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RESEARCH

Leptin levels and skeletal response: exploring functional treatment efficacy in overweight vs. normal-weight Class II patients

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Abstract

Purpose This prospective cohort study aimed to evaluate whether salivary leptin hormone levels correlate with skeletal and dental responses to functional therapy in normal-weight versus overweight skeletal class II malocclusion patients.

Methods Thirty-two patients with skeletal Class II division 1 malocclusion were divided into two groups: overweight and normal weight. All patients were treated with twin block appliances; their growth stage being about MP3cap. Lateral cephalometric x-rays and body mass index (BMI) percentiles were assessed before (T0) and at the end of the functional treatment (T1). Unstimulated saliva samples were collected from all patients at four time points (before, in the first month, in the third month and at the end of the functional treatment) using a noninvasive passive pouring method. Leptin levels were measured photometrically using an enzyme-linked immunosorbent assay (ELISA) kit.

Results Overweight patients exhibited higher salivary leptin levels and earlier skeletal maturation. Overjet correction was achieved in these patients with more incisor movement and they showed greater mandibular length increase. Correlation analysis revealed positive associations between leptin and the change of maxillary parameters as well as of soft tissue convexity. Negative correlations were observed between salivary leptin levels and changes in posterior facial height (PFH), PFH/AFH ratio (AFH: anterior facial height), and lower incisor inclination.

Conclusion Body weight significantly affected treatment timing and outcomes in Class II correction and should be considered in adolescent treatment planning.

Keywords Twin block · Obesity · Body mass index · Retrognathia · Treatment outcome

Leptinspiegel und skelettales Ansprechen: Eine Untersuchung der funktionellen therapeutischen Wirksamkeit bei übergewichtigen vs. normalgewichtigen Klasse-II-Patienten

Zusammenfassung

Zielsetzung Diese prospektive Kohortenstudie hatte zum Ziel zu untersuchen, ob der Leptinspiegel im Speichel mit den skelettalen und dentalen Ansprechen auf eine funktionelle Therapie bei normalgewichtigen Patienten im Vergleich zu übergewichtigen Patienten mit einer skelettalen Klasse-II-Malokklusion korreliert.

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Methoden Zweiunddreißig Patienten mit einer skelettalen Klasse-II/1-Malokklusion wurden in 2 Gruppen unterteilt: übergewichtige und normalgewichtige Patienten. Alle Patienten wurden mit Twin-Block-Apparaturen behandelt, dabei befand sich ihr Wachstumsstadium etwa bei MP3cap. Fernröntgenseitenaufnahmen und BMI(Body-Mass-Index)-Perzentilen wurden vor der funktionellen Behandlung (T0) und nach deren Abschluss (T1) ausgewertet. Von allen Patienten wurden an 4 Zeitpunkten (vor der Behandlung, im ersten Monat, im dritten Monat und nach Abschluss der funktionellen Behandlung) unstimulierte Speichelproben mittels einer nichtinvasiven passiven Gießmethode entnommen. Die Leptinspiegel wurden photometrisch mit einem ELISA(Enzyme-Linked Immunosorbent Assay)-Kit gemessen.

Ergebnisse Übergewichtige Patienten wiesen höhere Leptinspiegel im Speichel und eine frühere Skelettreifung auf. Bei diesen Patienten wurde die Overjet-Korrektur durch eine stärkere Bewegung der Schneidezähne erreicht, und sie zeigten eine stärkere Verlängerung des Unterkiefers. Die Korrelationsanalyse ergab positive Zusammenhänge zwischen Leptin und der Veränderung der Oberkieferparameter sowie der Weichgewebekonvexität. Negative Korrelationen wurden zwischen den Leptinspiegeln im Speichel und den Veränderungen der hinteren Gesichtshöhe (PFH), dem PFH/AFH-Verhältnis (AFH: vordere Gesichtshöhe) und der Neigung der unteren Schneidezähne beobachtet.

Schlussfolgerung Das Körpergewicht hatte signifikanten Einfluss auf den Behandlungszeitpunkt und die Ergebnisse bei der Klasse-II-Korrektur und sollte bei der Behandlungsplanung für Jugendliche berücksichtigt werden.

Schlüsselwörter Twin-Block · Adipositas · Body-Mass-Index · Retrognathie · Behandlungsergebnis

Introduction

Mandibular retrognathia is a primary cause of Class II malocclusion, and the ideal treatment goal is to optimize growth and development of the mandible. Convex profile and skeletal imbalance due to mandibular retrognathia can be corrected by functional appliances that position the mandible downwards and anteriorly which enhances mandibular growth in growing skeletal Class II patients [11, 18]. However, the long-term influence of functional appliances on true mandibular growth remains controversial, as some studies suggest that most of the observed correction is dentoalveolar or positional rather than due to genuine mandibular elongation [6]. The twin block appliance is one of the most preferred functional appliances due to its ease of use and patient comfort compared to monoblock appliances. It minimizes speech problems, enables upper jaw expansion and directs mandibular growth through its upper and lower components [3]. Starting treatment during adolescence is effective because cellular response and adaptive capacity are highest when growth is at its peak [4] and mandibular dimensions are increasing the most [2].

Childhood obesity is one of the major global health issues of the 21st century. Its prevalence has nearly doubled since 1980 and continues to rise at an alarming rate [25]. Regarding childhood obesity, 160 million children were obese in 2022, and over 390 million children and adolescents were overweight [27]. Body mass index (BMI; kg/m^2) is widely used to assess obesity based on the classification of the World Health Organization (WHO). BMI is commonly used to assess obesity and categorize individuals: the ≥ 85th percentile corresponds to overweight, the 15–85th percentile to normal weight [8]. Leptin, secreted by adipose tissue, increases with body fat mass [10] and declines with weight loss [23]. Obese adolescents were observed to show accelerated skeletal maturation and earlier dental development [19].

Leptin, derived from the Greek word ‘leptos’ (thin), is a protein encoded by the *Ob* gene, is composed of 167 amino acids, and is released from adipose tissue and regulates body weight [33]. The primary role of leptin is to regulate food intake and energy metabolism and to prevent obesity with a negative “feedback” effect on the hypothalamus. It also has various metabolic and endocrine functions and plays a role as a regulatory protein in various physiological processes including bone growth and endochondral ossification [19]. Leptin hormone is secreted more than normal in overweight patients due to excess adipose tissue [16, 22]. Studies in murine models showed that leptin affected chondrocyte populations in growth centers and increased IGF-I receptor expression [22]. These findings suggested that high circulating leptin levels in obese children may have a direct effect on bone growth centers.

While previous experimental research explored leptin’s effects on osteoclastic activity and ossification, its impact on the efficacy of functional orthodontic treatment remains unclear. This study aimed to compare functional treatment outcome based on salivary leptin levels in overweight and normal-weight Class II patients. The null hypothesis stated no difference in skeletal, dental, or soft tissue profile changes between groups treated with twin block appliances each.

Materials and methods

This prospective research project received ethics approval from the Clinical Studies Ethics Board of Bezmialem Vakif University (document number: 15310). Power analysis ($\alpha =$

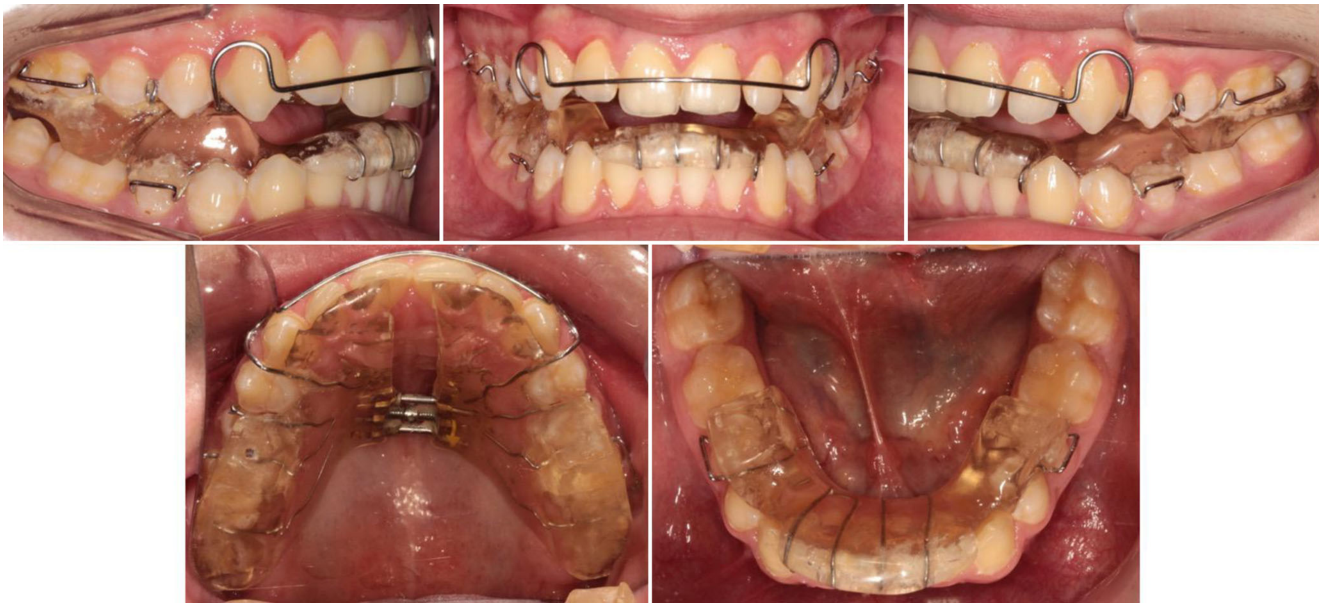

Fig. 1 Twin block appliance design used in this study. Note that the transverse expansion screw was applied in a minority of patients (5 patients) only

Abb. 1 In der Studie verwendetes Twin-Block-Appliance-Design. Zu beachten ist, dass die transversale Expansionsschraube nur bei einer Minderheit der Patienten (5 Patienten) eingesetzt wurde

0.05, power = 90%) using previous data suggested 14 patients per group [16] with an effect size of 0.8.

Inclusion criteria regarding orthodontic initial diagnosis:

- Skeletal Class II due to mandibular retrognathia(SNB < 78),
- Overjet > 5 mm,
- Normal vertical growth (SN-GoGn: 32° ± 6°),
- Minimal crowding of the dental arches (4 mm or less),
- Bilateral Class II molar/canine relationship, and
- MP3cap growth stage.

Exclusion criteria:

- Previous orthodontic treatment,
- Posterior crossbite or severe maxillary transverse deficiency,
- Congenital anomaly or syndrome,
- Salivary gland disorder, and
- Poor oral hygiene.

A total of 38 patients whose functional treatment was started and completed between 2018 and 2020 at the Orthodontic Department of Bezmialem Vakif University were enrolled. Six patients (2 overweight and 4 normal-weight) had to be excluded due to noncompliance. The remaining 32 subjects were divided into two groups:

- Group I: 16 overweight (BMI: 25–30 kg/m^2) and
- Group II: 16 normal-weight (BMI: 18.5–25 kg/m^2).

Body mass index (BMI) was evaluated by measuring the height and weight of individuals in the Department of Nutrition and Dietetics at Bezmialem Vakif University.

Appliance design

All patients were treated with the twin block appliance manufactured from thermosetting acrylic using Clark's design [7]. A vestibular arch was added to the upper part, and the buccal surface of the mandibular incisors was coated with acrylic unlike the original design. Interlocking bite blocks were set at 70° to the occlusal plane (Fig. 1). Expansion screws (Magnum 600-303-10, Dentarum, Ispringen, Germany) were added for 5 patients (2 overweight, 3 normal-weight) requiring transverse maxillary expansion and were activated twice per week. The patients were instructed to wear their appliance full-time except during meals. Sagittal advancement was set at 70% of maximum protrusion. Vertical opening in the premolar region exceeded resting vertical dimension by 2–3 mm. The upper bite block was trimmed 1 mm monthly posteriorly to facilitate molar eruption and to solve the pronounced curve of Spee.

Patient compliance with the twin block appliance was monitored at each follow-up visit through patient-reported daily wear time and clinical inspection of the appliance. Wear facets on the acrylic bite blocks and the overall intraoral fit were used as indirect indicators of regular usage.

Saliva collection method

Unstimulated saliva was collected from all patients at four different times; beginning of treatment (T0), 1st month (T1), 3rd month (T2), and end of treatment (T3) using a noninvasive passive drool method. Because of leptin level changes throughout the day in relation to hunger and satiety, salivary samples (5 mL) were collected between 9 and 12 noon, at least 1 h after a meal. Patients were instructed to eat and brush their teeth at least 1 h before the appointment and rinse their mouths thoroughly with water before collection to avoid contamination. They were seated upright with their heads tilted forward for 10 min, and a test tube was placed at the corner of the mouth to allow flowing saliva to drain into the test tube [16]. Samples were collected in Eppendorf tubes and stored in cryotubes at –80 °C until analysis.

Leptin concentration calculation

Saliva samples were thawed at room temperature, vortexed for 10–15 s, and centrifuged at 1500 rpm at 25 °C for 10 min. The supernatant was separated and the total protein amount was measured using the Bradford method [5]. The separated supernatants were measured photometrically at 450 nm with commercially purchased human leptin enzyme-linked immunosorbent assay (ELISA) kits. Results were calculated as pg/mL/mg protein. The analysis was carried out in the Medical Biochemistry R&D Laboratory of Bezmialem Vakif University.

Lateral cephalometric measurements

Lateral cephalometric films were taken using a digital X-ray device (Planmeca 2002 CC Proline, Helsinki, Finland). The distance between the midsagittal plane of the patients and the central beam was set as 155 cm, and the distance between the midsagittal plane and the film cassette was set as 12.5 cm. Patients were instructed to keep their tongue in a normal position in the mouth and without tension after swallowing, not to disrupt their head position, and to keep their teeth in centric occlusion during shots. X-rays were recorded from the patients at two time points (i.e., before treatment [T0] and at the end of functional treatment [T1]) and were analyzed using Dolphin Imaging Software (Version 8.0, Chatsworth, CA, USA) by a single author who was blinded to the groups.

A total of 47 parameters were evaluated on the lateral cephalometric radiographs and categorized into skeletal, dentoalveolar, and soft tissue measurements:

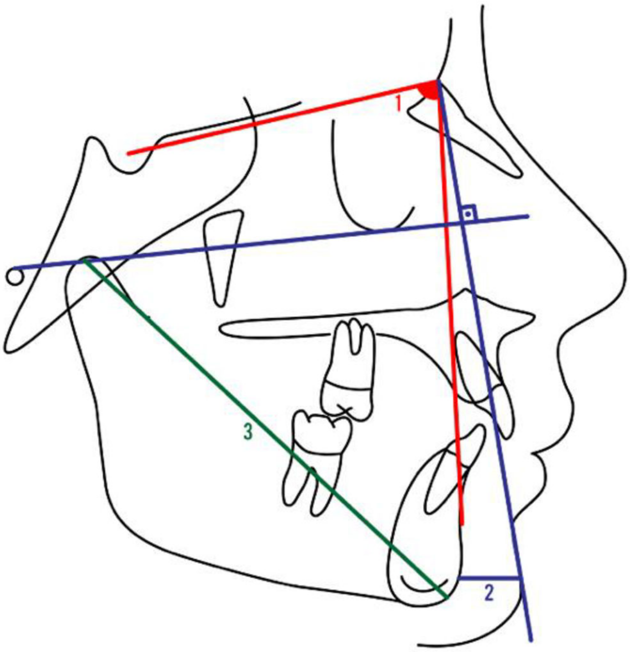

Fig. 2 Mandibular skeletal measurements used in the study. 1: SNB (°), 2: Na Perp–Pog (mm), 3: Co–Gn (mm)

Abb. 2 In der Studie verwendete Messungen am Unterkieferskelett. 1: SNB (°), 2: Na Perp–Pog (mm), 3: Co–Gn (mm)

- Maxillary skeletal measurements:
  SNA (°), Na Perp–A (mm), Co–A (mm), maxillary depth (mm), and maxillary height (mm).
- Mandibular skeletal measurements (Fig. 2):
  SNB (°), Na Perp–Pog (mm), and Co–Gn (mm)
- Maxillomandibular skeletal measurements:
  ANB (°), maxillomandibular difference (mm), Wits appraisal (mm), and Na–APog (°).
- Vertical measurements:
  Y-axis angle (°), SN–GoGn (°), FMA (°), SN–PP (°), Jarabak sum of angles (°), PP–MP (°), S–Go (mm), ANS–Me (mm), and posterior facial height/anterior facial height (PFH/AFH) ratio.
- Interdental measurements:
  Interincisal angle (°) and overjet (mm).
- Maxillary dentoalveolar measurements:
  U1–SN (°), U1–PP (°), U1–NA (°), U1–NA (mm), U1–NF(mm), U6–NF (mm), and U1–maxillary occlusal plane (°).
- Soft tissue measurements:
  Nasolabial angle (°), LL–E plane (mm), UL–E plane (mm), nasal projection (mm), TVL–A′ (mm), TVL–upper lip (mm), TVL–lower lip (mm), TVL–B′ (mm), TVL–Pog′ (mm), soft tissue convexity (mm), and mentolabial angle (°).

Statistical methods

All statistical analyses were performed using the SPSS (v20.0, IBM, Armonk, NY, USA). Shapiro–Wilk test confirmed normal distribution; hence, parametric tests were used (significance level was set at $p<0.05$). Independent t-tests compared intergroup differences. Independent-samples t-tests were applied to compare intergroup differences, while paired-samples t-tests evaluated intragroup changes between T0 and T1. For correlation analysis, since the distribution of Δ (T1–T0) values was nonnormal, Spearman's rank correlation test was used to assess the relationship between the treatment-induced changes (Δ values) in skeletal, dentoalveolar, and soft-tissue parameters and the mean salivary leptin levels. The repeatability of the measurements was calculated with Dahlberg's method error formula. Fifteen randomly selected lateral cephalometric radiographs were traced by the same clinician 15 days after the first measurement. The method error was calculated with the lowest for the nasolabial angle (0.0), and the highest for the L1-Md Occ Pl° (1.43). The results of a paired t-test showed that the data were free of systematic error ($p>0.05$). Interrater reliability was also assessed, and a high level of agreement was observed between the measurements of the two clinicians (ICC = 0.92, $p<0.001$).

Results

A total of 32 patients were enrolled in the study. Gender distribution and treatment durations were similar between groups. The mean duration of functional treatment was 10.75 ± 0.93 months in the overweight group and 11.13 ± 0.96 months in the normal-weight group ($p>0.05$). However, the overweight patients had a significantly younger mean age (11.31 ± 0.51 years) and higher salivary leptin levels at all time points compared to the normal-weight patients (Table 1).

Table 1 Statistical difference between groups in age and leptin values
Tab. 1 Statistischer Unterschied zwischen den Gruppen hinsichtlich Alter und Leptinwerten.

		n	$\overline{X}$±Sd	t	*p*
Age(year)	Overweight group	16	11.31 ± 0.51	–5.03	0.01*
	Normal-weight group	16	12.48 ± 0.77		
Treatment duration(month)	Overweight group	16	10.75 ± 0.93	–1.12	0.27
	Normal-weight group	16	11.13 ± 0.96		
Leptin 1st sample(mL/mg)	Overweight group	16	192.41 ± 6.03	9.93	0.01*
	Normal-weight group	16	166.47 ± 8.53		
Leptin 2nd sample(mL/mg)	Overweight group	16	195.12 ± 11.48	9.59	0.02*
	Normal-weight group	16	165.03 ± 5.05		
Leptin 3rd sample(mL/mg)	Overweight group	16	200.80 ± 22.55	6.32	0.03*
	Normal-weight group	16	164.19 ± 5.39		
Leptin 4th sample (mL/mg)	Overweight group	16	209.76 ± 33.42	5.14	0.04*
	Normal-weight group	16	166.06 ± 6.29		

SD Standard deviation
$P=0.05$
*paired samples t-test

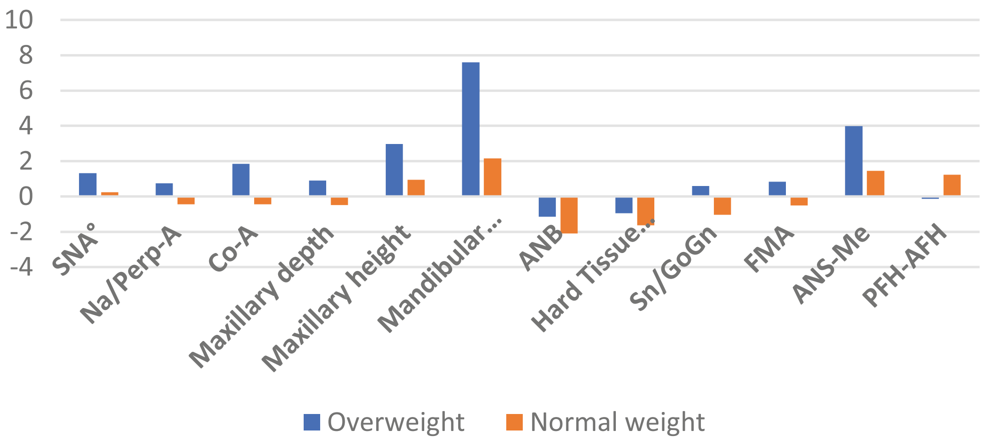

Fig. 3 Significant changes of skeletal parameters (Δ values)
Abb. 3 Signifikante Veränderungen skelettaler Parameter (Δ-Werte)

Table 2 Statistical difference between groups in maxillary and mandibular skeletal parameters

Tab. 2 Statistischer Unterschied zwischen den Gruppen hinsichtlich skelettaler Parameter des Ober- und Unterkiefers

	Overweight group			Normal-weight group			Δ Values		
	T0	T1	*P**	T0	T1	*p*	Overweight group	Normal-weight group	*P***
	$\overline{X}$ ± *SS*	$\overline{X}$ ± *SS*		$\overline{X}$ ± *SS*	$\overline{X}$ ± *SS*		$\overline{X}$ ± *SS*	$\overline{X}$ ± *SS*	
SNA°	77.08 ± 4.41	78.38 ± 5.09	*0.01**	78.82 ± 4.93	79.06 ± 4.93	0.25	1.31 ± 1.11	0.24 ± 0.81	*0.01**
Na/Perp-A	–3.38 ± 2.71	–2.64 ± 3.70	0.14	–1.66 ± 3.11	–2.09 ± 3.82	0.21	0.74 ± 1.92	–0.44 ± 1.35	*0.04**
Co-A	81.98 ± 4.40	83.83 ± 3.47	*0.01**	80.39 ± 2.72	80.14 ± 3.53	0.66	1.84 ± 1.78	–0.24 ± 2.19	*0.02**
Maxillary depth °	86.53 ± 2.78	87.43 ± 3.73	*0.09**	88.32 ± 3.32	87.83 ± 4.03	0.2	0.90 ± 1.99	–0.49 ± 1.45	*0.03**
Maxillary height°	23.88 ± 2.89	26.85 ± 3.28	*0.01**	23.19 ± 2.56	24.13 ± 2.01	*0.02**	2.97 ± 1.96	0.94 ± 1.48	*0.01**
SNB°	72.88 ± 4.18	75.35 ± 4.04	*0.01**	73.58 ± 3.62	75.89 ± 4.43	*0.01**	2.48 ± 1.07	2.31 ± 1.22	0.69
Na Perp-Pog	–11.06 ± 5.07	–8.84 ± 6.00	*0.01**	–9.02 ± 5.01	–6.91 ± 7.63	*0.01**	2.23 ± 2.78	2.11 ± 3.00	0.91
Mandibular length	106.96 ± 4.45	114.55 ± 4.33	*0.01**	103.11 ± 3.25	105.28 ± 3.82	*0.02**	7.59 ± 2.45	2.16 ± 3.26	*0.01**
ANB	4.18 ± 2.90	3.02 ± 3.12	*0.01**	5.25 ± 1.98	3.15 ± 1.99	*0.01**	–1.16 ± 1.21	–2.10 ± 1.19	*0.04**
Max-Mand Diff	21.14 ± 4.78	26.19 ± 5.43	*0.01**	16.62 ± 6.28	22.33 ± 2.29	*0.01**	5.05 ± 1.97	5.71 ± 6.37	0.69
Wits	7.03 ± 3.35	3.29 ± 2.79	*0.01**	6.11 ± 1.50	2.63 ± 2.20	*0.01**	–3.74 ± 1.75	–3.49 ± 1.50	0.67
Hard tissue convexity	2.56 ± 3.09	1.60 ± 3.37	*0.01**	3.21 ± 2.27	1.58 ± 2.58	*0.01**	–0.96 ± 1.23	–1.63 ± 0.92	*0.09**
Y axis angle	70.19 ± 4.83	69.55 ± 4.31	*0.06**	69.46 ± 4.40	68.22 ± 4.80	*0.06**	–0.64 ± 1.13	–1.24 ± 1.01	0.12
Sn/GoGn	30.30 ± 6.27	30.89 ± 5.43	0.33	29.12 ± 5.58	29.09 ± 5.99	*0.07**	0.59 ± 2.34	–1.03 ± 1.50	*0.06**
FMA	23.87 ± 4.29	24.70 ± 4.47	0.12	22.56 ± 4.70	22.04 ± 5.77	0.34	0.83 ± 2.00	–0.52 ± 2.09	*0.07**
Sn/PP	2.07 ± 3.39	2.34 ± 3.26	0.30	–0.77 ± 3.57	–0.57 ± 3.06	0.54	0.28 ± 1.03	0.20 ± 1.29	0.86
Sum of interior angles	393.33 ± 5.90	393.75 ± 5.34	0.36	392.03 ± 5.33	392.80 ± 5.86	*0.06**	0.42 ± 1.79	0.04 ± 1.63	0.07
Palatal mandibular angle	24.28 ± 5.94	24.38 ± 5.02	0.80	25.81 ± 5.95	25.41 ± 5.71	0.13	0.11 ± 1.61	–0.40 ± 2.17	0.13
S-Go	73.12 ± 5.18	76.64 ± 5.96	*0.01**	69.88 ± 3.66	72.99 ± 4.46	*0.01**	3.52 ± 3.57	3.11 ± 2.28	0.07
ANS-Me	62.07 ± 5.88	66.04 ± 6.46	*0.01**	57.99 ± 4.63	59.46 ± 4.53	*0.01**	3.98 ± 2.57	1.46 ± 2.10	*0.01**
PFH-AFH	66.29 ± 4.24	66.14 ± 3.78	0.80	67.21 ± 3.67	68.44 ± 4.35	*0.01**	–0.14 ± 2.22	1.23 ± 1.38	*0.04**

$P = 0.05$

*paired sample t-test

** Independent sample t-test

Hand–wrist maturational data indicated that all patients were classified as peak height velocity (MP3cap stage). Functional therapy with the twin block appliance effectively resulted in the correction of the class II molar relationship, reduction of overjet and overbite, and improvement of the skeletal discrepancy in both groups.

Cephalometric analysis

Skeletal parameters

All intergroup comparisons were based on the T0–T1 changes (Δ values). For the overweight patients in the maxilla significant increases were found for SNA ($\Delta = +1.31 \pm 1.11°$, $p = 0.01$), Na Perp–A ($\Delta = +0.74 \pm 1.92$ mm, $p = 0.04$), Co–A ($\Delta = +1.84 \pm 1.78$ mm, $p = 0.02$), maxillary depth ($\Delta = +0.90 \pm 1.99°$, $p = 0.03$), and maxillary height ($\Delta = +2.97 \pm 1.96$ mm, $p = 0.01$). These changes were significantly greater than those found in the normal-weight group (Table 2). For the mandible, both groups showed increases in SNB ($\Delta = +2.48 \pm 1.07°$ vs $+2.31 \pm 1.22°$, $p = 0.69$) and mandibular length (Co–Gn) ($\Delta = +7.59 \pm 2.45$ mm vs $+2.16 \pm 3.26$ mm, $p = 0.01$). The ANB angle decreased significantly in both groups, with a larger reduction in the normal-weight group ($p = 0.04$). Changes in Wits appraisal, maxillomandibular difference, and hard-tissue convexity were comparable between groups ($p > 0.05$). In the vertical dimension, overweight patients displayed a significantly greater increase in anterior facial height (ANS–Me; $\Delta = +3.98 \pm 2.57$ mm vs $+1.46 \pm 2.10$ mm, $p = 0.01$). Both groups showed an increase in posterior facial height (S–Go; $p < 0.01$) without a significant intergroup difference ($p = 0.07$). The PFH/AFH ratio increased only in normal-weight patients ($p = 0.04$). Other vertical parameters (Y-axis, FMA, SN/PP, sum of angles, palatal–mandibular angle) remained statistically unchanged for both groups. Figure 3 presents the significant changes (Δ values) observed in skeletal parameters.

Dentoalveolar parameters

Comparisons of the Δ values demonstrated significant differences in dental adaptation between the groups. Overjet decreased significantly in both groups ($p = 0.01$), with a greater reduction in overweight patients ($p = 0.01$). The interincisal angle increased significantly only in the overweight group ($p = 0.01$), resulting in a significant intergroup difference ($p = 0.02$).

In overweight patients, marked retroclination and retrusion of the upper incisors were observed (U1/SN, U1/PP, U1/NA (°), U1–NA (mm), U1–NF (mm), and U1–maxillary occlusal plane, all $p = 0.01$). These changes were not significant in the normal-weight group, and intergroup comparisons confirmed greater differences in overweight patients (all $p = 0.01$).

Both groups exhibited a significant proclination of the lower incisors (L1/NB, L1–NB mm; $p = 0.01$), which was more pronounced in overweight patients ($p = 0.02$ and $p = 0.01$).

Other mandibular parameters (IMPA, L1/A–Po, and L6–MP) showed no significant intergroup differences ($p > 0.05$). However, the L1/mandibular occlusal-plane angle followed opposite trends, decreasing in overweight and increasing in normal-weight patients ($p = 0.04$).

Soft-tissue parameters

Analysis of the Δ values revealed notable improvements in facial profile and perioral balance in overweight patients. Significant changes were found for subnasale vertical/LL

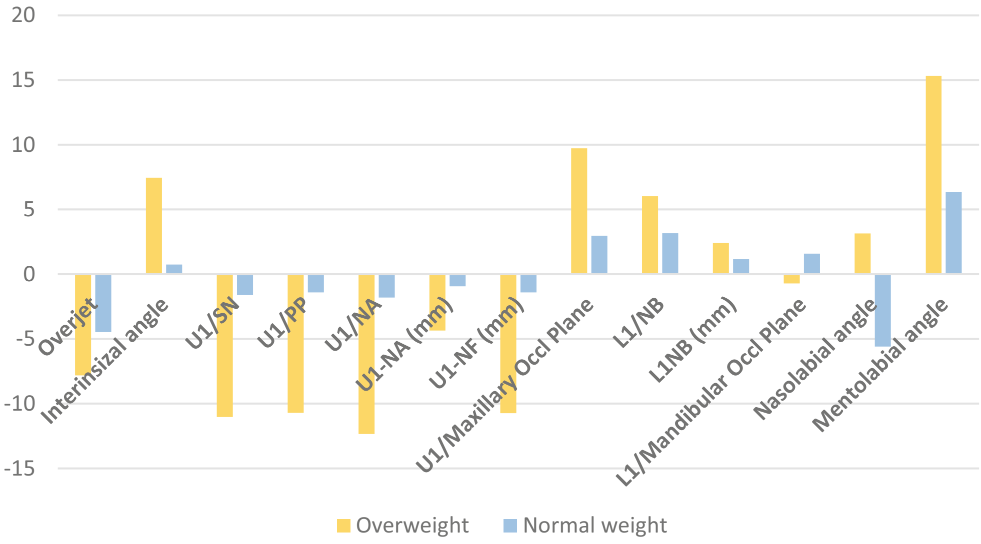

Fig. 4 Significant changes of dental and soft tissue parameters (Δ values)

Abb. 4 Signifikante Veränderungen von dentalen und Weichgewebeparametern (Δ-Werte)

Table 3 Statistical difference between groups in dentoalveolar and soft tissue parameters
Tab. 3 Statistischer Unterschied zwischen den Gruppen hinsichtlich dentoalveolärer und Weichgewebeparameter

	Overweight group			Normal-weight group			Δ Values		
	T0	T1	*p*	T0	T1	*p**	Overweight group	Normal-weight group	*p***
	$\overline{X}$ ± SS	$\overline{X}$ ± SS		$\overline{X}$ ± SS	$\overline{X}$ ± SS		$\overline{X}$ ± SS	$\overline{X}$ ± SS	
Overjet	11.34 ± 2.78	3.54 ± 1.37	0.01*	8.61 ± 2.22	4.13 ± 1.60	0.01*	–7.80 ± 3.32	–4.48 ± 1.79	0.01*
Interincisal angle	115.96 ± 12.61	123.41 ± 8.77	0.01*	122.54 ± 9.62	123.30 ± 6.44	0.61	7.45 ± 7.74	0.76 ± 5.78	0.02*
U1/SN°	115.29 ± 11.8	104.28 ± 8.50	0.01*	107.85 ± 11.01	106.25 ± 8.97	0.25	–11.02 ± 7.55	–1.60 ± 5.36	0.01*
U1/PP°	124.36 ± 12.20	113.64 ± 8.36	0.01*	114.08 ± 10.92	112.69 ± 8.75	0.34	–10.71 ± 7.78	–1.39 ± 5.68	0.01*
U1/NA°	38.24 ± 12.16	25.91 ± 9.44	0.01*	29.01 ± 10.92	27.20 ± 8.90	0.19	–12.34 ± 8.07	–1.81 ± 5.29	0.01*
U1-NA (mm)	10.14 ± 4.19	5.80 ± 3.42	0.01*	5.73 ± 3.14	4.80 ± 2.71	0.02*	–4.34 ± 2.50	–0.93 ± 1.35	0.01*
U1-NF (mm)	124.38 ± 12.22	113.64 ± 8.36	0.01*	114.08 ± 10.92	112.69 ± 8.75	0.34	–10.73 ± 7.81	–1.39 ± 5.68	0.01*
U6-NF (mm)	20.62 ± 2.31	21.88 ± 2.97	0.01*	17.94 ± 1.72	18.89 ± 2.28	0.03*	1.26 ± 1.20	0.95 ± 1.56	0.53
U1/Maxillary Occl Plane	48.23 ± 8.50	57.95 ± 6.28	0.01*	53.73 ± 7.80	56.72 ± 6.74	0.02*	9.73 ± 6.52	2.99 ± 4.61	0.01*
IMPA°	95.42 ± 5.41	98.58 ± 6.32	0.01*	97.57 ± 4.45	98.68 ± 4.32	0.4	3.16 ± 4.15	1.11 ± 5.08	0.22
L1/NB°	21.63 ± 4.85	27.68 ± 5.95	0.01*	23.19 ± 5.12	26.36 ± 4.08	0.01*	6.05 ± 3.84	3.18 ± 2.68	0.02*
L1NB (mm)	3.99 ± 2.03	6.43 ± 2.57	0.01*	3.61 ± 2.55	4.79 ± 2.23	0.01*	2.44 ± 1.27	1.18 ± 0.75	0.01*
L1/Apo	20.26 ± 5.69	27.36 ± 5.00	0.01*	20.82 ± 3.19	25.98 ± 2.24	0.01*	7.10 ± 4.52	5.16 ± 2.57	0.15
L6 -MP (mm)	28.56 ± 2.69	30.28 ± 3.23	0.01*	25.90 ± 2.23	26.90 ± 1.96	0.01*	1.71 ± 1.97	1.00 ± 1.31	0.24
L1/Mandibular Occl Plane	56.58 ± 6.07	55.87 ± 5.91	0.44	57.83 ± 3.30	59.41 ± 3.02	0.02*	–0.71 ± 3.55	1.58 ± 2.41	0.04*
Nasolabial angle°	112.43 ± 7.54	115.57 ± 9.42	0.15	114.13 ± 11.08	108.55 ± 6.91	0.07*	3.14 ± 8.27	–5.58 ± 11.42	0.02*
LL/E plane	–0.84 ± 3.44	–1.54 ± 2.45	0.37	–1.78 ± 2.84	–1.83 ± 3.04	0.87	–0.70 ± 3.03	–0.06 ± 1.35	0.44
UL/E plane	–1.25 ± 2.41	–3.81 ± 2.06	0.01*	–0.79 ± 2.29	–2.66 ± 2.66	0.01*	–2.56 ± 1.80	–1.87 ± 1.59	0.26
Nasal Projection	12.72 ± 1.73	13.68 ± 1.64	0.01*	12.54 ± 1.50	13.74 ± 1.91	0.01*	0.96 ± 0.99	1.21 ± 1.29	0.55
A/TVL	–29.56 ± 4.16	–28.13 ± 4.47	0.09*	–26.99 ± 3.70	–27.86 ± 4.51	0.49	1.43 ± 3.20	–0.87 ± 4.87	0.12
Subnasal Vertikal/UL	1.38 ± 1.19	0.74 ± 1.89	0.17	1.96 ± 2.42	1.68 ± 2.25	0.38	–0.64 ± 1.80	–0.29 ± 1.27	0.52
Subnasal Vertikal/LL	–5.06 ± 2.22	–2.48 ± 2.78	0.01*	–4.90 ± 2.09	–2.67 ± 3.12	0.01*	2.58 ± 2.65	2.23 ± 1.82	0.67
B/TVL	–37.93 ± 8.04	–33.26 ± 6.50	0.01*	–29.37 ± 19.75	–32.52 ± 7.47	0.59	4.68 ± 4.78	–3.15 ± 22.72	0.19
POG/TVL	–36.35 ± 8.77	–31.15 ± 6.72	0.01*	–32.58 ± 6.59	–30.56 ± 8.32	0.44	5.20 ± 5.37	2.02 ± 10.09	0.27
Soft tissue convexity	126.63 ± 5.15	127.49 ± 4.26	0.13	127.46 ± 3.31	128.49 ± 3.62	0.06	0.86 ± 2.17	1.03 ± 2.01	0.82
Mentolabial angle°	109.40 ± 10.68	124.72 ± 11.81	0.01*	123.00 ± 8.73	129.38 ± 7.26	0.02*	15.32 ± 16.40	6.38 ± 9.90	0.07*

$P=.05$
*paired sample t-test
** Independent sample t-test

($p = 0.01$), B/TVL ($p = 0.01$), Pog/TVL ($p = 0.01$), and mentolabial angle ($p = 0.01$). In the normal-weight group, only subnasale vertical/LL ($p = 0.01$) and mentolabial angle ($p = 0.02$) increased significantly. Nasal projection increased significantly in both groups ($p = 0.01$). Intergroup comparison revealed that the nasolabial angle exhibited opposite trends—it increased in overweight but decreased in normal-weight patients ($p = 0.02$). No significant differences were observed for LL/E-plane, UL/E-plane, A/TVL, soft-tissue convexity, or subnasale vertical/UL ($p > 0.05$; Table 3). Fig. 4 presents the significant changes (Δ values) in dental and soft tissue parameters.

Spearman correlation analysis was performed using the treatment-induced changes (Δ values) in cephalometric parameters between T0 and T1 to evaluate a possible relationship between mean salivary leptin levels and skeletal, dentoalveolar, and soft-tissue adaptations. The results revealed significant positive correlations between mean leptin levels and changes of Na Perp–A (r = 0.417, $p = 0.01$), maxillary depth (r = 0.411, $p = 0.01$), sum of interior angles (r = 0.365, $p = 0.03$), and soft-tissue convexity (r = 0.393, $p = 0.02$). Conversely, negative correlations were found between mean leptin levels and changes of posterior facial height (S–Go; r = –0.359, $p = 0.04$), PFH/AFH ratio (r = –0.405, $p = 0.02$), and lower incisor inclination (IMPA; r = –0.471, $p = 0.006$). No statistically significant correlations were detected for the remaining variables ($p > 0.05$).

Discussion

Twin block appliances have shown superior outcomes in Class II cases compared to other functional appliances. A greater significant increase in mandibular plane angle and gonial angle, and a greater decrease in overbite were found in patients treated with the twin block [9, 31]. One paper found out that among removable functional appliances, the twin block showed the highest increase in mandibular length [9]. Nevertheless, controversy remains regarding whether functional appliances exert a true long-term influence on mandibular growth or simply reposition the mandible temporarily. In this context, the twin block was selected in the present study to reliably assess the skeletal effects of leptin in response to a well-documented, efficient functional therapy.

Instead of chronological age, skeletal maturity assessed via hand–wrist radiographs was used as the selection criterium for this study. Doing so, it was observed that overweight patients were younger than those in the normal-weight group. Similar to Mack et al., our findings confirm that overweight patients exhibited faster skeletal and dental development [21].

Leptin levels can be measured using various methods, including plasma and saliva samples. Salivary leptin correlates strongly with serum levels and is ideal for noninvasive, repeated sampling [13, 17, 20]. Unstimulated saliva was preferred due to consistent leptin levels and minimal flow-rate variation [13].

The high reproducibility of our cephalometric measurements supports the reliability of the findings reported in this study. Intrarater reliability was confirmed by retracing 15 randomly selected lateral cephalometric radiographs 15 days after the initial measurement, with method errors ranging from 0.0° for the nasolabial angle to 1.43° for L1–mandibular occlusal plane (°). Paired t-tests showed no systematic error ($p > 0.05$). Interrater reliability was also excellent (ICC = 0.92, $p < 0.001$), indicating strong agreement between the clinicians. Although cephalometric tracing inherently involves some degree of subjectivity, these results suggest that measurement variability was minimal and unlikely to have affected the analysis of skeletal, dentoalveolar, or soft tissue changes observed in our sample to a greater extent. Therefore, the present findings can be considered reproducible, reinforcing the validity of our conclusions regarding treatment effects.

In order to assess whether the number of patients examined was sufficient, a post hoc power analysis was performed. The minimum sample size required to detect a significant difference was calculated using a type I error (α) of 0.05, a test power ($1-\beta$) of 0.8, and an effect size of 1.04, based on a two-sided alternative hypothesis (H1). Accordingly, at least 16 subjects per group (32 in total) were required. The calculated effect size was 1.04, which corresponds to a large effect. Thus, with the limitations of a post hoc analysis, the study seems to have been adequately powered to detect the observed effect size.

Significant increases in SNA, Co–A, and maxillary height were observed in the overweight group, whereas only maxillary height increased significantly in the normal-weight group. These findings should not be interpreted as true maxillary advancement but rather as positional changes resulting from the retraction of point A due to upper incisor retroclination. Illing et al. [15] previously emphasized that the position of point A can be influenced by the inclination of the upper incisors, and in the present study, the significant retroclination observed in the overweight group (U1–SN) likely accounted for the apparent increases in SNA and Co–A. Therefore, these findings are best explained by incisor-related positional effects rather than genuine skeletal changes.

Regarding mandibular changes, Cozza et al. [9] reported approximately 2 mm of additional mandibular growth (Co–Gn) during treatment with functional appliances compared to controls. The present study found a greater increase in mandibular length among overweight patients. This may be speculated to be attributable to the influence of leptin, which has been shown to stimulate chondrocyte activity in the mandibular condyle and increase IGF-I receptor expression, thereby, enhancing endochondral growth [22]. The observed increase in anterior facial height (ANS–Me) in the overweight group further supports enhanced condylar growth in both the vertical and sagittal directions. The mentioned findings are in agreement with a study published by Sadeghianrizi et al. [26], who demonstrated significantly greater mandibular and maxillary dimensions in obese adolescents compared to their normal-weight peers.

In this study, vertical skeletal parameters (Y-axis, SN/GoGn, FMA, SN/PP, palatal–mandibular angle) remained unchanged in both groups, likely because sagittal mandibular activation was prioritized in treatment design, preserving the patients' original vertical growth dimension. Similarly, Trenouth et al. [30] found no significant vertical changes following twin block therapy.

Overjet decreased significantly in both groups, with a greater reduction observed in overweight patients. The interincisal angle increased significantly only in the overweight group, reflecting enhanced incisor retroclination. Overweight patients exhibited marked retrusion and retroclination of the upper incisors (U1/SN, U1/PP, U1/NA, U1–NA mm, U1–NF mm, U1/maxillary occlusal plane; all $p = 0.01$), whereas changes of these parameters in the normal-weight group were minor.

Both groups demonstrated lower incisor proclination (L1/NB, L1–NB mm; $p = 0.01$), though the effect was more pronounced in overweight individuals. The dentoalveolar adaptations can be explained by the mechanical and muscular interactions induced by the functional appliance. The anterior and vertical positioning of the mandible during twin block therapy alters muscle resting length and activity, generating intermaxillary forces that promote distalization of maxillary teeth and mesial movement of mandibular teeth.

Notably, overweight individuals were observed to exhibit greater masticatory efficiency and bite force and tended to consume food more rapidly and in larger quantities [14, 34]. The increased muscular strength may amplify forces transmitted through the appliance, resulting in more extensive dentoalveolar movement. White et al. [34] provided electromyographic evidence showing significantly higher muscle activity during mastication in overweight subjects, supporting the greater degree of upper incisor displacement found in our overweight cohort.

Soft-tissue analysis revealed a significant increase in nasal projection and a reduction in UL–E plane distance in both groups. The nasolabial angle decreased more prominently in overweight patients, likely due to upper incisor retroclination and consequent upper lip retrusion. Both groups exhibited a reduction in the distance from subnasale vertical line to the lower lip (LL) and an increase in the mentolabial angle, reflecting favorable perioral adaptations. Additionally, significant forward positioning of soft-tissue pogonion (Pog/TvL) and the lower lip (B/TvL) was observed in the overweight group, consistent with mandibular advancement induced by the twin block therapy [28]. These adaptations—advancement of the lower lip, labiomental sulcus, and pogonion—corroborate previous findings and signify effective skeletal mandibular repositioning. The increase in nasal projection observed in both groups likely reflects normal nasal growth during the treatment period.

Spearman correlation analysis was performed using the treatment-induced changes (Δ values, T1–T0) of the cephalometric parameters to better understand the biological response to functional therapy, as recommended by Gratsia et al. [12]. The mean salivary leptin levels demonstrated positive correlations with Na Perp–A and maxillary depth, indicating that higher overall leptin concentrations were associated with greater anterior maxillary positioning. However, the significant retroclination of the upper incisors (U1–SN) observed in the overweight group may have partially influenced the apparent increases in SNA, Co–A, and maxillary height by inducing a retrusion of point A. A positive correlation between the mean leptin concentration and the soft-tissue convexity angle suggests that individuals with higher leptin levels exhibited greater anterior positioning of soft-tissue pogonion, which increases the N–Sn–Pg′ angle and results in a flatter facial profile and reduced convexity. Conversely, negative correlations were found between mean leptin concentration and posterior facial height (S–Go), PFH/AFH ratio, and lower incisor inclination (IMPA).

Our findings of accelerated mandibular growth and more pronounced dentoalveolar adaptations in overweight patients align with recent evidence from a scoping review by Michelogiannakis et al., concluding that although the direct association between obesity and altered orthodontic tooth movement remains inconclusive, obesity is consistently linked with changes in craniofacial morphology, advanced dentoskeletal maturation, and increased inflammatory responses [24]. These systemic influences may partly explain the greater skeletal and soft tissue adaptations observed in our overweight group and underscore the importance of incorporating BMI-stratified analyses in orthodontic research.

This study has certain limitations; the relatively small sample size may reduce the generalizability of the findings to the wider population. Due to ethical concerns an untreated control group was not recruited. Additionally, variations in patient compliance with appliance wear could have influenced the treatment outcomes, despite standardized instructions and monitoring. Randomized controlled longitudinal studies investigating other adipokines and hormonal biomarkers involved in growth modulation could further elucidate the biological mechanisms underlying treatment response.

Conclusion

Overweight patients exhibited higher salivary leptin levels throughout treatment. Mandibular length increased more in these patients, possibly reflecting leptin's osteogenic effects. Overjet correction involved greater skeletal as well as incisor movements in the overweight group. Thus, our null hypothesis stating no difference in skeletal, dental, or soft tissue profile changes had to be rejected. In addition, a positive correlations between the leptin concentration and some maxillary parameters, as well as soft tissue convexity, suggest a role of the hormone in sagittal development and soft tissue profile changes. These findings suggest that leptin may play a modulatory role in craniofacial growth and treatment response, highlighting the importance of considering body weight and hormonal profiles when planning functional therapy in adolescent Class II patients. In some of these cases earlier treatment initiation may be thought about.

Author contribution **E. Karaer** Conceptualization, Formal analysis, Data curation, Investigation, Methodology, Validation, Visualization; **S. Sahin** Conceptualization, Formal analysis, Methodology, Visualization, Writing – original draft; **G. Kurt** Conceptualization, Formal analysis, Methodology, Supervision, Validation, Writing – review and editing, Funding acquisition; **E. Guler** Methodology, Supervision, Review and editing KB; Investigation, Formal analysis, Resources.

Data availability statement The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of interest E. Karaer, S. Sahin, K. Bozali, E. Guler and G. Kurt declare that there are no competing interests.

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Ethical standards Written informed consent to participate was obtained from all participants (and from parents or legal guardians in the case of minors), in accordance with the Declaration of Helsinki and institutional ethical guidelines. The protocol of this study was approved by the Bezmialem Vakif University Local Ethics Committee (Approval Number: 09/10/2018 -15310). Consent for publication: Not applicable.

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