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Research Araştırma

Does the 2D:4D Ratio Exhibit Sexual Dimorphism in Sagittal Skeletal Malocclusions? A Retrospective Study

2D:4D Oranı Sagital İskeletsel Maloklüzyonlarda Cinsel Dimorfizm Gösterir Mi? Bir Retrospektif Çalışma

ABSTRACT

Objective: It is noteworthy that the 2D:4D ratio, also called as the ratio of the length of the second digit (2D) to the length of the fourth digit (4D), which has the ability to remain stable lifetime, is associated with various hormones and craniofacial skeletal development as a biomarker in early diagnosis. The aim of this study was to investigate the relationship between the 2D:4D ratio and sagittal skeletal malocclusions.

Materials and Method: A total of 117 patients (57 females, mean age 13.44±1.98; 60 males, mean age 13.56±2.14) with normal vertical angles were included, and the groups were divided into skeletal classes I, II and III according to the ANB angle. The skeletal Class I group consisted of patients with ideal values for both SNA and SNB angles. The skeletal groups were further divided into female and male subgroups by gender. SNA, SNB, SN/GoGn and ANB angles and ANS-PNS and Go-Pog lengths were measured on pretreatment lateral cephalometric radiographs. Digit length measurements were performed with a digital caliper capable of measuring up to 0.01 mm. The 2D:4D ratio was calculated for each group by dividing the 2D length by the 4D length. Statistical analyzes were performed with independent sample t-test and one-way ANOVA in normally distributed data, and Kruskal-Wallis and Man-Whitney U tests in non-normally distributed data. Statistical significance level was accepted as $p < 0.05$.

Results: There was no statistically significant difference between right and left 2D:4D ratios and right and left digit lengths of the same hand in skeletal classes. While statistically significant sexual dimorphism was observed in digit lengths and 2D:4D ratios in skeletal class Is, it was observed that the significance decreased as the severity of malocclusion increased. No significant difference was found in terms of sexual dimorphism in skeletal class IIIs. There was no significantly difference between the skeletal groups in terms of 2D:4D ratio and length measurements.

Conclusion: Sexual dimorphism was seen in all parameters, especially in skeletal Class I patients, and it was found that males had more 2D and 4D lengths and a lower 2D:4D ratio than females. It was also concluded that as the severity of malocclusion increased, the statistical significance of the parameters observed with sexual dimorphism decreased. The fact that sexual dimorphism is fully seen in skeletal class Is but not in skeletal Class III has led to the use of the 2D:4D ratio as a diagnostic biomarker in the early diagnosis of sagittal skeletal malocclusions by gender.

Key Words: 2D:4D Ratio; Sexual Dimorphism; Diagnostic; Skeletal Malocclusion; Orthodontics.

ÖZ

Amaç: Yaşam boyu sabit kalabilme özelliğine sahip olan ikinci parmağın (2D) uzunluğunun dördüncü parmağın (4D) uzunluğuna oranı olarak da adlandırılan 2D:4D oranının erken tanıda biyobelirteç olarak çeşitli hormonlar ve kraniofasiyal iskelet gelişimi ile ilişkili olması dikkat çekicidir. Bu çalışmanın amacı 2D:4D oranı ile sagittal iskelet malokluzyonları arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntem: Vertikal açıları normal olan toplam 117 hasta (57 kadın, ort. yaş 13.44±1.98; 60 erkek, ort. yaş 13.56±2.14) çalışmaya dahil edildi ve gruplar ANB açısına göre iskeletsel Sınıf I, II ve III olarak ayrıldı. İskeletsel Sınıf I grubu, hem SNA hem de SNB açıları için ideal değerlere sahip hastalardan oluşuyordu. İskeletsel gruplar ayrıca cinsiyete göre kadın ve erkek olarak alt gruplara ayrıldı. Tedavi öncesi lateral sefalometrik grafilerde SNA, SNB, SN/GoGn ve ANB açıları ile ANS-PNS ve Go-Pog uzunlukları ölçüldü. Parmak uzunluk ölçümleri 0,01 mm'ye kadar ölçüm yapabilen hassas dijital kumpas ile gerçekleştirildi. 2D:4D oranı, 2D uzunluğunun 4D uzunluğa bölünmesiyle her grup için hesaplandı. İstatistiksel analizler normal dağılan verilerde bağımsız örneklem t-testi ve tek yönlü ANOVA, normal dağılmayan verilerde Kruskal-Wallis ve Man-Whitney U testleri ile yapıldı. İstatistiksel anlamlılık düzeyi $p < 0.05$ olarak kabul edildi.

Bulgular: İskeletsel sınıflarda aynı elin parmak uzunlukları arasında ve sağ-sol 2D:4D oranları arasında istatistiksel olarak anlamlı farklılık bulunmadı. İskelet Sınıf I'lerde parmak uzunlukları ve 2D:4D oranlarında istatistiksel olarak anlamlı cinsel dimorfizm gözlenirken, maloklüzyonun şiddeti arttıkça bu anlamlılığın azaldığı gözlendi. İskeletsel Sınıf III'lerde hiçbir parametrede cinsel dimorfizm açısından anlamlı farklılık bulunmadı. 2D:4D oranı ve iskeletsel kaide uzunlukları açısından iskeletsel maloklüzyonlar arasında anlamlı farklılık bulunmadı.

Sonuç: Tüm parametrelerde özellikle iskeletsel Sınıf I hastalarda cinsel dimorfizm görülmüş ve erkeklerin 2D ve 4D uzunluklarının kadınlara göre daha uzun olduğu ve 2D:4D oranının daha düşük olduğu saptanmıştır. Ayrıca maloklüzyon şiddeti arttıkça cinsel dimorfizm ile gözlenen parametrelerin istatistiksel anlamlılığının azaldığı sonucuna varılmıştır. Cinsel dimorfizmin iskeletsel sınıf I'de tüm ölçümlerde görülmesi, ancak iskeletsel Sınıf III'lerde görülmemesi nedeniyle, cinsiyete göre 2D:4D oranının özellikle iskelet Sınıf III maloklüzyonlarının erken tanısında tanısal bir biyobelirteç olarak kullanılmasının yolunu açmıştır.

Anahtar Kelimeler: 2D:4D Oranı; Cinsel Dimorfizm; Tanı; Iskeletsel Maloklüzyon; Ortodonti.

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INTRODUCTION

Biomarkers are measurable indicators that enable the assessment of healthy or pathological processes, thereby helping to diagnose and prevent disease (1). One of these biomarkers, which is defined by the World Health Organization (WHO) as data that provides information about the relationship between a biological process and a potential hazard (2), is 2D:4D ratio. The 2D:4D ratio, which is the ratio of second digit (2D) to fourth digit (4D) length (3), has been reported to be stable, reproducible, and consistent for each individual as a biomarker (4). This ratio, which shows sexual dimorphism, tends to be lower in males than females due to the relatively longer 4D length of males (5). It has been reported that the 2D:4D ratio appears early in life and remains constant throughout the life (6).

Based on various indirect evidences in medicine, it has been reported that the 2D:4D ratio can be used as a retrospective non-interventional biomarker of prenatal androgen exposure (7). So in other words, since digit length and development of the gonads are controlled by Homeobox common genes, the 2D:4D ratio is thought to be a somatic marker of prenatal sex hormone exposure (5). This ratio is determined at the 13th or 14th week of intrauterine life (second trimester), and although it tends to vary between different ethnic groups, it shows a considerable lifetime constancy (4). The fact that the 2D:4D ratio has been confirmed to show sexual dimorphism in previous studies (8,9) has made this ratio the focus of researchs (10). In the amniocentesis samples, The digit ratio has been reported to be negatively correlated with testosterone due to prenatal androgen exposure and positively correlated with estrogen exposure (11). That is, this rate is expected to be lower in males because the male fetus is more exposed to testosterone than females (12). In the field of dentistry, various studies have been carried out from the investigating relationship of 2D:4D ratio with caries, taste sensitivity, periodontal disease, dental anxiety and nutrition to revealing forensic anthropometric relationships (10,13-16). Additionally, the relationship between the 2D:4D ratio, also called hormonal fingerprint, and human characteristics and behaviors has been shown in previous studies and it has been proven in the medical scenario that it can be used as an indirect marker in many diseases (4,12). However, there are limited studies in the literature investigating the relationship between the 2D:4D ratio and orthodontic malocclusion, (4,5,17) and, to the best of knowledge, they do not provide sufficient data on the type of malocclusion.

Determining of the growth period in the treatment of skeletal malocclusions is of crucial at the beginning, and hand-wrist radiographs as a diagnostic tool are considered as the gold standard because they are more reproducible, present the growth period in more detailed stages and provide easier detection (18). The fact that both hand-wrist radiographs and anatomical measurements of the digits, which are 2D and 4D lengths and 2D:4D ratio, exhibit similar reproducible and reliable features revealed that this current study is needed for orthodontic diagnosis. However, radiation exposure during radiography is not without risk, even in small doses, and causes somatic stochastic effects (19). In the literature, studies on non-invasive orthodontic diagnostic tools are not limited to the 2D:4D ratio, which is hormonal digitprint, but there are also studies on dermatoglyphics such as digitprints, palm prints, and lip prints, which have the potential to predict anomalies and malocclusions related to orofacial regions (20-22). However, although dermatoglyphics and lip prints can be used simply, conveniently and non-invasively to determine malocclusion at an early stage, it has also been reported that they are not completely reliable due to ethnic and environmental factors (23). It is seen that, unlike radiographs, non-invasive diagnostic tools such as saliva, gingival crevicular fluid and urine are used as biomarkers for orthodontic diagnosis (24). However, there are disadvantages such as differences in the collection method, processing and storage temperature of saliva, the fact that the technique is very sensitive due to the risk of contamination with blood and saliva during the collection of gingival crevicular fluid, and the need for different analyzes for each different biomarker (24). This has shown that there is still a need to investigate new non-invasive methods for accurate orthodontic diagnosis. In the light of all this knowledge, in the study, it will be clarified whether the 2D:4D ratio can be used as an orthodontic diagnostic tool in the diagnosis of sagittal skeletal malocclusions. Therefore, the aim of this study was to investigate the relationship between 2D length, 4D length, and 2D:4D ratio and sagittal skeletal malocclusions. It has been reported that the craniofacial complex consistently exhibits size-related sexual dimorphism (25). For this reason, it was also aimed to investigate whether 2D length, 4D length and 2D:4D ratios show sexual dimorphism in skeletal groups. The first null hypothesis of the study is that there is no difference in 2D:4D ratio between sagittal skeletal malocclusions. The second null hypothesis of the study is that 2D:4D ratios do not show sexual dimorphism in sagittal skeletal malocclusions.

MATERIAL AND METHODS

Study Design

This study was designed as a retrospective and single-center and was conducted by investigating the lateral cephalometric radiographs and orthodontic examination registration forms of the patients from the archive records. This study was approved by the Non-Interventional Clinical Research Ethics Committee of Zonguldak Bülent Ecevit University (protocol code 2023/11 and date 31/05/2023). Additional informed consent was not obtained since the study was conducted retrospectively through the investigation of archive records.

Samples and Groups

In this study, archive records of a total of 117 patients (57 female, mean age 13.44±1.98; 60 male, mean age 13.56±2.14) who referred for orthodontic treatment between August and December 2022 were included. The inclusion criteria of the study, which included 117 patients out of 543 whose records were collected during the orthodontic treatment examination, are as follows:

- No having prior orthodontic treatment,
- Normal skeletal vertical growth (SN/GoGn angle between 26 and 38 degrees),
- Normal SNA and SNB for skeletal Class I,
- Mandibular retrognathia with normal SNA for skeletal Class II,
- Maxillary retrognathia with normal SNB for skeletal Class III,
- Having lateral cephalometric radiographs with high resolution and good image quality.

Exclusion criteria from the study are as follows:

- Number and deformity of the digits or a history of trauma,
- Presence of congenital or hereditary syndrome,
- Having physical and systemic disability.

The patients were divided into three groups according to Steiner's ANB angle as skeletal Class I, II and III. For this, lateral cephalometric radiographs taken on a cephalometric x-ray device (Veraviewepocs 2D, J Morita Mfg. Corp., Kyoto, Japan) were evaluated. According to Steiner, skeletal sagittal classification is Class I if the ANB angle is between 0 and 4 degrees, Class II if it is greater than 4 degrees, and Class III if it is less than 0 degrees (26).

The group consisting of skeletal Class I patients was composed of patients with normal SNA (82°±2) and SNB (80°±2) angles according to Steiner. Thus, it was decided to compare skeletal Class I patients with ideal degrees in both vertical and sagittal direction with skeletal Class II and Class III groups. Since sagittal skeletal malocclusions, which are frequently encountered and treated in routine orthodontic practice, are caused by mandibular retrognathia for Class II and maxillary retrognathia for Class III, those with the opposite jaw in a normal position are included. In addition, it would also be revealed whether the 2D lengths, 4D lengths and 2D:4D ratios show sexual dimorphism in skeletal Class I patients with ideal skeletal norms, and they can be considered as a control group during statistical comparisons with other skeletal classes. The skeletal groups were further divided into subgroups according to gender as male and female. The measurements on the lateral cephalometric radiographs were performed using the Steiner cephalometric analysis via the Nemoceph NX (Nemotec, 2006, Madrid, Spain) cephalometric analysis program. Angular measurements on lateral cephalometric radiographs are SNA, SNB, ANB and SN/GoGn angles, while linear measurements are ANS-PNS (for maxillary length) and Go-Pog (for mandibular length) distances. The data on the angular and linear measurements performed according to the skeletal groups are presented in Table 1. The right and left 2D and 4D lengths of the patients were determined by investigating the orthodontic examination registration forms in the archive records. The 2D and 4D lengths of both hands were measured using a digital caliper (Insize digital caliper, code no 1112-150, INSIZE CO., LTD., Loganville, GA, USA) capable of measuring up to 0.01 mm by experienced orthodontists working in the Orthodontics Clinic. The distance between the midpoint of the proximal line crease separating the root of the digit from the palm of the hand and the digittips was accepted as digit length (27), and measurements were performed for both digits separately. First, the hands of the patients were positioned on a flat horizontal surface with the palms facing upwards and tense. The 2D and 4D lengths were then measured with the thumb abducted and slightly apart and the other four digits in the extended position (27). All measurements were repeated 3 times in patients and the arithmetic mean of these measurements was taken and counted as a single value for each length. The 2D lengths and 4D lengths were measured and recorded separately for each group. Also, the 2D:4D ratios were calculated and recorded for each group separately by dividing the 2D length by the 4D length.

Skeletal Groups	N	SNA Mean ±SD	SNB Mean ±SD	ANB Mean ±SD	SN/GoGn Mean ±SD	Maxillary length Mean ±SD	Mandibular Length Mean ±SD
Class I	34 (%29)	81.97±1.24	79.58±1.23	2.38±1.39	31.76±3.37	53.16±4.22	72.46±5.79
Class II	53 (%45)	81.96±3.54	75.96±3.46	6.00±1.09	32.52±3.76	53.10±4.26	69.62±6.91
Class III	30 (%26)	78.00±2.86	81.36±3.54	-3.36±2.45	31.00±5.01	51.60±5.27	71.96±7.20
Total	117 (%100)	80.94±3.32	78.40±3.78	2.54±4.13	31.91±4.03	52.73±4.54	71.04±6.75

N: sample size; SD: standard deviation.
Table 1. Angular and linear measurements of patients by skeletal groups.

Sample Size Calculation

The sample size of the study was carried out with the G*Power program (version 3.1.9.7; Franz Faul, Universität Kiel, Kiel, Germany). Accordingly, the effect size was determined as 0.88, taking into account the mean and standard deviation values, and when the α error probability was set as 0.05 and the (1 − β error prob) power of the study was determined as 95%, the real power of the study was calculated as 90% for at least 29 samples in each group.

Statistical Analysis

The normality distribution of the data was evaluated with the one-sample Kolmogorov-Smirnov test. Pairwise comparisons were performed with independent sample t-test in normally distributed data, while one-way ANOVA was used in intergroup comparisons. In the non-normally distributed data, Man-Whitney U test was used for pairwise comparisons, and Kruskal-Wallis was used for intergroup comparisons. The reliability analysis of cephalometric measurements repeated by the same orthodontist after 4 weeks in 10 randomized patients selected in each group was evaluated with intraclass correlation coefficients (ICCs) using Cronbach's α and two-way random effects. Statistical significance level was accepted as p-value < 0.05.

RESULTS

A strong intra-observer reliability was found in the skeletal groups for cephalometric measurements, with ICCs between 0.935 and 0.987 ($p < 0.001$). There was no statistically significant difference between the right and left hands in terms of 2D length, 4D length and 2D:4D ratio of skeletal class I patients with normal sagittal and vertical angles ($p > 0.05$). Similarly, there was no significantly difference between the 2D and 4D lengths of the right hand, and the 2D and 4D lengths of the left hand ($p > 0.05$). When the 2D and 4D lengths of skeletal Class I patients were evaluated according to gender, both 2D and 4D lengths were found to be significantly longer in males than in females ($p < 0.05$). The 2D:4D ratio was also found to be significantly lower in males than in females ($p < 0.05$). According to these results, it was observed that 2D length, 4D length and 2D:4D ratios exhibited sexual dimorphism in skeletal Class I patients. Statistical analysis results of skeletal Class I patients are shown in Table 2. There was no significant difference between the right and left hands of skeletal Class II patients in terms of 2D length, 4D length and 2D:4D ratios ($p > 0.05$). Likewise, no significant difference was found between the 2D and 4D lengths of both the right and left hands ($p > 0.05$).When the 2D and 4D lengths of skeletal Class II patients were evaluated according to gender, altered statistical results were seen compared to skeletal Class I patients. Although the right 2D length was longer and the right 2D:4D ratio was lower in males than in females, this differences were not statistically significant ($p > 0.05$). In addition, as expected, while the other digit lengths were significantly longer in males than females, the left 2D:4D ratio was found to be lower ($p < 0.05$). Statistical analysis results of skeletal Class II patients are presented in Table 3.
There was no significant difference between the right and left hands of skeletal Class III patients in terms of 2D length, 4D length and 2D:4D ratios ($p > 0.05$). Again, similarly, no significant difference was found between the 2D and 4D lengths of both the right and left hands ($p > 0.05$). When the 2D length, 4D length and 2D:4D ratios of skeletal Class III patients were evaluated according to gender, much more differed statistical results were encountered compared to skeletal Class I and Class II patients. In all measurements, in males compared the females, although the 4D length was longer than 2D length and the 2D:4D ratio was lower, these differences were not significant ($p > 0.05$). Statistical analysis results of skeletal Class III patients are given in Table 4.

There was no statistically significant difference between skeletal groups in terms of 2D lengths, 4D lengths, 2D:4D ratios, maxillary lengths and mandibular lengths (p>0.05). Statistical analysis results for the comparison of skeletal groups are presented in Table 5.

Parameters	Groups	N	Mean±SD	*p*-value
Parameters for digits				
2D length	Right hand	34	69.31±4.52	0.806 ^{t}
	Left hand	34	69.05±4.33	
4D length	Right hand	34	69.80±5.22	0.580 ^{t}
	Left hand	34	69.09±5.30	
2D:4D ratio	Right hand	34	0.992±0.031	0.376 ^{m}
	Left hand	34	1.001±0.035	
Parameters for hands				
Right hand	2D length	34	69.31±4.52	0.683 ^{t}
	4D length	34	69.80±5.22	
Left hand	2D length	34	69.05±4.33	0.973 ^{t}
	4D length	34	69.09±5.30	
Parameters for gender				
Right 2D length	Female	19	67.87±3.74	0.027 * ^{m}
	Male	15	71.14±4.87	
Right 4D length	Female	19	67.62±3.47	0.007 * ^{m}
	Male	15	72.56±5.85	
Right 2D:4D ratio	Female	19	1.001±0.021	0.033 * ^{m}
	Male	15	0.981±0.037	
Left 2D length	Female	19	67.39±3.25	0.008 * ^{m}
	Male	15	71.15±4.71	
Left 4D length	Female	19	66.89±3.30	0.006 * ^{m}
	Male	15	71.87±6.12	
Left 2D:4D ratio	Female	19	1.007±0.032	0.043 * ^{m}
	Male	15	0.990±0.038	

^{t}: independent sample t-test; ^{m}: Mann–Whitney U test; N: sample size; SD: standard deviation; *p*: significance level; *: *p*-value < 0.05.

Table 2. Statistical results of 2D and 4D lengths and 2D:4D ratios of the skeletal Class I patients.

Parameters	Groups	N	Mean±SD	*p*-value
Parameters for digits				
2D length	Right hand	53	69.17±6.21	0.812 [t]
	Left hand	53	69.45±6.10	
4D length	Right hand	53	70.14±6.29	0.907 [t]
	Left hand	53	70.29±6.40	
2D:4D ratio	Right hand	53	0.987±0.035	0.769 [m]
	Left hand	53	0.988±0.028	
Parameters for hands				
Right hand	2D length	53	69.17±6.21	0.425 [t]
	4D length	53	70.14±6.29	
Left hand	2D length	53	69.45±6.10	0.495 [t]
	4D length	53	70.29±6.40	
Parameters for gender				
Right 2D length	Female	26	67.51±4.47	0.055 [m]
	Male	27	70.77±7.24	
Right 4D length	Female	26	67.92±4.71	0.021 * [m]
	Male	27	72.28±6.93	
Right 2D:4D ratio	Female	26	0.995±0.034	0.078 [m]
	Male	27	0.979±0.034	
Left 2D length	Female	26	67.72±4.48	0.037 * [m]
	Male	27	71.12±7.02	
Left 4D length	Female	26	67.94±4.78	0.013 * [m]
	Male	27	72.55±7.02	
Left 2D:4D ratio	Female	26	0.997±0.025	0.025 * [m]
	Male	27	0.980±0.029	

[t]: independent sample t-test; [m]: Mann–Whitney U test; N: sample size; SD: standard deviation; *p*: significance level; *: *p*-value < 0.05.

Table 3. Statistical results of 2D and 4D lengths and 2D:4D ratios of skeletal Class II patients.

Parameters	Groups	N	Mean±SD	*p*-value
Parameters for digits				
2D length	Right hand	30	68.46±5.19	0.958 [t]
	Left hand	30	68.54±5.56	
4D length	Right hand	30	69.35±5.61	0.952 [t]
	Left hand	30	69.26±5.80	
2D:4D ratio	Right hand	30	0.987±0.027	0.871 [m]
	Left hand	30	0.989±0.025	
Parameters for hands				
Right hand	2D length	30	68.46±5.19	0.530 [t]
	4D length	30	69.35±5.61	
Left hand	2D length	30	68.54±5.56	0.625 [t]
	4D length	30	69.26±5.80	
Parameters for gender				
Right 2D length	Female	12	67.69±4.38	0.573 [m]
	Male	18	68.98±5.73	
Right 4D length	Female	12	67.80±5.21	0.415 [m]
	Male	18	70.38±5.78	
Right 2D:4D ratio	Female	12	1.001±0.029	0.134 [m]
	Male	18	0.979±0.024	
Left 2D length	Female	12	67.54±4.99	0.368 [m]
	Male	18	69.20±5.95	
Left 4D length	Female	12	67.15±5.37	0.200 [m]
	Male	18	70.66±5.79	
Left 2D:4D ratio	Female	12	1.006±0.021	0.08 [m]
	Male	18	0.978±0.022	

[t]: independent sample t-test; [m]: Mann–Whitney U test; N: sample size; SD: standard deviation; *p*: significance level; *: *p*-value < 0.05.

Table 4. Statistical results of 2D and 4D lengths and 2D:4D ratios of skeletal Class III patients.

Parameters	Skeletal Groups	Mean±SD	Statistical Value	*p*-Value
Right 2D length	Class I	69.31±4.52	0.220 [f]	0.803 [†]
	Class II	69.17±6.21		
	Class III	68.46±5.19		
Right 4D length	Class I	69.80±5.22	0.179 [f]	0.836 [†]
	Class II	70.14±6.29		
	Class III	69.35±5.61		
Right 2D:4D ratio	Class I	0.992±0.031	0.714 [h]	0.700 [††]
	Class II	0.987±0.035		
	Class III	0.987±0.027		
Left 2D length	Class I	69.05±4.33	0.268 [f]	0.765 [†]
	Class II	69.45±6.10		
	Class III	68.54±5.56		
Left 4D length	Class I	69.09±5.30	0.518 [f]	0.597 [†]
	Class II	70.29±6.40		
	Class III	69.26±5.80		
Left 2D:4D ratio	Class I	1.001±0.035	2.082 [h]	0.353 [††]
	Class II	0.988±0.028		
	Class III	0.989±0.025		
Maxillary length	Class I	53.16±4.22	1.269 [f]	0.285 [†]
	Class II	53.10±4.26		
	Class III	51.60±5.27		
Mandibular length	Class I	72.46±5.79	2.245 [f]	0.111 [†]
	Class II	69.62±6.91		
	Class III	71.96±7.20		

[f]: F-value for one-way ANOVA; [h]: H-statistic for Kruskal-Wallis; [†]: one-way ANOVA test; [††]: Kruskal-Wallis test; *p*: significance level; *: *p*-value < 0.05.

Table 5. Statistical results of comparison between skeletal groups.

DISCUSSION

The aim of this study was to investigate the relationship between 2D:4D ratio and sagittal skeletal malocclusions, which were inevitable in orthodontics, and to reveal the possible usability of this consistent ratio as a diagnostic tool in orthodontic practices, especially during early diagnosis. In this context, in the present study, no significant difference was found between the right and left hands in all skeletal groups in terms of 2D length, 4D length and 2D:4D ratios. Also, there is no significant difference was found between the 2D and 4D lengths of the same hand in each skeletal group. However, sexual dimorphism was seen in all measurements only in skeletal Class I, and the 4D length was longer in males than females, while the 2D:4D ratio was found to be lower. This has been reported in previous studies (5, 28). In addition, in skeletal Class II, the number of parameters found to be statistically significant in terms of sexual dimorphism in 2D length.

4D length and 2D:4D ratios decreased, and even in more severe sagittal skeletal malocclusion, which is skeletal Class III, statistical results of almost all parameters were not found significant for this feature. There are limited studies investigating the relationship of the 2D:4D ratio with craniofacial skeleton (25,29,30). In the study conducted by Valla et al. (25), which investigated the relationship between the 2D:4D ratio and the shape of the craniofacial skeleton in prepubertal children, it was reported that there was no sexual dimorphism in both craniofacial shape and 2D:4D ratios. On the other hand, in the study investigating the hypothesis that a more masculine facial appearance is associated with a lower 2D:4D ratio by Weinberg et al. (30), it was reported that mandibular prognathism increased with a decrease in the 2D:4D ratio in adult males, and a statistical relationship was observed between the 2D:4D ratio and face shape. Similarly, Premkumar et al. (31) reported that lower 2D:4D ratio is seen in mandibular prognathism and therefore this ratio can be used as a biomarker for early diagnosis of mandibular prognathism. In this present study, no significant difference was observed between sagittal skeletal classes in terms of 2D length, 4D length and 2D:4D ratios. The reason why it differs from the study of Weinberg et al. and Premkumar et al. might be that the skeletal Class III patients in the presented study consisted of patients with maxillary retrognathia rather than mandibular prognathia. However, sexual dimorphism was observed in skeletal Class I patients, with 4D longer and 2D:4D ratios lower in males than females in all measurements. Previous studies in the literature have mostly focused on the relationship between 2D:4D ratio and caries (1,5,32), and it seems that its relationship with malocclusion has not been comprehensively investigated in a specific methodological framework. For this reason, it is thought that the prominence of this present study as a research reveals the relationship between digit lengths and their ratios, which is a skeletal structure, and skeletal sagittal malocclusion with a systematic methodological approach, provides more reliable results. Lobud et al. (33) investigated the relationship between 2D:4D ratio and malocclusion classes, and reported that they did not find a relationship between 2D:4D ratio and malocclusion. In addition, Issrani et al. (5), in their study investigating the relationship of 2D:4D ratio, which also calling as hormonal fingerprint, with dental caries and malocclusion, reported that this ratio cannot be used both for caries and as an early marker of malocclusion. In the present study, no significant difference was found in the right and left 2D length, 4D length and 2D:4D ratios of patients in all skeletal groups. On the other hand, Priyanka et al. (4), in their study investigating the role of 2D:4D ratio in early detection of malocclusion, reported that as this ratio increases, malocclusion also increases significantly. Similarly, it has been reported that the prevalence of malocclusion increases with an increase in the 2D:4D ratio and that the 2D:4D ratio can be used as an early marker for malocclusion in the study by Garg et al. (17), which investigated the relationship of the 2D:4D ratio with the malocclusion group constituted according to the dental aesthetic index. In the present study, unlike these results, no significant difference was found between the skeletal groups in terms of 2D length, 4D length and 2D:4D ratios. However, statistical changes in sexual dimorphism findings of these lengths and ratios in each skeletal group were considerable. While statistically significant sexual dimorphic differences in length and ratios were observed in all measurements of skeletal Class I patients, these significant differences disappeared as the severity of malocclusion increased. It is thought that the reason for the different results of both the presented and literature studies was due to the different ethnic population and different methodological design of the studies. In order to avoid having to treat skeletal malocclusions via the orthognathic surgery due to late diagnosis, research on non-invasive approaches as an early diagnosis tool was carried out. In one of these studies, Achalli et al. (34), in which they investigated the relationship between digitprint models and skeletal malocclusions, reported that dermatoglyphics can be very helpful in the early diagnosis and prevention of malocclusion. Although there are other studies (20, 21) supporting that dermatoglyphics are an important marker in the early diagnosis of malocclusion, Eslami et al. (35) reported that dermatoglyphics did not show significant differences between skeletal malocclusions. The aim of the present study, which was carried out to reveal whether the 2D length, 4D length and 2D:4D ratios of the hands can be used in the early diagnosis of sagittal skeletal malocclusions, and also in terms of sexual dimorphism, was similar to the goals of dermatoglyphic studies. However, no significant differences were found between sagittal skeletal malocclusions in the orofacial region in terms of 2D:4D ratios, and maxillary and mandibular lengths.

The diagnostic value and indications of radiographs, which are considered indispensable for orthodontic treatment, are still controversial, and it is reported that studies examining the accuracy of cephalometric analyses and their effects on orthodontic diagnosis did not provide consistent results (19). In addition, since the minimum recording materials required for orthodontic diagnosis are never fully defined (36, 37), research on these non-invasive diagnostic methods, which is also away from the harmful effects of radiation, is important. However, when different non-invasive orthodontic diagnostic methods as a biomarker for the early diagnosis of malocclusion are examined in the current literature, it is seen that the results were unfortunately contradictory. Similarly, the lack of significant difference between skeletal classes in terms of 2D length, 4D length and 2D:4D ratios between skeletal classes in the presented study does not support the use of this ratio as a biomarker in the early diagnosis of skeletal malocclusion. Despite this, it was remarkable the number of parameters with statistically significant differences between females and males in terms of sexual dimorphism decreased as the severity of skeletal malocclusion increased. In the study, in addition to the fact that all patients had normal vertical angles, the skeletal Class I group consisted of patients with normal angles both maxillary and mandibular, enabling a more reliable comparison with other skeletal groups. Because it has been reported that different vertical growth patterns may affect the sagittal jaw relationship and therefore reduce the diagnostic accuracy (38). Moreover, standardizing the other groups to include skeletal Class II patients characterized by mandibular retrognathia and skeletal Class III patients characterized by maxillary retrognathia, which is frequently encountered in routine orthodontic practice, are the strengths of the study. However, the limitations of the study were the neglect of transversal skeletal dimensions, the absence of other sagittal skeletal position combinations that cause skeletal Class II and Class III malocclusions, and the non-homogeneous distribution of the sample size.

CONCLUSION

The first null hypothesis was accepted. The second null hypothesis of the study was rejected in skeletal Class I, partially accepted in Class II, and accepted in Class III. Sexual dimorphism was observed in all parameters in skeletal Class I patients in terms of 2D length, 4D length and 2D:4D ratio. It was notable that the parameters found statistically significant in digit length and ratios decreased as sagittal skeletal malocclusion became more severe for sexual dimorphism. This situation paved the way for the use of 2D:4D ratio in the early diagnosis of sagittal skeletal malocclusions in females and males by gender, and it was concluded that further studies should be planned in a larger sample group including different ethnic groups.

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