to the H line
H-A26db (mm)	The superoinferior component of the distance from the A26db to the H line
H-A26mb (mm)	The superoinferior component of the distance from the A26mb to the H line
H-A26p (mm)	The superoinferior component of the distance from the A26p to the H line
P-16db (°)	The pitch angle between the P line and the line that connects the A16db and C16db
P-16mb (°)	The pitch angle between the P line and the line that connects the A16mb and C16mb
P-16p (°)	The pitch angle between the P line and the line that connects the A16p and C16p
P-26db (°)	The pitch angle between the P line and the line that connects the A26db and C26db
P-26mb (°)	The pitch angle between the P line and the line that connects the A26mb and C26mb
P-26p (°)	The pitch angle between the P line and the line that connects the A26p and A26p
H -A (mm)	The superoinferior component of the distance from the A point to the H line
V-A (mm)	The anteroposterior component of the distance from the A point to the V line
H-ANS (mm)	The superoinferior component of the distance from the ANS point to the H line
V-ANS (mm)	The anteroposterior component of the distance from the ANS point to the V line
H-PNS (mm)	The superoinferior component of the distance from the PNS point to the H line
V-PNS (mm)	The anteroposterior component of the distance from the PNS point to the V line
H-P (°)	The pitch angle between the H line and the P line

RESULTS

ICC values of all measurements were found to be close to 1.00 (range= 0.958-0.991), indicating that all the skeletal and dental measurements could be repeated with an insignificant error that had no bearing on the outcomes. Based on the variable V-C16db (mm), the post-hoc power calculation showed a 99% power of the sample to represent the population, as well as an effect size of d=1.6 at α=0.05.

When lateral cephalometric values were examined, significant increases in SNA, ANB, IMPA and overjet values and a significant decrease in SN-GoMe were observed (p=0.004, p=0.001, p=0.001, p=0.000 and p=0.029, respectively) (Table 2).

For molar movement evaluation on CBCT, the paired sample t-test showed significant increases in all linear measurements in the coronal plane (p<0.05), except for the C16p-C26p values (p=0.119) (Table 3). The angular measurements in the coronal plane showed significant decreases in the 16mb and 26mb values (p=0.043 and p=0.001, respectively) (Table 3). There were significant increases in the distances of the dental points to the vertical reference line (V line) and the horizontal

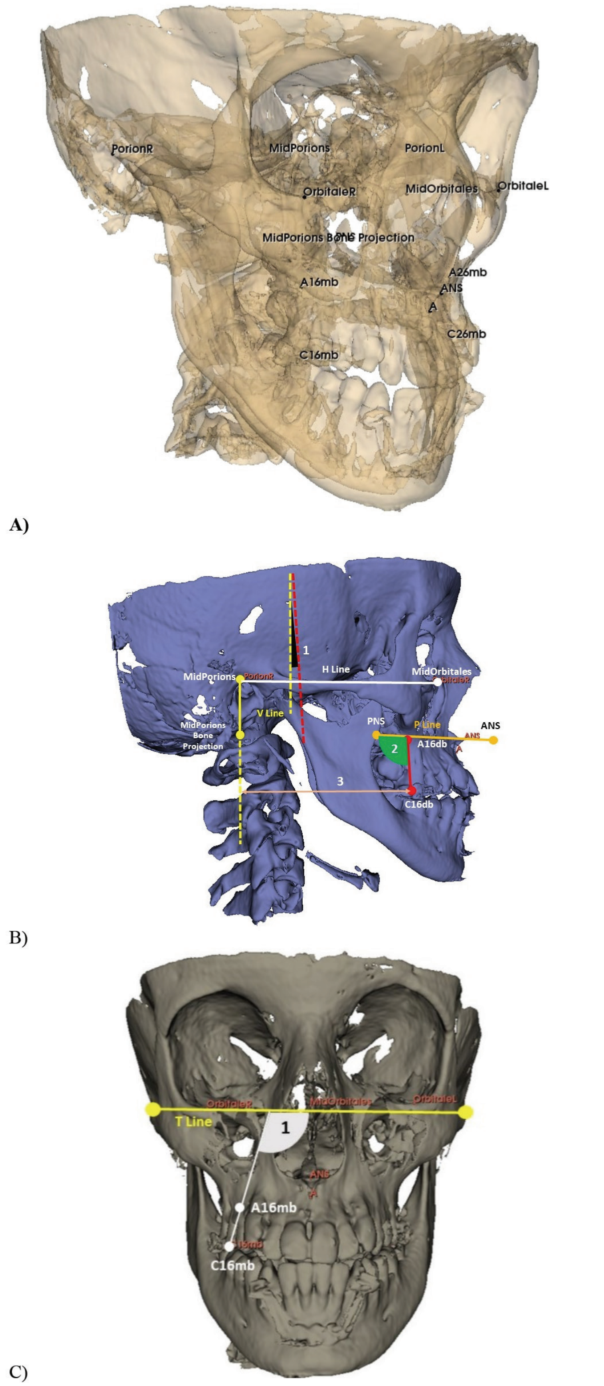

Figure 2. A) Points marked on the three dimensional head model B) Schematization of measurements and some reference lines. 1: V-16db (°), 2: P-16db (°), 3: V-C16db (mm). C) Schematization of measurements and T line from frontal view. 1: 16db (°)

reference line (H line) measured in millimeters in the sagittal plane (p≤0.001) (Table 3). Significant increases were found in all angular measurements made in the sagittal plane compared to the V line (p<0.05) (Table 3). In the angular measurements performed in the sagittal plane relative to the palatal reference line (P line), significant increases were observed in the P-16p, P-26mb, and P-26 p-values (p=0.002, p=0.007, and p=0.025, respectively) (Table 3). The skeletal measurement results showed significant increases in terms of the V-A, V-ANS, and V-PNS values (p=0.000, p=0.000, and p=0.005, respectively) (Table 3).

To evaluate expansion difference at the coronal and apical level, an independent samples t-test was performed on the millimetric measurements made at the coronal plane. A significant difference was found between the values at the coronal level and those at the apical level, and higher values were found at the apical level (p=0.021) (Table 4). To interpret differences in sagittal movements at the coronal and apical levels, an independent samples t-test was performed between the V-C and V-A (mm) results, and there was a significant difference in favor of the C points (p=0.000) (Table 4). A paired samples t-test was applied to determine whether the movements at the apical and coronal levels relative to the H line were due to dental extrusion or skeletal movement (Table 4).

DISCUSSION

Mesialization of the maxillary posterior teeth and resultant incisor proclination, or lack of space for permanent canines, are among the most frequently encountered side effects of facemask treatment.[3] Class III orthopedic treatments using skeletal anchorage units are preferred particularly because they reduce dental side effects.[8] Although no clear consensus has been reached in the literature about the movement of maxillary molar teeth, the hybrid hyrax appliance is deemed safe for clinical usage because it is supposed to reduce these negative effects by keeping the maxillary molar teeth in their original positions. Therefore, our study aimed to examine the movement of maxillary molar teeth in patients treated with hybrid hyrax-Mentoplate appliances. There are not many publications in the literature discussing the movement of maxillary molar teeth and also most of these have been made based on intraoral models and lateral cephalometric X-rays.[1,2,4,8] CBCT data of patients were used in our study to examine the crown and root movements and minimize errors caused by superimposition or magnification in 2D images. Thus, this is the first study to examine the molar movement in 3D according to the authors' knowledge.

For the evaluation of the cephalometric analysis aimed for the efficiency of the treatment for individuals in the study group, SNA and ANB angles increased but the SNB angle remained same.[5,13-15] Once more, the overbite showed little change, but the overjet showed a notable increase.[5,13-15] These findings are consistent with related research in the literature. The SN-GoMe value decreased, while comparable investigations found no change in contrast to our findings.[5,13-15] This discrepancy could be caused by variations in study groups and methodologies. As reported in similar studies, no change was found UI-SN angle, but a significant increase was observed in IMPA in this study.[5,13-15] Şar et al.[16] explained this situation by the elimination of lip pressure by the hooks of the plates applied to the anterior mandible region.

Table 2. Cephalometric values of the study sample before and after treatment

	T0			T1			ΔT1-T0			
	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	p
SN-GoMe (°)	41.10	40.50	1.85	39.70	40.00	2.16	-1.40	-1.50	1.71	0.029[a*]
SNA (°)	75.90	76.50	3.00	79.20	79.50	3.91	3.30	2.00	2.71	0.004[a**]
SNB (°)	78.80	79.00	2.74	78.50	78.00	2.72	-0.30	-0.50	1.64	0.576[a]
ANB (°)	-2.80	-2.00	1.99	0.50	0.50	2.01	3.30	3.00	2.06	0.001[a**]
UI-SN (°)	107.40	108.00	4.58	109.50	109.00	5.42	2.10	1.00	5.30	0.242[a]
IMPA (°)	80.00	80.00	5.16	87.20	88.00	3.01	7.20	7.00	4.89	0.001[a**]
Overjet (mm)	-0.24	0.10	1.12	2.59	2.55	1.15	2.83	2.85	1.37	0.000[a***]
Overbite (mm)	0.80	0.05	1.62	0.52	-0.05	1.56	-0.28	-0.15	0.97	0.327[b]

[*]$p<0.05$, [**]$p<0.01$, [***]$p<0.001$; [a]Paired samples t-test, [b]Wilcoxon signed-rank tests
SD: Standard deviation

Table 3. Changes in measured parameters over time

		T0			T1			Δ T1-T0		
		n	Mean	SD	n	Mean	SD	Mean	SD	p
CORONAL PLANE	C16db -C26db (mm)	10	53.24	2.46	10	55.45	2.87	1.03	1.25	0.000[***†]
	C16mb-C26mb (mm)	10	50.32	2.16	10	51.35	2.72	2.21	1.04	0.029[*†]
	C16p-C26p (mm)	10	42.26	2.8	10	43.8	2.89	1.53	2.82	0.119[†]
	A16db-A26db (mm)	10	49.65	3.3	10	52.13	3.95	2.49	1.38	0.000[***†]
	A16mb-A26mb (mm)	10	47.29	3.53	10	49.73	3.73	2.44	1.21	0.000[***†]
	A16p-A26p (mm)	10	32.02	3.06	10	34.84	3.16	2.82	1.4	0.000[***†]
	16db (°)	10	93.66	6.02	10	92.96	7.36	-0.71	2.67	0.425[†]
	16mb (°)	10	93.18	7.15	10	90.68	5.66	-2.5	3.36	0.043[*†]
	16p (°)	10	103.49	6.22	10	102.71	4.38	-0.78	3.31	0.473[†]
	26db (°)	10	97.92	6.58	10	97.34	7.59	-0.59	2.62	0.495[†]
	26mb (°)	10	96.93	5.98	10	94.79	5.99	-2.14	1.29	0.001[***†]
	26p (°)	10	106.51	5.31	10	105.29	6.56	-1.21	3.3	0.275[†]
SAGITTAL PLANE	V-C16db (mm)	10	53.64	3.34	10	59.67	4.63	6.04	3.75	0.001[***†]
	V-C16mb (mm)	10	58	3.45	10	64.14	4.62	6.14	3.41	0.000[***†]
	V-C16p (mm)	10	51.86	3.57	10	58.88	4.58	7.02	3.17	0.000[***†]
	V-A16db (mm)	10	56.94	3.7	10	61.24	3.46	4.3	1.82	0.000[***†]
	V-A16mb (mm)	10	59.41	3.56	10	63.81	3.26	4.4	1.75	0.000[***†]
	V-A16p (mm)	10	54.59	3.99	10	58.74	3.63	4.15	1.92	0.000[***†]
	V-C26db (mm)	10	54.07	3.36	10	59.68	4.14	5.61	3.06	0.000[***†]
	V-C26mb (mm)	10	58.37	3.43	10	64.07	4.56	5.7	2.85	0.000[***†]
	V-C26p (mm)	10	52.31	3.35	10	58.6	4.59	6.29	3.26	0.000[***†]
	V-A26db (mm)	10	57.19	4.26	10	61.17	3.8	3.98	1.89	0.000[***†]
	V-A26mb (mm)	10	59.85	3.96	10	63.93	3.78	4.07	1.93	0.000[***†]
	V-A26p (mm)	10	55.1	4.07	10	59.19	3.35	4.09	1.79	0.000[***†]
	V -16db (°)	10	-10.23	5.55	10	-4.85	6.95	5.38	6.81	0.034[*†]
	V-16mb (°)	10	-4.6	5.97	10	0.62	6.86	5.22	6.05	0.023[*†]
	V-16p (°)	10	-8.53	6.37	10	0.19	7.44	8.73	5.65	0.001[***†]
	V-26db (°)	10	-9.8	4.98	10	-4.61	5.75	5.19	6.57	0.034[*†]
	V-26mb (°)	10	-4.49	6.61	10	0.41	8.34	4.91	5.68	0.023[*†]
	V-26p (°)	10	-8.85	3.01	10	-1.98	6.8	6.88	6.6	0.009[**†]

Table 3. Continued

		T0			T1			Δ T1-T0		
		n	Mean	SD	n	Mean	SD	Mean	SD	p
SAGITTAL PLANE	H -C16db (mm)	10	40.68	1.87	10	43.51	2.16	2.83	1.94	0.001***†
	H-C16mb (mm)	10	41.55	1.69	10	43.89	1.9	2.34	1.54	0.001***†
	H-C16p (mm)	10	40.94	1.54	10	43.9	2.04	2.95	1.19	0.000***†
	H-A16db (mm)	10	22.18	2.12	10	24.63	2.62	2.44	1.61	0.001***†
	H-A16mb (mm)	10	22.76	1.88	10	24.82	2.12	2.06	1.26	0.001***†
	H-A16p (mm)	10	22.37	1.91	10	25.1	2.59	2.73	1.52	0.000***†
	H-C26db (mm)	10	40.07	1.53	10	42.51	2.26	2.43	0.98	0.000***†
	H-C26mb (mm)	10	41.15	1.56	10	43.13	1.93	1.98	0.92	0.000***†
	H-C26p (mm)	10	40.45	1.65	10	42.63	2.3	2.18	1.35	0.001***†
	H-A26db (mm)	10	21.84	2.32	10	23.9	3.06	2.06	1.28	0.001***†
	H-A26mb (mm)	10	22.69	2.16	10	24.59	2.61	1.89	0.96	0.000***†
	H-A26p (mm)	10	22.35	2.57	10	24.54	2.97	2.18	1.48	0.001***†
	P -16db (°)	10	81.78	4.29	10	85.73	5.74	3.95	6.41	0.74‡
	P-16mb (°)	10	87.41	4.66	10	91.49	5.43	4.09	5.74	0.051†
	P-16p (°)	10	83.47	4.86	10	91	6.18	7.53	5.38	0.002**†
	P-26db (°)	10	82.22	4.95	10	85.52	3.68	3.29	5.19	0.076†
	P-26mb (°)	10	85.31	4.84	10	90.92	6.93	5.61	5.11	0.007**†
	P-26p (°)	10	83.15	2.76	10	88.34	5.09	5.19	6.11	0.025*†
SKELETAL MEASUREMENTS	H -A (mm)	10	27.9	1.39	10	27.86	1.57	-0.04	1.52	0.93†
	V-A (mm)	10	83.09	4.27	10	86.42	4.19	3.33	1.55	0.000***†
	H-ANS (mm)	10	20.63	2.13	10	20.77	2.36	0.14	0.79	0.584†
	V-ANS (mm)	10	88.08	4.01	10	90.83	4.68	2.75	1.15	0.000***†
	H-PNS (mm)	10	19.38	1.44	10	20.54	1.81	1.16	1.32	0.022*†
	V-PNS (mm)	10	39.17	4.8	10	41.04	4.43	1.87	1.26	0.005‡
	H-P (°)	10	1.54	1.88	10	0.23	2.63	-1.31	1.9	0.057†

†Paired samples t-test, ‡Wilcoxon signed-rank tests, *p≤0.05, **p≤0.01, ***p≤0.001
SD, standard deviation; mm, millimeters; °, degree

Table 4. Evaluation of alterations at the coronal and apical level

		Mean	SD	p
Expansion	A	2.58	1.29	0.021*
	C	1.59	1.88	
V-mm	A	3.60	2.10	0.000**
	C	6.13	3.16	
H-mm	A	2.23	1.34	0.246
	C	2.45	1.35	

p-values for Independent Samples t-test
*p≤0.05, **p≤0.001
SD: Standard deviation, mm: millimeters

When molar movements are examined via CBCT, except for the C16p-C26 p-values, there were significant increases in all distance measurements as a result of 1 week of RME. 2.58 mm of increase at the apical level and 1.59 mm of increase at the coronal level were observed, with a significant difference between them. Consistent with these results, all angular measurements on the coronal plane decreased, although this decrease was statistically significant for only two of these measurements. Contrary to studies in the literature examining the amount of expansion at the apical and coronal levels, in this study, the amount of expansion at the apical level was found to be greater than that at the coronal level.[17,18] Since it is known that RME can affect the circummaxillary and midpalatal sutures, the palatal bone halves may have been inclined inwardly by the Class III elastic force vector that was applied throughout the time needed for the recalcification of the sutures following expansion.[19] This can also explain the reduction in angular measurements examined in the coronal plane. Further research is necessary to determine why this change is greater at the apical level than at the coronal level.

There are a limited number of studies in the literature examining maxillary molar movement after force application in the orthopedic treatment of Class III malocclusions with skeletal anchorage support. In our study, the angles of the maxillary first molars relative to the V line for each cusp were found to be significantly increased after the treatment. Compared to the V line, the amount of mesial movement increased significantly at both the coronal and apical levels, while the degree of increase was higher at the coronal level. Therefore, an increase in angles compared to the V line is expected. In this study, considering the 3.33 mm forward movement of point A relative to the V line, the degree of maxillary molar movement was found to be 2.8 mm at the coronal level and 0.27 mm at the apical level. The angles measured relative to the P line, a significant change was observed in some measurements, but not in all of them. It was found that the P line made a slight anterior rotation compared to the H line, although this change was not significant. In light of all this information, the increase in angular measurements and the almost complete absence of mesial movement at the apical level can be attributed to two reasons: the slight anterior rotation in the palatal line may have masked the mesial movement of the molar at the apical level, or as stated in previous studies, the wire may have been bent due to elastic forces.[2]

Wilmes et al.[1] examined the mesial movement of maxillary molar teeth on intraoral models of 10 patients to whom hybrid hyrax-facemasks were applied. They reported that during the facemask treatment, mesial movements of 0.4 mm for the maxillary first right molar and 0.3 mm for the maxillary first left occurred.[1] Although there were individuals with a similar mean age and similar characteristics to those in our study, variations in treatment methods or intermaxillary elastic strengths could account for the difference between the study conducted by Wilmes et al.[1] and this study. Wilmes et al.[1] used 5 oz 1/4 inch elastics during treatment. Over time, the decrease in the strength of elastics as the maxilla comes forward may have caused a decrease in the mesial movement of the molar teeth. Tarraf et al.[5] also examined individuals treated with the same technique as in this study, reported mesial tipping in the maxillary molars, and attributed the result to bending in the wire.

Nienkemper et al.[8] examined the effects of a hybrid hyrax-facemask combination on 16 individuals with a mean age of 9.5 on lateral cephalometric X-rays and reported a statistically insignificant mesial movement of 0.4 mm relative to point A in the maxillary molar teeth. Although the treatment period was shorter than the one in this study, the predominance of the skeletal effect of the orthopedic forces (400 gr on each side) due to the younger mean age may be the reason for the lack of a significant movement in the molars.[3]

Ngan et al.[2] reported 0.6 mm of mesial movement in maxillary molars in individuals with a mean age of 9.8 years, whom they treated with hybrid hyrax-facemasks, and they attributed the result to the bending in the wire. It is thought that the results of other studies were lower than those in our study due to the dominance of the skeletal effect brought about by the mean ages of the included patients.[3,8]

Miranda et al.[4] performed skeletal Class III orthopedic treatments with hybrid hyrax with Miniscrew Anchored Maxillary Protraction (MAMP) protocol, and they reported 1.96 mm of mesial movement in the maxillary molars. The fact that the elastic forces in this study were smaller than those in similar studies mentioned before, and the mean age of the patients in this study was smaller than the aforementioned previous study may be the reason for the differences in our results.[4]

Considering the results of the aforementioned studies and the results we obtained in our study, factors such as age and orthopedic strength may affect the sagittal movement of molar teeth. To minimize this effect, we recommend the use of more rigid appliances, and since there are some publications regarding the drift of miniscrews under orthodontic and orthopedic forces, the effects of miniscrews under orthopedic force should also be examined.[20-22] Without analyzing miniscrew movements, it is impossible to pinpoint the exact reason for this, even though bending in the appliance or palatal plane rotation may contribute to concealing it.

While the results of the present study did not show a significant change at point A relative to the H line, the Independent Samples t-test showed a significant extrusion at both the apical (2.23 mm) and coronal (2.45 mm) levels in all teeth. In a previous study of Yıldırım et al.[13], they also reported a significant extrusion in maxillary molar teeth, and the degree of this extrusion was higher than that in this study. The small number of patients in that study may be the cause of the higher degree of molar extrusion.[13] Kamel et al.[23] applied the MAMP with Alternate RME and Constriction protocol to individuals with a mean age of 11 and reported 1.43 mm of extrusion, which was smaller than the value in our results. Methodological differences and the fact that the elastic force used by the authors was smaller than that in this study may be the reason for this difference. In light of these findings, even if there is skeletal anchorage support, the bending in the wire of the anchorage device, the movements of the miniscrews, and in addition to these, the vector of the elastic force should be taken into consideration. In cases where extrusion is undesirable, precautions may need to be taken for vertical control.

In the skeletal measurements, no significant change was observed in the H-P values. The fact that there was no change at point A in the supero-inferior direction according to the H-A measurements supported this result. Upon reviewing research with a similar methodology to that in this study, although Yıldırım et al.[13] and the study conducted by Willman et al.[15] revealed results supporting this study, Katyal et al.[14] reported a statistically significant but clinically insignificant anterior rotation of 0.8°. In terms of the sagittal movement of point A, Willmann et al.[15] reported a forward movement value of 2.67 mm, and Tarraf et al.[5] found a value of 4.06 mm. Even though the age group covered by Willmann et al.[15] was younger than the one in this study, the elastic force in their study was smaller, explaining why they reported less movement than that in this study. The reason why Tarraf et al.[5] reported more sagittal movement than us at point A may be the longer treatment duration in their study compared to the one in this study.

Study Limitations

The lack of a control group, small sample size, and the inability to evaluate changes after the long-term follow-up of treated patients can be considered as limitations. In addition, the increased vertical growth direction of the individuals in this study group can be considered as a limitation. It is thought that the inclusion of individuals with different vertical growth patterns and a control group with long-term follow-up results in future studies may also contribute to the literature.

CONCLUSION

According to the results of the present study, the use of Class III intermaxillary elastics may affect the transverse width of the maxilla at both the coronal and apical levels, in favor of the apical level due to immature bone in the midpalatal suture after expansion. Examined on the sagittal plane, the molar teeth exhibit clear mesial movement due to mesial tipping. In this treatment technique, dental extrusion occurs in the molar teeth despite the usage of skeletal anchorage. However, considering that this study is a pilot study, caution should be taken in interpreting the results.

Ethics

Ethics Committee Approval: The study was approved by the Marmara University Faculty of Medicine Non-Drug and Medical Device Research Ethics Committee (approval no.: 09.2024.623, date: 08.07.2024).

Informed Consent: All included patients have an informed consent form in their files.

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Footnotes

Author Contributions: Concept - G.Y., E.O.O.; Design - G.Y., E.O.O.; Data Collecting and Processing - G.Y.; Analysis or Interpretation - G.Y., E.O.O.; Literature Search - G.Y., E.O.O.; Writing - G.Y., E.O.O.

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Original Article

Orthodontic Forces Interrupt Root Formation in Immature Teeth: Myth or Fact? A Pilot Study

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Main Points

- Root dimensions do not differ between the treated and untreated groups.
- Post-treatment changes include a reduction in the distobuccal and palatal root length of molars.
- Developing roots achieve normal length after rapid maxillary expansion and fixed orthodontic treatment.

ABSTRACT

Objective: To assess the effects of rapid maxillary expansion (RME) and orthodontic treatment with fixed appliances on the developing roots of anchor teeth compared with completely formed roots.

Methods: Pre- and post-treatment cone-beam computed tomography (CBCT) scans of 19 patients (mean pre-treatment age 10.9±1.3, mean post-treatment age 13.66±1.29) with incompletely formed roots who had undergone RME and orthodontic treatment with fixed appliances were selected. In addition, 15 CBCT scans of age- and sex-matched untreated controls (mean age 13.69±1.08) with completely formed roots of the same teeth were obtained. Pre- and post-treatment CBCT records of the experimental group were segmented and reconstructed to obtain linear and volumetric measurements of the roots for comparison with the control group. Changes in the root dimensions were analyzed using the paired t-test; Independent Student's t-test was used for comparisons between the groups.

Results: All premolars in the experimental group showed a statistically significant increase in root length and volume post-treatment ($p<0.05$), with the greatest increase seen in the second premolar. The distobuccal and palatal root lengths of the molars decreased significantly after treatment in the experimental group. The comparison of post-treatment root dimensions between the experimental and untreated control groups showed no significant difference.

Conclusion: The teeth with developing roots attain normal root length after RME and orthodontic treatment with fixed appliances, with no significant differences in root length and volume compared with teeth with completely formed roots.

Keywords: Maxillary expansion, orthodontic treatment, developing teeth, root formation

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INTRODUCTION

Dental root development is a complex process that initiates after crown formation and continues for two to three years after the eruption of teeth in the oral cavity.[1,2] Thus, root elongation and apex formation are susceptible to intrinsic and extrinsic factors like trauma and mechanical force application, potentially leading to short and malformed roots.[3,4]

One of the commonly used orthodontic treatment modalities during the developmental stages of teeth is rapid maxillary expansion (RME).[5] In this treatment method, heavy orthopedic forces are transmitted to the bone with anchorage from the posterior teeth.[5,6] Although this procedure successfully corrects transverse discrepancy, some adverse effects on the buccal cortical bone and roots of the anchor teeth have been reported.[7,8] Resorption of the completely formed roots of the anchor teeth is one of the potential side effects of RME.[7,9] It is associated with radicular volume loss, especially on the buccal aspect of roots.[7,8,10,11] Additionally, root resorption is also a possible consequence of fixed orthodontic treatment due to factors such as treatment duration, direction, magnitude of force, and amount of tooth movement.[12,13] This side effect of orthodontic treatment on completely formed roots leads to the suggestion that it could also disrupt the root development process in developing teeth.[7]

Some radiographic studies evaluated the effect of orthodontic treatment on developing teeth and showed less root resorption and achievement of normal root length after completion of treatment.[14,15] In contrast, another study reported that RME and reverse headgear treatment at an early age can inhibit maxillary and mandibular root development.[16] These studies primarily utilized either periapical or panoramic radiographs. However, a separate study using CBCT in patients with clefts found no significant changes in the root length of developing roots after RME.[17]

Three-dimensional evaluation with CBCT provides high-definition images and produces multiplanar reformatted images allowing 2D views in all three dimensions.[18] Additionally, it enables the estimation of changes in root dimensions occurring over a period of time compared with other methods.[7] Despite this advantage, there is a paucity of literature exploring the effect of orthodontic treatment on developing dental roots using CBCT.

Whether orthodontic treatment disrupts root formation and affects the morphology and length remains unclear. Therefore, the objective of this retrospective pilot study was to three-dimensionally evaluate the effects of RME and orthodontic treatment with fixed appliances on the length and volume of the developing roots of anchor teeth by comparing them with an untreated control group. The null hypothesis was that RME and orthodontic treatment had no significant effect on the length and volume of developing roots of anchor teeth.

METHODS

This retrospective pilot study was conducted at the Department of Orthodontics, Boston University Henry M. Goldman School of Dental Medicine. CBCT records were collected from the department repository, and ethics approval was granted by the Institutional Review Board of Boston University (approval no.: H-32515, date: 10.12.2018). A sample of patients for the experimental group was selected based on the following inclusion criteria: aged 8-12 years, good quality pre (T1) and post-treatment (T2) CBCT records of patients treated with RME, no history of craniofacial anomaly or syndrome, no history of craniofacial trauma or surgery, no amalgam restorations or root canal fillings, and no extracted premolars or molars. Patients had maxillary constriction with unilateral or bilateral posterior crossbite or transverse discrepancy, as diagnosed with compensated molar inclination.[19] The treatment method employed was RME with a Hyrax appliance soldered to the bands of the maxillary first permanent molar, with the Hyrax wire extending to the first premolars for anchorage. The data were collected from the same provider and subjected to a commonly used activation protocol of one turn per day (0.25 mm/turn) until the palatal cusps of the maxillary molars were in contact with the buccal cusps of the mandibular molars. The expander was retained for 3 months post-expansion, followed by fixed orthodontic treatment with an edge-wise appliance. All teeth in the study group received orthodontic forces during treatment before the completion of root apexification. Most teeth received direct force from the RME along with the fixed orthodontic appliances, whereas some of the second premolars received only force from the fixed orthodontic appliance. The same repository was searched for an untreated control group (pre-treatment patients) matched to the sex and post-treatment age of the experimental group, with the absence of restorations or root canal fillings, and the absence of any craniofacial anomaly or syndrome.

Patients in the experimental group (n=19) with a mean pre-treatment age of 10.9±1.3 years and post-treatment age of 13.66±1.29 years were matched with an untreated control group (n=15) with a mean age of 13.69±1.08 years. In the experimental group, roots of premolar teeth were incompletely formed with open apex at different stages of tooth development. We report the root formation stages as defined by Nolla.[20] The second premolars were in stages 7 and 8, and the first premolars were in stages 8 and 9 of tooth development at T1 in the experimental group, while the apices of the first molars were fully formed (Nolla stage 10). The apices of the roots were closed and fully formed in the control group (Table 1). In the experimental group, two CBCT scans were performed (T1 and T2) with a mean treatment duration of 2.7 years. All CBCT scans were taken using the same i-CAT machine (Imaging Sciences International, Hartfield, PA, USA) at 120 KVp and 0.5 mm nominal focal spot size, rendering a 17.0 cm x 23 cm field of view with a 0.3 mm voxel size image. DICOM images of both groups were imported and processed using

Mimics software (version 21.0 Materialize, Leuven, Belgium). The maxillary first molar and first and second premolars on both right and left sides were segmented manually. A custom bone threshold was initially set (range: 226 to 3071), the masks were then cleaned manually for accurate tooth segmentation, and three-dimensional images were reconstructed with the edit and region grow functions for the measurements (Figure 1). The same threshold values were used for the segmentation of each patient's pre- and post-treatment records.[21]

The reconstructed images of each tooth were divided into crown and root sections by a plane passing through the cementoenamel junction (CEJ) perpendicular to the long axis of the tooth for root volume measurement. Since the CEJ is curved as it circles the tooth, an interactive multiplanar reconstruction function was used for image orientation, such that the planes were adjusted along the long axis of the tooth and in the axial view, sagittal and coronal planes were adjusted to intersect at the center of the tooth at the level of buccal and palatal CEJ. Subsequently, three points were marked on the buccal, mesial, and palatal surfaces to form the reference plane (Table 2).

Table 1. Characteristics of cases according to root formation stage

Characteristics	Experimental results at T2	Control	p-value
Root formation	Nolla Stage 10 Closed Apex	Nolla Stage 10 Closed Apex	
n	19	15	
Mean age in years (SD)	13.66 (1.29)	13.69 (1.08)	0.93
Males, n (%)	7 (36.8%)	4 (26.6%)	0.7
Females, n (%)	12 (63.15%)	11 (73.3%)	0.6

*Significance at $p<0.05$
SD, standard deviation.

Measurements

1. Root length: Root length was measured using the axial guided navigation method,[22] in which the axial cursor is moved in the sagittal and coronal multiplanar reconstruction to determine the cusp tip and root tip. The linear distance between the cusp tip and the root apex was measured. In developing roots, the distance from the cusp tip to the center of the most apical part of the root was measured. The lengths of all three molar roots were measured, and only the buccal roots of premolars were measured, as some of the premolars had fused buccal and palatal roots.

2. Volume measurements: The volume of the rendered 3D root models was measured by the software after dividing the crown and root with the CEJ plane.

Statistical Analysis

The normality of the data distribution and the equality of variances were assessed using the Shapiro-Wilk, Kolmogorov-Smirnov, and Levene's tests. The data showed normal distribution and equal variances. Therefore, the experimental group's changes in root length and volume were compared between pre- and post-treatment using the paired t-test. The Independent Student's t-test was used to compare mean ages and changes in root values between groups.

The intraclass correlation coefficient was used to analyze intraobserver reliability. For this purpose, a random sample (10% of the overall sample) was re-segmented and re-measured by the same researcher T.D. 2 weeks apart. The reliability was

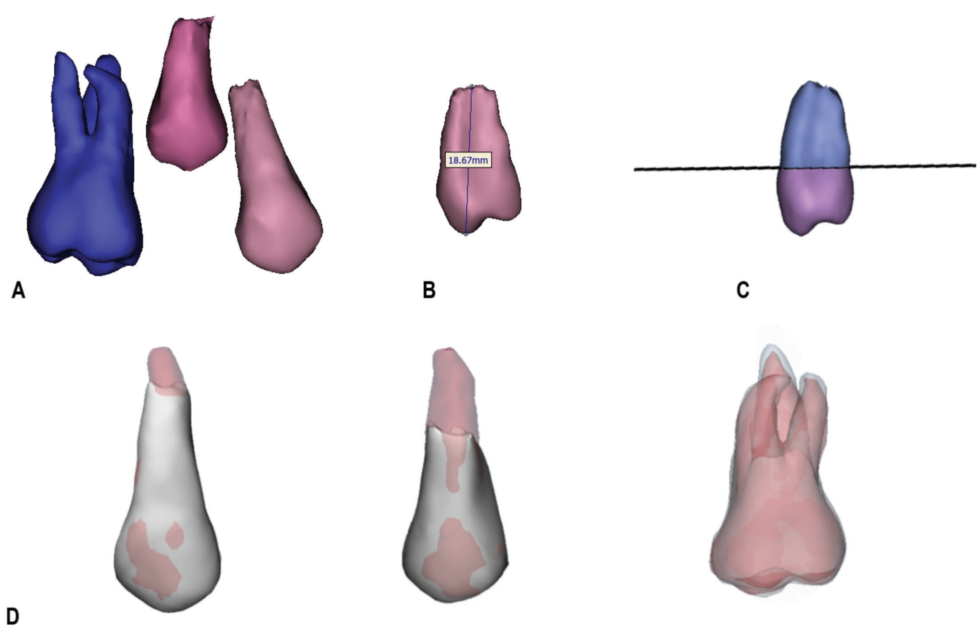

Figure 1. Three-dimensional reconstruction and measurement: **A)** Segmented and reconstructed images of maxillary first molar and premolars at T1; **B)** Root length measurement; **C)** CEJ plane dividing crown and root; **D)** Superimposition of T1 (White) and T2 (Red) images showing increase in root length of premolars and decrease in palatal and distobuccal root length of molars

further tested using a paired t-test, Bland-Altman level of agreement, and Dahlberg's method error.

All statistical analyses were performed using SAS Software Version 9.4 (SAS Institute Inc., Cary, NC, USA), with the significance level set at 0.05.

RESULTS

Overall, the measurements were found to have excellent reliability for all parameters studied, with interclass correlation values of >0.96, and method errors, as described in Supplementary Table 1.

The average pretreatment age of patients in the experimental group was 10.9±1.3. There was no significant difference between the post-treatment age of the experimental group (13.66±1.29) and the age of the control group (13.69±1.08) ($p>0.05$), with similar sex distributions (Table 1).

In the experimental group, there was a significant increase in the root lengths of the first and second premolars between T1 and T2. The greatest increase was observed in the roots of the right and left second premolars, with mean increases of 4.62±2 mm and 4.76±2.17 mm, respectively. A statistically significant decrease of 0.47 and 0.56 mm in the distobuccal and palatal root lengths of the right first molar, and 0.40 and 0.71 mm in the distobuccal and palatal root lengths of the left first molar were observed. No significant difference was observed in the mesiobuccal roots of the right and left molars (p-values of 0.83 and 0.7, respectively. There was a statistically significant increase in root volume of the right and left second and first premolars ($p<0.05$), however, the roots of the right and left first molars showed no significant change in volume post-treatment with a p-value of 0.64 and 0.38, respectively (Tables 3 and 4).

The comparison of post-treatment root length and root volume between the experimental and untreated control groups showed no statistically significant differences for all teeth (Tables 5 and 6).

DISCUSSION

As very few radiographic studies have looked into the effects of orthodontic treatment on developing roots, the objective of the present retrospective study was to determine the effects of RME and orthodontic treatment with fixed appliances on the length and volume of the developing roots by comparing them with an untreated control group.[14,15,23]

In the experimental group, the root length and volume of the maxillary premolars significantly increased after treatment (Tables 3 and 4). These results were consistent with a study on changes in the roots of developing teeth after orthodontic treatment, which showed an increase in the root length of immature incisors after treatment.[15] This implies that orthodontic treatment generally has little effect on teeth with immature roots. Another study compared the effects of rapid and slow maxillary expansion treatment on the developing roots of all the teeth.[16] The results of panoramic

Table 2. Reference points and the CEJ plane

Points and planes	Description
Buccal CEJ point	A point at the intersection of the coronal plane with the center of the buccal surface at the CEJ level.
Palatal CEJ point	A point at the intersection of the coronal plane with the center of the palatal surface at the CEJ level.
Mesial CEJ point	A point at the intersection of the sagittal plane with the center of the mesial surface at the CEJ level.
CEJ plane	At the level of the CEJ determined by the buccal, palatal, and mesial CEJ points.

CEJ, cementoenamel junction.

Table 3. Comparison of root length (mm) of right (R) and left (L) first molar and premolars between pre (T1) and post (T2) in Group 1 (experimental group)

Tooth	T1 (Mean±SD)	T2 (Mean±SD)	T2-T1 difference	p-value
First molar (R)				
MB	18.99±1.26	18.96±1.29	-0.02	0.834
DB	19.07±1.33	18.60±1.44	-0.47	0.004*
P	21.18±1.33	20.62±1.23	-0.56	0.002*
First molar (L)				
MB	19.25±1.37	19.21±1.60	-0.04	0.701
DB	19.08±1.24	18.68±1.56	-0.40	0.010*
P	21.17±1.37	20.46±1.51	-0.71	0.003*
Second premolar (R)	14.94±2.27	19.56±1.31	4.61	<0.001*
Second premolar (L)	14.88±2.55	19.64±1.39	4.76	<0.001*
First premolar (R)	16.91±2.48	19.79±1.66	2.87	<0.001*
First premolar (L)	16.82±2.49	19.98±1.33	3.16	<0.001*

*Significance at $p<0.05$
MB, mesiobuccal root; DB, distobuccal root; P, palatal root; SD, standard deviation.

Table 4. Comparison of root volume (mm³) of right (R) and left (L) first molar and premolars between pre (T1) and post (T2) in Group 1 (experimental group)

Tooth	T1 (Mean±SD)	T2 (Mean±SD)	T2-T1 difference	p-value
First molar (R)	538.45±70.38	532.27±83.61	-6.18	0.647
First molar (L)	516.02±90.88	498.83±83.31	-17.19	0.383
Second premolar (R)	165.42±47.36	222.74±42.00	57.31	<0.001*
Second premolar (L)	159.83±44.57	203.83±37.86	43.99	<0.001*
First premolar (R)	193.80±60.39	227.21±42.83	33.41	0.001*
First premolar (L)	189.02±61.49	214.71±40.33	25.68	0.019*

*Significance at $p<0.05$
SD, standard deviation.

Table 5. Comparison of post-treatment root length (mm) between the experimental group (Group 1) and the untreated control group (Group 2)

Tooth	Group 1 T2 (Mean±SD)	Group 2 T1 (Mean±SD)	Group 1 and Group 2 (Mean±SD)	p-value
First Molar (R)				
MB	18.9±1.3	18.7±1.4	0.2±1.33	0.635
DB	18.6±1.4	18.6±1.6	-0.05±1.5	0.923
P	20.6±1.2	20.2±1.6	0.3±1.44	0.462
First Molar (L)				
MB	19.2±1.6	18.8±1.3	0.3±1.51	0.472
DB	18.6±1.5	18.7±1.5	-0.03±1.54	0.940
P	20.4±1.5	20.6±1.7	-0.1±1.62	0.723
Second Premolar (R)	19.5±1.1	19.8±1.9	-0.3±1.62	0.576
Second Premolar (L)	19.6±1.4	19.9±1.8	-0.2±1.63	0.621
First Premolar (R)	19.7±1.7	20.1±1.7	-0.3±1.7	0.544
First Premolar (L)	19.9±1.3	20.1±1.7	-0.1±1.55	0.766

*Significance at $p<0.05$
Group 1: experimental; Group 2: control
Group 1-Group 2: difference between two groups, SD: standard deviation
MB, mesiobuccal root; DB, distobuccal root; P, palatal root; R, right; L, left

Table 6. Comparison of post-treatment root volume (mm³) between the experimental and control groups

Tooth	Group 1 T2 (Mean±SD)	Group 2 T1 (Mean±SD)	Group 1 and Group 2 (Mean±SD)	p-value
First Molar (R)	532.2±83.6	533.8±105.8	-1.5±93.99	0.961
First Molar (L)	498.8±83.3	513.4±99.3	-14.6±90.66	0.644
Second Premolar (R)	222.7±42.0	229.1±59.4	-6.4±52.46	0.713
Second Premolar (L)	203.8±37.8	218.8±49.5	-15.0±43.35	0.322
First Premolar (R)	227.2±42.8	236.9±48.8	-9.7±45.54	0.541
First Premolar (L)	214.7±40.3	230.8±47.4	-16.1±43.58	0.291

*Significance at $p<0.05$
Group 1: experimental; Group 2: control
Group 1-Group 2: difference between two groups, SD: standard deviation
R, right; L, left

radiographs revealed a significant increase in root length only in the second premolars of the maxillary arch after RME and reverse headgear treatment. The authors concluded that root development was disrupted in all other maxillary teeth. These contrasting results may be due to the use of headgear with RME and different treatment durations, as the root changes in that study were measured after expansion and protraction treatment (mean duration 8.15±2.4 months). However, in the present investigation, changes in the roots were evaluated after the completion of fixed orthodontic treatment, which encompasses the entire period of root development. In addition, the difference in results could be attributed to the use of panoramic radiographs in the previous study, as it has limitations due to the use of a focal trough. This feature makes root assessment challenging and may lead to an overestimation of root resorption. Da Silva Filho et al.[14] also studied the effect of leveling with a 2x4 appliance on the developing roots of incisors and found no disruption in root development. This assessment was conducted using periapical radiographs after 7 months of treatment.[14]

Additionally, in the present study, a reduction in the lengths of the distobuccal and palatal roots of molars was observed, with the palatal root of the left first molar being mostly affected (0.71 mm of length reduction). However, these values are clinically insignificant.[24] In addition, no significant changes in mesiobuccal root length and overall molar root volume was noted after treatment (Tables 3 and 4). The discrepancy between molars and premolars could be attributed to the different root formation stages, as the molar roots were fully formed compared with the premolar roots, which were still developing before treatment. This indicates that immature teeth are generally not affected by orthodontic treatment. The differences observed in teeth could also be the result of variations in anchorage, as during the RME phase, the Hyrax appliance was soldered to the bands on the molars while the premolars were anchored with the Hyrax wires. However, previous studies have shown no significant difference in root changes between banded and non-banded anchor teeth following RME.[9]

The changes in molar roots, nonetheless, are consistent with the findings of previous research. Cardinal et al.[17] evaluated the three-dimensional effect of RME on the developing roots of molars in patients with cleft molars, with a mean age of 10.7 years. The authors compared the effect of different types of rapid maxillary expanders on developing roots and found no difference in the root length of molars with both open and closed apices when evaluated three months after expansion. Other research on root resorption after RME showed maximum changes in the palatal and mesiobuccal roots of the molar.[8,11] In contrast, another study measuring apical root resorption on CBCT scans after non-extraction fixed orthodontic treatment found maximum effects on the distobuccal roots of maxillary molars.[22] However, our results indicated that the distobuccal and palatal roots were affected. The discrepancies may be due to the differences in treatment duration or the effect of fixed orthodontic treatment after RME. A recent study compared the extent of root resorption in patients treated with tooth-borne and bone-borne RME and found significant reductions in volume and length in both groups, with a greater reduction in the tooth-borne group.[25] This result can be attributed to the absence of direct forces on the teeth. We did not observe any effect on root maturation. However, the use of a bone-borne RME could potentially reduce changes in root length and volume.

In addition, no significant effect was observed on the root volume of the molars after treatment. This finding could be attributed to either the small volumetric changes or the use of CBCT images with voxel sizes of 0.3 mm (300 µm). However, there is no consensus on the optimal voxel size for assessing radicular volume. A previous study showed that CBCT images with a 0.3-mm voxel size were effective in detecting external root resorption.[26] Conversely, another study found that CBCT with 300 µm underestimated volumetric measurements compared to smaller voxel sizes.[27] More recent research reported no significant differences in sensitivity and specificity between 120, 200, 250, and 300 µm voxel sizes.[28]

In comparison with the control group with untreated normal roots, the post-treatment root dimensions of the experimental group showed no significant difference, which implies attainment of normal root dimensions (Tables 5 and 6). Similarly, Rosenberg[29] reported that incompletely formed premolars and canines reached normal root length after Begg orthodontic treatment. In addition, other authors reported that immature teeth reached a normal root length after treatment compared with fully formed roots, which is in agreement with our findings.[23] These studies were assessed radiographically without a control group, whereas in the present study, changes in developing roots were evaluated three-dimensionally and compared with normal roots. Our results also corroborate those of a recent histological investigation, which showed the attainment of normal root length and less root resorption in immature teeth after treatment compared with completely formed roots.[30]

In this study, the control group was selected randomly from a large CBCT repository and matched to the posttreatment age and sex of the experimental group to ensure a valid comparison. During the selection process, the criteria were the completion of root development, age and sex matching, absence of restorations or root canal fillings, and absence of any craniofacial problems or syndromes. Therefore, the possibility of having short roots or small teeth in the control group can be considered a random error that should not cause any bias in the results. The exclusion of a second time point in the control group was due to the method of comparing root length and volume, not the amount of root formation, during the same period of time. The final root length comparison was thought to be more clinically relevant since the final root length and surface area had the greatest impact on actual tooth movement. Therefore, adding a longitudinal dataset would diverge from our hypothesis.

Study Limitations

A potential limitation of this study is the small sample size, which is typical for a pilot study. The comparison between the control and experimental groups did not show statistical significance, possibly because of the small sample size. To assess the required number of subjects, a post-hoc analysis was performed using G*Power 3.1.9.7 (Franz Faul, Universität Kiel, Germany) with an effect size of 0.37. The results indicated that a sample size of 119 per group was required to achieve 80% power with a type I error of 0.05. However, ethical considerations regarding radiation exposure limited the number of cases in the untreated control group. Also, future research using surface-based deviation 3D analysis would be beneficial to assess the exact areas of surface changes.[25,31]

From a clinical perspective, the results of this study can help dentists better understand root changes in immature teeth after orthodontic treatment. Early treatment does not appear to have a negative impact on root formation. However, to obtain a definite inference, further long-term studies with appropriate sample sizes are necessary.

CONCLUSION

This pilot study suggests that RME and orthodontic treatment with fixed appliances do not interrupt normal dental root formation, which supports early orthodontic and orthopedic treatment. Larger-scale studies are needed to confirm these findings.

Ethics

Ethics Committee Approval: Ethical permission was granted by the Institutional Review Board of Boston University (approval no.: H-32515, date: 10.12.2018).

Informed Consent: Retrospective pilot study.

Acknowledgments

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Footnotes

Author Contributions: Concept - M.M.; Design - L.A.W., M.M.; Data Collection and/or Processing - T.D.; Analysis and/or Interpretation - T.D., A.A.A., M.S., M.M.; Literature Search - T.D., M.S.; Writing - T.D., A.A.A., L.A.W., M.S., M.M.

Conflict of Interest: The authors have no conflicts of interest to declare.

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Supplementary Table 1. Intra-rater reliability using paired t-tests, Bland and Altman limits of agreement, and Intraclass correlation and Dahlberg method error

Variable	Paired t-test	Bland and Altman limits of agreement				Intraclass correlation (ICC)			Dahlberg method error
	MD (M1-M2)	SD	p-value	Lower 95% CI	Upper 95% CI	ICC	Lower 95% CI	Upper 95% CI	
UR_1M_PRL	-0.04	0.14	0.495	-0.20	0.11	0.99	0.98	1	0.055
UL_1M_PRL	-0.01	0.09	0.798	-0.10	0.08	0.99	0.99	1	0.025
UR_1M_MBRL	-0.25	0.38	0.165	-0.65	0.14	0.98	0.89	0.99	0.047
UL_1M_MBRL	0.03	0.13	0.537	-0.10	0.18	0.99	0.99	1	0.035
UR_1M_DBRL	0.33	0.52	0.179	-0.21	0.88	0.96	0.75	0.99	0.173
UL_1M_DBRL	-0.01	0.18	0.899	-0.20	0.18	0.99	0.98	1	0.037
UR_2PM_BRL	0.17	0.18	0.1	-0.02	0.36	0.99	0.98	1	0.021
UL_2PM_BRL	-0.005	0.08	0.899	-0.09	0.08	1	0.99	1	0.013
UR_1PM_BRL	0.09	0.15	0.217	-0.07	0.25	0.999	0.99	1	0.022
UL_1PM_BRL	-0.05	0.14	0.39	-0.21	0.09	0.99	0.99	1	0.019
UR_1M_RV	-3.24	23.20	0.746	-27.59	21.11	0.99	0.93	0.99	0.098
UL_1M_RV	1.99	30.41	0.879	-29.92	33.90	0.98	0.90	0.99	0.129
UR_2PM_RV	2.71	5.69	0.296	-3.26	8.68	0.99	0.98	1	0.05
UL_2PM_RV	0.22	6.49	0.937	-6.58	7.03	0.99	0.96	0.99	0.037
UR_1PM_RV	2.64	10.13	0.552	-8.00	13.28	0.99	0.96	0.99	0.076
UL_1PM_RV	-1.82	4.50	0.367	-6.55	2.90	0.99	0.99	1	0.019

*Significance at $p<0.05$
M1, one measurement; M2, two measurement; CI, confidence interval; MD, mean difference; SD, standard deviation; UR, upper right; UL, upper left; 1M, first molar; PRL, palatal root length; MBRL, mesiobuccal root length; DBRL, distobuccal root length; 2PM, second premolar; 1PM, first premolar; BRL, buccal root length; RV, root volume.

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Original Article

Gender-based Comparison of Pharyngeal Airway Between Class I and Class III Patients During MP3cap Growth Period

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Main Points

- The dimensions of the nasopharyngeal area were similar across different malocclusion groups and genders.
- The inferior pharyngeal space was larger in girls with Class III malocclusion compared to boys with the same condition.
- Girls displayed a more extensive head posture than boys in both Class I and Class III malocclusions.
- When planning orthodontic treatment during the growth and development period, it is important to consider the age, gender, and malocclusion characteristics in relation to the pharyngeal airway.

ABSTRACT

Objective: To compare the pharyngeal airway size and area between Class III patients exhibiting optimal vertical growth direction and Class I patients at the MP3cap stage, considering gender differences.

Methods: This retrospective study analyzed pre-treatment cephalograms of a total of 180 patients with Class I (45 girls, 45 boys) and Class III (maxilla or maxillo-mandibular origin) (45 girls, 45 boys) malocclusions. Linear and angular measurements were conducted on lateral cephalograms utilizing the GNU Image Manipulation Program (GIMP 2.10.18, NY, USA; https://www.gimp.org/). The pharyngeal airway areas were computed utilizing AUTOCAD (Autodesk 2018, San Rafael, CA, USA). The Independent Samples t-test and Mann-Whitney U test were employed for comparative analysis of variables across groups. The forward selection method was employed in conjunction with regression analysis.

Results: No significant differences were observed in the nasopharyngeal area (NA; mm^2) across the malocclusion groups and genders. In Class III girls, the oropharyngeal area (OA; mm^2), retroglossal (RG; mm^2) area, and superior pharyngeal space (SPS; mm) were significantly larger than those of Class III boys, and Class I girls ($p<0.05$). The inferior pharyngeal space (IPS; mm) was significantly larger in Class III girls compared to Class III boys ($p<0.05$). Girls with Class I/III malocclusions demonstrated a more pronounced head posture than boys ($p<0.05$).

Conclusion: The findings indicate the necessity of accounting for gender-specific variations in Class I and III patients, as well as evaluating pharyngeal airway characteristics in orthodontic diagnosis and treatment planning. In Class III girls, the OA and RG areas, as well as the superior and inferior pharyngeal spaces, were larger compared to Class III boys.

Keywords: Airway, Class I, Class III malocclusion, pharyngeal

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INTRODUCTION

The pharyngeal airway is a complex structure closely associated with the maxilla and mandible. The etiology of Class III malocclusion and the variability of the maxillomandibular sagittal relationship are associated with alterations in airway and breathing patterns.[1] In recent years, the number of studies evaluating the relationship between malocclusions and the pharyngeal airway has increased in the literature.[2,3] Although numerous studies have assessed the impact of various treatments for skeletal Class III malocclusion on the pharyngeal airway[4-7] there is a paucity of research examining the pharyngeal airway in untreated Class III patients. Furthermore, disparate findings have emerged, attributed to variations in age, gender, and methodological approaches among the studies.[2,3,8-11] Thus, it is essential to investigate the relationship between Class III malocclusion and the pharyngeal airway within homogeneous groups.

This study aimed to compare the pharyngeal airway size and area between Class III patients exhibiting optimal vertical growth and Class I patients during the MP3cap growth period, across both genders. The number of studies establishing pharyngeal airway normative values in Class I patients is limited, and current research frequently includes a small sample size and skeletal measurements.[12-14] Consequently, our secondary objective was to establish the normative values of airway dimensions in Class I subjects exhibiting optimal sagittal and vertical growth patterns, underscoring the necessity for additional research.

METHODS

This retrospective study examined the pre-treatment lateral cephalograms of 180 patients (90 boys and 90 girls) with Class I (45 girls, 45 boys) and Class III (45 girls, 45 boys) malocclusions, referred to the orthodontic clinic of the University. Parents of all participating children were informed, and the study protocol received approval from the Measurement and Evaluation Ethics Sub-Working Group of the Gazi University (approval no.: 2020-465, date: 08.09.2020). Informed consent forms were obtained from each patient.

Power analysis was performed utilizing G*Power 3.1.9.7 (University of Düsseldorf, Düsseldorf, Germany) to ascertain the necessary sample size for the skeletal Class I and III malocclusion groups. This study utilized data from analogous prior research as references for the ANB angle, nasopharyngeal airway area, and oropharyngeal airway area.[16] The sample size of 87 patients per group at $\alpha=0.05$ provides a statistical power of 95% for this study; however, it was increased to 90 to achieve equal gender distribution. The inclusion criteria for the Class I group were established as follows: ANB angle ranging from 0 to 4°, SN/GoGn angle between 26 and 38°, MP3cap growth development period (the epiphysis of the middle phalanx of the third finger is equal to or wider than the metaphysis, with lateral sides exhibiting initial capping towards the metaphysis), and chronological age between 10 and 14 years. The inclusion criteria for the Class III group were: a negative ANB angle, a skeletal Class III anomaly originating from the maxilla or maxillo-mandibular region, Angle Class III malocclusion, an SN/GoGn angle ranging from 26° to 38°, anterior crossbite, MP3cap growth development period, and a chronological age between 10 and 14 years (Figure 1).

The study analyzed 11088 patients from the digital archive of the orthodontic department, excluding individuals with ANB angles exceeding 4°, SN/GoGn greater than 38°, SN/GoGN less than 26°, and those not in the MP3cap growth and development stage, as well as those exhibiting accelerated or retarded growth with a deviation of more than one year between chronological and skeletal ages. Furthermore, individuals with a prior history of orthodontic treatment, upper airway pathology, or oral respiration were excluded from the study. Patient selection for each malocclusion class and gender group was conducted using random number generation in Excel, yielding 45 randomly selected patients per group. Figure 1 illustrates the flow chart developed for patient selection criteria.

Lateral cephalograms were obtained under standardized conditions, with the head stabilized using a cephalostat, teeth in centric occlusion, and the Frankfort horizontal plane aligned parallel to the floor. Linear and angular measurements of lateral cephalograms were conducted by a single researcher utilizing the GNU Image Manipulation Program (GIMP 2.10.18, NY, USA; https://www.gimp.org/). Fifteen lateral cephalograms from each group were randomly selected, re-digitized, and recalculated by the same researcher two weeks later to assess the reliability of the method. The pharyngeal airway areas were calculated utilizing AUTOCAD (Autodesk 2018, San Rafael, CA, USA). Cephalometric radiographs were aligned based on a plane with a specified measurement in millimeters, after which the "Measure" command was utilized to select the corner points of the airway region for measurement purposes. Linear measurements and airway areas were ultimately compared across the groups (Figure 2, Table 1).

Statistical Analysis

Data analysis was conducted using IBM version 20.0 (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test was employed to assess normality. The statistical analysis utilized the Independent Samples t-test and the Mann-Whitney U test for comparing variables between groups. A significance level of $p<0.05$ was deemed statistically significant. A multiple linear regression analysis was conducted to identify cephalometric measurements that may influence pharyngeal airway measurements.

The multiple linear regression analysis utilized the "forward selection" method to select independent variables for inclusion in the model. Independent variables with a p-value less than 0.20 were deemed eligible for inclusion in the multiple linear regression model.

RESULTS

The measurements for each parameter were evaluated for reliability using the intra-class correlation coefficient, yielding statistically significant results (p<0.001), which indicates high reliability. The chronological ages of girls with skeletal Class I (137.2±9.1 months) and Class III (138.9±11.2 months) malocclusions were comparable. No significant differences were observed in the ages of boys with Class III (145.4±9.8 months) and Class I (143.8±9.4 months) malocclusions. The chronological and skeletal ages of boys with Class I malocclusions were significantly greater than those of girls with Class I malocclusions (p=0.001, p<0.001, respectively). The chronological and skeletal ages of the Class III boys were significantly higher than those of the Class III girls (p<0.01, p<0.001; respectively).

Comparisons Between Malocclusions

Boys with Class I malocclusion had higher Co-A and ANB values, and a smaller SNB angle than boys with Class III malocclusion (p<0.001). In Class I boys, AA'-Pm' and AA-PNS dimensions were found to be significantly larger than those in Class III boys (p<0.05).

The Co-A length, SNA, and ANB angles were significantly higher in skeletal Class I girls compared to Class III girls (p<0.001, p<0.01, p<0.001; respectively). The SNB angle and Co-Gn distance were observed to be smaller in Class I girls compared to Class III girls (p<0.001, p<0.05, respectively). The oropharyngeal area (OA) and retroglossal (RG) area were significantly smaller in skeletal Class I girls compared to Class III girls (p<0.001, p=0.001; respectively). Class III girls exhibited greater nasopharyngeal height (S-PNS) and upper airway

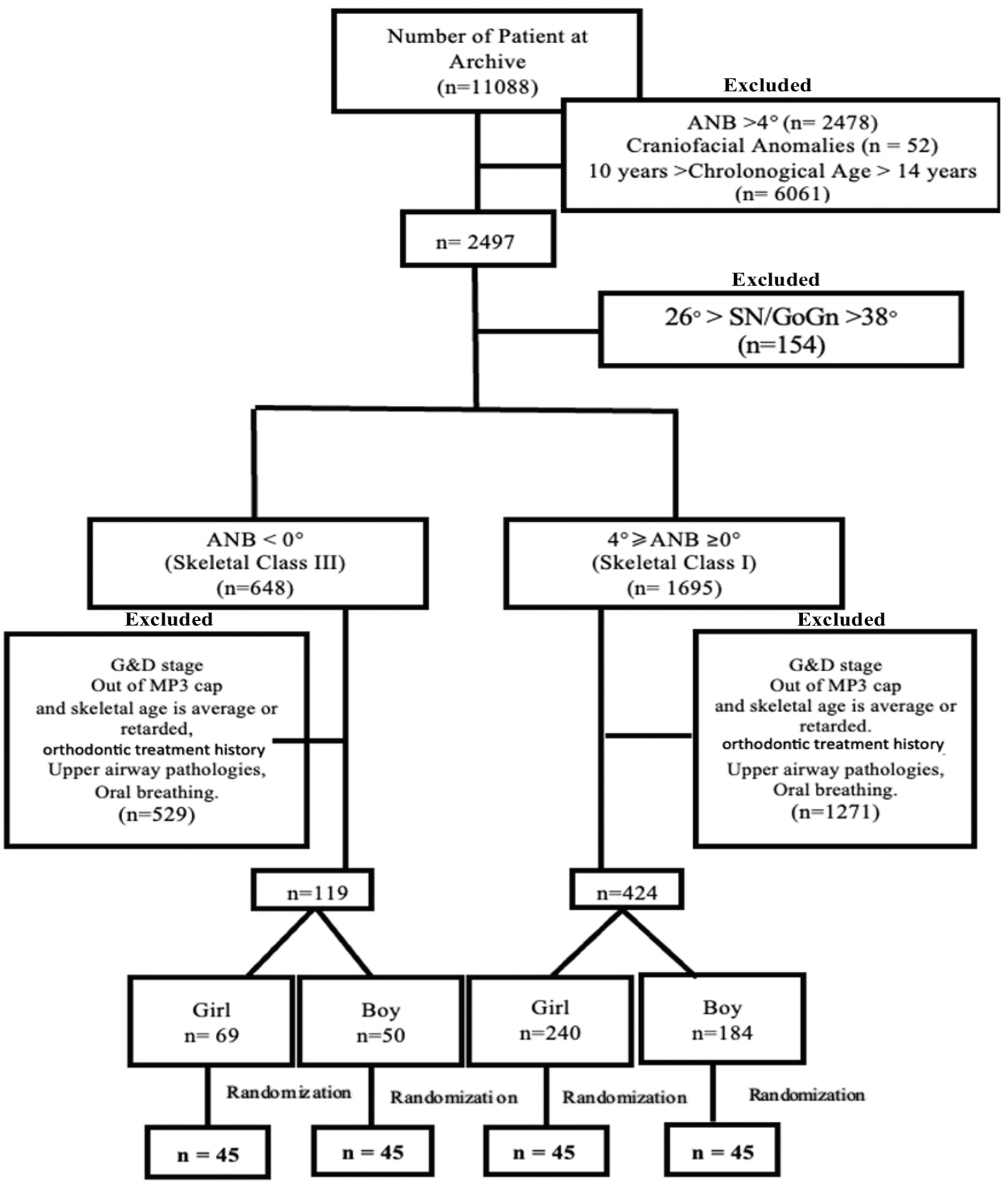

Figure 1. Flow chart for patient selection criteria

width (SPS), along with a more anterior and lower hyoid bone position compared to Class I girls (p<0.05) (Tables 2, 3).

Comparisons Between Gender

Mandibular effective length (Co-Gn) was found to be greater in Class I boys than Class I girls (p<0.01). N-Me, ANS-Me, and H-SN dimensions were found to be greater whereas SNB angle is smaller in Class I boys than in Class I girls (p<0.001). The S-PNS in Class I boys was found to be greater than in Class I girls (p<0.01). Girls with Class I malocclusion have a more extensive head position than boys due to SN/CVT angle (p<0.05).

The skeletal measurements of boys and girls exhibiting Class III malocclusion were comparable. In Class III girls, OA (p<0.05), RG (p<0.01), SPS (p<0.05), lower airway width (IPS) (p<0.05), and airway width at epiglottis level (eb-Peb) (p<0.05) were found to be greater than those in Class III boys. The hyoid position relative to the mandible (H-MP) was significantly lower in Class III girls compared to Class III boys (p<0.01). Class III girls exhibit a more pronounced head position compared to Class III boys (p<0.001) (Tables 2, 3).

Regression Analysis

The multiple linear regression analysis utilizing the "forward selection" method indicated that in Class III boys, cephalometric measurements and NA are significantly explained by SNA, while RP area is significantly explained by N-Me (p<0.05) (Tables 4, 5). The regression model indicates that the RP area is explained by the N-ANS and Co-A variables, while NA is explained by the Co-Gn length in Class III girls (p<0.05) (Tables 4, 5).

DISCUSSION

Orthodontic treatment may potentially affect the upper airway.[15] Narrowing of the upper respiratory tract can lead to snoring and obstructive sleep apnea (OSA), adversely impacting sleep quality.[15] Recent investigations indicate that patients with OSA display dentofacial morphological characteristics linked to a constricted upper airway, including a retrusive mandible, a vertical mandibular plane, a dorsally positioned tongue, and an extended soft palate.[17] The literature discusses the impacts of various orthodontic, orthopedic, functional, and orthognathic surgical interventions on the upper airway.[4-7] Additionally, several studies evaluated the upper airway according to various types of malocclusions.[2,3,7,11,18] However, these studies often had a wide distribution of ages among the malocclusion groups, based on chronological age, or evaluated both genders together. Buyukcavus et al.[2] did not consider the vertical dimension in their classification of Class III patients, grouping them solely based on the ANB, SNA, SNB values as maxillary retrognathism, mandibular prognathism, or a combination of them. In our study, we classified the patients based on the Co-A and Co-Gn values, the ideal SN/GoGn angle range was chosen considering the vertical dimension known to affect the airway. This study represents the first evaluation of airways in Class III patients during the MP3cap growth period. This study

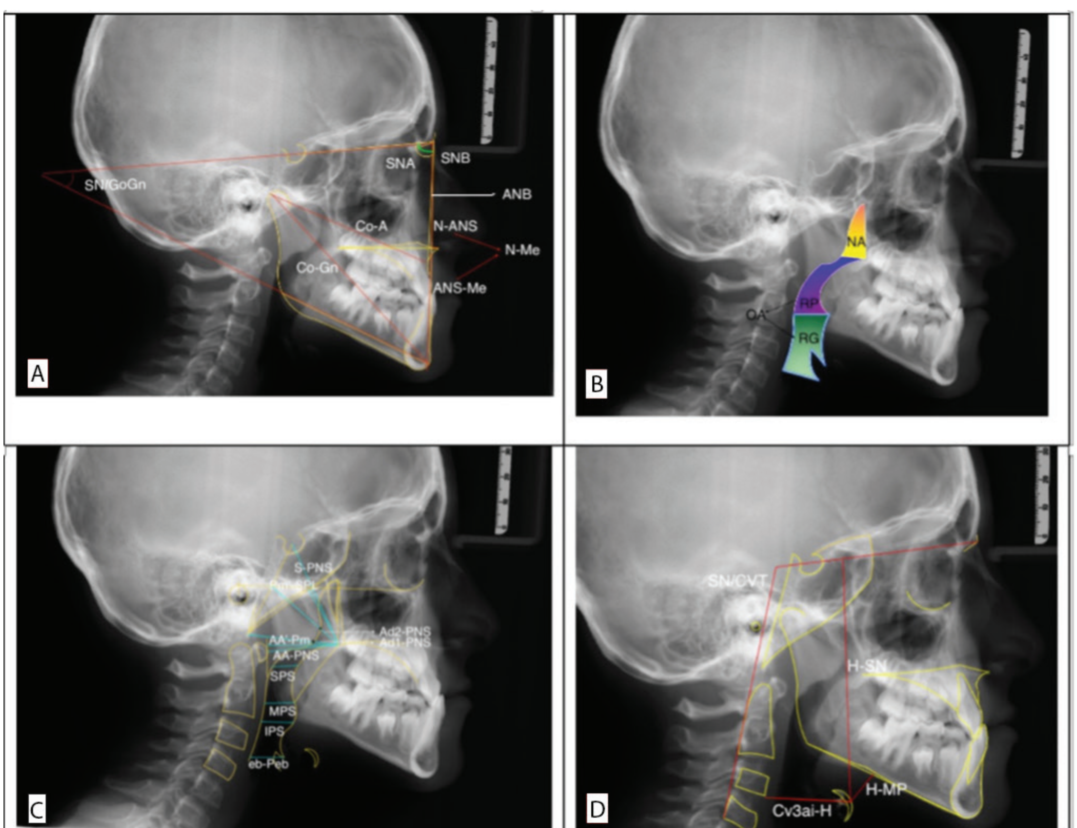

Figure 2. Skeletal landmarks and measurements used in study

establishes the normative values of airway dimensions in patients with Class I dentofacial structure during the MP3cap growth period for both genders.

Bench et al.[19] reported that the level of the hyoid bone descends with chronological age. Developmental changes are observed in both pharyngeal airway depth and hyoid position with chronological age.[19,20] The sagittal nasopharyngeal airway is narrowest at five years of age, increases until ten slightly decreases between 10-11 years of age, and increases again after 11 years of age.[20] However, there is no study in the literature that has considered skeletal ages during airway evaluation and several studies have reported a significant but low correlation between chronological ages and skeletal ages in girls.[21,22] Utilizing comparable skeletal ages and growth periods may reduce the influence of age, yielding more precise data in evaluating airway dimensions and facilitating a deeper comprehension of airway development and changes during growth. Boys in both malocclusion groups demonstrated greater skeletal and chronological ages compared to girls, with a statistically significant difference observed. This disparity is due to the earlier onset of the growth spurt (MP3cap) in girls compared to boys during the growth and development phase.

The gold standard method for diagnosing OSA is polysomnography (PSG).[23] However, cone-beam computed tomography (CBCT) has gained popularity as a convenient and less time-consuming diagnostic tool, especially due to its relatively lower cost as compared to PSG.[24] While lateral cephalograms created using CBCT images are considered a practical and convenient method to assess the airway, there may be differences observed on the right and left sides.[25] The lateral cephalogram is a simple, low-cost, and easily renewable 2-dimensional image that is more suitable for retrospective studies. Pracharktam et al.[26] evaluated the upper airway passage in two positions, sitting upright and lying down, and reported similar airway measurements between the two positions using 2D cephalograms. In our study, lateral cephalograms were taken while the patients were in their natural upright position.

Table 1. Skeletal landmarks and measurements utilized in the study

Nazopharyngeal area (NA; mm^2)	The posterior wall has a convex contour from the upper point of the pterygomaxillary fissure to point ad2, where the tangent to the sphenoid bone curvature intersects the posterior pharyngeal wall. It continues with a concave contour to point ad1, where the Ba-PNS line intersects the posterior pharyngeal wall. This area is bounded below by the palatal plane and in front by the PTV plane, which is perpendicular to the FH plane from point Pm.
Oropharyngeal area (OA; mm^2)	The area bounded above by the palatal plane, below by the base of the epiglottis, posteriorly and anteriorly pharyngeal wall.
Retropalatal area (RP; mm^2)	The area of the region that extends from the level of the hard palate to the caudal limit of the soft palate.
Retroglossal area (RG; mm^2)	The area extends from the caudal border of the soft palate to the base of the epiglottis.
S-PNS (mm)	The distance between point S and PNS.
ad1-PNS (mm)	The distance between ad1 (the point where the Ba-PNS line intersects the posterior pharyngeal wall) and PNS.
ad2-PNS (mm)	The distance between ad2 (the point where the line extending from the midpoint of the Ba-S line intersects the posterior pharyngeal wall) and PNS.
AA'-Pm' (mm)	The distance between the points where the perpendiculars from the most anterior projecting point of the atlas and the pterygomaxillary point intersect the palatal planes.
Pm'-SPL (mm)	The distance from Pm to the vertical projection point of the line perpendicular to the FH plane on the pharyngeal wall, to the tangent line of the sphenoid bone's lower boundary, starting from Basion.
AA-PNS (mm)	The distance between the point where the tangent drawn perpendicularly from the most anterior point of the atlas intersects the palatal plane and PNS.
MPS (mm)	The distance between the lowest point of the soft palate (P) and the point where the line drawn parallel to the FH plane from this point intersects the pharyngeal wall (Pp).
SPS (mm)	The distance between the points where the anterior and posterior pharyngeal walls intersect lines drawn parallel to the FH plane from the midpoint of the soft palate.
IPS (mm)	The distance between the points where a line drawn parallel to the FH plane from the most anterior and inferior edge of the 2nd cervical vertebra (CV2ai) intersects the anterior and posterior pharyngeal walls.
eb-Peb (mm)	The distance between the point where the line extending parallel to the FH plane from the vallecula epiglottis intersects the posterior pharyngeal wall and the vallecula epiglottis.
H-MP (mm)	The perpendicular distance from the most anterior point of the hyoid bone to the mandibular plane.
H-SN (mm)	The perpendicular distance from the most anterior point of the hyoid bone to the SN plane.
Cv3ai-H (mm)	The distance between the most anterior and inferior point of the 3rd cervical vertebra and the most anterior point of the hyoid bone.
SN/CVT (°)	The angle between the SN and CVT planes.

FH: Frankfort horizontal

Table 2. Comparison of the skeletal measurements of boys and girls with Class I and III malocclusions

Measurements		Class I			Class III			Class I vs Class III	
		Boys	Girls	p-value	Boys	Girls	p-value	Boys p-value	Girls p-value
Maxillary	SNA (°)	79.4±2.9	79.7±3.3	0.622	78.2±4.4	77.7±3.3	0.591	0.121	0.005**
	Co-A (mm)	79.5±4.0	78.0±4.5	0.097	76.2±4.6	74.8±3.5	0.102	**<0.001*** **	**<0.001*** **
Mandibular	SNB (°)	77.0 (68-85)	77.0 (70-85)	**<0.001*** **	81.0 (71-90)	80.0 (74-88)	0.694	**<0.001*** **	**<0.001*** **
	Co-Gn (mm)	102.6±5.5	99.4±5.9	**0.010** **	104.2±5.5	102.0±5.4	0.062	0.155	**0.028* **
Maxillo-mandibular	ANB (°)	2.3±1.1	2.6±1.1	0.292	-2.8±2.0	-2.7±1.3	0.691	**<0.001*** **	**<0.001*** **
Vertical	SN/GoGn (°)	34.4±2.5	33.6±2.5	0.159	33.3±3.0	34.2±2.7	0.131	0.072	0.274
	N-Me (mm)	109.3±5.8	104.2±5.9	**<0.001*** **	107.1±9.9	106.7±6.3	0.820	0.196	0.060
	N-ANS (mm)	48.8±3.3	47.6±3.2	0.095	49.2±2.8	48.3±2.8	0.154	0.537	0.262
	ANS-Me (mm)	61.0 (50-71)	57.0 (45-65)	**<0.001*** **	58.0 (50-71)	58.0 (50-71)	0.695	0.107	0.115

Data were presented as mean±standard deviation or median (min.-max.)
P<0.05 as statistically significant
*p=0.05; **p=0.01; ***p=0.001

Table 3. Comparison of the pharyngeal airway measurements of boys and girls with Class I and III malocclusions

Measurements	Class I			Class III			Class I vs Class III	
	Boys	Girls	p-value	Boys	Girls	p-value	Boys p-value	Girls p-value
NA (mm²)	270.9±79.6	261.3±80.1	0.569	268.0±68.9	253.8±72.5	0.341	0.857	0.643
OA (mm²)	491.4±126.2	461.5±108.2	0.230	483.9±125.6	551.1±126.0	0.013	0.777	**<0.001*** **
RP (mm²)	270.7±52.7	248.6±62.2	0.074	276.8±70.6	270.7±60.1	0.659	0.643	0.090
RG (mm²)	224.0 (31-571)	212.9±88.3	0.831	217.0 (8.0-382)	280.4±100.0	0.002	0.693	**0.001*** **
S-PNS (mm)	42.2±2.8	40.4±2.1	**0.001*** **	42.1±2.7	41.7±3.0	0.482	0.908	**0.015* **
ad1-PNS (mm)	19.0 (11-25)	19.0 (7-28)	0.543	19.0 (12-28)	19.0 (7-25)	0.538	0.789	0.234
ad2-PNS (mm)	15.0 (7.0-24)	15.0 (5-23)	0.842	15.0 (10-23)	14.0 (7-38)	0.068	0.202	0.478
AA'-Pm' (mm)	27.8±3.1	27.4±3.3	0.575	26.1±3.4	26.8±3.5	0.343	0.016*	0.384
Pm'-SPL (mm)	29.0±3.7	27.7±3.3	0.096	28.0±3.3	27.8±3.2	0.744	0.200	0.922
AA-PNS (mm)	28.8±3.0	28.6±3.0	0.699	27.2±3.0	27.8±3.3	0.346	0.011*	0.256
MPS (mm)	10.0±2.9	9.2±2.7	0.181	9.3±2.4	10.0±2.0	0.190	0.254	0.131
SPS (mm)	10.6±2.3	10.8±2.6	0.735	10.6±2.3	12.0±2.8	**0.010** **	0.964	**0.032* **
IPS (mm)	9.0 (4.0-14)	9.7±3.2	0.526	9.0 (6-18)	10.7±2.9	**0.014* **	0.769	0.135
eb- Peb (mm)	13.7±2.3	14.4±3.1	0.178	13.2±2.8	14.6±3.5	**0.046* **	0.394	0.873
H-MP (mm)	11.0±4.0	12.0 (5-24)	0.474	11.8±3.9	15.0 (6-31)	**0.004** **	0.342	**0.007** **
H-SN (mm)	94.4±7.0	88.5±7.5	**<0.001*** **	95.7±6.8	93.6±6.2	0.123	0.384	**0.001*** **
Cv3ai-H (mm)	24.3±2.8	24.5±2.8	0.704	24.6±3.0	25.8±2.8	0.060	0.559	**0.030**
SN/CVT (°)	103.1±8.3	108.0±10.3	**0.015* **	101.8±9.2	108.9±8.7	**<0.001*** **	0.465	0.650

Data were presented as mean±standard deviation or median (min.-max.)
P<0.05 as statistically significant
*p=0.05; **p=0.01; ***p=0.001

Table 4. Results of the multiple linear regression analysis of cephalometric measurements with NA in Class III girls and boys

Gender	Independent variables	B	SE	β	p-value	95% CI (Upper-Lower)	Regression
Boys	SNA (°)	5.839	2.208	0.374	**0.011***	(1.388;10.291)	F=6.997 p=0.011 adj. R^2=0.120
Girls	Co-Gn (mm)	4.110	1.959	0.305	**0.042***	(0.159;8.061)	F=4.401 p=0.042 adj. R^2=0.072

adj. R^2: Adjusted explained variance
*P<0.05 as statistically significant
B, non-standardized coefficient; β, standardized coefficient; SE, standard error; CI, confidence interval; NA, nasopharyngeal area

Table 5. Results of the multiple linear regression analysis of cephalometric measurements with RP in Class III girls and boys

Gender	Independent variables	B	SE	β	p-value	95% CI (Upper-Lower)	Regression
Boys	N-Me (mm)	2.692	1.021	0.377	**0.012***	(0.631;4.752)	F=4.039 p=0.025 adj. R^2=0.121
	SNB (°)	3.215	2.242	0.205	0.159	(-1.311;7.740)	
Girls	N-ANS (mm)	7.820	2.959	0.361	**0.012***	(1.849;13.792)	F=5.752 p=0.006 adj. R^2=0.178
	Co-A (mm)	4.795	2.342	0.280	**0.047***	(-0.067;9.522)	

adj. R^2: Adjusted explained variance
*P<0.05 as statistically significant
B, non-standardized coefficient; β, standardized coefficient; SE, standard error; CI, confidence interval

Bozzini et al.[27] employed a 40-second protocol for CBCT scanning, sufficient for patients to hold their breath and stabilize their head position. Hong et al.[28] employed a 15-second time protocol for CBCT scanning. The duration required to obtain lateral cephalometric radiographs in our study was 14.9 seconds. The short duration facilitates breath-holding in patients, resulting in more dependable radiographs for airway evaluation.

Ucar et al.[29] observed that low-angle patients exhibited a greater nasopharyngeal airway area and upper airway dimensions than high-angle patients. Alhammadi et al.[30] reported that vertical positioning of the mandible enhances airway volume while accommodating collapse resulting from the posterior position of the mandible. Only patients exhibiting optimal vertical growth patterns were included in this study to minimize variation. Since the literature shows differing opinions on the relationship between gender and airway dimensions,[10,14,31] the airway was evaluated separately for each gender in this study.

Jena et al.[9] reported that skeletal parameters, particularly mandibular prognathism, influence airway dimensions. This study included only Class III patients from the maxilla or maxillomandibular regions, excluding those from the mandible. The present study indicates that Class III boys exhibited significantly lower measurements of pharyngeal width in the anteroposterior direction at the adenoid level (AA-PNS, AA'-Pm') compared to Class I boys. Class III girls exhibited a significantly larger OA and RG area in comparison to Class I girls. Furthermore, SPS and IPS measurements exhibited greater values in Class III girls. The observed results may be attributed to the inferior and anterior positioning of the hyoid bone, along with an extended head posture in Class III girls. Consistent with our findings; Iwasaki et al.[10] reported that Class III patients exhibited a wider oropharyngeal airway than Class I patients at 8 years of chronological age using CBCT images. Trenouth and Timms reported a positive correlation between oropharyngeal airway and mandibular length in children aged 10 to 13.[32] However, Takemoto et al.[13] found that the lower pharyngeal airway size was larger in Class III girls originating from the mandible compared to those in Class I; however, no significant differences were noted in the sizes of the upper airway. The study found that an anterior mandibular position in girls aged 7-8 years correlates with an increased width of the lower pharyngeal airway.

Takemoto et al.[13] observed no significant differences in upper airway dimensions between Class III and Class I girls at the age of 8. Zhong et al.[33] classified Class I and Class III Chinese children according to mandibular plane angle and ANB angle, revealing no significant differences in upper pharyngeal space measurements. Chan et al.[34] similarly found no significant differences in the nasopharyngeal region across various malocclusions. The authors found that NA was comparable in both Class III and Class I groups across genders. The patients in our study had an average age of approximately 12 years, and the growth and development of the airway were found to be more stable, as reported by Taylor et al.[35].

Ceylan and Oktay[11] reported a negative impact of an elevated ANB angle on the dimensions of the NA in their study, which evaluated both genders collectively and compared Class I, II, and III malocclusions. All subjects in the study were aged between 13 and 15 years. No significant differences in NA were observed between Class I and Class III malocclusion groups across both genders. The regression analysis indicated that NA is explicable by SNA in Class III boys and Co-Gn in Class III girls. No significant difference was observed in the SNA angle between Class III and Class I boys. The anticipated increase in NA for Class III girls, linked to the rise in mandibular effective length, was not observed. This absence of difference may be explained by the malocclusion stemming from maxilla-mandibular discrepancy and a reduced SNA angle. The authors found that an increased ANB angle correlated with a decrease in OA and noted a higher positioning of the hyoid bone in Class III children compared to Class I children. In contrast to that study, our research indicates that the hyoid bone is positioned lower, and the OA was larger exclusively in Class III girls.

A significant regression model was identified in Class III girls, linking RP area, upper anterior facial height, and upper maxillary effective size. Bozzini et al.[27] reported a moderate positive correlation between nasal area and facial height, as well as between the RP area and upper anterior facial height in Class III girls approximately 26 years of age.

Gökçe et al.[14] conducted a comparison of pharyngeal measurements between male and female adults with Class I malocclusion, revealing statistically significant greater sagittal pharyngeal dimensions in males, with the exception of craniocervical angles related to head posture. Our study revealed that only S-PNS was significantly greater in Class I boys, while other pharyngeal measurements were comparable between genders within the Class I malocclusion group. This discrepancy may be attributed to the age differences between our study and that of Gökçe et al.[14].

Hellsing et al.[36] found correlation between head position and cervical lordosis, on lateral cephalograms; increase in the size of the pharyngeal airway. Huggare et al.[37] found that head extension positively influenced nasorespiratory function. The present study noted an increase in airway dimensions in Class III females, characterized by an extended head (an increase of 200 in the SN/OPT angle) and a lowered hyoid bone position. In contrast to our study, Alves et al.[25] evaluated adult patients and found that RP and RG volumes were significantly larger in Class III males compared to Class III females.

The McNamara analysis[12] indicates that in the Ann Arbor adult samples, the average upper airway measurement is 17.4 mm, with a tendency for this measurement to increase with age. The mean lower airway measurements range from 10 to 12 mm, with no significant changes observed with age. In the present study, we found that the median [minimum, maximum (min., max.)] upper airway measurements (ad1-PNS) for Class I and Class III boys were 19 (11, 25) mm and 19 (7, 28) mm, respectively. The median lower airway measurements (IPS) were 9 (4, 14) mm and 9 (6, 18) mm, respectively. The median (min., max.) upper airway measurements (ad1-PNS) for Class I and Class III girls were 19.0 (7-28) mm and 19.0 (7-25) mm, respectively. The median lower airway measurements (IPS) were 9.7±3.2 mm and 10.7±2.9 mm, respectively. The findings underscore the importance of gender differences in airway measurements.

Our results indicate that the airway must be thoroughly assessed in orthodontic diagnosis and treatment planning, considering age-related factors for each gender. In particular, the application of treatments that narrow the airway and induce clockwise rotation of the mandible may be approached with reduced clinical concern in females, given that this area is wider compared to males of the same age. Furthermore, implementing multidisciplinary treatments in conjunction with ENT specialists would be advantageous.

Strengths and Limitations

All patients' radiographs were obtained using the same cephalometric radiography device, in a consistent environment, and with subjects positioned in a natural head posture. Furthermore, patients were chosen within a defined age range (10-14 years) and at the same growth and development stage (MP3cap) to minimize age-related variations. Additionally, to control for gender effects, measurements were assessed independently for each gender and subsequently compared across genders.

Multiple measurements were conducted to characterize the airway, thus eliminating dependence on a singular parameter. The study participants demonstrated optimal vertical growth direction.

A limitation of this study may be the absence of assessment for body mass index or obesity scores, attributable to its retrospective design. Additional limitations include the absence of longitudinal follow-up and the reliance on two-dimensional evaluation for assessing the pharyngeal airway. Future research should employ longitudinal designs to monitor alterations in airway dimensions over time. Additionally, focusing on Class III patients with mandibular prognathism and integrating comprehensive clinical evaluations of breathing by ear, nose, and throat specialists would be advantageous.

CONCLUSION

There are no differences in the nasopharyngeal area dimensions when comparing different malocclusion groups or genders. In Class III girls, the oropharyngeal, RG, and superior pharyngeal space were larger than Class III boys, and larger than Class I girls. The inferior pharyngeal space was larger in Class III girls than Class III boys. Girls with both Class I and Class III malocclusions exhibited a more extensive head posture compared to boys.

Ethics

Ethics Committee Approval: The study protocol received approval from the Measurement and Evaluation Ethics Sub-Working Group of the Gazi University (approval no.: 2020-465, date: 08.09.2020).

Informed Consent: Informed consent forms were obtained from each patient.

Footnotes

Author Contributions: Surgical and Medical Practices - M.K., E.K.; Concept - M.K., E.K.; Design - E.K.; Data Collection and/or Processing - M.K.; Analysis and/or Interpretation - B.Ç.; Literature Search - M.K., B.Ç., E.K.; Writing - M.K., B.Ç., E.K.

Conflict of Interest: The authors have no conflicts of interest to declare.

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Original Article

A Comparative Study of Proximal Caries Formation and Decay, Missing, Filled Teeth Scores in Clear Aligners and Fixed Orthodontic Treatments

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Main Points

- The total number of caries lesions increased with the use of fixed and clear aligner treatments.
- Clear aligners had no significant effect on reducing the risk of proximal caries compared with fixed orthodontic appliances.
- Fixed orthodontic treatment significantly increased the Decay, Missing, Filled Teeth (DMFT) score, whereas clear aligner therapy caused no statistical change in the DMFT scores.

ABSTRACT

Objective: This study aimed to evaluate proximal caries formation and Decay, Missing, Filled Teeth (DMFT) scores during clear aligner (CA) therapy compared with fixed orthodontic treatment.

Methods: A total of 50 patients with a mean age of 19.9 years were divided into two equal groups (n=25) according to treatment method. Both CA and fixed appliance (FA) patients had low-to-medium levels of crowding. Caries formation and DMFT scores were assessed via radiographic and clinical examination before treatment (T0) and at the end of a six-month observation period (T1). The numbers of caries lesions and fillings was analyzed using a Two-Way Analysis of Variance with a significance level of 0.05.

Results: Significant statistical differences were found for both groups ($p<0.001$). The amount of proximal caries significantly increased in both groups, whereas the increase in non-proximal caries was only statistically significant in the FA group. DMFT scores also increased significantly in both groups, with the FA group showing a higher increase at the end of the observation period.

Conclusion: Although CAs had an advantage in decreasing the overall risk of caries, no distinct advantage was found in reducing the risk of proximal caries lesions. The DMFT index was significantly higher in fixed orthodontic treatment patients than in CA treatment patients.

Keywords: Removable appliances, clear aligners, demineralization, fixed appliance, orthodontics

INTRODUCTION

Fixed orthodontic treatment with brackets, wires, and ligatures is associated with an increased risk of caries because it promotes saliva bacteria and plaque accumulation. Kiliçoğlu et al.[1] found that fixed devices, especially on molar surfaces, hinder proper oral hygiene, leading to an elevated risk of caries in inaccessible proximal areas. The proximal area is inaccessible for physiological cleansing, and the risk of caries lesions is elevated in this area when the patient lacks proper oral hygiene.[2]

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Difficulty in mechanical cleaning contributes to increased plaque accumulation. Consequently, neighboring teeth may experience demineralization on their contact surfaces.[3]

In contrast, clear aligners have a significant benefit in reducing the formation of new caries during orthodontic therapy. A recent review about the effects of different orthodontic appliances on periodontal health and oral flora stated that the majority of the literature showed that biofilm formation on clear aligners was less than that on fixed appliances because clear aligners could be removed and changed after a time period and patients treated with aligners showed better compliance in oral hygiene.[4]

Clear aligners, which require 20-22 hours of daily use, impede natural cleaning and remineralization mechanisms by preventing saliva flow onto teeth. Consequently, plaque accumulation occurs under the aligners, thereby affecting the oral flora.[5-7]

Although clear aligners reduce demineralization risk on buccal surfaces compared with fixed appliances, they may still lead to severe decay, periodontal issues, and even tooth loss. Proximal areas require thorough hygiene and may carry an increased caries risk.[8]

Previous studies mostly focused on white spot lesions and the total amount of caries lesion formations during clear aligner therapy,[9] but no study has assessed the risk of proximal caries in patients using clear aligners.

The present study aimed to evaluate proximal caries formation and Decay, Missing, Filled Teeth (DMFT) scores during the first six months of clear aligner treatment compared with fixed orthodontic treatment. The null hypothesis is that approximal caries formation and DMFT scores do not differ between the two treatment modalities.

METHODS

This prospective study included 50 patients who sought orthodontic treatment at an Orthodontic Clinic of Kırıkkale University Faculty of Dentistry. Sample size estimation was performed using G-Power (Version 3.1.2., Franz Faul, Universitat-Kiel, Germany) based on a previous study investigating the effect of orthodontic treatment on the DMFT index and caries formation. With equal group sizes, an effect range of 0.40, and a significance level of 0.05, the power analysis indicated a power level of 0.80 for 50 patients.

Patients included in the study had permanent dentition, demonstrated the ability to maintain oral hygiene, and showed no signs of plaque buildup, inflammation, or spontaneous gingival bleeding. Additionally, they had moderate dental crowding between 2 and 5 mm. Patients were excluded if they exhibited increased caries activity, xerostomia, periodontal tissue loss, or advanced periodontal disease. Those with systemic diseases affecting oral tissues and saliva flow, craniofacial syndromes, poor oral hygiene, or those who refused to provide informed consent were also excluded from the study.

This study was approved by Kırıkkale University Clinical Research Ethics Committee (approval no.: 05/01, date: 29.04.2021). Patients were informed about the study and treatment details before beginning treatment and signed informed consent forms, which were approved by the institutional review board. Patients were selected according to inclusion/exclusion criteria from two groups who consulted the Kırıkkale University Faculty of Dentistry, Clinic of Orthodontics for orthodontic treatment between the years 2021 to 2023:

Fixed Orthodontic Appliances (FA) Group: Twelve males and thirteen females (n=25) with a mean age of 17.7 years. Standard 0.022-inch slot metal brackets with MBT prescription (Master Series, American Orthodontics, Sheboygan, WI, USA), bondable molar tubes on first and second molars were used, along with standard wire sequencing. 0.016 and 0.019x0.025-inch heat activated thermal nickel-titanium and stainless-steel wires were used in order.

Clear Aligners (CA) Group: Twelve males and thirteen females (n=25) with a mean age of 21.8 years. Attachments were used selectively for tooth movements. Aligners were worn for at least 20 h per day with specific usage instructions.

Attachments were used only for specific tooth movement needs and for anchorage control in the CA group. Patients were asked to use their aligners for at least 20 h per day. The first two aligners were used for 15 days, and the rest of the single aligners were used for 10 days. Patients in both groups had mild to moderate crowding. None of the patients underwent orthodontic extractions or interproximal enamel reduction on the canines, premolars, or molars.

Pumice prophylaxis was administered, and standard oral hygiene instructions, including brushing three times a day, were given before appliance placement for all patients. The FA group used orthodontic toothbrushes and interdental brushes. They were advised to avoid foods that could damage fixed appliances.

The CA group avoided chewing while wearing aligners, brushed their teeth after meals, and cleaned the aligners with toothbrushes under running tap water. A single expert planned treatment for both groups, informing patients of the restrictions and disadvantages associated with each treatment system.

Records and Time Points

Before treatment (T0), we obtained cephalometric, panoramic, and bite-wing radiographs, intraoral and extraoral photographs, and 3D intraoral scanning models. Radiographs obtained at T0 and at the end of the observation period (T1) were used for caries assessment. The same phosphor-plate bite-wing radiographs (Primax RDX-58, Film Speed E, Berlin, Germany), panoramic device (Op 2D Panorex, Kavo, Germany), and patient positioning were used for radiographic records. Only radiographs without irradiation, positioning, or procedural errors were used in this study.

The post-treatment records were collected with brackets and attachments, and treatment was continued after the observation period.

Radiographic Analysis

Radiographic classification was used for caries assessment. All radiolucent demineralization areas on radiographs were considered caries. An expert examiner randomly assessed all radiographic images and re-analyzed some of the radiographs to evaluate intraclass correlation coefficient (ICC). The assessment included decalcifications and fillings in the canines, premolars, and first and second molars. However, the mesial proximal faces of the canines and distal proximal sides of the second molars were excluded due to bite-wing film size limitations and inexact contact with the third molar teeth. The number and location of caries lesions were recorded and classified as proximal or non-proximal caries/fillings. Lesions observed at T0 were treated and considered fillings at T1. Secondary lesions around or under existing fillings were not recorded at T1; only newly formed lesions were included. To assess caries formation differences between groups, we used the World Health Organization-recommended DMFT index system as follows:

[DMFT = {untreated} + {filling} + {missing teeth}][10]

Twenty percent of the total radiographs were reassessed after one month by the same examiner to analyze the methodological error.

Statistical Analysis

We performed statistical analyses using SPSS 24 (IBM Systems, USA). The normal distribution of data was verified using a Shapiro-Wilk test. Two-way analysis of variance (two-way ANOVA) with Bonferroni's post-hoc test was used to assess the changes in proximal and non-proximal caries amounts and the DMFT score between the two groups at different time points. The ICC method was used to assess observer reliability. The significance level was set at 0.05.

RESULTS

The mean ICCs were 0.84 for the fixed treatment group (FA) and 0.88 for the clear aligner group (CA), indicating high consistency in radiographic assessment.

At the time of T1 examinations: Patients in the FA group had undergone orthodontic therapy for 15.7±13.9 months. Patients in the CA group had undergone orthodontic therapy for 15.2±14.1 months. Table 1 presents the sex-specific incidence. Table 2 presents the descriptive and statistical significance.

The increase in proximal caries amounts and the time-group interaction were statistically significant: [$F_{(1, 48)}=14.59$, $p<0.001$]. Specifically, only the FA group exhibited a significant increase after the observation period ($p<0.001$). No significant main effect of group was found: [$F_{(1, 48)}=0.785$, $p=0.38$].

The number of non-proximal caries increased significantly in FA group: [$F_{(1, 48)}=24.3$, $p<0.001$]. There was no significant interaction between time and group or main effect of group on parameters: [$F_{(1, 48)}=0.568$, 0.455].

The mean DMFT score of the CA group increased by 0.52 points, whereas that of the FA group increased by 1.68 points after the observation period. The overall increase in DMFT scores was significant: [$F_{(1)}=30.250$, $p<0.001$]. Both time and group had a significant effect on DMFT scores: [$F_{(1, 48)}=8.410$, $p<0.001$]. The FA group exhibited a higher overall increase in DMFT scores after the observation period. For visual reference, Figure 1 illustrates the patterns of all analyzed parameters.

DISCUSSION

The current study revealed that clear aligners were not effective in decreasing the risk of proximal caries when

Table 1. Ratio of the number of new caries formations and fillings through the observation period to the total number of examined subjects (incidences) according to sex

Group	Caries type	Gender	N	Incidence
CA	Proximal	F	13	2.84
	Non-proximal	M	12	4
	Proximal	F	13	2.46
	Non-proximal	M	12	3.41
FA	Proximal	F	13	2.84
	Non-proximal	M	12	2.91
	Proximal	F	13	4.92
	Non-proximal	M	12	3.16

N, Number; CA, Clear Aligners;; FA, Fixed Orthodontic Appliances; F, Female; M, Male

Table 2. Caries lesion numbers according to time points and statistical significance

Variable	Group	Time	Mean	SD	p-value
Proximal caries + fillings	CA	T0	3.04	3.95	
		T1	3.4	4.09	
	FA	T0	2.16	2.44	**
		T1	2.88	2.32	
Non-proximal caries+ fillings	CA	T0	2.84	2.81	
		T1	2.92	2.9	
	FA	T0	3.28	3.54	**
		T1	4.08	3.55	
DMFT*	CA	T0	5.24	5.61	**
		T1	5.76	5.83	
	FA	T0	6.08	4.99	**
		T1	7.76	4.44	

*Significant main effect of the group ($p<0.05$)
**Statistical significance between time points ($p<0.05$)
SD, standard deviation; DMFT, Decay, Missing, Filled Teeth; CA, Clear Aligners; FA, Fixed Orthodontic Appliances

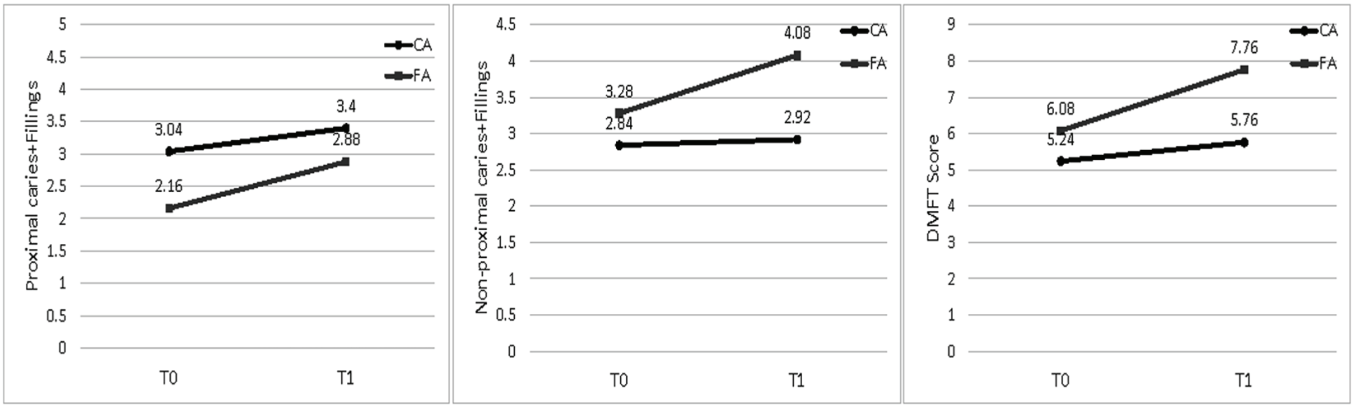

Figure 1. Changes in proximal and non-proximal caries and DMFT scores with the time
DMFT, Decay, Missing, Filled Teeth; CA, Clear Aligners; FA, Fixed Orthodontic Appliances

compared with fixed orthodontic appliances. While previous studies highlighted the key advantages of clear aligners for reducing caries risk, most studies focused solely on buccal surfaces. However, the proximal areas pose greater challenges during oral hygiene applications, and the impact of the type of orthodontic appliance on these surfaces remains unclear.

The alteration of buccal enamel surface characteristics during fixed orthodontic treatment, including etching and resin bonding procedures, contrasts with clear aligner therapy.[5] Unlike composite resin attachments placed only when needed in clear aligner therapy, fixed appliances exhibit a different pattern of bacterial colonization. This discrepancy may have contributed to the observed differences in caries risk between the two approaches.

The surface and chemical characteristics of adhesive materials used in traditional fixed orthodontic appliances and clear aligners significantly affect bacterial retention in the buccal areas.[11] As a result of microbiota changes, enamel demineralization, manifesting as white spot lesions, occurs in 2-97% of patients undergoing fixed orthodontic treatment.[12] Consistent with our findings, the fixed treatment group exhibited a significant increase in non-proximal caries due to plaque accumulation around appliances on the buccal surfaces. Several researchers have evaluated the concentrations of *Streptococcus mutans* and Lactobacilli in saliva, revealing that these bacterial counts peak around 12 weeks after the start of fixed orthodontic treatment.[13-15]

Mummolo et al.[16] found that 40% of fixed appliance patients experienced increased demineralization after 6 months of treatment, necessitating more remineralization agents. In contrast, patients who underwent clear aligner implantation exhibited demineralization in only 10% and patients who underwent removable appliance implantation in 13.3% after the same duration.[15]

Interestingly, our findings indicated that fixed treatment increased the risk of non-proximal caries, whereas the risk of proximal caries remained relatively stable regardless of the appliance used. Similarly, Sifakakis et al.[17] no difference in the salivary counts of cariogenic bacteria was observed between adults treated with clear aligners or fixed appliances. Good oral hygiene likely played a role in the present study, as our study included only patients with favorable hygiene practices.

Orthodontic appliances, such as brackets and bands, pose challenges for thorough proximal cleaning. Although cleaning agents are effective for anterior teeth during full-arch fixed orthodontic treatment, they are less efficient for difficult-to-reach posterior areas. Posterior teeth inherently carry a higher risk of caries even without orthodontic intervention.[17] The oral environment relies on natural cleaning mechanisms facilitated by saliva, tongue movement, and cheek motion. Aligners covering tooth surfaces can disrupt this natural cleaning process.[11]

Saliva plays a crucial role in oral health. Decreased saliva flow contributes to gingival diseases and caries.[18] Patients with xerostomia and advanced periodontal diseases were excluded from the study due to their impact on DMFT scores and tooth loss.

Clear aligners, when worn for 20-22 hours per day and removed only during eating and brushing, have demonstrated effectiveness. However, previous studies have suggested that clear aligners may negatively impact oral hygiene, potentially leading to bacterial colonization and biofilm formation, both intricately linked to caries and periodontal diseases.[4,19,20] While clear aligners prevent some pH-balancing effects of saliva enzymes during full-time use, their ease of mechanical cleaning contributes to overall better oral hygiene. Abu Ebaid and Acar's[21] research supports this, showing that clear aligners minimally affect saliva pH and dental plaque accumulation compared to several fixed orthodontic appliances. Fernley et al.[22] found an inverse relationship between saliva carbonic anhydrase concentration and caries prevalence, highlighting the importance of salivary factors in oral health.

Our study revealed no significant main effect of the appliance used on the increase in the number of caries lesions over time. However, the DMFT scores significantly increased in both groups. Clear aligners did not effectively reduce the risk of proximal caries, possibly because of their limited impact on saliva cleaning effects.

Interestingly, fixed appliances increased the DMFT index more than clear aligners. This difference can be attributed to easier cleaning and reduced plaque accumulation on the buccal surfaces in patients with clear aligners.

In our study, bite-wing radiography was used to assess proximal caries. These radiographs demonstrated higher sensitivity than both panoramic radiographs and visual-tactile examination for diagnosing proximal caries.[23] Newman et al.[24] combined panoramic and bite-wing radiographs for successful proximal caries diagnosis. We adhered to this approach by utilizing both radiographic techniques. Periapical radiographs were intentionally avoided to minimize unnecessary X-ray exposure while assessing the same area. Gribben[25] emphasized the importance of error-free radiographs for valid evaluations, and we followed World Health Organization criteria[26] in evaluating diagnostically excellent radiographs.

Dental crowding complicates oral hygiene, increasing the risk of plaque accumulation and caries.[27] To standardize the sample, we excluded patients with excessive crowding. Only individuals with good oral hygiene were included to minimize the impact of oral hygiene on the study results. The interproximal reduction (IPR) of enamel tissue can lead to surface irregularities and plaque accumulation.[27] To eliminate this potential effect, we excluded patients who required IPR of their canines, premolars, and molars.

Study Limitations

The distal surfaces of the second molars, where caries formation is more common, were not included in our study because of the absence of universally present third molars for proximal contact. Additionally, nutritional content was not controlled because this parameter is challenging to regulate. Instead, patients with similar hygiene and caries activities were included for standardization.

Future randomized controlled trials that carefully monitor pretreatment complexity and treatment outcomes are necessary to minimize variations among pre-treatment groups and provide a comprehensive understanding of the effects of aligners on proximal caries formation. In clinical practice, thorough monitoring of proximal caries formation throughout orthodontic treatment remains crucial, regardless the type of appliance used.

CONCLUSION

New caries formed in non-proximal areas were more common during fixed orthodontic treatment. Clear aligners provide an advantage in reducing the risk of non-proximal caries compared with fixed appliances. However, no significant difference was observed in proximal caries formation between the two treatment modalities, indicating that clear aligners do not significantly reduce the risk of proximal caries. Patients undergoing fixed orthodontic treatment experienced a significantly greater increase in the DMFT index compared to those receiving clear aligner treatment. Despite the overall decrease in caries risk with clear aligners, the possibility of proximal caries formation remains and should not be overlooked. In clinical practice, vigilant monitoring of proximal caries formation throughout orthodontic treatment is essential, regardless of the appliance used.

Ethics

Ethics Committee Approval: This study was approved by Kırıkkale University Clinical Research Ethics Committee (approval no.: 05/01, date: 29.04.2021).

Informed Consent: Patients were informed about the study and treatment details before beginning treatment and signed informed consent forms, which were approved by the institutional review board.

Footnotes

Author Contributions: Surgical and Medical Practices - S.Ç., B.S.A.; Concept - B.S.A.; Design - S.Ç.; Data Collection and/or Processing - S.Ç.; Analysis and/or Interpretation - B.S.A.; Literature Search - S.Ç., Writing - S.Ç., B.S.A.

Conflict of Interest: The authors have no conflicts of interest to declare.

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Original Article

Prediction of Skeletal Age Through Cervical Vertebral Measurements Using Different Machine Learning Regression Methods

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Main Points

- The least absolute shrinkage and selection operator regression exhibited the highest predictive accuracy in estimating vertebral skeletal age.
- Vertebral depth of concavities emerged as a significant predictor of skeletal age in both sexes.
- Vertebral skeletal age estimation did not demonstrate a clinical advantage over chronological age.
- Vertebral skeletal age estimation showed greater variability in boys than in girls, indicating lower consistency with hand-wrist skeletal age assessment.

ABSTRACT

Objective: To compare skeletal ages determined using three different regression methods from measurements made on cervical vertebrae from lateral cephalometric radiographs (LCRs) with the skeletal age determined from hand-wrist radiographs (HWRs).

Methods: LCRs and HWRs of 794 individuals (329 boys, 465 girls) aged 7-18 years were examined. The hand-wrist skeletal age of the participants was determined using the Greulich-Pyle (GP) atlas. Forty-four linear and nine angular morphometric measurements in the C2-C5 vertebrae were made in LCRs. Vertebral skeletal age (VSA) was determined in both sexes using Ridge, the least absolute shrinkage and selection operator (LASSO), and ElasticNet regression methods. The study results were evaluated using R2 (explainability power). Bland-Altman analysis was performed to determine the consistency of chronologic age (CA), GP age, and VSAs.

Results: LASSO regression showed the highest explainability power for VSA, with boys at 0.783 and girls at 0.741. In both sexes, the vertebral depth of concavities had high beta coefficients, and the posterior height of C3 vertebrae (TVup-TVlp) had the highest beta coefficient in boys in LASSO regression. The width of the limits of agreement in both CA and VSA graphs of GP age was wider in boys than in girls. The width of the limits of agreement of CA-VSAs was wider in girls than in boys.

Conclusion: Although high R2 values were obtained, VSA showed no superiority over CA in the assessment of skeletal age, and no significant clinical advantage was observed. For the Turkish population, using GP age may be more accurate for determining skeletal age in orthodontic treatment planning.

Keywords: Orthodontics, hand-wrist radiograph, cephalometry, cervical vertebrae, machine learning

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INTRODUCTION

Assessing growth potential during pre-adolescence and adolescence is crucial, and various indicators such as body height and weight, sexual maturation, chronologic age (CA), dental development, and skeletal development can be used to identify growth stages. The identification of the growth and development stage of an individual has a significant impact on the diagnosis, treatment planning, and treatment outcome of orthodontic treatment. Although CA is commonly used, it may not always be a reliable indicator for growth stages due to variations in the timing, velocity, and duration of growth among individuals.[1] Skeletal age is commonly evaluated in orthodontics via hand-wrist radiographs (HWRs) or lateral cephalometric radiographs (LCRs).[2]

The Greulich-Pyle (GP) atlas is commonly used to determine patients' skeletal age by evaluating the maturation of the hand and wrist bones. The main use of skeletal age in orthodontic treatment is the determination of the timing of orthopedic treatment or the confirmation of the end of growth.[3] HWRs are considered the gold standard; the other most commonly used method for evaluating skeletal maturity in orthodontics is cervical vertebral maturation (CVM), which is based on assessing the maturation stage of the cervical vertebrae.[4,5] It is often suggested that HWRs in orthodontics should be limited to cases where the information obtained is considered essential for treatment planning and cannot be obtained by other means, given the importance of minimizing radiographic exposure.[6]

To objectify skeletal age assessment and make it more efficient, many artificial intelligence (AI) systems have been developed to increase diagnostic accuracy mostly via HWRs.[7] Due to the significant correlation between hand-wrist bone and CVM, most AI studies have focused on classifying developmental phases and comparing AI-based classifications with human diagnoses. However, skeletal age estimation has not been thoroughly studied. The clinical application of these studies was limited because they focus on evaluating success metrics rather than automated systems.[8,9] To address this gap, this study aims to evaluate cervical vertebrae maturity using a quantitative method of morphologic changes.

Regression-based methods determine how independent factors affect a dependent variable by identifying a non-deterministic function representing the independent variables' effect on the dependent variable's mean. While regression procedures are straightforward, they require a suitable model for data fitting. Predictions can be made by applying the parameters obtained in a clinical application into the regression formula.[10] Ridge, The least absolute shrinkage and selection operator (LASSO), and ElasticNet are regression models are commonly used in multiple linear regression problems to prevent overfitting. Optimizing the selection of the proper technique and fine-tuning the hyperparameters via cross-validation is essential for constructing a model that effectively manages bias and variance, thereby enhancing predicted accuracy.[11]

The explainability power (R^2) provides valuable information regarding the degree to which the analyzed data can understand the dependent variable. The higher the R^2 value, the higher the capacity of the obtained data to describe the dependent variable.[12-14] The predominant methodology in the scholarly literature for estimating skeletal age through vertebral parameters involved stepwise regression analysis.[15-18] To our knowledge, no previous study in the literature includes a quantitative approach with AI regression methods to determine skeletal age through LCRs.

Although correlation analysis can compare actual and regression-predicted skeletal age studies, it only evaluates the connection between variables, not their differences.[15,17] The Bland-Altman analysis offers an alternative approach by quantifying the agreement between two quantitative measures by calculating the mean difference and agreement limits. However, Bland-Altman plots only depict the range of agreement without indicating whether it is acceptable. Acceptable limits must be determined based on predefined clinical requirements, biologic considerations, or other relevant goals.[19] Also, there is limited research explicitly addressesing R^2 in skeletal age determination using vertebral measurements and assessing the compatibility and repeatability [vertebral skeletal age (VSA) -GP age] of this method through Bland-Altman analysis.[20]

The aim of this study was to develop a predictive model of VSA by using Ridge, LASSO, and ElasticNet regression models.

The null hypothesis of the study was that there would be no significant difference between the vertebral age prediction models developed using Ridge, LASSO, and ElasticNet regression.

METHODS

Study Design

The study received ethical approval from the Research Ethics Committee of Recep Tayyip Erdoğan University (date: 02.02.2023 and protocol number: 33) and involved a retrospective analysis of LCRs and HWRs from patients referred for orthodontic treatment at the Department of Orthodontics, Faculty of Dentistry at Recep Tayyip Erdoğan University. The study was conducted in accordance with the applicable ethical principles of the World Medical Association Declaration of Helsinki of 1964 and later versions.[21] Informed written consent forms, which included the use of patient records in scientific studies, were obtained from all patients at the beginning of treatment. Patients who met specific criteria were included in the study, including individuals of Turkish ethnicity, between the ages of 7-18 years, with good quality LCRs and HWRs, normal growth and development, no systemic disease, no congenital deformities, no bone syndromes, no previous hand-wrist injury, and good nutrition without serious illness. LCRs and HWRs were taken on the same day and all LCRs included in the study were of sufficient quality, with a clear view of the cervical spine (C2-C5).

The LCRs and HWRs were acquired using a Planmeca Promax 2D S2 imaging unit (Planmeca Oy; Helsinki, Finland) with specific exposure parameters (66 kVp, 10 mA, 10.5 s in LCRs, 60 kVp, 4 mA, and 10.5 s in HWRs). During LCR acquisition, ear rods, and nasal support were used to stabilize the head, and the Frankfort horizontal plane was set parallel to the floor. HWRs were obtained using a specific focus-to-film distance of 170 cm and 30° angulation of the thumb to allow for the depiction of the sesamoid bone.

In the sample size calculation performed considering the number of independent variables as 53, the adjusted R^2=0.686 result in the study of Varshosaz et al.[15], 95% confidence (1-α), 95% test strength (1-β), and f2=2.185 effect size, the minimum required number of samples was determined as 69.

A total of 1257 individuals' LCRs and HWRs were reviewed, and radiographs from 463 individuals who did not meet the inclusion criteria were excluded from the study. We analyzed 794 sets of radiographs (LCR and HWR) of untreated subjects (329 boys, 465 girls) and identified 27 cervical vertebral reference points (Figure 1) for the analysis and obtained 44 linear and nine angular morphometric measurements (Figures 2 and 3), which were located in the C2-C5 vertebrae. The GP age was determined using the HWR images.

All LCRs were calibrated using a 45-mm-long bar, and linear and angular measurements were performed by an orthodontist with 4 years of orthodontic clinical experience using AudaxCeph version 4.2.0.3101 software. To assess the intra-rater and inter-rater agreement, a random sample of 393 LCRs and HWRs was chosen. The measurements were repeated after 1 month by the same orthodontist with 4 years of clinical experience to determine intra-rater reproducibility. Another orthodontist with 10 years of clinical experience performed the measurements to evaluate inter-rater reliability. The intraclass correlation coefficient (ICC) was used to assess the measurement error.

Regression Methods

Ridge, LASSO, and ElasticNet are all regression models used in multiple linear regression problems to prevent overfitting. Choosing the appropriate method and tuning the hyperparameters through cross-validation are crucial for building a model that balances bias and variance, thus improving predictive performance.[12,14]

Multicollinearity occurs when independent variables in a regression model are highly correlated, making it difficult to determine each variable's effect. This issue can be detected using the variance inflation factor (VIF) and tolerance values. A VIF above 10 or a tolerance below 0.2 indicates multicollinearity. Regularization techniques such as Ridge, LASSO, and ElasticNet address multicollinearity by adding a penalty term to the regression model, which helps shrink the coefficients of correlated variables.

Ridge regression incorporates an L2 penalty, the sum of squared coefficients, into the loss function. This technique is particularly effective when dealing with many small and approximately equal coefficients because it distributes the values evenly among correlated variables. By using the lambda (λ) parameter, Ridge regression controls the strength of the L2 regularization.

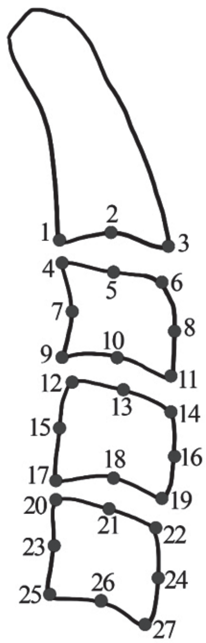

Figure 1. 1.SVp: The most posterior point of the lower edge of the 2nd cervical vertebra, 2.SVd: The deepest point of the concavity at the lower edge of the 2nd cervical vertebra, 3.SVa: The most anterior point of the lower edge of the 2nd cervical vertebra, 4.TVup: The most posterior point of the upper edge of the 3rd cervical vertebra, 5.TVum: Midpoint of the upper edge of the 3rd cervical vertebra, 6.TVua: The most anterior point of the upper edge of the 3rd cervical vertebra, 7.TVpm: Midpoint of the posterior border of the 3rd cervical vertebra, 8.TVam: Midpoint of the anterior edge of the 3rd cervical vertebra, 9.TVlp: The most posterior point of the lower border of the 3rd cervical vertebra, 10.TVd: The deepest point of the concavity at the lower edge of the 3rd cervical vertebra, 11.TVla: The most anterior point of the lower border of the 3rd cervical vertebra, 12.FVup: The most posterior point of the upper edge of the 4th cervical vertebra, 13.FVum: Midpoint of the upper edge of the 4th cervical vertebra, 14.FVua: The most anterior point of the upper edge of the 4th cervical vertebra, 15.FVpm: Midpoint of the posterior edge of 4th cervical vertebra, 16.FVam: The midpoint of the anterior edge of the 4th cervical vertebra, 17.FVlp: The most posterior point of the lower edge of the 4th cervical vertebra, 18.FVd: The deepest point of the concavity at the lower edge of the 4th cervical vertebra, 19.FVla: The most anterior point of the lower edge of the 4th cervical vertebra, 20.FiVup: The most posterior point of the upper edge of the 5th cervical vertebra, 21.FiVum: Midpoint of the upper edge of the 5th cervical vertebra, 22.FiVua: The most anterior point of the upper edge of the 5th cervical vertebra, 23.FiVpm: Midpoint of the posterior edge of 5th cervical vertebra, 24.FiVam: The midpoint of the anterior border of the 5th cervical vertebra, 25.FiVlp: The most posterior point of the lower border of the 5th cervical vertebra, 26.FiVd: The deepest point of the concavity at the lower edge of the 5th cervical vertebra, 27.FiVla: The most anterior point of the lower border of the 5th cervical vertebra

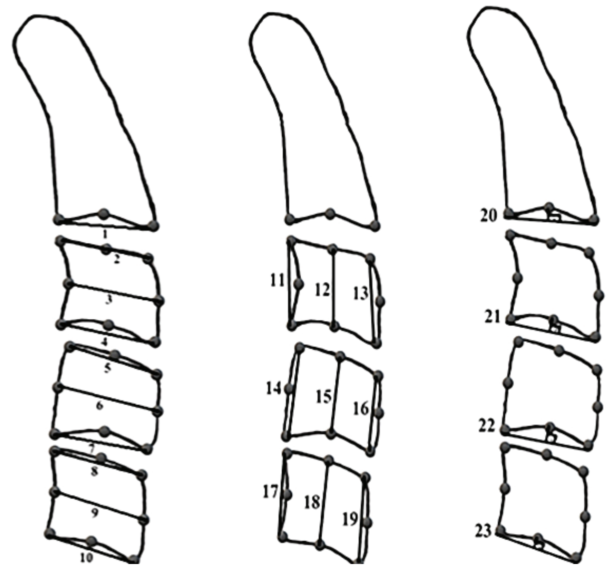

Figure 2. 1st SVp-SVa, 2nd TVup-TVua, 3rd TVpm-TVam, 4th TVlp-TVla, 5th FVup-FVua, 6th FVpm-FVam, 7th FVlp-FVla, 8th FiVup-FiVua, 9th FiVpm-FiVam, 10th FiVlp-FiVla, 11th TVup-TVlp, 12th TVum-TVd, 13th TVua-TVla, 14th FVup-FVlp, 15th FVum-FVd, 16th FVua-FVla, 17th FiVup-FiVlp, 18th FiVum-FiVd, 19th FiVua-FiVla, 20th SVD, 21st TVD, 22nd FVD, 23rd FiVD

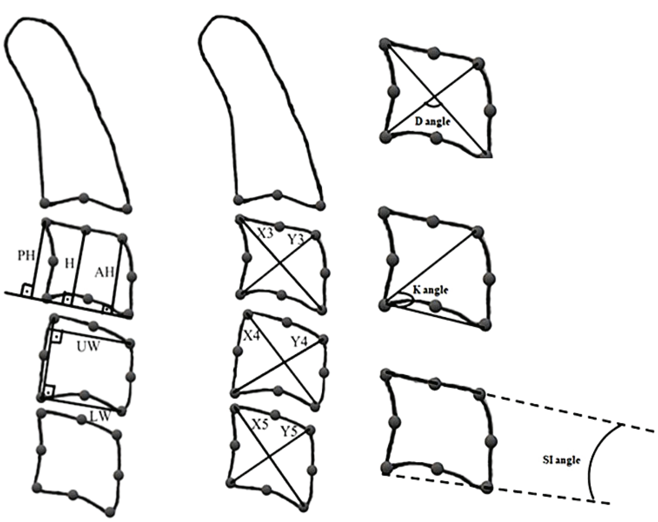

Figure 3. PH3, H3, AH3, PH4, H4, AH4, PH5, H5, AH5, UW3, LW3, UW4, LW4, UW5, LW5, X3, Y3, X4, Y4, X5, Y5, D3 angle, D4 angle, D5 angle, K3, K4, K5, SI3, SI4, SI5

This regularization term penalizes large coefficients, thereby reducing their variance without eliminating any variables, and mitigating multicollinearity in the model.[12] LASSO regression applies an L1 penalty, which is the sum of the absolute values of coefficients. This approach can shrink some coefficients to zero, effectively performing variable selection by eliminating less important predictors. This makes it particularly useful when only a few predictors are expected to be significant. LASSO regression uses the lambda (λ) parameter to control the strength of the L1 regularization, which penalizes the absolute values of the coefficients and enables variable selection by shrinking some coefficients to zero.[13] ElasticNet combines both L1 and L2 penalties, offering a balance between Ridge and LASSO regressions. This approach is advantageous when multiple correlated predictors are present, and some need to be eliminated. ElasticNet regression uses lambda (λ) and alpha (α) parameters. Lambda (λ) controls the overall strength of the regularization, and alpha (α) determines the mix between L1 and L2 regularization. When alpha is 0, ElasticNet behaves like Ridge regression; when alpha is 1, it behaves like LASSO regression. Values between 0 and 1 provide a balance between the two methods. The optimal values of the regularization parameters in Ridge, LASSO, and ElasticNet regression are determined by minimizing the mean squared error.[14]

The performance of these models is typically evaluated using metrics such as R^2 and the Akaike information criterion (AIC) (to measure the model's fit and complexity).[12,14] Cross-validation is a method used to evaluate the performance of machine-learning models. Among various methods, k-fold cross-validation is the most widely used. The dataset is divided into k parts, and each of the k parts is used separately as the test dataset, and the remaining dataset is used as the training dataset. This process is repeated k times, and the mean of the test errors obtained each time is used to predict the model's performance. K-fold cross-validation method ensures that all the samples in the dataset are used to train the model. After k cross-validation, the mean error is calculated for the training and test data and expresses how much the predicted values deviate from the actual values. A lower mean error value means a better fit and more accurate predictions. Cross-validation, especially k-fold cross-validation, is often used to tune the hyperparameters (lambda and alpha), ensuring that the model generalizes well to new data.[12,14]

Statistical Analysis

Statistical analysis was performed using the Eviews v12 program (IHS Markit Ltd, London, UK). Descriptive statistics were calculated as mean, standard deviation, median, minimum/maximum (min./max.), Kurtosis, and Skewness. Vertebral morphometric measurements were included to generate a calculated VSA. The ENET-ElasticNet regularization method was used for estimating skeletal age. Estimation was made using Ridge, LASSO, and ElasticNet regression models included in the method. Lambda hyperparameter was used in Ridge and LASSO methods and the optimal lambda value was determined according to the min./max. ratio (0.0001) according to the minimum mean square error within 50 periods. In ElasticNet regression, both lambda and alpha editing parameters were used and the alpha value was automatically taken as 0.5. Bland-Altman analysis was used to assess the agreement among different methods of age estimation, including the GP age, VSA (Ridge, LASSO, ElasticNet), and CA. Limits of agreement were identified.

RESULTS

Measurement Error

The intra-rater and inter-rater agreements were estimated using the intra-class correlation coefficient (ICC) and were found to be excellent for all vertebral measurements (ICC ≥0.977, and ICC ≥0.960, respectively). Both intra-observer and inter-observer agreements of GP skeletal age were 0.997 (95% confidence interval: 0.996 to 0.997) with excellent reliability.

The First Phase of the Regression Methods

The descriptive statistics in the study are demonstrated for each sex (Table 1). Independent variables with VIF values greater than 10 are shown in bold (Table 2). Our study was conducted separately for both girls and boys.

Statistical analysis consisted of two parts. In the first part, all independent variables (vertebral measurements) were evaluated. The target variable was GP age. To obtain the VSA, three regression methods were used. In the second part, the analyses were repeated with the variables with the highest beta coefficients obtained from each regression model.

In the initial phase of the statistical analysis, the lambda values were chosen based on minimum mean square error values. The beta coefficients and lambda values for each regression model were determined separately for boys and girls, and the results are presented in Table 3. The R^2 values obtained in the first stage of the statistical analysis were between 0.799 and 0.804.

In boys, all variables except one in the Ridge and ElasticNet regressions and 15 variables in the LASSO regression had non-zero beta coefficients. In girls, all variables in the Ridge and ElasticNet regressions and all variables except 11 in the LASSO regression had non-zero beta coefficients.

The Second Phase of the Regression Methods

Due to the high number of independent variables (n=53) statistically evaluated in our study, in the second part of the analysis, the beta coefficients were examined to determine which variables had the greatest impact on the regression models and to select the most important variables for clinical applicability. Separate analyses were conducted for boys and girls, and the eight variables with the highest coefficients in each regression model were chosen.

For both girls and boys, eight measurements with the highest coefficients were selected in each regression model, and a total of 24 measurements were determined. In boys, for the elimination of 24 measurements selected for the second part of the statistical analysis, the first three measurements (SVD, FiVD, FVD) were common to all three regression models and had the highest beta coefficients, and PH3, TVD, TVup-TVlp, and Y3 measurements, which were common to all three models, were selected. In addition, UW3, which was common to ElasticNet and Ridge regressions was selected. For boys, the selected measurements were SVD, FiVD, FVD, PH3, TVD, TVup-TVlp, Y3, and UW3 (Figure 4a, Table 4). In girls, for the elimination of 24

Table 1. The descriptive statistics for each sex

	Boys=329		Girls=465	
Measurements	Mean	Standard deviation	Mean	Standard deviation
Skeletal age	12.9	3.1	13.6	2.7
SVp-SVa	13.2	1.5	11.8	1.1
TVup-TVua	13.1	1.6	11.9	1.3
TVpm-TVam	13.8	1.6	12.9	1.3
TVlp-TVla	13.9	1.4	12.7	1.2
FVup-FVua	13.5	1.7	12.4	1.3
FVpm-FVam	13.7	1.7	12.7	1.4
FVlp-FVla	14.0	1.7	12.8	1.3
FiVup-FiVua	13.6	2.0	12.4	1.5
FiVpm-FiVam	13.8	1.9	12.7	1.4
FiVlp-FiVla	14.4	1.9	13.2	1.4
TVup-TVlp	10.8	2.5	11.2	2.0
TVum-TVd	9.4	2.2	9.9	1.7
TVua-TVla	9.0	2.6	10.0	2.4
FVup-FVlp	10.6	2.4	10.9	2.0
FVum-FVd	9.2	1.9	9.6	1.7
FVua-FVla	8.5	2.2	9.3	2.2
FiVup-FiVlp	10.4	2.4	10.8	2.1
FiVum-FiVd	9.3	1.9	9.5	1.6
FiVua-FiVla	8.3	2.1	9.1	2.0
SVD	1.2	0.7	1.4	0.6
TVD	0.9	0.7	1.1	0.7
FVD	0.8	0.6	1.0	0.6
FiVD	0.7	0.6	0.9	0.6
X3	18.7	2.6	18.1	2.0
Y3	14.5	2.1	14.1	1.7
X4	18.4	2.6	17.8	2.1
Y4	14.8	2.2	14.4	1.8
X5	18.3	2.7	17.6	2.1
Y5	15.2	2.4	14.7	1.8
D3 angle	109.2	12.1	99.6	11.7
D4 angle	111.7	10.6	103.4	10.9
D5 angle	113.7	10.0	105.2	10.4
K3 angle	36.4	8.2	42.9	8.4
K4 angle	33.8	6.6	39.3	7.3
K5 angle	32.2	6.1	37.3	6.5
SI3 angle	8.7	5.3	6.9	5.7
SI4 angle	9.6	4.9	8.0	4.8
SI5 angle	9.5	4.8	8.5	4.5
PH3	10.6	2.5	11.0	2.0
H3	10.1	2.6	10.8	2.0
AH3	8.7	2.6	9.6	2.3
PH4	10.5	2.4	10.8	2.0
H4	9.7	2.3	10.4	2.0
AH4	8.2	2.2	9.1	2.1
PH5	10.4	2.4	10.7	2.1
H5	9.7	2.2	10.2	1.9
AH5	8.1	2.1	8.9	2.0
UW3	12.5	1.5	11.4	1.2
LW3	13.8	1.4	12.5	1.2
UW4	12.9	1.7	11.9	1.3
LW4	13.8	1.7	12.7	1.3
UW5	13.2	1.9	12.1	1.4
LW5	14.3	1.9	13.1	1.5

Table 2. Tolerance and VIF values in boys and girls

Measurements	Boys		Girls	
	Tolerance	VIF	Tolerance	VIF
FVup-FVlp	0	**26202.8**	0	**13112.1**
AH3	0	**3996.27**	0.001	**1840.53**
AH4	0	**3782.6**	0	**5082.87**
AH5	0	**2757.9**	0	**2051.75**
SI3 angle	0.003	**324.895**	0.004	**284.422**
SI4 angle	0.004	**226.826**	0.004	**250.702**
SI5 angle	0.008	**133.063**	0.006	**178.519**
D3 angle	0	**2681.55**	0	**2326.59**
D4 angle	0	**2017.23**	0	**2474.24**
D5 angle	0.001	**1416.93**	0.001	**1722.65**
FiVD	0.184	5.429	0.138	7.267
FiVlp-FiVla	0.001	**1481.23**	0.001	**947.5**
FiVpm-FiVam	0.046	**21.886**	0.092	**10.886**
FiVua-FiVla	0	**2072.05**	0.001	**1479**
FiVum-FiVd	0.026	**37.796**	0.026	**38.321**
FiVup-FiVlp	0	**10946.8**	0	**34200**
FiVup-FiVua	0.001	**670.271**	0.001	**850.398**
FVD	0.137	7.278	0.105	9.536
FVlp-FVla	0.001	**1441.84**	0.001	**810.977**
FVpm-FVam	0.049	**20.232**	0.066	**15.11**
FVua-FVla	0	**3653.2**	0	**4776.87**
FVum-FVd	0.019	**51.932**	0.019	**51.533**
FVup-FVua	0.001	**1114.8**	0.001	**747.306**
H3	0.007	**144.1**	0.008	**127.789**
H4	0.01	**103.722**	0.009	**109.27**
H5	0.013	**75.204**	0.012	**80.036**
K3 angle	0	**2676.69**	0	**2289.14**
K4 angle	0.001	**1527.84**	0.001	**1992.53**
K5 angle	0.001	**917.457**	0.001	**1358.53**
LW3	0.002	**578.674**	0.001	**772.953**
LW4	0.001	**1185.02**	0.002	**632.613**
LW5	0.001	**1133.61**	0.001	**844.341**
PH3	0	**18165.8**	0.001	**1177.72**
PH4	0.001	**1125.44**	0.001	**1337.63**
PH5	0.001	**1018.7**	0.001	**847.303**
SVD	0.353	2.835	0.405	2.47
SVp-SVa	0.311	3.216	0.395	2.529
TVD	0.091	**10.972**	0.084	**11.935**
TVlp-TVla	0.002	**635.172**	0.001	**973.426**
TVpm-TVam	0.058	**17.144**	0.091	**10.958**
TVua-TVla	0	**3760.9**	0.001	**1771.12**
TVum-TVd	0.014	**71.786**	0.014	**69.296**
TVup-TVlp	0.001	**1308.24**	0	**8472.63**
TVup-TVua	0.001	**731.716**	0.002	**481.131**
UW3	0.002	**504.403**	0.003	**368.668**
UW4	0.001	**952.503**	0.002	**652.179**
UW5	0.001	**685.526**	0.001	**741.698**
X3	0.001	**1729.68**	0.001	**979.453**
X4	0.001	**1753.84**	0.001	**1404.84**
X5	0.001	**1302.94**	0.001	**1081.78**
Y3	0.002	**492.202**	0.003	**330.541**
Y4	0.001	**682.317**	0.002	**615.488**
Y5	0.002	**572.438**	0.002	**521.382**

Independent variables with a VIF value of 10 or more are demonstrated in bold
VIF: The variance inflation factor

measurements selected for the second part of the statistical analysis, SVD, FVD, TVum-TVd, TVpm-TVam, UW4, and Y3, which are common to all three regression models and have high beta coefficients were selected.

In addition, FiVD, which is common to Ridge and ElasticNet regression, and UW5, which is common to LASSO and Ridge regression, were selected. For girls, the selected measurements were SVD, FVD, TVum-TVd, TVpm-TVam, UW4, Y3, FiVD, and UW5 (Figure 4b, Table 4). The lambda values and beta coefficients were recalculated based on new datasets created separately for each sex.

In the second phase of the statistical analysis, the lambda values were chosen based on minimum mean square error values. The minimum mean square error for boys was obtained at lambda values 0.0762, 0.000148, and 0.002344 for the Ridge, LASSO, and ElasticNet, respectively. For girls, the minimum mean square error was obtained at lambda values of 0.04913915, 0.00003718, and 0.00000113 for the Ridge, LASSO, and ElasticNet regression, respectively.

The R^2 values obtained in the second stage of the statistical analysis were between 0.740 and 0.783. The highest R^2 in both boys and girls was obtained using LASSO regression (respectively, R^2=0.783, 0.741) (Table 5), and the performance of each regression model was assessed using 10-fold cross-validation.

The means and errors for both the training and test datasets from the initial and second parts of the analyses are presented in Table 6.

Vertebral skeletal age formulas obtained in each regression model in boys:

Ridge regression: VSA=0.318*FVD + 0.561*FiVD + 0.307*PH3 + 0.487*SVD - 0.059*TVD + 0.33*TVup-TVlp + 0.025*UW3 + 0.252*Y3 + 0.889

LASSO regression: VSA=0.185*FVD + 0.534*FiVD + 0.019*PH3 + 0.448*SVD + 0*TVD + 0.647*TVup-TVlp + 0*UW3 + 0.259*Y3 + 0.868

ElasticNet regression: VSA=0.323*FVD + 0.564*FiVD + 0.306*PH3 + 0.483*SVD – 0.048*TVD + 0.326*TVup-TVlp + 0.031*UW3 + 0.249*Y3 + 0.906

Vertebral skeletal age formulas obtained in each regression model in girls:

Ridge regression: VSA=0.528*FiVD + 0.909*FVD + 0.638*SVD + 0.023*TVpm-Tvam + 0.508*TVum-TVd -0.138*UW4 - 0.064*UW5 + 0.456*Y3 + 1.988

LASSO regression: VSA=0.481*FiVD + 0.935*FVD + 0.614*SVD + 0*TVpm-Tvam + 0.513*TVum-TVd -0.149*UW4 - 0.065*UW5 + 0.494*Y3 + 1.892

Table 3. The model results obtained according to the minimum mean square error as a result of the Ridge, LASSO, and ElasticNet regression models in boys and girls in the first part of the analysis

	Boys			Girls		
	Ridge	LASSO	ElasticNet	Ridge	LASSO	ElasticNet
Lambda	0.809	0.000398	0.000027	0.05002	0.000012	0.0000012
SVp-SVa	-0.01	0	-0.005	0.029	0.023	0.019
TVup-TVua	0.04	0.032	0.039	-0.058	-0.026	-0.035
TVpm-TVam	-0.001	0	0.003	0.164	0.205	0.137
TVlp-TVla	0.024	0	0.023	-0.07	-0.083	-0.065
FVup-FVua	0.015	0.001	0.017	0.104	0.104	0.084
FVpm-FVam	0.028	0.014	0.027	-0.062	-0.087	-0.04
FVlp-FVla	0.012	0	0.012	-0.056	-0.046	-0.067
FiVup-FiVua	0.018	0	0.018	0.05	0.014	0.046
FiVpm-FiVam	0	0	0	0.098	0.1	0.08
FiVlp-FiVla	-0.006	0	-0.002	-0.05	-0.075	-0.047
TVup-TVlp	0.045	0.072	0.043	0.051	0.021	0.054
TVum-TVd	0.047	0.057	0.045	-0.173	-0.259	-0.11
TVua-TVla	0.025	0.014	0.025	-0.007	0	0.005
FVup-FVlp	0.038	0.061	0.037	0.042	0.01	0.043
FVum-FVd	0.023	0.008	0.025	-0.038	-0.014	-0.021
FVua-FVla	0.03	0.014	0.031	-0.032	-0.036	-0.004
FiVup-FiVlp	0.035	0.051	0.033	0.009	0	0.015
FiVum-FiVd	0.012	0	0.016	0.022	0	0.011
FiVua-FiVla	0.025	0.008	0.026	-0.014	0	0.002
SVD	0.234	0.307	0.215	0.211	0.186	0.218
TVD	0.103	0.06	0.107	0.046	-0.016	0.106
FVD	0.146	0.123	0.144	0.374	0.418	0.362
FiVD	0.183	0.178	0.178	0.112	0.06	0.116
X3	0.023	0.032	0.024	-0.033	-0.029	-0.022
Y3	0.052	0.072	0.048	0.11	0.139	0.098
X4	0.021	0.03	0.022	-0.044	-0.048	-0.026
Y4	0.029	0.027	0.028	0.063	0.036	0.062
X5	0.019	0.022	0.019	-0.017	0	-0.01
Y5	0.017	0.007	0.018	0.069	0.059	0.06
D3 angle	-0.01	-0.012	-0.01	-0.024	-0.039	-0.021
D4 angle	-0.012	-0.014	-0.012	-0.029	-0.045	-0.023
D5 angle	-0.011	-0.012	-0.011	-0.023	-0.028	-0.018
K3 angle	0.008	0	0.008	0.017	0.012	0.014
K4 angle	0.013	0.003	0.013	0.031	0.03	0.023
K5 angle	0.011	0	0.011	0.025	0.022	0.02
SI3 angle	0.012	0	0.011	0.014	0.012	0.011
SI4 angle	0.013	0	0.013	-0.002	0.002	-0.001
SI5 angle	0.02	0.011	0.019	-0.007	-0.002	-0.006
PH3	0.047	0.07	0.045	0.072	0.076	0.071
H3	0.039	0.048	0.036	0.095	0.116	0.064
AH3	0.03	0.021	0.029	0.029	0	0.03
PH4	0.039	0.052	0.038	0.036	0	0.041
H4	0.031	0.032	0.031	0.091	0.085	0.071
AH4	0.034	0.033	0.034	0.001	0	0.016
PH5	0.035	0.043	0.034	0.016	0	0.02
H5	0.033	0.037	0.032	-0.014	-0.001	0.002
AH5	0.029	0.017	0.029	0.002	0	0.014
UW3	0.049	0.046	0.047	0.099	0.068	0.076
LW3	0.025	0	0.023	-0.019	0	-0.021
UW4	0.023	0.014	0.023	0.157	0.228	0.128
LW4	0.015	0.001	0.015	-0.052	-0.025	-0.06
UW5	0.018	0.001	0.018	0.11	0.165	0.091
LW5	-0.006	0	-0.002	-0.027	-0.005	-0.032
c	2.869	5.309	2.756	8.661	12.86	7.636
df	53	53	53	53	53	53
L1 Norm	4.693	6.964	4.53	11.861	15.918	10.475
R-squared	0.801	0.801	0.8	0.802	0.804	0.799
AIC	0.521	0.522	0.522	0.426	0.424	0.429

LASSO: Least absolute shrinkage and selection operator, AIC: Akaike information criterion

Table 4. Definitions of vertebral measurements used for the regression formula

Vertebral measurements	Definitions
TVup-TVlp[a]	The vertical distance between the uppermost and lowest points of the posterior edge of the 3rd cervical vertebra.
FiVD[ab]	The vertical distance from the deepest point of the 5th cervical vertebra to the plane between the most anterior and posterior points of its lower edge
SVD[ab]	The vertical distance from the deepest point of the 2nd cervical vertebra to the plane between the most anterior and posterior points of its lower edge
Y3[ab]	The most anterior point of the upper border of the 3rd cervical vertebra and the most posterior point of the lower border.
FVD[ab]	The vertical distance from the deepest point of the 4th cervical vertebra to the plane between the most anterior and posterior points of its lower edge
PH3[a]	The distance of the perpendicular from the highest point of the posterior edge of the 3rd cervical vertebra to the plane formed by the most anterior and most posterior points of the lower edge
UW3[a]	The horizontal distance of the perpendicular descending from the highest point of the anterior edge to the plane formed between the upper and lower points of the posterior edge of the 3rd cervical vertebra.
TVD[a]	The vertical distance from the deepest point of the 3rd cervical vertebra to the plane between the most anterior and posterior points of its lower edge
TVum-TVd[b]	The vertical distance between the uppermost and lowest points of the medial edge of the 3rd cervical vertebra.
UW4[b]	The horizontal distance of the perpendicular descending from the highest point of the anterior edge to the plane formed between the upper and lower points of the posterior edge of the 4th cervical vertebra.
UW5[b]	The horizontal distance of the perpendicular descending from the highest point of the anterior edge to the plane formed between the upper and lower points of the posterior edge of the 5th cervical vertebra.
TVpm-TVam[b]	The horizontal distance between the midpoints of the anterior and posterior edges of the 3rd cervical vertebra.

[a]Only boys; [b]Only girls; [ab]Both boys and girls

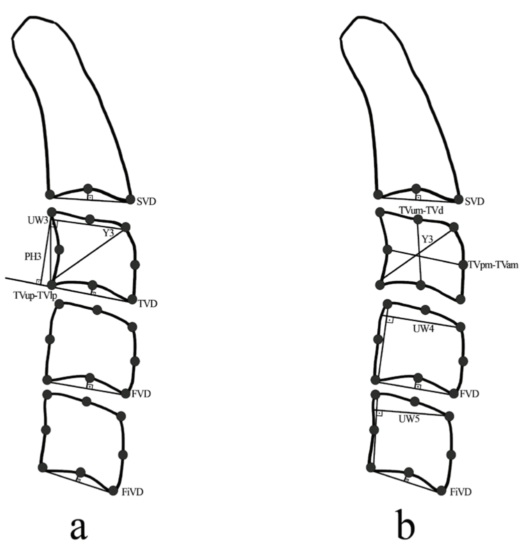

Figure 4. a) The vertebral measurements used for the second phase of the statistical analysis in boys, **b)** The vertebral measurements used for the second phase of the statistical analysis in girls

ElasticNet regression: VSA=0.543*FiVD + 0.891*FVD + 0.642*SVD + 0.033*TVpm-Tvam + 0.498*TVum-TVd - 0.126*UW4 - 0.055*UW5 + 0.435*Y3 + 1.985

The highest power of explainability was obtained using LASSO regression for both girls and boys (Table 5).

Bland-Altman Analysis

Figures 5 and 6 display the Bland-Altman plots illustrating the consistency of inter-age measurements for boys and girls, respectively, including CA, GP age, Ridge regression age, LASSO regression age, and ElasticNet age. The plots depict a solid line indicating zero bias, the middle-dashed line represents the bias, and the outer dashed lines define the limits of agreement.

DISCUSSION

This study identified key findings in skeletal age prediction using Ridge, LASSO, and ElasticNet regression models. Among these, LASSO regression demonstrated the highest R^2 values (0.783 in boys and 0.741 in girls). Additionally, in both sexes, the vertebral depth of concavities exhibited high beta coefficients, highlighting their significance in skeletal age estimation. The Bland-Altman analysis indicated that the limits of agreement for GP age with CA and VSA were wider in boys than in girls, whereas the limits of agreement between CA and VSA were wider in girls than in boys.

Furthermore, although LASSO exhibited the highest R^2, the observed differences in predictive accuracy among Ridge, LASSO, and ElasticNet regression models suggest that the assumption of equal model performance does not hold. The performance variations among models differed, leading to the rejection of the null hypothesis (H_0), which stated that there would be no difference between VSA prediction models developed using Ridge, LASSO, and ElasticNet regression.

Morphologic changes in the cervical vertebrae are considered useful indicators of skeletal development, although the CVM method has some limitations, such as subjectivity and inadequate validity and reproducibility.[22] We attempted to overcome these restrictions by assessing VSA using morphometric measurements. CVM and hand-wrist methods may be consistent,[9,23] making them reliable skeletal maturity indicators, especially when HWR images are unavailable.[24]

The sample sizes in the literature for skeletal age estimation from vertebral measurements varied from 66 to 958 individuals. Our study sample size was larger than in many studies in the literature, except for Roman et al.'s[24] study.[15-17,25]

There are noticeable differences between boys and girls in the timing of the growth spurt (pre-peak, peak, and post-peak). Hägg and Taranger[26] reported that pubertal growth spurts begin on average at the age of 10 years in girls and 12 years in

Table 5. The model results obtained according to the minimum mean square error as a result of the Ridge, LASSO, and ElasticNet regression models in boys and girls in the second part of the analysis

Boys	Ridge	LASSO	ElasticNet	Girls	Ridge	LASSO	ElasticNet
Lambda	0.0762	0.000148	0.002344	Lambda	0.04913915	0.00003718	0.00000113
TVup-TVlp	0.330	0.647	0.326	FVD	0.909	0.935	0.891
FiVD	0.561	0.534	0.564	SVD	0.638	0.614	0.642
SVD	0.487	0.448	0.483	FiVD	0.528	0.481	0.543
Y3	0.252	0.259	0.249	TVum-TVd	0.508	0.513	0.498
FVD	0.318	0.185	0.323	Y3	0.456	0.494	0.435
PH3	0.307	0.019	0.306	UW4	-0.138	-0.149	-0.126
UW3	0.025	0.000	0.031	UW5	-0.064	-0.065	-0.055
TVD	-0.059	0.000	-0.048	TVpm-TVam	0.023	0.000	0.033
C	0.889	0.868	0.906	C	1.988	1.892	1.985
df	8	6	8	df	8	7	8
L1 Norm	3.229	2.959	3.236	L1 Norm	5.251	5.143	5.207
R-squared	0.782	**0.783**	0.781	R-squared	0.74	**0.741**	0.74
AIC	0.267	0.254	0.267	AIC	0.294	0.289	0.295

LASSO: Least absolute shrinkage and selection operator, AIC: Akaike information criterion

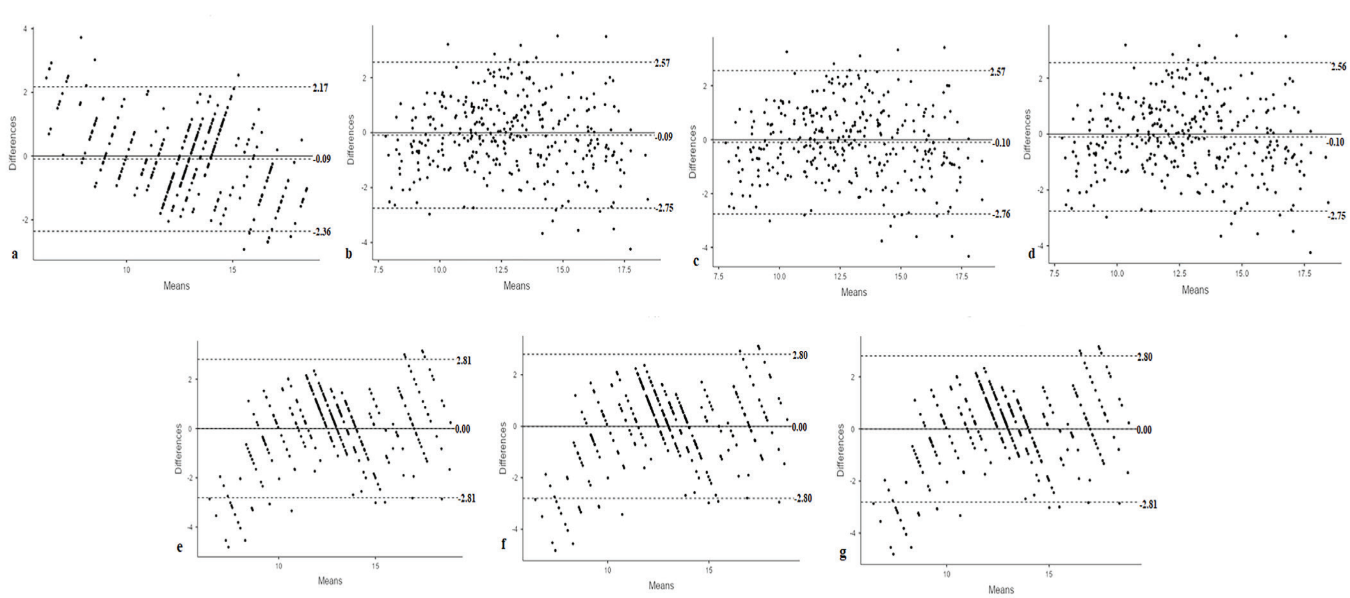

Figure 5. The X-axis represents the means of the 1st and 2nd measurements. The Y-axis represents the differences between the 1st and 2nd measurements. The solid line in the purple area indicates zero bias. The dashed middle line defines bias. The dashed outer lines define the limits of agreement. **a)** The Bland-Altman plot of the consistency between chronologic age (CA) and Greulich-Pyle (GP) age in boys. **b)** The Bland-Altman plot of the consistency between chronologic age (CA) and Ridge regression age in boys. **c)** The Bland-Altman plot of the consistency between chronologic age (CA) and LASSO regression age in boys. **d)** The Bland-Altman plot of the consistency between chronologic age (CA) and ElasticNet regression age in boys. **e)** The Bland-Altman plot of the consistency between Greulich-Pyle (GP) age and Ridge regression age in boys. **f)** The Bland-Altman plot of the consistency between Greulich-Pyle (GP) age and LASSO regression age in boys. **g)** The Bland-Altman plot of the consistency between Greulich-Pyle (GP) age and ElasticNet regression age in boys

boys. Fishman[27] also reported that the pubertal growth spurt ended at the age of 14.77 years in girls and 16.4 years in boys. In the present study, VSA was determined separately in boys and girls because the difference in growth and development between the sexes is often considered important.[24,26,27]

Previous studies examined C2-C5,[9,28,29] C2-C4,[4,8,30] and C3-C4[15-17,25] vertebrae for estimating skeletal age and maturation from cervical vertebrae. In our study, we focused on evaluating C2-C5 vertebrae.

The age range of the sample of our study (7-18 years) was wider than in Caldas et al.'s[25] study (7-15.9 years), Mito et al.'s[17] study (7-14.9 years), and Alhadlaq and Al-Maflehi's[16] study (10-15 years).

Caldas et al.[25] reported that the anterior (TVua-TVla), median (TVum-TVd), and posterior (TVup-TVlp) heights of the C3 vertebrae increased between 10 and 13 years, and the anterior (FVua-FVla), median (FVum-FVd), and posterior (FVup-FVlp) heights of the C4 vertebrae increased between the ages of

Table 6. Means and errors of test and training set in the first and second analyses for boys and girls

SEX (first and second analysis)	Regression model	Lambda	Test Set means	Train set means	Test set errors	Train set errors
Male (first analysis)	**Ridge**	0.809	2.016	1.849	0.159	0.017
	LASSO	0.000398	2.048	1.849	0.164	0.016
	ElasticNet	0.000027	2.018	1.847	0.159	0.017
Male (second analysis)	**Ridge**	0.07621	2.134	2.039	0.149	0.016
	LASSO	0.000148	2.132	2.031	0.152	0.017
	ElasticNet	0.000002	2.135	2.038	0.149	0.016
Female (first analysis)	**Ridge**	0.05002	1.613	1.456	0.121	0.013
	LASSO	0.000012	1.636	1.437	0.17	0.018
	ElasticNet	0.0000012	1.633	1.467	0.17	0.018
Female (second analysis)	**Ridge**	0.04913915	2.016	1.915	0.192	0.021
	LASSO	0.00003718	2.018	1.911	0.191	0.021
	ElasticNet	0.00000113	2.016	1.918	0.192	0.021

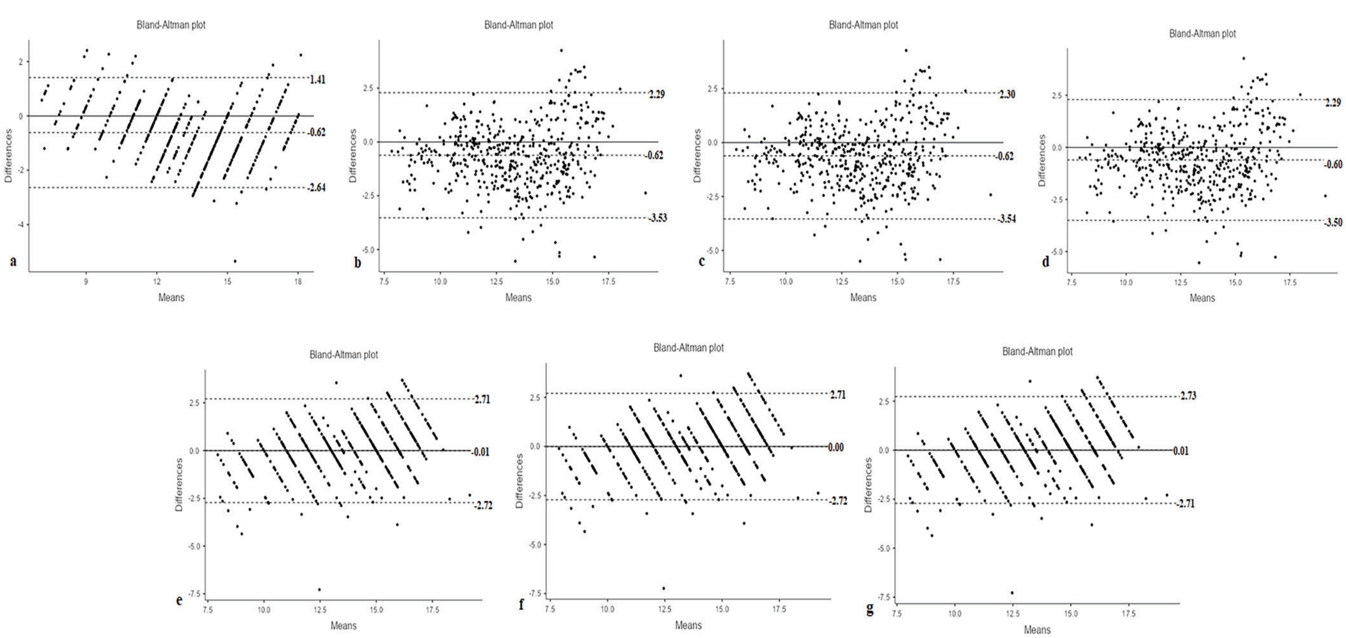

Figure 6. The X-axis represents the means of the 1st and 2nd measurements. The Y-axis represents the differences between the 1st and 2nd measurements. The solid line in the purple area indicates zero bias. The dashed middle line defines bias. The dashed outer lines define the limits of agreement. **a)** The Bland-Altman plot of the consistency between chronological age (CA) and Greulich-Pyle (GP) age in girls. **b)** The Bland-Altman plot of the consistency between the chronologic age (CA) and Ridge regression age in girls. **c)** The Bland-Altman plot of the consistency between chronologic age (CA) and LASSO regression age in girls. **d)** The Bland-Altman plot of the consistency between chronologic age (CA) and ElasticNet regression age in girls. **e)** The Bland-Altman plot of the consistency between Greulich-Pyle (GP) age and Ridge regression age in girls. **f)** The Bland-Altman plot of the consistency between Greulich-Pyle (GP) age and LASSO regression age in girls. **g)** The Bland-Altman plot of the consistency between Greulich-Pyle (GP) age and ElasticNet regression age in girls

11-13 years in girls. In addition, they reported that the anterior (Tvua-Tvla), median (Tvum-TVd), and posterior (Tvup-TVlp) heights and median width (TVpm-Tvam) of the C3 vertebrae increased between 12 and 15 years, but no significant changes were observed in the C4 vertebral measurements in boys.[25] Mito et al.[17] reported that the anterior, median, and posterior heights of the C3 and C4 vertebrae increased rapidly from age 10 to 13 years in girls.

Alhadlaq and Al-Maflehi[16] reported an increase in the heights of the C3 and C4 vertebrae between 10-15 years, but the median width did not change in this period in boys. In the present study, the median height of the C3 vertebrae (TVum-TVd) in girls and the posterior height of the C3 vertebrae (TVup-TVlp) in boys had high beta coefficients, and the coefficients of C3 height measurements were high. However, the concavity depth of all vertebrae may have been more pronounced than C4 height measurements due to the wider age range compared to other studies,[16,17,25] and the higher number of independent variables. Roman et al.[24] found that the most influential variable in determining the vertebral maturation period was the vertebral depth of concavity.

Likewise, concavity depth at the lower border of C4 (FVd) and C3 (TVd) vertebrae in girls and concavity depth at the lower border of C5 (FiVD) and C2 (SVD) vertebrae in boys were found to be the most influential variables in skeletal age estimation.

Generally, stepwise regression has been used in studies to obtain VSA.[15-18] Varshosaz et al.[15] reported that the anterior length of the fourth vertebrae was the most important variable for determining skeletal age by performing a stepwise multivariable regression analysis. The focus of the present study was to introduce different regression models for detecting VSA. The power of explainability in their study was R^2=0.686, whereas, in our study, it was R^2=0.741 in girls and R^2=0.783 in boys.[15] Although both studies were conducted in similar age groups, our study provided separate evaluations for boys and girls. Difference in variables, sample size, ethnic differences, and the use of different regression models may have influenced the results.

Although many studies have reported that evaluating cervical vertebrae with morphologic and morphometric methods yields successful results in skeletal age estimation,[16,17,23-25,29,31] Beit et al.[20] reported that methods based on vertebral morphology were insufficient for estimating skeletal age. In addition to the ratio measurements in their study, the SI angle, which was also included in our study, was included. When the first part of the statistical analysis was examined in our study, the beta coefficient of the SI angle was found to be low, likewise in the study of Beit et al.[20]. Thus, the SI angle was excluded from the second part of the statistical analysis. The explanatory power of this study model (R^2=0.783 for boys, R^2=0.741 for girls) was found to be higher than for Beit et al.[20] (R^2=0.693 for boys and R^2=0.671 for girls). Although our R^2 values are higher than those in the studies by Varshoaz et al.[15] and Beit et al.[20], the clinical advantage was insufficient to predict the skeletal age.

It is important to evaluate the differences between the two methods to assess their compatibility and reproducibility. Bland-Altman analysis was used to examine the agreement between GP age, CA, and VSA.

Varshosaz et al.[15] evaluated the relationship using the correlation method and stated that LCRs are useful for skeletal age estimation and might be an alternative to HWRs, with the advantage of radiation reduction. In the study of Beit et al.[20], the limit of agreement between CA and GP skeletal age (in boys ULA: 2.1, LLA: -1.7; in girls ULA: 2.2, LLA: -1.2) was found to be better than in our study (in boys ULA: 2.17, LLA: -2.36, in girls ULA: 1.41, LLA: -2.64). They reported that the agreement between CA and GP age was higher than the agreement between GP age and VSA in both sexes.[20] In our study, in both CA and VSA (Ridge, LASSO, Elastic Net) graphs of GP age, the width of the limits of agreement was wider in boys than in girls (Figures 5a, e, f, g, 6a, e, f, g). The width of the limits of agreement of CA-VSA (Ridge, LASSO, ElasticNet) was wider in girls than in boys (Figures 5b, c, d, 6b, c, d). Similar to our findings, by comparing GP age with VSA and CA, Beit et al.[20] reported that VSA was not superior to CA. Therefore, differences in interpretation based on statistical analysis methods are important.

In studies performed to obtain VSA, ratio or angular measurements were generally used.[15-17,20,25] In the present study, only linear and angular measurements were included. Although image magnification was mentioned as a disadvantage in the use of linear measurements,[16] the power of explainability in our study was higher than the ratio measurements used in other studies.[15,20]

Circumpubertal growth differences are more closely related to skeletal age than CA. Variations in the maturation stage are closely associated with changes in when and how much growth happens. Comprehending the development of the oro-facial region is crucial for orthodontic therapy. Determining skeletal age is important in creating effective orthodontic treatment plans because patients grow at different times, durations, and velocities. Orthodontic treatment for growth modification requires proper patient selection, appliance prescription, and compliance. Clinical decisions involving extra-oral traction forces, functional appliances, extraction vs. non-extraction therapy, or orthognathic surgery are primarily based on growth considerations.[32,33]

The methods mentioned in our study have provided useful but limited information on determining the timing of orthopedic treatment or confirming the end of growth. Clinicians should know the average differences between chronologic and skeletal ages for each sex and identify ages when there is good concordance or within clinically acceptable limits of treatment or purpose. Suri et al.[32] reported that a 0.5-year difference between skeletal and CA was acceptable in clinical practice. Despite observing high R^2 values, no significant clinical advantage was observed when comparing it with CA in the present study.

Study Limitations

Skeletal age is influenced by ethnic factors.[34] To avoid ethnic influences on skeletal growth and development, only individuals of Turkish ethnicity were included in this study. Although GP atlas assessment has been reported to exhibit minimal inter-observer and intra-observer discrepancies, it should be noted that this evaluation is inherently subjective.[35]

Future studies should be conducted using a group-based approach, employing larger sample sizes and encompassing diverse age ranges within the groups. Variations in vertebral maturations may exhibit dissimilarities across distinct age cohorts. Evaluations can be made about which vertebral variables play a more important role in different age groups.[16,17,25]

This study had several strengths. First, with a sample size of 794 individuals (329 boys, 465 girls), it included a larger dataset than many previous studies evaluating skeletal age through cervical vertebrae measurements, except for Roman et al.'s[24] study.[15-17,25] Second, by incorporating multiple regression models (Ridge, LASSO, and ElasticNet), this study enabled a comparative assessment of different predictive methodologies, providing insights into their strengths and weaknesses. Additionally, the Bland-Altman analysis enhanced reliability by quantifying the agreement between VSA and GP skeletal ages, thereby improving the interpretability of the findings. However, some limitations should be acknowledged. The retrospective design and the the inclusion of only a single ethnic group may limit the generalizability of the results. Future research should incorporate longitudinal data, investigate the influence of ethnic variability on skeletal age prediction, and validate findings using external datasets to improve model robustness and clinical applicability.

CONCLUSION

In our study, the difference in skeletal age estimation was greater than 0.5 years, which does not provide enough information in clinical practice. Relying on VSA alone to determine the skeletal age of individuals within the Turkish population is insufficient for determining the timing of orthopedic treatment or confirming the end of growth.

Ethics

Ethics Committee Approval: The study received ethical approval from the Research Ethics Committee of Recep Tayyip Erdoğan University (date: 02.02.2023 and protocol number: 33).

Informed Consent: Informed written consent forms, which included the use of patient records in scientific studies, were obtained from all patients at the beginning of treatment.

Footnotes

Author Contributions: İ.Y., M.G.; Concept - İ.Y., M.G.; Design - İ.Y., M.G.; Data Collection and/or Processing - İ.Y., M.G.; Analysis and/or Interpretation - İ.Y., M.G.; Literature Search - İ.Y., M.G.; Writing - İ.Y., M.G.

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Original Article

Evaluation of the Effect of Low-level Laser Therapy on Leveling Mandibular Anterior Crowding

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Main Points

- Low-level laser therapy has no effect on the acceleration of tooth movement during leveling.
- Low-level laser therapy reduced the leveling duration; however, the difference was not statistically significant.
- Except for day 1 of leveling, there was no decrease in pain levels.

ABSTRACT

Objective: This study aims to evaluate the effect of low-level laser therapy (LLLT) on leveling mandibular anterior crowding and associated pain levels.

Methods: This double-blinded, parallel, randomized clinical trial included 30 participants who were randomly assigned to the laser group or the control group, with Little's irregularity index of 4-8 mm in the mandibular canine-canine region. Nickel-titanium archwires measuring 0.012 inches were tied with elastomeric ligatures and changed every 14 days throughout the leveling process. The leveling duration was recorded in days, from the bonding application to the end of leveling. Irradiation was performed at an 810-nm wavelength using a gallium-aluminum-arsenide diode laser device with a power output of 100 mW and an energy density of 8 J/cm^2. Laser applications were performed after archwire ligation (day 0), on days 3, 7, and 14 and every 14 days until leveling was completed. The leveling duration was calculated, and pain levels were evaluated using a visual analogue scale (VAS) after archwire ligation (hour 0), at hours 2 and 6 and on days 1, 3, 7, 14, and 21.

Results: The leveling duration showed no significant differences between the laser and control groups (p=0.170). Group comparison results of the VAS scores at hour 6 (p=0.001) and day 1 (p=0.006) exhibited significantly reduced pain levels in the laser group compared with the control group.

Conclusion: Although LLLT is not effective in reducing the leveling duration, it significantly reduces pain levels at hour 6 and on the 1st day.

Keywords: Low-level laser therapy, orthodontics, crowding, pain measurement

INTRODUCTION

A prolonged treatment duration not only causes a decrease in patient compliance but also increases the risk of various side effects, such as root resorption, periodontal problems, and white spot lesions.[1] Reducing the treatment duration requires increasing the rate of tooth movement.[2] Therefore, accelerating tooth movement is one of the primary goals of orthodontists.[3] Tooth movement can be accelerated by stimulating alveolar bone remodeling with surgical and non-surgical procedures.[1,4] Invasive surgical procedures are less preferred by

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clinicians and patients due to the possibility of pain, discomfort, and damage to the tooth root.[5,6] Photobiomodulation is often preferred as a mechanical/physical stimulation, which is a non-surgical procedure classified into two subcategories.[7] However, pharmacological methods, the other category, are mostly performed at the level of animal experimentation. They have systemic and local side effects, and clinical dose applications are not yet sufficient.[8] Low-level laser therapy (LLLT), known as photobiomodulation, is reported to accelerate tooth movement by altering cellular activity in tissues through exposure to laser beams in the visible red to near-infrared spectrum.[9] LLLT is also reported to be effective in alleviating orthodontic pain and accelerating tooth movement.[10-12]

For this purpose, light-emitting diodes (LEDs) or low-level lasers (LLL) can be used.[6] Although the number of studies evaluating the effect of extraoral and intraoral LED applications on accelerating tooth leveling and alignment has increased, only four studies have investigated the use of LLLT.[13-16] However, in all studies where LLLT was applied, archwires were changed during the process. To date, no study has examined the effect of LLLT on mandibular anterior tooth leveling without archwire changes.

Based on this background, this study aims to investigate the effect of LLLT on leveling mandibular anterior crowding and pain levels. The null hypothesis states that LLLT has no effect on leveling mandibular anterior crowding or pain levels.

METHODS

Trial Design

A total of 30 participants (22 women and 8 men) who underwent non-extraction fixed orthodontic treatment with the straight-wire technique at the Department of Orthodontics, Van Yüzüncü Yıl University Faculty of Dentistry between February 2020 and October 2022 were enrolled in this double-blinded, parallel, randomized clinical trial. The approval of the Van Yüzüncü Yıl University Faculty of Medicine, Clinical Research Ethics Committee was obtained to conduct this study (approval no.: 24, date: 05.05.2020). After the study was explained, informed consent forms, prepared according to the Declaration of Helsinki, were signed by all participants and their legal guardians for those under the age of 18. The Consolidated Standards of Reporting Trials flowchart of patient recruitment, follow-up, and entry into data analysis is shown in Figure 1.

Participants and Eligibility Criteria

The following inclusion criteria were applied: no previous orthodontic treatment; complete permanent dentition; cephalometric evaluation and model analysis indicating non-extraction treatment with skeletal Class I malocclusion, maxillary and mandibular incisor positions and inclinations within retrusive and/or normal values, and a mandibular canine to canine Little's irregularity index (LII) of 4-8 mm; no congenital anomalies, dental structural disorders, crowns, or extensive restorations in the mandibular anterior teeth; no pregnancy, lactation, smoking, systemic problems, or related medications that could impact alveolar bone metabolism and tooth movement; good oral hygiene; no plaque accumulation, gingival inflammation, or alcohol use. Correspondingly, participants with temporomandibular joint disorders, parafunctional habits, or those requiring anchorage mechanisms, such as miniscrews and lingual arches in the mandible, were excluded from the study.

Interventions

Clinical Procedures

After the participants were assigned to the laser and control groups, fixed orthodontic treatment with the straight-wire technique was initiated using 0.018-inch slot stainless steel Roth brackets (Gemini Roth System, 3M Unitek, Monrovia, CA, USA). Bonding procedures were performed using the same orthodontic adhesive according to the manufacturer's instructions (Transbond™ XT, 3M Unitek, Monrovia, CA, USA). Polymerization was conducted using a LED source (Elipar FreeLight 2; 3M ESPE, St. Paul, MN, USA).

During the leveling phase, 0.012-inch nickel-titanium (NiTi) archwires (3M Unitek, Monrovia, CA, USA) were secured with elastomeric ligatures (QuiK-StiK™, 3M Unitek, Monrovia, CA, USA), which were changed every 14 days during laser applications. The archwire was not replaced at these appointments unless deflection was observed. Patients and their parents were informed about prolonged treatment duration due to bracket failures and were instructed to contact the orthodontist immediately in case of any issues.

Laser Parameters and Procedure

An 810 nm semiconductor continuous-wave gallium-aluminum-arsenide (Ga-Al-As) diode laser device (Cheese Diode Laser, Wuhan Gigaa Optronics Technology Co. Ltd.,

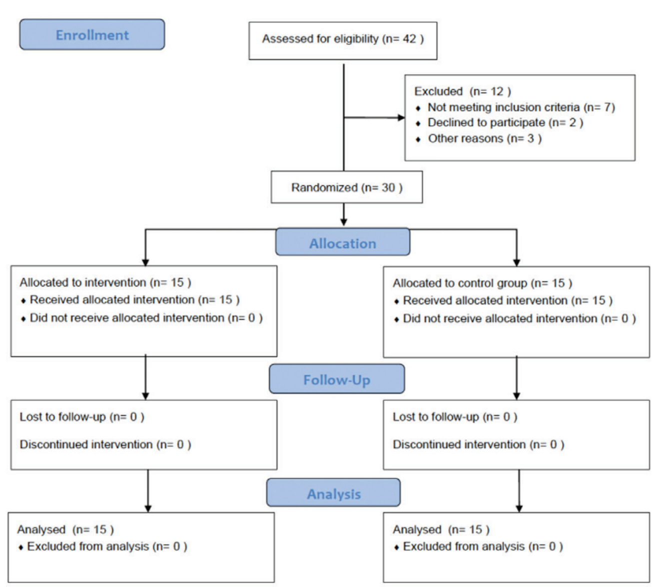

Figure 1. Consolidated Standards of Reporting Trials flowchart

Figure 2. The application of LLL onto the cervical and apical midpoint of the mandibular anterior teeth roots
LLL, low-level lasers

Wuhan, China) was used in this study. The laser operated at a power output of 100 mW, an energy density of 8 J/cm^2, and an exposure time of 10 seconds was used in this study. The laser tip, held perpendicularly and in contact with the mucosa, had a radius of 4 mm and a spot area of approximately 0.125 mm^2.

A total of 12 irradiations, each lasting 10 seconds, were applied to two areas on the vestibular surfaces of the mandibular anterior teeth, one on the cervical third and one on the apical third (Figure 2). These applications were conducted immediately after archwire ligation (day 0) and subsequently on days 3, 7, and 14 and then every 14 days until leveling was completed.

Both the participants and the clinician wore protective goggles during the application to protect against the possible adverse effects of the laser beam. All laser applications were performed by the same investigator (Y.T.). In the control group, a placebo procedure was conducted by the same researcher on the indicated days, without pressing the pedal of the laser device. This approach ensured an effective assessment of individual pain levels (Y.T.). The second researcher, who determined whether the leveling was complete, and the participants in the study were blinded to group assignments.

Leveling Assessment

The leveling of mandibular anterior crowding was assessed using the objective grading system of the American Board of Orthodontics Phase III clinical examination by an orthodontist with 5 years of experience (Y.K.).[17] To evaluate the treatment outcomes, mandibular alginate impressions of the participants were taken to obtain plaster models before treatment and at the end of leveling. After these plaster models were scanned using iTero intraoral scanner (iTero Element 2, Align Technology, San Jose, CA, USA) and the digital orthodontic models were exported as stereolithography (STL) files and imported into OrthoCAD software (Align Technology, San Jose, CA, USA) to calculate LII by another investigator (Y.T.). To assess the measurement reliability, 10 pre-treatment STL files were remeasured 1 month after the first measurement. The reliability was evaluated using the intraclass correlation coefficient (ICC) and showed strong intraexaminer reliability (ICC =0.997).

When LII was 0.5 mm or less, the date of completing the leveling of mandibular anterior crowding was noted on the patient card. The leveling duration was calculated and recorded in days, from the bonding application to the end of leveling.

Pain Assessment

The participants' pain experiences were measured using a questionnaire containing the visual analogue scale (VAS), a 10 cm horizontal line with 0 representing no pain and 10 representing the worst pain possible. The patients were asked to consider the most severe pain they had experienced in the past, accept this as 10, and place a mark on the scale reflecting their current pain. The pain assessment was conducted immediately after the bonding procedure and ligation of 0.012-inch NiTi archwires (hour 0), at hours 2 and 6, and on days 1, 3, 7, 14, and 21. All individuals were given detailed information about when and how to fill in the forms (Y.T.). However, to prevent any issues during the completion of the forms, a timetable indicating which form should be filled out at what time and on which day was prepared.

Sample Size Calculation

The sample size was calculated with G*Power 3.1.2 (Franz Faul, Universität Kiel, Kiel, Germany) using the results of a previous randomized controlled clinical trial.[13] Considering the results of the laser and control groups of this study, the effect size (d, effect size) calculated for equal groups was determined to be 1.89. For a type I error (α=0.05) and 99% power, the sample size was calculated as 24 participants, with a minimum of 12 for each group. However, assuming a 15% exclusion rate, a total of 30 participants were included in this study, with 15 in each group.

Randomization

The participants were randomly assigned to the laser and control groups by coin flip, with an allocation ratio of 1:1. An operator, independent of the study, performed the random allocation. Women and men were separately randomly assigned to the laser and control groups to ensure insignificant differences between the groups in terms of gender (laser: 11 women, 4 men; control: 11 women, 4 men). Furthermore, care was taken to ensure that LII was similar in both groups.

Statistical Analysis

Descriptive statistics for the studied variables were presented as mean, standard deviation, minimum, and maximum values. The normality assumption of the variables was tested using the Shapiro-Wilk test. In the comparison of quantitative data between the two groups, the Student's t-test was used for normally distributed groups, whereas the Mann-Whitney U test was used for non-normally distributed groups. All statistical analyses were performed using the Number Cruncher Statistical System 2007 (Kaysville, UT, USA), and the level of statistical significance was defined as 1% and 5%.

RESULTS

Throughout the study, there were no patient drop-outs (Figure 1). Additionally, no bracket failures were observed in any of the participants during the leveling duration. The mean ages of the participants in the laser and control groups were 15.61±1.28 and 17.16±2.76 years, respectively, with mean LIIs of 6.57±0.29 and 6.45±0.22 mm, respectively. Intergroup comparison results showed no significant differences in terms of mean age and LII (Table 1).The comparison results regarding the leveling duration of the laser and control groups are shown in Table 2. The mean leveling duration was 111.8±42.9 days in the laser group and 135.67±49.65 days in the control group. The differences in mean leveling duration between the laser and control groups were found to be insignificant. Group comparison results of the VAS scores identified a reduced pain level in the laser group compared with the control group; however, only the differences at hour 6 and on day 1 were found to be significant. The differences at hours 0 and 2 and on days 3, 7, 14, and 21 were insignificant (Table 3).

Table 1. Descriptive statistics

	Groups	Mean±SD	Min.	Max.	p-value
Age (year)	Laser	15.61±1.28	13.08	18.25	0.059
	Control	17.16±2.76	12.5	21.08	
Little's irregularity index (mm)	Laser	6.57±0.29	4.35	8.00	0.749
	Control	6.45±0.22	4.24	8.08	

Student's t-test was performed, $p<0.05$.
SD, standard deviation; Min., minimum; Max., maximum

Table 2. Comparison of the mean leveling duration of laser and control groups

	Groups	Mean±SD	Min.	Max.	p-value
Leveling duration (day)	Laser	111.8±42.9	61	185	0.170
	Control	137.67±49.65	50	216	

Student's t-test was performed, $p<0.05$.
SD, standard deviation; Min., minimum; Max., maximum

DISCUSSION

In recent years, research has focused on accelerating tooth movement and reducing treatment time.[18,19] This study which investigated the effect of LLLT on both the leveling of mandibular anterior crowding and the level of pain during leveling. The results showed no significant differences between the laser and control groups in terms of mean leveling duration. However, when comparing the groups' VAS scores, pain levels were significantly lower in the laser group than in the control group only at hour 6 and on the 1st day. Therefore, the null hypothesis was partially accepted.

In the literature, there are studies reporting that LLLT accelerates orthodontic tooth movement,[5,13,14,20,21] as well as studies reporting no significant effect.[15,22-25] One study reported that low-dose laser application decreased the acceleration of orthodontic tooth movement.[26] Variability in the study results may be due to factors such as the dose of laser irradiation, radiation mode, energy density, application location and duration, different tooth movements, and the fact that some studies are animal experiments. Due to the variability of results, more experimental and randomized clinical trials are

Table 3. Intergroup comparison results of visual analog scale (VAS) scores recorded at different time-intervals

		Laser	Control	p-value
0th hour	**Mean±SD**	0.53±0.83	0.73±1.49	0.691
	Min.	0	0	
	Max.	3	5	
2nd hour	**Mean±SD**	1.87±0.92	2.87±1.55	0.092
	Min.	0	1	
	Max.	3	5	
6th hour	**Mean±SD**	2.67±1.29	5.60±1.50	0.001**
	Min.	1	3	
	Max.	5	10	
1st day	**Mean±SD**	3.07±1.58	5.27±2.22	0.006**
	Min.	1	2	
	Max.	5	10	
3rd day	**Mean±SD**	2.67±1.45	4.0±2.54	0.181
	Min.	0	1	
	Max.	5	10	
7th day	**Mean±SD**	1.27±1.33	2.47±1.96	0.074
	Min.	0	0	
	Max.	4	7	
14th day	**Mean±SD**	1.40±1.06	1.50±1.30	0.931
	Min.	0	0	
	Max.	4	4	
21th day	**Mean±SD**	1.0±0.93	1.67±0.90	0.256
	Min.	0	0	
	Max.	3	3	

Mann-Whitney U test was performed, $p<0.05$, $^{**}p<0.01$
SD, standard deviation; Min., minimum; Max., maximum

needed.[24,27] Therefore, when designing the study, we aimed to standardize the type of photobiomodulation (LED or LLLT) and other factors that may affect tooth acceleration.

It is stated that the most important disadvantage of LEDs is their semi-monochromatic structure. Additionally, LEDs have limitations such as a wide wavelength, spot size, and the difficulty of achieving the power obtained with laser applications.[28] A broad review of the literature presented that an extraoral LED device was used in three studies,[5,20,21] an intraoral LED device was used in three studies,[6,29,30] and LLLT was used in one study,[13] in which the effect of photobiomodulation on leveling duration was evaluated. Although methodological differences existed between the LED studies, their results showed a significantly decreased leveling duration due to increasing tooth movement.[5,6,20,21,29,30] The leveling duration in this study was determined to be longer than in the studies of Nahas et al.,[20] Shaughnessy et al.,[6] and Okla et al.[30] and shorter than in the studies of Lo Giudice et al.[21] and Caccianiga et al.[29] However, due to their structure, LEDs have been reported to provide the same effect on cellular activity as low-dose laser applications. The lack of standardization in studies makes research results and LED applications controversial in photobiomodulation.[28] The recommended wavelength for LLLT is in the range of 600-1200 nm.[20] At this wavelength, the laser beam is well absorbed by pigmented tissues and less absorbed by hemoglobin and water, providing good penetration into the tissues.[31] Additionally, wavelengths from 780 nm to 930 nm are reported to accelerate tooth movement effectively, according to a systematic review that investigated the effect of different wavelengths of Ga-Al-As diode lasers.[32]

Previously published studies have shown that the biostimulatory effect of LLLT depends on the energy density, with stimulation observed at low energy densities and inhibition observed at higher ones.[2,20,33] A systematic review found that diode lasers with energy densities of 2.5, 5, and 8 J/cm^2 were more effective than those with energy densities of 20 and 25 J/cm^2, though the optimal dose remains uncertain.[2] A review of previous studies revealed variations in energy density and exposure time. In the study by Al-Sayed Hasan et al.[13] the energy density was observed to be 2.5 J/cm^2 and 15 seconds/point in the study by 7.5 J/cm^2 and 3 seconds/point in the study by Qamruddin et al.,[10] and 25 J/cm^2 and 23 seconds/point in the study by Limpanichkul et al.,[22] respectively. In light of this information, an 810 nm diode laser device with an energy density of 8 J/cm^2 and an exposure time of 10 seconds/point was preferred in this study.

The small mesio-distal dimensions of mandibular anterior teeth reduce the interbracket distance. Therefore, NiTi archwires with low hardness and high elasticity should be preferred during leveling to minimize binding and notching due to crowding.[34] Profitt, Bennett, and McLaughlin also recommended using round archwires that apply light force during leveling.[35] Camacho and Cujar,[16] Ghaffar et al.,[14] and Al-Sayed Hasan et al.[13] changed the diameter and cross-section of the archwires during treatment. In this study, 0.012-inch NiTi archwires were used unchanged until leveling was completed to standardize the factors that could affect tooth movement.

A study evaluating malocclusion types, their distribution by gender, and the degree of maxillary and mandibular crowding determined that moderate crowding was most common in the anterior mandible.[36] The mesio-distal dimensions of mandibular molars and the displacement of the mandible due to growth and development were found to be effective in the higher incidence of mandibular anterior crowding.[37] Additionally, LII was used as the preferred method for assessing crowding in four recent studies examining the effect of photobiomodulation on the leveling of anterior teeth.[6,13,20,21] Therefore, participants with moderate mandibular anterior crowding, as determined by LII, were included in this study. Camacho and Cujar[16] evaluated the effect of LLLT on tooth movement, reporting an average reduction in treatment duration of 167 days (30% less) with laser application (30% less). However, evaluating the effect over the total treatment period suggests that many factors, including the end of orthodontic treatment, may affect the results. Two other studies investigating the rate of tooth leveling found statistically significant differences.[13,14] Al-Sayed Hasan et al.[13] evaluated the leveling and alignment of the maxillary anterior teeth in patients treated with four first premolar extractions. The leveling and alignment duration was found to be 81.23 days in the laser group and 109.23 days in the control group. Although these durations are shorter than those in our study, the intergroup differences are partially similar-28 days in the study by Al-Sayed Hasan et al.[13] and 23.87 days in our study. These discrepancies might result from the treatment plan, where the leveling and alignment of the maxillary anterior teeth were evaluated after the extraction of the first premolar in the study by Al-Sayed Hasan et al.[13]

Ghaffar et al.[14] also reported LLLT in the mandibular anterior region as 68.2 days in the laser group and 109.5 days in the control group. The difference between the results of these two studies and our study may also be due to the change in archwires.[13,14] In the study by El-Shehawy et al.,[15] patients were treated with conventional NiTi archwires in a standardized sequence of 0.012, 0.014, and 0.016 inches during the leveling and alignment phase for 12 weeks. At the end of this period, it was reported that no significant difference was observed in the leveling and alignment of the lower anterior region between the laser-treated group and the control group.

Relatively few studies have compared the effect of LLLT on pain level during leveling with a control group.[14,38,39] Among the available studies using the VAS scores, the evaluations were performed immediately after the initial archwire placement, at hour 2, and on days 1, 2, 3, and 7 in patients who had non-extraction fixed orthodontic treatment in the study by Celebi et al.[39] In contrast, Al-Sayed Hasan et al.[12] assessed pain at hours 1 and 6 and on days 1, 2, and 3 in patients who had undergone four first premolar extractions. Both studies reported no significant intergroup differences. In this study, group comparison results at hour 6 and on day 1 showed significantly reduced pain levels in the laser group compared with the control group. These discrepancies might be explained by differences in laser parameters and application protocols, as well as in age and gender distributions. Furthermore, whereas the maxillary dental arch was evaluated in these studies, the mandibular dental arch was evaluated in our study. Ghaffar et al.[14] used the VAS every day for the first 7 days to assess pain associated with initial archwire placement. The laser group reported statistically significantly lower mean pain scores than the control group only on the 5th day. The pain scores are compatible with the study of Ghaffar et al.,[14] which is the most similar study to the methodology of this study. However, the fact that this study shows laser therapy to be effective on pain only at hour 6 and on day 1 necessitates a discussion about the clinical significance of this method. At this point, pharmacological methods, such as analgesics, could be preferred instead of LLLT.

Study Limitations

The main limitations of this study include a small sample size, single wavelength LLL application, the inability to standardize the amount of crowding, the assessment of only the leveling, and the failure to investigate the rate of tooth movement over time. Therefore, future studies with larger sample sizes, different LLL wavelengths and application protocols, and an evaluation of both leveling/alignment and the rate of tooth movement over time are recommended.

CONCLUSION

The leveling duration showed no significant differences between the laser and control groups. Group comparison results of the VAS scores at hour 6 and on day 1 exhibited significantly reduced pain levels in the laser group compared with the control group.

Ethics

Ethics Committee Approval: The approval of the Van Yüzüncü Yıl University Faculty of Medicine, Clinical Research Ethics Committee was obtained to conduct this study (approval no.: 24, date: 05.05.2020).

Informed Consent: Informed consent forms was obtained.

Footnotes

Author Contributions: Surgical and Medical Practices - Y.T.; Concept - Y.K.; Design - Y.K.; Data Collection and/or Processing - Y.T.; Analysis and/or Interpretation - Y.T., Y.K.; Literature Search - Y.T., Y.K.; Writing - Y.T., Y.K.

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Review

Primary Failure of Eruption: A Rare but Desperate Condition for Orthodontic Treatment

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Main Points

- Primary failure of eruption has a genetic basis.
- Orthodontic forces cause ankylosis in teeth affected by primary failure of eruption.
- Primary failure of eruption may cause posterior open bite.

ABSTRACT

Tooth eruption is a highly complex mechanism that is controlled by many factors. Various mechanical, systemic, or genetic factors can cause eruption disorders. Primary failure of eruption (PFE) is known as an eruption disorder occurring due to non-syndromic genetic factors. It is frequently seen in the first and second molars and causes posterior open bite. It can be observed unilaterally or bilaterally. Studies show that mutations in many different genes that control the tooth eruption mechanism, mainly the *PTH1R* and *KMT2C* genes, constitute the genetic basis of PFE. Primary eruption disorders are very difficult to treat. It is known that the application of active orthodontic forces causes local ankylosis in the tooth and the failure of the tooth to return to its normal position. For this reason, determining the correct diagnosis and treatment method is very important. Although there are different treatment methods, the results of research about the success of these treatment methods are quite limited. This review aims to explain the etiology, diagnosis, and treatment of PFE in light of current genetic studies.

Keywords: Eruption disorders, orthodontics, posterior openbite, PTH1R, unerupted tooth

INTRODUCTION

In addition to the change in the direction of tooth eruption, there are basically two types of serious eruption anomalies. These anomalies are classified as primary and secondary eruption disorders.[1] Eruption disorders can occur due to a syndrome or develop in a non-syndromic manner. In both cases, it is crucial to differentiate between local or mechanical factors (e.g., adjacent teeth, cysts, lateral pressure of the tongue, or syndromes) and the disorder of the eruption mechanism.[2] If there is no systemic condition or any obstacle in the eruptive path that would prevent tooth eruption, this condition is called primary failure of eruption (PFE).[3] PFE was initially introduced by Proffit and Vig[4] and later redefined by Frazier-Bowers et al.[5,6] It represents a rare genetic anomaly affecting tooth eruption, with a prevalence of 0.06%.[7]

Tooth eruption refers to tooth movements that occur from the time the tooth is in the dentoalveolar structure to the time it begins to function in the mouth.[8] It is a coordinated and complex mechanism, and cellular,

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genetic, and systemic factors can affect this process.[1] The understanding and clinical management of the molecular and genetic mechanisms associated with tooth development and eruption disorders is quite difficult.[9]

Tooth eruption disorders have a wide clinical spectrum, from delayed eruption to the failure of eruption. Different alveolar bone apposition/resorption mechanisms can cause different clinical consequences such as PFE, ankylosis, eruption disorders due to insufficient arch distance, and impaction of the canines.[10]

Tooth eruption and loss are complicated processes that occur through the coordinated work of osteoclasts, osteoblasts, periodontal ligament cells, and dental follicle cells.[10] Before the eruption process begins, osteoclast precursors are organized in the dental follicle, and these cells combine to transform into osteoclasts that then resorb the alveolar bone, creating the pathway necessary for eruption.[10]

The majority of tooth eruption disorders are seen as a result of a change in the eruption direction of the first molars (ectopic eruption). At this stage, early diagnosis and treatment provided by the application of natural forces that will allow eruption are very important in preventing malocclusions. The most common teeth erupting in an ectopic position are the upper permanent molars and canines.

Studies have shown that PFE generally has a genetic etiology.[2] Current studies have revealed that *PTH1R* and *KMT2C* gene mutations cause primary eruption disorders. The currently known genetic etiology of PFE distinguishes it from other eruption disorders. In addition to systemic or syndromic diseases such as Albers-Schönberg Osteopetrosis, Odontodysplasia, and Cleidocranial Dysplasia, a differential diagnosis should be made with other eruption disorders such as mechanical eruption disorder (MFE) and ankylosis with clinical symptoms such as immobility, infraocclusion, and a metallic sound on percussion.[2]

CLINICAL AND RESEARCH RESULTS

Etiology

Typically, local factors such as odontomas, cysts, supernumerary teeth, and jaw fractures which often affect only one tooth and create a physical barrier to the eruption path are the main cause of eruption disorders. Other potential obstacles arise from mispositioned or malformed tooth buds, dilacerations, or ankylosis. While this type of eruption disorders is generally observed in the upper incisors and canines, the first or second molars are rarely affected.[11] Eruptions caused by disorders which are less frequently observed than those caused by physical causes occur in systemic diseases or syndromes such as ectodermal dysplasia, cleidocranial dysostosis, down syndrome, apert syndrome, Gardner's syndrome, hyperpituitarism, and hyperthyroidism. An even more rarely observed eruption disorder is PFE.[11]

Recent studies have revealed that this dental phenotype is genetically linked to mutations in the *PTH1R* and *KMT2C* genes. Additionally, the products of the *Periostin* (*POSTN*), *Ameloblastin* (*AMBN*), and *Amelogenin* (*AMELX*) genes are crucial in tooth development processes and contribute to eruption disorders through various mechanisms. AMELX, an enamel matrix protein, is recognized as a negative regulator of osteoclastogenesis which acts by suppressing the expression of RANKL and M-CSF.[12] Phenotypic variations are based on genetic, epigenetic, and environmental factors, but information about the pathophysiological mechanism leading to PFE is quite limited.[13] Studies have shown that that viral infections in the nerve pathways cause dental anomalies and eruption disorders, but no definitive conclusion can be reached due to various inadequacies in information on this subject.[14] It is anticipated that in the near future, it may become standard practice for orthodontists to collect saliva samples or cheek swabs for genetic testing when necessary. This advancement could lead to more personalized treatment plans and a better understanding of genetic effects on dental and craniofacial development.[15] Interestingly, a relationship between PFE and osteoarthritis was observed in some families affected by PFE, but this does not indicate a direct relationship between the two conditions.[15]

Decker et al.[17] were the first to report that a variant in *PTH1R* is associated with PFE.[16]

PTH1R

PTH1R is located on chromosome 3p21-p22.1.[17] It has been reported that parathyroid hormone (PTH) and PTH-dependent peptide (PTHrP) are the main modulator cells for osteoprotegerin (OPG), which is the osteoclastogenesis inhibitory factor, and RANKL, which is the main modulator cell of osteoclastogenesis.[18]

PFE is an autosomal dominant genetic disease that develops as a result of the heterozygous PTH1R mutation inactivating the functions of PTH1R and shows a phenotype only in the teeth.[19,20]

It is observed that a PTH1R ligand (PTHrP) affects the presence and activity of the dental enamel organ, especially the stellate reticulum of the dental follicle, and the tooth eruption mechanism (Figure 1). A lack of PTHrP production in dental follicle cells which is essential for the physiological root resorption of deciduous teeth and the proper eruption of permanent teeth causes teeth that initially follow a normal development process to be encapsulated by bone.[8,21]

After the link between PTH1R and PFE was established, more than 60 different PTH1R variants have been identified in patients with PFE.[20] Subramanian et al.[19] suggested that these PTH1R variants impair signal transduction in periodontal tissue cells, thereby causing primary failure of tooth eruption. Furthermore, mutations in PTH1R are known to lead to severe growth retardation and skeletal dysplasia.[22]

KMT2C

As a result of detailed clinical and molecular genetic analyses, it was determined that potential pathogenic mutations that may occur in the *KMT2C* gene may form the genetic basis of PFE.[9] The heterozygous splice site mutation in KMT2C causes primary eruption disorder with an autosomal dominant character in humans.[9]

Diagnosis

Since PFE has a family history, the simplest diagnostic approach is to check occlusion status in the parents of suspected patients. The next step is the exclusion of local and systemic causes of eruption failure such as regional odontodysplasia, neoplasms, odontogenic and non-odontogenic tumors, cysts, mucosal barriers-scar tissue, hypothyroidism, and hypoparathyroidism.[16]

Disorders caused by endocrine factors have not been observed in PFE or MFE patients (at least in light of the information we have to date). The main differential diagnosis should be made between mechanical obstruction (ankylosis) in the eruption path of the tooth and disorders in the eruption mechanism. The most accurate way to distinguish these two conditions is to determine the prognosis of the affected teeth.[4]

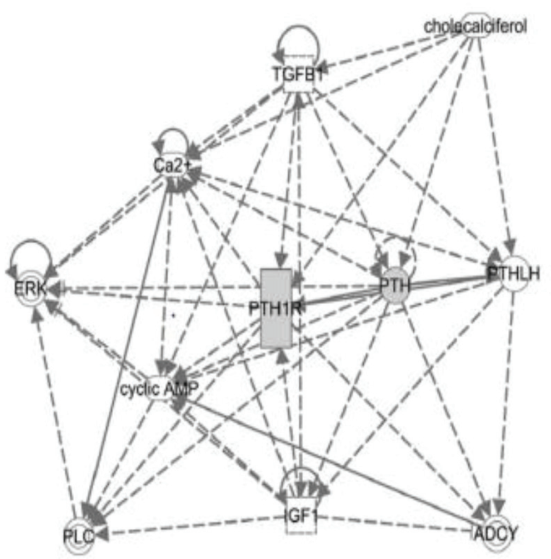

Figure 1. Scheme prepared to investigate the connection between the *PTH1R* gene and the molecular basis of tooth eruption[10]

PFE is mainly characterized by eruption disorders in the posterior teeth and vertical growth retardation in the alveolar process in the affected area. Eruption disorders of the permanent first and second molars are quite uncommon but have a significant clinical impact. Their ability to continue to develop without damage is also important for craniofacial growth.[23] Therefore, the accurate diagnosis and treatment of PFE are important as they will also affect craniofacial growth.

The average age of patients diagnosed with PFE is 13.65 years.[24] Typically, the teeth with the highest PFE rates (excluding the third molars) are the first and second molars in all four quadrants of the mouth.[24]

In a study involving 31 patients who met the inclusion criteria, 15 were diagnosed with PFE. In 100% of the cases, the first permanent molars were affected, while the second molars were affected in 93% of the cases.[25] In another study, 269 teeth were included, of which 87 (32%) were first molars, and 47 (17%) were second molars.[26]

Apart from PFE, other eruption disorders that cause posterior open bite (Table 1) are MFE and indeterminate failure of eruption (IFE). To apply the correct and effective treatment, a differential diagnosis must be made between these two eruption disorders.[4]

Other Types of Eruption Failures That Should Be Considered in Differential Diagnosis of PFE

It has been observed that a single permanent tooth is typically affected in MFE, and this tooth is usually the first or second premolar. Clinical observations have shown that the affected tooth is in infraocclusion, and a metallic sound is heard on percussion. Radiographs typically showed areas of ankylosis on the proximal sides of the teeth, but these could not be distinguished on the labial and lingual surfaces.[27]

Table 1. Table of eruption disorders that cause posterior open bite[4]

Classification	Number of affected tooth	Impact on neighboring teeth	Clinical appearance of ankylosis	Affected teeth visible intraorally	Typical treatment response	Proposed cause of failure
MFE	Usually only first molars	Adjacent teeth normal	Yes	Maybe	Other teeth respond, affected teeth might respond to luxation	Ankylosis, possible other obstruciton
PFE	Unilateral or bilateral, can involve whole quadrants	Distal teeth also affected	No	Usually some portion of at least 1 tooth	No response to orthodontic force	Failure of eruption mechanism
IFE	Too early to determine	Unknown at this stage	No	Maybe	Depends on final diagnosis	Ankylosis or PFE
Other	Any	Unknown	No	Yes	Might respond but tends to relapse	Possible tongue or soft-tissue interference

MFE, mechanical eruption disorder; PFE, primary failure of eruption; IFE, indeterminate failure of eruption

The teeth distal to the most mesially affected tooth are usually normal, and this is the most characteristic feature of MFE in the process of differential diagnosis with PFE. In cases where PFE is suspected based on genetics, genetic screening is recommended for determining the right treatment option.[28] The responses of the affected tooth or teeth to orthodontic forces would also be different.[4]

IFE is a diagnosis made in very young patients, where the distinction between PFE and MFE is not clear, to determine whether the teeth distal to the most mesially affected tooth are affected.[29]

According to a study conducted on 97 patients by Frazier-Bowers et al.[5] (Figure 2), PFE was observed in 39%, IFE was observed in 33%, MFE was observed in 20%, and 8% could not be included in a category.[4] Based on the aforementioned study, the most common eruption disorder causing posterior open bite was PFE.

The frequent involvement of the premolar and molar teeth in both PFE and ankylosis prompts the question of whether these eruption disorders are part of the same spectrum. PFE is more likely to be diagnosed when ankylosis lacks a discernible physical or mechanical cause and is determined to have a genetic origin. The primary distinction in diagnosing ankylosis versus PFE relies on clinical observations. Therefore, accurate clinical assessment leads to an accurate diagnosis.[8,10]

In secondary eruption disorders, the tooth has passed through the bone barrier and erupted but remained in infraocclusion. The situation in which the affected tooth begins to erupt in the mouth but then stops erupting or fails to fully occlude, which is observed in teeth affected by primary eruption disorders, is a characteristic feature that causes confusion in terms of definition with secondary eruption disorders. When teeth with secondary eruption disorders were examined histologically, ankylosed areas were observed at their roots.[1]

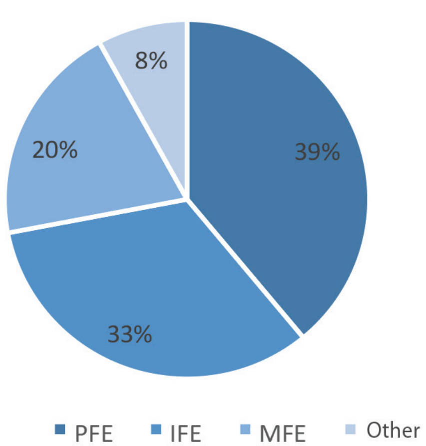

Figure 2. Scatter chart of eruption disorders causing posterior open bite according to percentages[4]
MFE, mechanical eruption disorder; PFE, primary failure of eruption; IFE, indeterminate failure of eruption

Teeth affected by PFE may vary in number, type (deciduous or permanent), and symmetry.[13] PFE has been observed to typically affect multiple posterior teeth. It was determined that all teeth distal to the most affected mesial tooth were also affected and showed similar infraocclusion characteristics.[27] This feature is very important in making a differential diagnosis with MFE. PFE was also reported in cases where other dental anomalies such as peg-shaped lateral teeth and infraoccluded primary molars are present.[6]

Although it is known that posterior teeth are often affected, it was observed that anterior teeth can also be affected. It was stated that in cases where anterior teeth are affected, posterior teeth are also affected.[14] The incidence of PFE did not show a notable difference between the maxilla and mandible.[4] Available clinical findings show that PFE is often observed unilaterally, but it can also be observed bilaterally. This suggests that while PFE affects the teeth on one side of the jaw, it might not cause any eruption disorder in any of the teeth on the other side. It can affect both primary and permanent dentition. The affected permanent tooth may later become ankylosed. It can be observed in a single individual not in other family members of theirs. There is no significant difference in the frequency of observation between the sexes. Dilacerations can be observed in the roots of the affected molar teeth.[11]

In the retrospective comparative study conducted by Avalos-Hernández et al.,[30] CBCT images of 40 teeth affected by PFE and 40 unaffected teeth were analyzed. As a result, the coronal dimensions of molars affected by PFE were smaller, and the mesial and distal root lengths were shorter by approximately 2 mm.[30] Upper molars affected by PFE also showed a characteristic inclination toward the palatal and distal directions, which could be considered diagnostic.[30]

Subtypes of PFE

Studies have shown two subtypes of PFE (Figure 3). It has been reported that in Type 1 PFE, the loss of tooth eruption capacity is related to a certain chronological time, and in Type 2, it is related to a certain root development phase. The eruption potential of teeth affected in Type 2 cases varies. A combination of Types 1 2 was observed in most reported PFE cases.[6]

In Type 1 cases, an open bite progressing from the anterior to the posterior is observed. The eruption defect which is known to be genetically screened for Type 1 is known to be present in all affected teeth at the same developmental stage. A similar and high degree of eruption failure was observed in all teeth from the most mesial tooth to the most distal tooth.[14] For Type 1 cases, a more commonly observed form, teeth distal to the affected first molar exhibit a more severe infraocclusion that causes posterior lateral open bite.[15]

In Type 2 cases, an open bite progressing from the anterior to the posterior is similarly observed. However, various eruption disorders are observed in multiple quadrants.[3] Eruption failure is also observed in the second molar teeth.[10] Although the teeth distal to the most mesially affected tooth have a higher

Figure 3. a) Intraoral image of an 18-year-old female patient with PFE Type 1, b) Intraoral image of a 17-year-old female patient with PFE Type 2, c) Intraoral image of a 15-year-old female patient with PFE Type 1 and Type 2 observed together.[11]
PFE, primary failure of eruption

eruption potential, they are still inadequate compared to normal teeth.[14] In a Type 3 case, which can be described as a combination of Type 1 and 2 according to some sources, it has been observed that Types 1 and 2 occur together in different quadrants of the same patient.

Pathogenesis

It is known that several genes including *PTH1R*, *AXIN2*, *MSX1*, and *PAX9* play critical roles in odontogenesis. There is compelling evidence suggesting that PFE is typically an autosomal dominant heterogeneous condition linked to mutations in the *PTH1R* gene and genes involved in the activation of the cAMP/PKA pathway, which are crucial for tooth eruption. However, not all individuals with PFE exhibit mutations in these known genes, and the genetic basis of PFE remains largely unexplored.[31]

Treatment

Although PFE is rare, when it occurs in both the maxilla and the mandible, a severe posterior open bite may occur, which is very difficult to treat and has unpredictable outcomes.[6] Open bite, which occurs as a result of the affected teeth being below the normal occlusal level, can occur unilaterally or bilaterally.

Various multidisciplinary treatment methods are available for the disorders that occur with PFE, especially posterior open bite. Orthodontists and pedodontists are the first to encounter patients with PFE. Still, surgeons and prosthetists will most likely be involved in the management of PFE.[15] Clinicians should consider basic molecular mechanisms when treating simple and complex dental complications resulting from eruption anomalies.[1]

In a study involving 22 cases of teeth affected by PFE, various treatment approaches were reported as follows: unsuccessful orthodontic treatments following extraction (n=6), extraction of affected teeth (n=7), orthodontic extrusion of unaffected teeth (n=1), alignment of upper and lower labial segments (n=1), segmental osteotomy (n=1), and overdentures (n=1). Additionally, 5 patients did not receive any treatment.[14]

Proffit and Vig[4] and Frazier-Bowers et al.'s[5] research suggested that extracting teeth affected by PFE could be a suitable treatment method. For young patients, occlusal stability can be maintained with direct or indirect composite practices until implant placement becomes feasible. Adult patients with mild infraocclusion may not necessarily require treatment but should undergo regular monitoring.[14]

In addition to tooth extraction, surgical interventions or distraction osteogenesis (DOG) may be considered as further treatment options for managing PFE. For example, this is valid in cases where PFE is very severe and where it is necessary to extract the affected teeth and then shift the teeth distal to the first molar into the extraction space (as in cases of Type 2 PFE). One approach to help improve tooth positioning may be to perform single-tooth osteotomies or corticotomies.[15] Since it is known that teeth affected by PFE do not respond well to orthodontic forces, alternative treatment options should be considered. It has not been possible to determine whether the teeth affected by PFE do not respond to orthodontic forces alone and whether the combined surgical and orthodontic approach is quite successful or not due to the lack of studies in this field.[15]

Orthodontic Treatment Methods

In cases where an eruption malfunction is observed in the first molar teeth, this condition can be diagnosed early, and the early extraction of the first molar tooth and the orthodontic mesialization of the second molar tooth can be a good treatment alternative. Nevertheless, for this treatment to be applied, there must be no eruption disorder in the second molar tooth.[10] While orthodontic extrusion, another treatment method, can be an effective method in the presence of MFE in which the eruption mechanism is not impaired, it cannot be a successful treatment method for PFE because it causes immediate ankylosis in the teeth affected by PFE if orthodontic forces are applied.[3] This makes PFE a challenging condition for orthodontists. Therefore, due to the high failure rate of orthodontically assisted eruption in individuals with PFE, it is crucial to conduct a genetic diagnosis before initiating any orthodontic treatment.[13] A genetically confirmed PFE diagnosis will protect both patients and orthodontists from years of unnecessary treatments and the harmful effects of orthodontic forces on the affected area as well as the unaffected area.[32]

A 28-year-old male patient with unilateral posterior open bite secondary to PFE of maxillary molars presented to our clinic (Figure 4). The maxillary right first molar exhibited partial impaction, and the maxillary right second and third molars were completely impacted (Figure 5). These conditions coincided with the characteristics of PFE. After the extraction of the right first molar, the second molar was erupted with orthodontic forces (Figures 6 and 7).

A case report[33] presented a nine-year-five-month-old female patient who was referred due to the failure of eruption of the maxillary right permanent first molar. A modified Nance palatal arch with a distal extension was fabricated, along with the bonding of an orthodontic button for traction. However, the tooth did not respond to the initial orthodontic forces applied. A follow-up periapical radiograph taken six months later revealed areas indicative of ankylosis. Subsequently, a surgical subluxation was performed, followed by the immediate application of orthodontic forces. Though some initial movement was noted, continuous movement was not achieved, necessitating a second surgical subluxation five months later. Following this intervention, the tooth responded favorably. The orthodontic button was subsequently repositioned to optimize the loading vector. Six months later, the first molar was successfully aligned in its correct position, and the orthodontic appliances were removed. At the end of the 12-month follow-up, radiographic analyses confirmed that the tooth was properly aligned with the occlusal plane of adjacent teeth, preserving the integrity of both dental and periodontal structures. By the end of the four-year follow-up, the tooth remained stable in the desired position, effectively occluding with its antagonist.

Figure 4. Panoramic radiograph taken before treatment. Right maxillary first molar to third molar positioned below the occlusal plane

Surgical Treatment Methods

The integration of cementum and dentin with the alveolar bone prevents orthodontic tooth movement and necessitates surgical approaches such as vertical DOG or minimal segmental osteotomy for the affected teeth.[34] A segmental osteotomy of the alveolar bone affected by PFE can be performed to reposition the segment and improve the occlusal plane. A bone graft can be placed between the bone segment and the base of the alveolar bone when necessary. There are certain risk factors for both jaws. For the maxilla, the thick and poorly elastic palatal mucosa impedes the movement of the segment, whereas there is a risk of causing damage to the inferior alveolar nerve when performing this procedure in the mandible.[16]

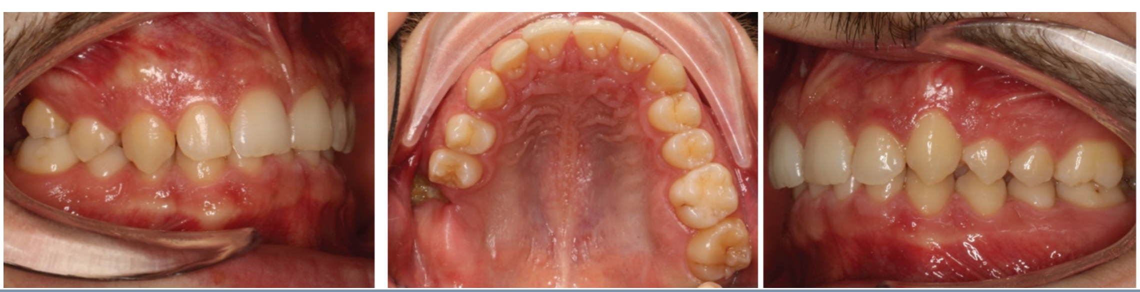

Figure 5. Introral photographs before treatment

Figure 6. Midtreatment occlusal view

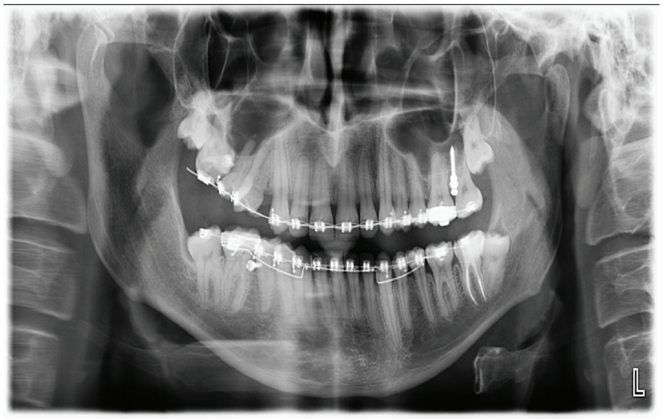

Figure 7. Midtreatment panoramic radiograph

DOG, commonly used in patients with lateral open bite, has some drawbacks in terms of controlling the direction of growth. The linear movement of the distraction device often results in the displacement of the segment towards the palatal side during bone growth. In such cases, the floating bone concept may offer a more effective approach, allowing for the three-dimensional control of the segment's position by continuously applying pressure before complete bone healing. Previously, researchers applied DOG to the maxillary alveolar bone in a PFE case with severe lateral open bite, controlling segment position using elastic traction and removing the device before complete bone healing. This approach successfully improved dental arch morphology and achieved stable occlusion.[16]

Prosthetic Treatment Methods

Prosthodontic treatment is often the only treatment available for these patients. In cases where PFE is milder, a prosthetic approach and the camouflage of the eruption problem with crowns would be a good treatment option.[15]

Depending on the extent of tooth eruption, treatment options such as overlay crowns or overlay removable partial dentures can be considered when the tooth crown is sufficiently visible in the oral cavity. It is generally recommended to not place fixed restorations before vertical growth is completed.[3] This approach ensures that the restoration will properly accommodate any future changes in the tooth's position as vertical growth continues, thereby optimizing long-term treatment outcomes.

CONCLUSION

Since tooth eruption is a multifactorial mechanism, it is known that many different factors can cause tooth eruption disorders. The possibility of PFE comes to mind in cases where eruption disorders are observed despite the absence of any physical disability or systemic disease. The most important feature that distinguishes PFE from other eruption disorders is its genetic etiology. Studies have shown that defects in the *PTH1R* and *KM2TC* genes cause PFE. In addition to these genes, it is known that other genes responsible for regulating the tooth eruption mechanism could also be considered candidate genes for PFE.

It can be stated that the infraocclusion of the posterior teeth is the most distinguishing feature of PFE, especially when it is observed bilaterally. Another important distinguishing feature is that all teeth distal to the most mesial tooth affected by PFE are also affected. Since it is known that orthodontic forces applied for treatment cause ankylosis in teeth affected by PFE, genetic screening is recommended for diagnostic purposes in patients with suspected PFE.

An orthodontic treatment approach to teeth affected by PFE would not be appropriate. Therefore, surgical and prosthetic approaches are recommended, but one may still argue that treatment methods are quite limited since very few cases explaining treatment options have been reported.

Footnotes

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Review

Effectiveness of Surgical and Non-Surgical Techniques for Accelerating Orthodontic Tooth Movement in Fixed Appliances and Aligners: A Systematic Review

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Main Points

- This review identifies corticotomy and photobiomodulation (PBM) as key techniques for accelerating orthodontic tooth movement, enhancing treatment efficiency and reducing discomfort.
- PBM, in particular, shows promise due to its non-invasive and painless nature, although further research is needed to optimize its protocols.
- The study calls for more randomized controlled trials to better integrate acceleration techniques with modern orthodontic appliances, and suggests that advancements in stimulation devices could make treatments more tailored and accessible to patients.

ABSTRACT

Several procedures have been proposed as adjuvant treatments in orthodontics to accelerate orthodontic tooth movement (OTM). This review aimed to evaluate and compare the effectiveness of surgical and non-surgical techniques in accelerating tooth movement, ascertain the influence of different orthodontic appliances on the rate of tooth movement and analyze their clinical applicability as supportive approaches in orthodontic treatment. A bibliographic search was carried out in April 2024 across Pubmed, Scopus, Web of Science, and the Cochrane Library using combinations of keywords and Medical Subject Heading terms relevant to the topic. The search had no time restriction and was limited to studies published in English. A total of 76 articles were included in this systematic review. Corticotomy exhibited the highest acceleration potential among surgical techniques but is highly invasive and associated with considerable pain and discomfort. Among non-surgical techniques, vibration and photobiomodulation (PBM) showed the most promising results due to their non-invasiveness and effectiveness in accelerating tooth movement. This review provides a comprehensive overview of techniques for accelerating OTM. The literature remains limited in involving surgical and non-surgical procedures using orthodontic aligners, highlighting the need for further research. Considering all the pros and cons, PBM appears to be the most promising technique; however, its effectiveness is yet suboptimal. Future efforts should be dedicated to optimizing PBM protocols to stimulate specific remodeling phenomena, ensuring its establishment as a safe, effective, painless, and non-invasive acceleration technique.

Keywords: Accelerated orthodontic tooth movement, corticotomy, low-intensity pulsed ultrasound, non-surgical techniques, photobiomodulation, surgical techniques, vibration

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INTRODUCTION

The prolonged duration of the orthodontic treatment is a primary obstacle to patient adherence, especially among adults.[1] Therefore, shortening treatment time and manipulating the biological response to orthodontic forces to accelerate orthodontic tooth movement (OTM) have been key challenges in modern orthodontics. Several techniques have been proposed to improve the rate of tooth movement while minimizing long-term iatrogenic damage.[2] Extended orthodontic treatment is one of the definitive risk factors for root resorption and periodontal problems. On the contrary, shorter treatment times are associated with a lower risk of root resorption, reduced enamel demineralization, and improved patient compliance.[3]

Orthodontic movement involves several periodontal processes, including an acute inflammatory response, necrosis, and tissue degeneration in the compression side of stressed teeth, as well as intense bone remodeling on the tension side.[4,5] The potential of coadjuvant treatments in accelerating OTM depends on their ability to modulate tissue remodeling. Thus, understanding the mechanisms underlying acceleration techniques is pivotal for selecting and optimizing the most appropriate approach. Besides, factors such as patient comfort, usability, and endorsement of the intervention must be taken into account to meet expectations and ensure their quality of life during the procedure.[6,7]

Surgical procedures such as corticotom,[8] accelerated osteogenic orthodontics,[9,10] piezocision,[11] corticision,[12] and micro-osteoperforation (MOP)[13] have been proposed as effective methods to accelerate the orthodontic movement. However, these techniques require surgical intervention, posing higher risks and costs, along with prolonged postoperative discomfort. These drawbacks have fostered interest in non-surgical acceleration methods, which offer non-invasive and painless alternatives.[14] Such techniques include vibration stimuli,[15] electromagnetic stimulation,[16] extracorporeal shock waves,[17] low-intensity pulsed ultrasound,[18,19] photobiomodulation (PBM),[20] and the injection of biomaterials, supplements, or hormones.[21] These approaches can be considered more appealing to patients due to their reduced invasiveness and effectiveness.[22]

Despite the growing investigation on this topic in recent years, the scientific literature lacks systematic and focused information from randomized controlled trials (RCTs) comparing the effectiveness of different surgical and non-surgical techniques for accelerating OTM. Indeed, recent systematic reviews have provided novel insights into the implementation of these techniques.[23,24] However, the available evidence remains limited, and the effects of different orthodontic approaches, including fixed and removable appliances, have yet to be explored. This review addresses this gap by identifying the most effective ways for modulating the biological response and accelerating OTM with minimal side effects. The scientific and empirical knowledge offered by the current systematic review will assist clinicians in defining the most suitable acceleration technique for each case, ultimately improving treatment duration and pain management.

METHODS

This review was conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020.[25]

Eligibility Criteria

The Population, Intervention, Comparison, Outcomes, and Study design strategy (Table 1),[26] was used to formulate the guiding questions for this study: "Which technique for accelerating tooth movement, surgical or non-surgical, is most effective and associated with less tissue damage and discomfort?" and "How does the type of orthodontic appliance influence acceleration rates?"

Based on these questions, the following eligibility criteria were defined:

Inclusion Criteria

- Clinical RCTs investigating surgical and non-surgical acceleration techniques as coadjuvants of orthodontic treatment using fixed appliances and clear aligners;

- Studies published in English.

Exclusion Criteria

- Meta-analyses, systematic and narrative reviews, case reports, comments, theses, dissertations, and any publication type other than clinical RCTs;

- Studies conducted on preclinical models (e.g., *in vitro* or animal studies);

- Studies with a sample size of less than 10 participants.

Table 1. Implementation of the PICOS strategy

Population	Patients undergoing orthodontic treatment with fixed appliances or aligners, without age, sex or background restrictions.
Intervention	Surgical and non-surgical techniques for acceleration of orthodontic tooth movement.
Comparison	Control groups (e.g., no intervention group, contralateral tooth/teeth groups), baseline conditions, or distinct acceleration methods.
Results	Velocity/amount of tooth movement, biological effects of acceleration techniques on the periodontium.
Study design	Randomized controlled trials.

Information Sources and Search Strategy

The bibliographic search was carried out in PubMed (via the National Library of Medicine), Scopus, Cochrane Library, and Web of Science databases between April 23 and 25, 2024. The retrieved articles were analyzed without any time restrictions, and only studies published in English were considered. The same advanced search was applied across all databases, targeting titles, abstracts, and keywords using the terms listed in Table 2.

Selection Process

An advanced search was initially performed using the specified keywords in each database. Duplicate articles were removed using Mendeley's citation tool. The titles and abstracts of the identified, potentially relevant articles were submitted for preliminary evaluation by two authors (AG and MC). Then, the selected studies were read in full and assessed for eligibility.

Data Collection Process and Items

After evaluating the articles, the relevant data were extracted and organized in a table. The extracted information included publication details (name of the first author and year of publication), population under study (sample size and group distribution), tested treatments (types of treatments/interventions compared and studied), intervention characteristics (required movements, intervention description, and evaluation duration), and key findings, such as orthodontic movement rates, differences between groups, and complications during procedures and/or the recovery period.

Effect Measures, Synthesis Methods, and Certainty Assessment

In this study, surgical and non-surgical techniques for enhancing and accelerating orthodontic movement were compared and evaluated, emphasizing the type of orthodontic intervention (either conventional appliances or aligners). Only clinical RCTs with 10 or more participants were selected for the qualitative synthesis. The effect measures included the mean difference in tooth movement or treatment duration between the groups. Statistical comparisons were assessed between the groups.

Data were presented chronologically in two tables - one for surgical techniques and the other for non-surgical techniques -, standardizing the collected information for a clear and intuitive comparison of the interventions and reported outcomes.

Risk of Bias Assessment

The quality assessment was conducted using the Effective Public Health Practice Project (EPHPP) tool, a standardized method for evaluating the risk of bias in clinical studies. The complete quality assessment data are provided as supplementary materials.

RESULTS

Article Selection

A bibliographic search yielded 499 articles, of which 143 were duplicates and thus removed. An additional 29 manuscripts were obtained from citation searching and added for screening. After reading the titles and abstracts, 299 articles were selected for further analysis. Five reports were not retrieved, and 218 studies were excluded based on eligibility criteria, resulting in 76 articles being selected for qualitative synthesis. This process is represented in Figure 1.

Profile of the Included Studies

Publication Year

The highest number of articles on the selected topic was published by 2020 (n=12, 18.2%),[22,27-37] with the first publication appearing in 2004.[38] Figure 2 reflects the rapid growth in publication, which is associated with the growing knowledge and expertise in the techniques discussed here.

Type of Acceleration Intervention

Thirty-three articles on surgical techniques to accelerate OTM were selected. Numerous studies investigated the effects of multiple surgical acceleration methods,[8,9,12,13,27,39-45] mainly comparing modified corticotomies [such as MOP and periodontology-assisted accelerated osteogenic orthodontics (PAOO)] with conventional corticotomy. In summary, 13 articles examined the effectiveness of piezocision to accelerate OTM,[8,11,13,27,38,40-42,44,46-49] 12 focused on MOP,[28-30,42,43,50-56] eight used traditional corticotomy,[1,8,9,27,43-45,57] five addressed periodontally accelerated orthodontics,[9,38,39,58,59] two utilized laser-assisted flapless corticotomy,[40,60] and one studied corticision.[12] Regarding non-surgical techniques, 45 articles were selected: 28 assessed

Table 2. Search strategy employed in the electronic search

Type of study	Search Strategy
PubMed Scopus Cochrane Library Web of Science	[“accelerated orthodontics” OR “accelerated orthodontic movement” OR “accelerated tooth movement” OR “orthodontic movement” OR “tooth acceleration” OR “tooth movement acceleration” OR “dental acceleration” OR “accelerating dental movement”) AND (“surgery techniques” OR “surgical techniques” OR corticotomy OR “micro-osteoperforation” OR microosteoperforation OR piezocision OR “accelerated osteogenic orthodontics” OR “periodontally accelerated osteogenic orthodontics” OR “noninvasive techniques” OR “non-invasive techniques” OR “nonsurgical techniques” OR “non-surgical techniques” OR “growth hormone” OR parathormone OR steroid OR “nonsteroidal anti-inflammatory drugs” OR “non-steroidal anti-inflammatory drugs” OR NSAIDs OR i-PRF OR “vitamin D3” OR micronutrients OR “electromagnetic fields” OR vibration OR ultrasound OR “mechanical force” OR “mechanical stimulus” OR “mechanical stimulation” OR photobiomodulation OR PBM OR phototherapy OR “low level light therapy” OR “low-level light therapy” OR “low level laser therapy” OR “low-level laser therapy” OR PBM OR “laser therapy” OR “laser irradiation” OR “light therapy” OR “light irradiation” OR “low power laser therapy” OR “low-power laser therapy” OR LLLT OR PBM OR “low energy laser” OR “low-energy laser” OR “low intensity laser” OR “low-intensity laser”]

the potential of PBM,[13,14,22,33-35,37,56,61-80] eight investigated the application of vibratory stimuli,[31,81-87] four analyzed the efficacy of the injection of biomaterials, supplements, or hormones [e.g., platelet-rich fibrin (PRF)[88-90] and platelet-rich plasma (PRP)[21,90]], two implemented vitamin D supplementation,[91,92] one used low-intensity pulsed ultrasound stimulation (LIPUS),[32] one employed electromagnetic stimulation,[16] and one assessed the impact of extracorporeal shock waves on the rate of OTM.[17]

Two studies compared the effects of one surgical and one non-surgical technique: PBM vs. piezocision[13] and PBM vs. MOP;[56] however, only the first study included a control group (with no acceleration technique). Importantly, each study was

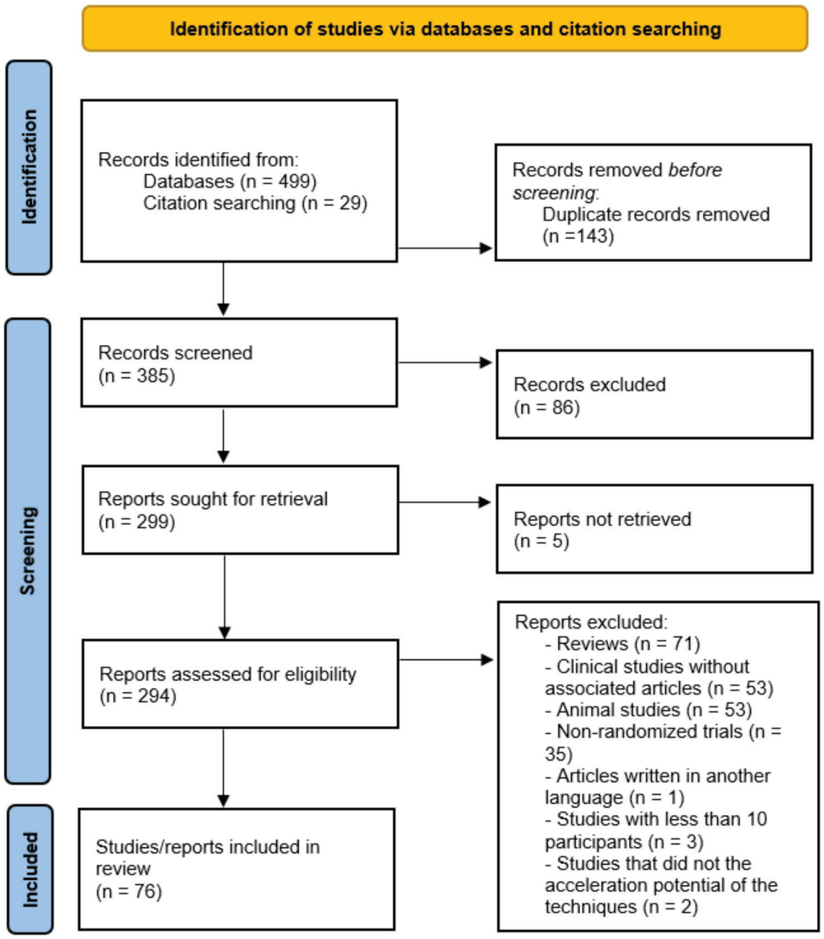

Figure 1. PRISMA flowchart of the studies identified through electronic search

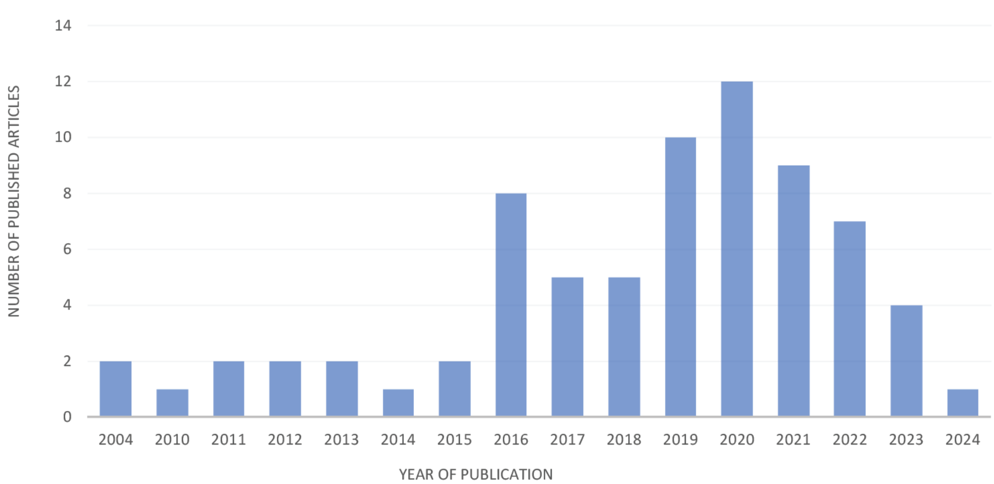

Figure 2. Distribution of the included articles by year of publication

presented only once in Supplementary Tables 1 or 2, including the experiments in which multiple techniques were assessed. Nevertheless, studies comparing two acceleration methods are further discussed below.

Type of Orthodontic Intervention

Conventional treatment with fixed appliances was the preferred orthodontic intervention, with no aligner interventions being registered among the studies describing surgical techniques. In contrast, three studies investigated the efficacy of non-surgical techniques for accelerating tooth movement with aligners - two focused on vibration[85,86] and one on PBM.[69]

Data Extraction, Systematic Synthesis, and Certainty of Evidence

The most relevant features from the revised studies were extracted and organized into tables for a more dynamic, easy-to-read, and systematic analysis. This approach enables the reader to efficiently compare protocols and results obtained from studies using surgical (Supplementary Table 1) and non-surgical (Supplementary Table 2) acceleration techniques.

Each study associated orthodontic procedures with movement-related variables, serving as proxies for the accelerating abilities of each technique (i.e., amount of tooth movement, treatment duration, and movement rate). In some cases, unit conversions were performed to uniformize the stimulation parameters across studies, facilitating comparison (e.g., mechanical vibrational forces presented in gf were converted into Newton). Movement-related values were statistically compared between groups, typically with conventional orthodontic treatment (control) vs orthodontic treatment with acceleration techniques. A few studies compared two or more acceleration approaches. Occasionally, biological outcomes, such as cytokine expression and root resorption signals, were monitored and compared between groups.

For statistical analysis, the majority of studies assessed the magnitude of difference between groups with a significance level of 5% (95% confidence interval).

Results of Syntheses

Supplementary Tables 1 and 2 present the compiled data from the studies investigating the accelerating potential of surgical and non-surgical techniques, respectively.

Results of Individual Studies

Traditional Corticotomy

The traditional alveolar corticotomy is a surgical technique involving an intentional lesion of the cortical bone that consists of reflecting full-thickness flaps to expose buccal alveolar bone, followed by a series of interdental cuts through the cortical bone, which scarcely penetrate the medullary bone. It has been previously shown that corticotomy can increase the rate of OTM two to four times in the first days compared to the single use of a conventional appliance alone.[1] Initially, corticotomies were believed to accelerate tooth movement through alveolar bone segmentation, mass tooth movement, and an associated bone block. However, the regional accelerator phenomenon (RAP) is now the most widely accepted explanation, involving a complex regional mechanism encompassing both soft and hard tissues, and is characterized by the acceleration of normal vital tissue remodeling processes, enhancing tissue healing and defensive reactions.[93] This phenomenon causes a reduction in bone density due to increased remodeling space, which starts within a few days after the procedure, peaks between one and two months, and lasts for two to four months.[57]

Shoreibah et al.[57] conducted one of the early RCT studies on surgical acceleration techniques, demonstrating that corticotomy can decrease the total time of orthodontic treatment. However, the procedure was associated with a slight (non-significant) decrease in bone density and root resorption post-intervention.

A few years later, Al-Naoum et al.[1] showed that while corticotomy was highly effective in accelerating the OTM, it was accompanied by increased pain, discomfort, and swelling compared to conventional orthodontic treatment, thereby highlighting the primary drawbacks of traditional corticotomy from the patients' perspective. By 2023, Gopalakrishnan et al.[45] compared the effects of a soft tissue flap-only procedure and a single-cut corticotomy on the rate of canine retraction, revealing no significant differences between the two surgical methods.

At the time of this review, no relevant studies were found that combined corticotomy with orthodontic treatments using aligners.

Although corticotomy is highly effective in accelerating OTM, it is also invasive and aggressive for patients. As a result, minimally invasive surgical techniques with high acceleration efficiency have been developed, known as flapless corticotomies, which do not require flap elevation.[27] Consequently, all other surgical acceleration methods are modified corticotomies, including MOP, PAOO, corticision, piezocision, and laser-assisted corticotomy.

Laser-assisted Flapless Corticotomy

One of the earliest flapless corticotomy techniques was performed using a laser due to its ability to create clear, dry, and less traumatic incisions, which also made the procedure more convenient for patients.[94]

Jaber et al.60 reported that although corticotomy procedures effectively reduced treatment time, it is considered one of the most invasive techniques for accelerating OTM. Approximately 50% of patients experienced extreme pain and discomfort while eating during the first two days, which subsided to mild pain in about 67% of patients within eight weeks post-intervention. Furthermore, around 80% of patients presented moderate to severe swelling immediately after the procedure, which significantly reduced within a week.60 Alfawal et al.40

also investigated the effect of laser-assisted corticotomy compared to MOP intervention, as detailed in Section 3.5.6 (MOP).

Periodontology-assisted Accelerated Osteogenic Orthodontics

PAOO is a technique that combines alveolar corticotomy, bone graft materials, and orthodontic forces for the rapid correction of malocclusions. The technique is performed using releasing incisions, with full-thickness flaps reflected labially and lingually. Alveolar decortication, in conjunction with medullary penetration, is performed to enhance bleeding, followed by the placement of a bio-absorbable grafting material over the injured bone.[9]

Chandra et al.[9] examined the use of corticotomy with a recombinant human bone morphogenetic protein type-2 (rhBMP-2) graft and demonstrated its efficacy in shortening overall treatment duration. Notably, an increase in bone density at the corticotomy sites was observed compared to conventional corticotomy without the graft. rhBMP-2 exhibited regenerative and osteoinductive properties, mitigating dentoalveolar bone loss by enhancing local bone density.

Also, Bahammam[39] compared the effectiveness of two xenografts-a bovine xenograft and bioactive glass-using the PAOO technique to treat adult patients with moderate dental crowding.The study concluded that the combination of orthodontic treatment and PAOO was effective in accelerating the OTM in adult patients, with the additional ability to reduce the risk of root resorption. The bovine xenograft, when used with modified corticotomy, resulted in an increase in bone density than bioactive glass.[39]

In line with previous results, the conclusions drawn by Wu et al.[38] also support the effectiveness of accelerated osteogenic orthodontics techniques in reducing treatment time, albeit using a modified approach-improved accelerated osteogenic orthodontics. This treatment integrates PAOO with piezosurgery-assisted corticotomy (piezocision). In their study, the average treatment period was reduced by more than six months in patients with skeletal class III malocclusion.[90] Piezosurgery-assisted corticotomies limited to the buccal surface were performed, involving vertical incisions in interradicular spaces, bone graft application, and meticulous flap repositioning. The rate of tooth movement in the PAOO group was superior to that of the conventional orthodontic treatment group.[38]

In addition, Alsino et al.[59] investigated the effect of PAOO with a bone xenograft (Bone-D®) on correcting lower anterior teeth crowding. The study found that PAOO accelerated alignment and leveling, while differences in dental arch width between the canines and second premolars were clinically negligible. Moreover, no significant periodontal tissue damage was observed.

To date, no studies have assessed the ability of PAOO to accelerate orthodontic treatments with aligners.

Corticision

Corticision, derived from "cortical bone incision," involves performing small incisions in the tissue, typically with a blade, without flap elevation. This approach is associated with less tissue damage and pain.[12,95]

The only RCT that performed corticision, conducted by Sirri et al.,[12] reported a 1.2 fold faster alignment of lower anterior teeth compared to conventional orthodontic treatment. No significant differences in apical root resorption were found, although the maximum root resorption index was observed for the experimental group. Additionally, the distribution of dehiscence formation was similar between the groups, revealing that corticision did not promote gingival recession.

Piezocision

Piezocision is a more conservative and less invasive alternative to the conventional corticotomy technique. It involves the use of an ultrasonic cutting instrument to make incisions in the cortical bone without requiring a flap elevation.[96] This method has evolved as a new approach for manipulating cortical bone, causing minimal damage to adjacent tissues, reducing discomfort, and enhancing patient acceptance.

All the reviewed articles on piezocision involved the use of fixed appliances. For instance, some studies reported that piezocision reduced treatment duration by 59% compared to conventional orthodontic treatment alone while also minimizing anchorage loss of posterior teeth without adversely affecting periodontal health.[47,97] Moreover, another study showed that despite the piezocision being minimally invasive and requiring a longer surgical procedure, it is proved to be more efficient in reducing treatment duration compared to conventional corticotomy.[40]

However, Abbas et al.[44] observed that corticotomy resulted in greater canine movement rates in the first and third months than piezocision. This difference was attributed to the more extended corticotomy surgery, which may have increased the RAP due to prolonged tissue exposure, manipulation, and invasiveness.

Furthermore, Alfawal et al.[40] demonstrated that both piezocision and laser-assisted flapless corticotomy without grafting are highly effective in accelerating canine retraction using minimally invasive techniques. In this study, the canine retraction rate in both experimental groups was approximately 25% higher compared to the control.[40] Although laser corticotomy is 2.5 times faster than conventional orthodontic treatment (i.e., without acceleration techniques) and causes less pain and discomfort than piezocision,[40] Charavet et al.[46,48] highlighted that piezocision may be contraindicated in patients with a high gingival smile line because of high susceptible to develop small scars.

In addition, Khlef et al.[8,27] compared traditional corticotomy and graft corticotomy and found no statistically significant differences in retraction rates, skeletal, dental, and tissue variables, or root resorption. Conversely, Fernandes et al.[41] reported that both alveolar corticotomy and piezocision techniques were ineffective in accelerating canine retraction, ascribing to the intervention's failure to activate the RAP in the medullary bone, which compromised bone remodeling and occlusal contacts during retraction.

In another study, Jivrajani and Bhad Patil[35] showed that the piezocision procedure increased iatrogenic root resorption by 44% when used in conjunction with orthodontic forces. The authors suggested caution, as its application close to the root may cause iatrogenic damage to adjacent roots.

Micro-osteoperforation

MOP is a minimally invasive, graftless, and flapless transmucosal bone puncture technique that effectively reduces treatment time with minimal surgical damage.[52] This technique consists of producing multiple transmucosal perforations within the maxillary interproximal alveolar bone to elicit RAP near the targeted region for OTM.[51] Similar to other surgical techniques, MOP facilitates tooth movement by activating osteoclasts through RAP, which is associated with decreased bone density. Additionally, the depths of MOP boreholes may influence the RAP intensity.

As outlined in the abovementioned acceleration techniques, all studies using MOP applied conventional orthodontic treatment with fixed appliances. Specifically, the study carried out by Attri et al.[54] indicated that OTM acceleration occurred after MOP was performed every 28 days during the retraction period, with patients reporting minimal discomfort after the procedure.

Similarly, Sivarajan et al.[51] observed that MOP could increase the overall retraction of mini-implant-supported canines over 16 weeks, though the difference was not statistically significant. Pain was reported by several patients, with approximately 60% describing it as moderate and 15% as severe.[51]

MOP was found to significantly increase the expression of cytokines and chemokines, which are known for recruiting osteoclast precursors and stimulating their differentiation, potentially reducing orthodontic treatment time by up to 62%, with no associated adverse effects.[53] However, a study comparing molar and mesial migration with MOP depths ranging from 3 to 6 mm observed no clinically significant difference in tooth movement.[28]

Similarly, Aboalnaga et al.[50] stated that MOP was not able to accelerate the rate of canine retraction, did not increase posterior anchorage, and led to changes in root resorption. Furthermore, patients experienced mild to moderate transient pain that disappeared in about seven days.[98-101] Nonetheless, this study did not evaluate the effect of different numbers, sites, and repetitions of MOP on the rate or type of tooth movement, nor did it assess the effect of different total treatment durations. Additionally, the findings by Babanouri et al.[29] indicated the effectiveness of MOP in accelerating tooth movement over three months; however, this corroborates with a previous study suggesting that increasing the number of MOP from 3 to 6 mm was not clinically significant, as it did not proportionally reduce treatment time). Meanwhile, Jaiswal et al.[52] reported that doubling MOP accelerated tooth movement by 25% compared to a single MOP. This increase also led to significantly higher IL-1-β levels, which is in line with the increased osteoclastic activity observed after the second MOP.[30] Teh et al.[30] investigated the effects of MOP on the horizontal and vertical distribution of mandibular trabeculae using perforation intervals of four, eight, and twelve weeks. An increased orthodontic movement rate was observed at all intervals, with the most notable acceleration at the four-week interval. This effect is plausible due to the RAP induced by MOP, which enhanced alveolar bone turnover and thus accelerated OTM.[30] Moreover, Bansal et al.[55] stated that MOP facilitated by mini-implants significantly accelerated tooth movement for up to nine weeks without causing significant pain, discomfort, root resorption, or loss of marginal alveolar bone height.

Notably, Alqadasi et al.[42] compared the effects of MOP and piezocision on the acceleration of orthodontic movement in adults and observed that both techniques significantly increased the rate of tooth movement compared to conventional treatment after three months. None of the techniques caused root resorption nor increased vertical bone loss.

Alfailany et al.[43] compared the effects of MOP, traditional corticotomy, and conventional orthodontic treatment (without acceleration procedures) on maxillary canine retraction for treating Class II division 1 malocclusion. The results revealed that both MOP and corticotomy increased the canine retraction rate during the first two months. However, this effect withered after three months, as well as at the end of retraction, suggesting a transient acceleration ability of the tested techniques.

Overall, recent studies emphasize that tooth acceleration primarily occurs in the immediate post-corticotomy stage (both traditional and flapless), ascribing this to the regional acceleratory phenomenon, which accumulates after the surgical procedure. This leads to increased bone turnover and reduced bone density, thereby accelerating OTM.[8,27,57,60] Importantly, traditional and flapless corticotomies were associated with similar OTM rates, while minimally invasive interventions (e.g., piezocision, MOP) showed less tissue damage and discomfort, making them preferable to flap-associated corticotomy.[27,40,43]

Injection of Biomaterials, Supplements, or Hormones

Recent studies have explored the effect of PRP and PRF as promising alternatives for accelerating OTM. These approaches enhance bone regeneration, wound healing, and grafting, with less risk of bone and periodontal loss because of their high contents of growth factors, which are gradually released. The primary difference between these techniques resides in their preparation. Briefly, PRP requires the addition of an anticoagulant solution to the patient's blood sample, followed by multiple centrifugation steps and homogenization with a buffy coat. In contrast, PRF consists of blood collection, centrifugation, and substrate extraction from the top liquid layer.[98] Typically, PRF contains more healing factors and stem cells and is associated with less trauma.[98]

Although these techniques have the potential to accelerate treatment, they remain considerably controversial in the orthodontic field, as evidenced by the two studies reviewed in the current work. Karakasli and Erdur[89] stated that PRF could be an effective method to shorten treatment duration, while Zeitounlouian et al.[88] indicated that retraction rates after PRF were comparable to the control sides, with the exception of the second month, over a five-month period. These results suggest that the supposed accelerating effect of platelet concentrates may be associated with a transient increase in tooth movement rate, implying that repeated injections may be necessary for sustained effects.

Furthermore, Al-Bozaie et al.[21] investigated the impact of PRP to accelerate en-masse anterior canine retraction. The authors found no significant differences in the OTM rate compared to the control, although teeth in the PRP group were mainly retracted by controlled tipping and partially by translation.

Interestingly, a separate study by Ammar et al.[90] compared the acceleration potential of PRP and PRF, as well as a control group with no acceleration procedure. The results showed a significant acceleration in retraction movement after PRF compared to PRP in the second and fourth months, though no differences were observed in the first and third months. Both PRP and PRF led to an increase in overall movement related to the control.

Mechanical Vibration

Vibration stimulus has gained interest over the last decades as a non-invasive modality that triggers a catabolic cascade, stimulating cellular differentiation and significantly increasing the proliferation of osteoclastic and fibroblastic cells, especially on the alveolar bone. These processes accelerate bone metabolism, suppress bone loss, and ultimately increase the rate of tooth movement.[102-104]

The reported outcomes of the reviewed studies were analyzed based on the type of orthodontic treatment adopted in each study:

a) Conventional treatment with fixed appliances

Mayama et al.[81] studied the application of vibration of 5.2±0.5 gf (approximately 0.05 N at 10.2±2.6 Hz) in the canine retraction region using a customized stimulation device. The vibration was applied for 3 minimum (min) once a month. It was observed that static orthodontic force with supplemental vibration significantly accelerated canine retraction and reduced the number of visits to complete treatment. In line with these results, Liao et al.[83] examined the effects of vibration (50 Hz, 0.2 N, 20 g) applied for 10 min/day on the buccal surface of the maxillary canine and found a substantial increase in both closed space and canine distalization in the vibration group.

In contrast, Taha et al.[31] reported no statistically significant differences in canine retraction and pain perception between stimulated and non-stimulated groups, ascribing these results to the small sample size and short study duration.[31]

Similarly, DiBiase et al.[84] investigated the effect of vibratory force on space closing using the AcceleDent for 20 min/day but identified no significant differences.

Some studies have also focused on the use of vibrating electric toothbrushes. Leethanakul et al.[82] indicated that the application of vibrating stimuli using an electric toothbrush during orthodontic treatment increased IL-1β secretion and accelerated OTM by 59% over three months. Conversely, Kannan et al.[87] found no significant differences in distal canine movement between the experimental and control sides with the application of vibratory stimulus. They emphasized the need to determine the optimal frequency range to consolidate this modality as an effective method for OTM acceleration in orthodontics.

b) Treatment with aligners

Regarding the existing evidence on the impact of mechanical vibration on tooth movement rate, Lombardo et al.[86] demonstrated that low-frequency vibrations (30 Hz, 0.25 N), applied for 20 min/day with aligners replaced at 7-and 14-day intervals, produced no statistically significant difference in OTM accuracy. However, adding 20 min of daily low-frequency vibration with a 14-day aligner replacement schedule improved the accuracy of rotation of maxillary incisors by 10%.[86] Furthermore, vibration combined with a 14-day aligners replacement interval enhanced the accuracy of buccolingual and mesiodistal tipping of maxillary canines and buccolingual tipping of maxillary molars by 13-16% compared to a 7-day replacement schedule.[86]

Besides, Katchooi et al.[85] found no evidence to support that the vibratory stimulus delivered with the AcceleDent Aura device affected aligner treatment efficacy or completion rates in adult patients.

Low-intensity Pulsed Ultrasound Simulation

LIPUS is a recently employed technique that utilizes high-frequency mechanical vibrations (>20000 Hz) to stimulate and accelerate the biological processes associated with OTM.[18,99] The only RCT investigating the effects of LIPUS was conducted by El-Bialy et al.,[32] who evaluated the impact of ultrasonic waves (1.5 MHz, 1 kHz pulse, power density of 30 mW/cm^2) on the rate of OTM and root resorption. The study concluded that ultrasound stimulation increased the rate of tooth movement by 29% and resulted in less root resorption compared to contralateral control teeth.[32] Similar conclusions were drawn from observational studies utilizing LIPUS intervention.[19,100]

Electromagnetic Stimulation

The use of pulsed electromagnetic fields (PEMFs) in medicine has been documented for years, extending from their application in orthopedics for fracture treatment. The piezoelectric effect in bone results from the generation of opposite polarities in response to tension and compression forces. Electrical currents generated by orthodontic forces within the alveolar bone can stimulate the directional response, resorption, and deposition involved in the bone remodeling process.[16]

Again, the only study using electromagnetic fields used orthodontic treatment with fixed appliances, and no research has explored the combination of electromagnetic stimulation and aligner therapy. Showkatbakhsh et al.[16] revealed that 1-Hz PEMFs increased the OTM by 1.57±0.83 mm compared to the control group, which underwent similar orthodontic treatment without the utilization of acceleration techniques and required 5.0±0.6 months for completion.

Extracorporeal Shockwave Therapy

Extracorporeal shockwave therapy applied during orthodontic treatment may accelerate tooth movement by stimulating osteogenesis, angiogenesis, and revascularization. Several cytokines and growth factors are released by the influence of shockwaves, which promotes neovascularization, osteoblastic differentiation, and tissue growth.[17] In this regard, Falkensammer et al.[17] performed a study involving 26 patients, where the stimulated group received a single shockwave treatment with 1000 impulses targeted at the tissue of interest. No statistically significant differences were observed in OTM and periodontal status. These findings suggest that a single application of extracorporeal shockwave treatment does not accelerate OTM.

Supplementation with Vitamin D

Drugs and nutritional supplements, such as vitamin D, have been used to accelerate OTM, with promising results. Several studies describe the use of prostaglandin-E, cytokines, and the activator receptor of nuclear factor kappa-B ligand (RANKL), among others, which have been associated with increased tooth movement rate. These biomolecules alter the morphology and activity of osteoclasts and osteoblasts through the intracellular increase of cyclic adenosine monophosphate levels, mRNA synthesis, and RANKL secretion.[92] The active form of vitamin D, named calcitriol, is a potent stimulator of osteoclast activity but can also promote osteoblastic differentiation, depending on environmental conditions. It facilitates the differentiation of osteoclast precursors, increases osteoclast activity, and stimulates osteoblast differentiation and bone mineralization in a dose-dependent manner.

In one of the two revised studies reporting the utilization of calcitriol supplementation for accelerating OTM, a dose of 50 pg administered at intervals of up to 12 weeks effectively accelerated OTM.[92] The other study, which examined the effects of different calcitriol doses, showed that a 25 pg dose increased the canine movement rate by roughly 51% compared to the control. This reduction in treatment time and cost was observed on the experimental side at week 12 and, to a lesser extent, on the control side.[92] Furthermore, doses of 15 and 40 pg of calcitriol resulted in an OTM acceleration of about 10% when compared to the control.[91]

Photobiomodulation

Currently, PBM is one of the most promising approaches for OTM acceleration. Light in the red and near-infrared regions exhibits a biostimulating effect on bone remodeling, promoting the proliferation and differentiation of osteoclastic, osteoblastic, and fibroblastic cells. This therapeutic modality has been proven to not only accelerate OTM but also prevent external root resorption, modulate the inflammatory response, and alleviate pain and discomfort observed during OTM.[101]

a) Conventional treatment with fixed appliances:

Of the 28 revised PBM studies, only one did not use fixed orthodontic appliances. Among the 27 studies resorting to conventional treatment, 24 observed an increased rate of OTM compared to the control, despite variations in stimulation regimens,[1,13,14,22,34-37,61-64,66-68,70-74,76,77,79,80] while other two found no significant differences between the irradiated and control groups.[65,78] One study comparing OTM rates after PBM and MOP intervention observed that MOP induced a more rapid tooth movement.[56] Another study assessed the effectiveness of PBM and full-thickness mucoperiosteal flap (FTMPF) in reducing the treatment time but found no significant differences.[37] Moreover, one study compared the pain levels following OTM accelerated by PBM and piezocision, reporting significantly lower pain and discomfort in the PBM group during the first two weeks of canine retraction compared to the control and piezocision groups.[13]

Besides, Abdarazik et al.[37] compared the accelerating effect of a particular and minimally invasive type of corticotomy-elevation of an FTMPF, which includes the surface mucosa, submucosa, and periosteum without microperfuration-with the same intervention accompanied by low-intensity PBM. Their findings indicated that FTMPF accelerated OTM by 25%, whereas PBM reduced this rate by 20%. Thus, as expected, FTMPF was shown to be more effective in accelerating OTM.[37]

Meanwhile, Nahas et al.[73] found that PBM was effective in reducing the time needed to resolve inferior anterior issues. The authors also observed an energy loss of about 80-95% as the photic beams reached the target tissue (alveolar bone), resulting in approximately 12 J/cm^2 reaching the cells from an initial delivery dose of 108 J/cm^2.

In addition to the OTM rate, the PBM studies in this review also monitored other changes, such as the modulation of the inflammatory response induced by OTM. In fact, the results published by Üretürk et al.[70] suggested that the application of a low-intensity 820 nm laser caused an increase in IL-1 β and TGF- β1 levels in the gingival crevicular fluid (GCF). Similarly, Yassaei et al.[67] noted that using a 980 nm diode laser during tooth distalization significantly increased IL-6 concentration in the irradiated group. On the contrary, Ekizer et al.[68] used a 618 nm LED device at 20 mW/cm^2 for 20 min/day over 21 days and found no effect on IL-1 β levels in the GCF.[68]

Furthermore, Jivrajani and Bhad Patil[35] stated that low-intensity 980-nm laser therapy has a biostimulation effect, demonstrated by the increased concentration of matrix metalloproteinase-9 (MMP-9) in the GCF during the first three months of treatment. MMP-9 is a well-described bone resorption factor widely studied to assess bone remodeling status.

b) Treatment with aligners

Regarding the use of PBM as a coadjuvant therapy to accelerate OTM with aligners, Caccianiga et al.[69] proposed that the PBM produced the same rate of OTM as the control group, even after 12 h, following 22 h of aligner use per day without PBM.

Risk of Bias Assessment

The complete assessment of methodological quality is presented in Supplementary Table 3. Briefly, the EPHPP classified 45 clinical studies as having a low risk of bias,[1,8,9,12-14,16,17,21,22,29-32,34,35,40,43,44,46,47,50,54,55,57-60,62,63,66,68,71,72,74-76,80-82,84-86,90,92] 27 studies as having a moderate risk of bias,[11,27,28,33,37-39,41,42,45,48,49,51-53,56,61,64,65,67,69,70,77-79,88,89] and four studies as having a high risk of bias.[73,83,87,91] The criterion most likely to contribute to bias was blinding, as researchers were aware of the group or individual from which the sample was collected, potentially compromising the impartiality of the evaluation.

DISCUSSION

The present systematic review analyses and compares the surgical and non-surgical techniques currently used in the clinical context, considering their potential to enhance OTM during orthodontic treatments. It also examines the side effects associated with each technique and how different types of orthodontic appliances influence the rate of OTM. The review aims to provide a reproducible methodological approach for generating scientific and practical knowledge, ultimately optimizing the clinical applicability of OTM acceleration methods in the future.

Briefly, the current surgical techniques include: (1) traditional corticotomy, which significantly enhances OTM due to the RAP, facilitating tissue remodeling and healing.[93] This method can triple the rate of OTM in the initial post-operative days.[93] However, it is invasive, often causing significant discomfort and swelling in a majority of patients shortly after the procedure.[9,27] The effect of this technique when used with aligners has yet to be studied; (2) laser-assisted flapless corticotomy, which avoids flap elevation and uses a laser to create clear and small incisions in the cortical bone, resulting in minimal bleeding and tissue damage. This technique has been proven to accelerate OTM with minimal pain and discomfort for the patient;[40,60] (3) PAOO, a technique that merges corticotomy, bone grafting, and orthodontic forces to correct malocclusions swiftly. It not only accelerates OTM but also increases bone density at the corticotomy sites, potentially reducing the risk of root resorption.[38] However, there is no evidence supporting its efficacy with aligners; (4) corticision, a minimally invasive periodontal procedure in which small incisions are made in the cortical bone to stimulate tissue remodeling. This review includes a single study that compared the effect of corticision on the alignment of crowded lower anterior teeth, specifically evaluating external apical root resorption and bone defects. The study showed that corticision greatly conserves tissue integrity compared to conventional non-accelerated methods of alignment;[12] (5) piezocision, a less invasive approach, involves making ultrasonic incisions in the cortical bone without flap lifting, thereby reducing patient discomfort and recovery time.[97] Despite its benefits, piezocision may not be suitable for patients with high gingival smile lines due to the potential risk of scarring;[95,96] and (6) MOP, which involves transmucosal bone punctures to elicit RAP, enhancing osteoclast activity and accelerating OTM.[43,51] Despite being minimally invasive, the effectiveness of MOP in reducing treatment time remains controversial, with some studies noting minimal impact on OTM rates.[30]

Concerning non-surgical acceleration techniques, the following were reviewed: (1) injection of biomaterials, supplements, or hormones (e.g., PRF, PRP): while promising, the use of these agents to accelerate OTM is not consensual, with contradictory outcomes reported.[21,48,90,96] Their effectiveness might be transient, suggesting that repeated applications could be necessary for prolonged effects.[48] Importantly, a comparative study found that the PRF group showed longer-lasting acceleration effects compared to PRP, suggesting that the former may be the preferred option;[90] (2) mechanical vibration: vibrational stimuli can expedite OTM by stimulating cellular activity and bone metabolism.[102] However, the effectiveness of this approach varies markedly across studies, with some reporting significant enhancements in OTM rates while others find negligible effects;[85,87] (3) LIPUS: growing evidence suggests that ultrasound stimulation can effectively improve OTM rates and reduce root loss by modulating the remodeling processes occurring in the periodontium;[19,32,100] (4) electromagnetic stimulation: the application of PEMFs has shown potential in accelerating OTM by influencing electrical currents in the alveolar bone.[16,17] However, evidence is limited to its use with fixed appliances, and there is no data on its use with aligner therapy; (5) shockwave therapy: while theoretically promising due to its potential to stimulate osteogenesis and angiogenesis, shockwave therapy has not demonstrated significant effectiveness in accelerating OTM in practical settings;[17] (6) vitamin D supplementation: the potential of calcitriol, the active form of vitamin D, to stimulate osteoclastic and osteoblastic activity, thereby enhancing OTM, has been documented.[91] Dose-dependent responses highlight the need for tailored treatment plans;[91] (7) PBM:

this technique uses light to stimulate cellular activity in the alveolar bone and periodontal ligament, showing promising results in accelerating OTM, reducing pain, and modulating inflammatory responses.[74,76,79,80] However, the effectiveness is highly dependent on parameters of the light used, such as intensity and wavelength, which are yet to be optimized in clinical settings. Notably, the only study combining OTM with aligners and PBM found no light-induced acceleration effect. The authors hypothesize that improvements in the OTM rate may be due to biostimulation of bone turnover,[69] highlighting the necessity of further research to investigate the appropriate aligner and PBM protocol for stimulating bone remodeling and reducing treatment time. Indeed, confirming the best PBM protocol for aligner treatment is pivotal, as this orthodontic intervention is increasingly appealing to patients due to its comfort and ease of management.[69]

Although there is a lack of RCT studies on low-intensity electrical stimulation, preliminary reports suggest that electrical stimuli can effectively augment the en-masse retraction rate of the upper anterior teeth, accompanied by mild to moderate pain.[103,104]

Overall, the RCTs reviewed reveal that most surgical and non-surgical techniques identified can accelerate OTM, while some require optimization of technical parameters. Studies comparing surgical methods with non-surgical methods, such as MOP vs. PBM[56] and FTMPF vs PBM,[37] displayed that surgical techniques are associated with higher OTM rates. Despite the fact that surgical methods like corticotomy and PAOO have the potential to accelerate OTM, they also carry higher levels of invasiveness and discomfort. These techniques should, therefore, be only applied after a careful diagnosis to maximize patient benefits. This demonstrates the importance of considering factors beyond the acceleration technique, including the overall impact on the patient's quality of life.

Despite advancements in minimally invasive surgical techniques such as piezocision and MOP, corticotomy showed the highest acceleration potential. The extent of tissue damage created during these procedures has a direct effect on the intensity of the RAP, thus playing an important role in the effectiveness of these techniques.

Non-surgical methods, such as mechanical vibration and PBM, offer less invasive alternatives, though their efficacy may vary. Nevertheless, several studies point to a satisfactory accelerating efficacy of these techniques, with patients expressing high satisfaction. Notably, Nahas et al.[73] highlighted that the irradiation dose plays a determining factor in the effectiveness of PBM in accelerating OTM. Thus, subdosing may explain the less satisfactory results in studies that did not observe an increased OTM rate after irradiation.

Importantly, while most current scientific evidence predominantly focuses on fixed appliances in surgical contexts, some RCTs have explored non-surgical techniques combined with both fixed and non-fixed appliances,[69,85,86] revealing significant differences in accelerating OTM. Specifically, surgical techniques demonstrate superior efficacy in reducing treatment duration.[56] However, time efficiency alone cannot dictate method selection, as surgical interventions entail greater invasiveness and are associated with considerable levels of discomfort and pain. Indeed, all surgical techniques in this review displayed statistically significant differences in accelerating OTM, with particular relevance to MOP, piezocision, and especially corticotomy, reducing treatment duration by several months, in some cases, by more than half a year. However, several adverse effects have been reported, such as experiencing moderate to severe pain and discomfort during feeding.[1,13,60] In addition, swelling and a challenging recovery period lasting two to four weeks have been reported. These outcomes suggest that surgical techniques may not be suitable for all patients, highlighting the necessity for careful consideration of the associated risks and benefits.

This has driven further research and developments in non-surgical acceleration techniques. At the same time, not all studies showed statistically significant efficacy in accelerating OTM;[78,84] both vibration and PBM exhibit promising outcomes, with the latter offering the additional benefit of modulating inflammatory responses and reducing pain scores. The absence of adverse effects, such as discomfort and pain, fosters the potential utilization of these acceleration techniques, including in the pediatric population.

Acceleration techniques for tooth movement have been studied for decades, evolving to reduce and minimize two major drawbacks of orthodontic treatment, namely prolonged duration and pain, thus promoting treatment acceptance among patients and clinicians. This review highlights a diverse array of both surgical and non-surgical approaches aimed at accelerating OTM. All being considered, corticotomy and PBM are the most commonly used techniques, with stronger evidence supporting their effectiveness in accelerating OTM. PBM stands out as a promising, non-invasive, painless, and effective biostimulatory approach for accelerating the coadjuvant of OTM in the future. This is reflected by the increasing number of studies employing this technique over the last few years. However, further scientific and clinical investigations are required to refine PBM protocols and consolidate their use in orthodontic practice.

Study Limitations

This review provides comprehensive insights into various acceleration techniques but has some limitations:

• Limited Research on Aligners: A major limitation is the absence of studies assessing the effectiveness of acceleration techniques, specifically with aligners. Most research focuses on traditional fixed appliances, restricting the applicability to patients using newer aligner technologies.

• Variability in Study Designs: The included studies vary in design, sample size, methodology, and outcome measures, leading to inconsistencies that hinder definitive conclusions, thereby compromising the robustness of the reported results. Additionally, variations in treatment protocols, such as frequency, duration, and intensity of interventions, further hamper comparisons and limit the generalizability of findings.

• Short-term Focus: Many studies primarily report short-term outcomes, often neglecting long-term effects such as stability of tooth position, overall oral health, and the risk of relapse.

• Patient-Related Factors: The review may not fully account for patient-specific variables, including age, general health, bone density, and oral hygiene, which can significantly influence treatment effectiveness and potential side effects.

• Pain and Discomfort: While the review addresses pain and discomfort associated with some techniques, it may not adequately capture the patient experience or quality of life, both of which are crucial for evaluating the practicality and acceptability of such interventions.

•Invasive Nature of Some Techniques: Procedures like corticotomy and PAOO could be a barrier to widespread adoption due to their invasiveness. The severe pain and swelling linked to these methods could deter patients from choosing these options. This concern is often highlighted throughout this review, anticipating that non-invasive alternatives may be preferable, particularly for some groups of patients, such as children.

• Limited Discussion on Cost-Effectiveness: The review does not address the cost-effectiveness of these acceleration techniques. The additional expenses of advanced surgical procedures or devices may not be justified by the reduction in treatment time from a patient's perspective.

CONCLUSION

As a starting point, this review addresses a critical gap by providing extensive theoretical knowledge to support decision-making in a clinical setting. Nonetheless, additional studies are needed before confident conclusions can be drawn regarding the optimal clinical protocols to follow.

Addressing these limitations in future research could enhance understanding and refine the application of orthodontic acceleration techniques, particularly when evaluating their long-term outcomes in conjunction with newer orthodontic appliances like aligners. The lack of RCTs assessing the efficacy of surgical techniques in aligner therapy hinders the analysis of their efficacy in accelerating OTM using non-fixed appliances. Consequently, further investigation and research are warranted to bridge this knowledge gap. Integrating these methods into standard orthodontic treatment could significantly reduce treatment time and improve patient outcomes. Importantly, expanding the range of stimulation device options would more easily meet patients' expectations in a way that broadens the available solutions, suitable for their individualized needs, potentially leading to more tailored, affordable, and effective treatment options. Notably, the development of new PBM devices could make their purchase more feasible and provide a more likely acquisition, which could ultimately foster the utilization of home-based accelerating interventions and expand their usage.

Other information

The systematic review was registered in the PROSPERO database under registration ID 545573, and the protocol is available on the PROSPERO website. The title was later amended to reflect a focus on the comparison of acceleration techniques using conventional and fixed versus removable appliances. Nevertheless, the focused question, eligibility criteria, and search criteria remained unchanged.

Footnotes

Author Contributions: Concept - F.S.S., T.P.; Design - A.G., F.M.; Data Collection and/or Processing - A.G., G.B., M.C., F.M.; Analysis and/or Interpretation - A.G., F.M.; Literature Search - G.B., M.C.; Writing - A.G., F.M., F.S.S., T.P.

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Supplementary Tables 1-3: https://l24.im/vlXHz