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Analytic study of the differences in cephalometric parameters in German class II/III orthodontic patients

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Abstract

Objectives

The objective of this investigation was to assess and contrast cephalometric parameters in German individuals undergoing orthodontic treatment for skeletal class II and III anomalies, while examining how these measurements vary according to age and gender.

Materials and Methods

A total of 386 German orthodontic patients (ages 5.3–53 years) were studied, with an even distribution by gender. Participants were classified as having a skeletal class II (n = 210, 54.4%) or class III (n = 176, 45.6%) using the individualized ANB method of Panagiotidis and Witt. Lateral cephalograms were digitally analyzed to compare cephalometric differences between groups and subgroups.

Results

Significant differences were observed between classes II and III, as well as among the subgroups. Skeletal deformities were more pronounced at older ages (> 21 years). Class III patients had a more prognathic mandible (SNB angle) and a greater skeletal discrepancy (as assessed by the Wits appraisal). Males with class III malocclusion exhibited a more open vertical configuration (NL/ML angle, NL-NSL angle, Gonion angle). Dental compensation increased with age, with being more proclined and lower incisors being more retroclined in class III patients. Correlations among sagittal, vertical, and dental variables were identified.

Conclusions

The differences in cephalometric parameters between various malocclusion classes and subgroups, particularly in terms of gender and age, underscore the potential influence of these factors.

Introduction

A high percentage of the contemporary population has an orthodontic treatment need, as recently demonstrated in large epidemiological studies in Germany [1, 2]. In other countries, a high prevalence of malocclusions is also reported, such as 48% in Saudi Arabia Prevalence of malocclusion and orthodontic treatment needs among adolescents in Najran City [3] or 36% in Italy [4]. However, variations occur due to the population being assessed and the indices applied. Among the various indications of orthodontic treatment, correcting the sagittal relationship of the jaw bases, specifically skeletal class II and III, plays a significant role. This aligns with the recently published finding that an increased (larger than 3 mm) or decreased (smaller than 1 mm) overjet, often associated with skeletal class II or III, when correctly

positioned upper and lower jaw fronts, is a frequent reason for orthodontic treatment in Germany [5]. Skeletal classification refers to the sagittal (anteroposterior) alignment between the maxillary and mandibular bones. It can be divided into three groups: whereas patients with skeletal class I present a neutrobasal jaw relation, that is an ideal sagittal position of the upper and lower jaw, cases with class II have a distobasal jaw relation, and those with class III a mesiobasal jaw relation. The term skeletal class only refers to the phenotype, which describes the position of the maxillary and mandibular bones concerning each other, without considering the etiological factor, since the extent of prognathism can vary in the maxilla and the mandible as well as in both jaws [6–8].

A cephalometric analysis, which is mainly conducted with lateral cephalograms, is required to diagnose the skeletal class of an individual. Various approaches to defining an individual's skeletal class are described in the literature, and differences occur due to the parameter assessed and the kind of norm values needed to interpret the measured parameter. For example, the skeletal class can be determined using the ANB angle, introduced by Riedel [9], or the Wits appraisal, established by Jacobson [10]. The average values can be distinguished between empirical and individualized ones. Whereas the first is based on average values, representing a healthy population's mean of a predefined value for a specific parameter, the latter reflects the individual present correlation between different craniofacial structures. Since the first attempt to individualize the average value of ANB for the determination of skeletal classification by Steiner in 1953 [11], various techniques have been presented, among which a graphic solution, the harmony box of Segner and Hasund [12, 13], and mathematical ones, such as Predictive mathematical models used to calculate ANB [14, 15] and Wits parameters are frequently applied [16].

As indicated by the individualized average values in an individual patient, some correlations exist between the anatomic structures within the craniofacial skeleton. This idea was already introduced by Enlow et al. [17], who described the balance of the craniofacial structures in terms of growth and shape. However, the degree of correlation and the contributing structures vary according to differences in the specific population regarding ethnicity, age, and gender, which should be considered when choosing cephalometric average values [18–22].

After analyzing the parameter variations between the different subgroups and the correlations, it may be helpful to perform a principal component analysis (PCA). PCA, established by Pearson in 1901 [23], and is used to reduce the dimensionality of a multivariate dataset without losing significant information by generating new, uncorrelated variables called principal components.

Recently, we conducted a study on Arab orthodontic patients to investigate differences across subjects exhibiting skeletal malocclusion types II and III and to analyze the performance of different machine learning models [24]. However, to our knowledge, studies are still seeking such outcomes in a German orthodontic population, but differences are expected due to the other ethnicities, as already mentioned. Hence, the aim of this study was primarily to identify discrepancies in cephalometric parameters between German orthodontic skeletal class II and III patients and among different age and sex groups employing multiple group comparison tests, the study explored how cephalometric parameters correlate

within particular gender and age groups, as well as how these features vary between different demographic segments, and finally PCA was done to explore the ability to reduce the dimensionality of our data, and to reveal the most important variables to the diagnosis process.

Material and Methods

Ethical Statement and Sample Size Consideration

This observational, multi-center diagnostic study was conducted among German orthodontic patients treated at various dental specialty offices, in collaboration with the Orthodontics unit of the University Hospital in Regensburg, Germany. Before collecting the samples, ethical approval was granted by the university's designated ethics board for this project (Ethics reference code 19-1596-101, 13 November 2019). In this study we included the maximum available patients that were enrolled in the defined period of the study. Throughout the study, we followed the ethical approval guidelines as well as the Declaration of Helsinki. Besides, this study followed the STROBE Statement for observational studies.

Cephalometric data collection

In this study, only orthodontic specialist practices across Germany or in the Orthodontics unit of the University Hospital in Regensburg were considered for inclusion. The patients were classified according to the definition of Panagiotidis and Witt [15]: $ANB_{individual}$ [15] = -35.16 + (0.4 x SNA) + (0.2 x ML-NSL), and the Calculated_ANB = $ANB_{measured}$ – $ANB_{individual}$

Inclusion criteria

- Skeletal class II - SCIIMO: Calculated_ANB>1,5°
- Skeletal class III - SCIIIMO: Calculated_ANB<-1,5°
- Pre-treatment lateral cephalograms available from patients' records with the possibility of calibration and anamnestic information as evident from the patient's records, including demographic data (age, gender).

Exclusion criteria

* Skeletal class I patients

* No available pre-treatment cephalometric parameters, and anamnestic information

* Patients who couldn't sign an informed consent form

In the present study, slightly different limits of acceptance were applied (± 1.5 °) than initially proposed by Panagiotidis and Witt (± 1°) [15] to exclude borderline cases from the analysis. Based on the Calculated_ANB, patients were retrospectively allocated to the group's skeletal classes II and III. The

relevant cephalometric variables are explained in Figures 1A and 1B and Table 1. All cephalometric analyses were performed by two raters, who were calibrated prior to the measurements. Both intrarater and interrater correlations were determined based on repetitive measurements of 50 cephalometric X-rays, which were chosen by using a random generator. Utilizing the test-retest method, each rater obtained all 50 cephalometric measurements twice, with a minimum gap of two weeks between the two measurements. Subsequently, reliability was assessed, which ranged between 0.92 and 0.99 for interrater reliability and 0.90 and 0.99 for intrarater reliability.

Based on Calculated_ANB, all patients were allocated to sagittal skeletal groups (classes II and III) to investigate group-specific differences in cephalometric variables. Furthermore, subgroups were established within each group to measure the inter-group variation in both gender and age. In detail, the subgroups were:

- gender: male, female
- age: 0 < Age < 13, 14 < Age < 20, Age > 21
- combination of age and gender

After detecting the variations in cephalometric measurements across the (sub)groups, the correlation between those parameters was determined.

Data Analysis

Intrarater- and interrater reliability were tested. Analyses of the data were conducted using the R statistical environment (https://www.r-project.org/). Cephalometric variables between patients with skeletal class II and III were compared for statistical significance via a single-factor analysis of variance procedure with post-hoc analyses. Then, Spearman correlation was conducted between the different cephalometric parameters. PCA was used to explore the ability to reduce the dimensionality of our data and reveal the most critical cephalometric parameters. The PCA was performed first while including gender and age, and then the PCA was performed again while not including these covariates. Finally, Results were considered statistically significant and highly significant if $p < 0.05$ and 0.01, respectively.

Results

Patients

Finally, the investigation comprised 386 participants, 210 (54.4%) with skeletal class II and 176 (45.6%) with skeletal class III. Patient ages in the study sample spanned from 5.3 to 53 years. On average, class II individuals were 13 ± 6.6 years old, and class III patients were 14 ± 6.3 years old. Regarding how the sample was divided by sex, it was similar in both groups: among skeletal class II patients, 60% were female (n = 125), and in class III 54% were female (n = 95). Details of the study cohort, covering both

demographic and cephalometric variables, are shown in Tables 2A and 2B for skeletal class II and III subjects, correspondingly.

As illustrated in Fig. 2, the computed ANB, representing the discrepancy between measured and individualized ANB angles, clearly differs among individuals diagnosed with skeletal class II and class III malocclusions in all genders and ages. The highest density was observed in adult class II subjects of both sexes, whereas in adult class III patients, the density was the most negligible.

Cephalometric variables: effect of skeletal class, gender, and age.

In Tables 3A-E, the results of cephalometric comparisons across skeletal class II and III categories, as well as among subgroups defined by age and sex within one malocclusion group, are presented. Statistical significance was assessed using multiple comparisons and post hoc Tukey tests. Patients with skeletal class II malocclusion presented with partly significantly different cephalometric measurements than class III patients. Furthermore, significant differences were found within each skeletal malocclusion group (class II, class III) according to gender and age, as revealed by multiple comparison tests. Only the significant and relevant results are presented in the tables.

Analyzing each skeletal class separately in Table 3A, it becomes evident that among class II patients, more and more significant differences occur between the age and gender-dependent subgroups than in class III patients. In skeletal class II, adult patients (age > 21) present with significantly higher retroinclined front teeth than younger ones, and this finding is reinforced in males. The degree of dysgnathia, i.e., of the skeletal class, increased in adult patients, irrespective of the kind of dysgnathia (skeletal class II and III). In line with this finding, adult male patients had significantly more retrognathic mandible (SNB angle) than younger (female) patients in class II cases.

As shown in Table 3B, the extent of the difference between class II and III patients was exceptionally high if one group consisted of the oldest patient group (Age > 21).

The comparisons between class II and III patients, which include gender and age, are presented in (Tables 3C-3E) for cephalometric indices reflecting skeletal height, anteroposterior relationships, and dental alignment, respectively. In the vertical direction, class III patients tended to have more divergent jaw bases than class II patients (NL/ML angle), although this was only significant in males. Furthermore, in class III, there was a more substantial extent of counterclockwise rotation of the maxilla, especially in adults and in males (NL-NSL angle). The Gonion angle was significantly higher in class III patients, especially in males, indicating a more vertical growth pattern in this group. When age was considered as an independent variable, the most significant differences in the Gonion angle were identified for the groups “III_0 < Age < 13-II_14 < Age < 20” and “III_0 < Age < 13-II_Age > 21”, i.e., in the event that children with class III malocclusion were part of the comparison. Corresponding to the positive difference, compared with class III individuals, class II patients showed a more pronounced vertical growth pattern as reflected by the facial axis. This contradicts the observations made at the Gonion and NL/ML angles. Also contradictory to the previous findings is that the difference was highest in females. Considering

age, it was found that the highest difference occurred when adult class II patients (II_Age > 21) were included in the comparison.

Regarding the sagittal direction shown in (Table 3D), patients with class III exhibited a markedly more forward-positioned mandible than class II subjects (SNB angle). Whereas gender alone did not lead to further significant discrepancies, it is evident that age influenced the degree of difference between class II and III, as it was most dominant in adult patients (III_Age > 21-II_Age > 21, 8.18°). Corresponding to the severity of mandibular protrusion, the parameter “Wits appraisal” was significantly more negative in subjects with skeletal class III than in class II, as determined by the definition of skeletal class. The most significant differences could be observed for adult (Age > 21) and male patients (III_Age > 21-II_Age > 21, -11.83 °).

Evaluating the dental parameters, class III and class II patients presented a trend toward dental compensation for their skeletal malocclusion. Accordingly, class III patients had significantly more proclined and retroclined upper and lower incisors, respectively, than class II patients. Furthermore, when adult class II patients were considered in the analysis, the maxillary front teeth had a greater interposition in class III cases compared to class II cases, also indicating dental compensation.

Heatmaps of Spearman Correlation

The heatmap correlation matrices are presented in Figs. 3–5 and are based on calculations of the Spearman correlation. Figure 3 illustrates, separately for class II (Fig. 3A) and class III (Fig. 3B), how the cephalometric parameters are associated without considering the effects of age and gender. In both classes, there was a strong correlation between specific dental variables, which measure either the same or influence the size of another variable: first, the variable + 1/NA angle showed a perfect negative correlation with the parameters + 1/NL angle (SCIIMO- ρ=-0.923, SCIIIMO- ρ=-0.812, P < 0.01) and + 1/SNL (SCIIMO- ρ=-0.948, SCIIIMO- ρ=-0.852, P < 0.01) and an almost perfect positive correlation with + 1 / NA (mm) (SCIIMO- ρ = 0.878, SCIIIMO- ρ = 0.699, P < 0.01). -1/ML was strongly negatively correlated with − 1/NB angle (SCIIMO- ρ = -0.514, SCIIIMO- ρ = -0.634, P < 0.01), and − 1/NB (mm) (SCIIMO- ρ=-0.766, SCIIIMO- ρ=-0.826, P < 0.01). Interincisal angle was correlated with the tilt of the upper and lower anterior teeth and their position. Concerning the skeletal variables, in both classes a pronounced inverse correlation between the parameters PFH / AFH ratio and ML - NSL angle became obvious (SCIIMO- ρ = -0.963, SCIIIMO- ρ = -0.932, P < 0.01)—furthermore, ML - NSL angle was inversely related with Facial-Axis (SCIIMO- ρ = -0.679, SCIIIMO- ρ = -0.689, P < 0.01), and exhibited a direct linkage with Gonion angle (SCIIMO- ρ = 0.716, SCIIIMO- ρ = 0.627, P < 0.01), and ML-NL angle (SCIIMO- ρ = 0.844, SCIIIMO- ρ = 0.825, P < 0.01). Demonstrating the connection between vertical and sagittal aspects, the PFH/AFH ratio presented a positive and significant correlation with SN-Pg angle (SCIIMO- ρ = 0.770, SCIIIMO- ρ = 0.681, P < 0.01), and SNB measurement (SCIIMO- ρ = 0.645, SCIIIMO- ρ = 0.596, P < 0.01). ML-NSL angle presented a strong opposing relationship with SN - Pg angle (SCIIMO- ρ = 0.-780, SCIIIMO- ρ = -0.749, P < 0.01), and SNB angle (SCIIMO- ρ = 0.-653, SCIIIMO- ρ = -0.665, P < 0.01). In terms of sagittal orientation, a strong direct correlation existed between SNA angle on the one hand and SNB

angle (SCIIMO- ρ = 0.847, SCIIIMO- ρ = 0.833, P < 0.01), and SN-Pg angular value (SCIIMO- ρ = 0.734, SCIIIMO- ρ = 0.753, P < 0.01) on the other. Furthermore, SNB angle showed a perfect positive correlation with SN-Pg angle (SCIIMO- ρ = 0.931, SCIIIMO- ρ = 0.962, P < 0.01). Class II and III subjects presented comparable cephalometric parameter correlations besides minor differences.

Gender and Age variation

Figures 4 and 5 show the heatmap correlation matrices for skeletal classes II and III, respectively, and are separated into different age and gender groups to evaluate the influence of these independent variables (Figs. 4A-4F) and (Figs. 5A-5F). Firstly, it is evident that as age increases, more correlations between cephalometric parameters can be observed in both malocclusion classes, but particularly in class II. In adult patients, male subjects tended to have more correlations than females in both classes. In male and female children (age < 13), Calculated_ANB demonstrated a moderate linkage with other parameters in both malocclusion classes. Especially male patients with class II presented more significant associations of the Calculated_ANB at the two higher age groups: adolescent males (14 < age < 20) showed the strongest association with Calculated_ANB, and Wits appraisal (ρ = 0.873, P < 0.01) and Gonion angle (ρ = -0.773, P < 0.01). In contrast. In adult males (age > 21) the Calculated_ANB was strongly correlated with Wits index (ρ = 1.00, P < 0.01), Facial-Axis (ρ = 0.886, P < 0.05), PFH/AFH (ρ = 0.829, P < 0.05) (positive), and with Gonial Angle (ρ = -0.943, P < 0.01), NL-ML (ρ = -0.829, P < 0.05) angle and ML-NSL angle (ρ = -0.829, P < 0.05) (negative).

In patients with skeletal class III, the strongest correlations were also found in male adults. Calculated_ANB showed a negative correlation with SNB angle (ρ=-0.783, P < 0.05), SN-Pg angle (ρ=-0.783, P < 0.05), Facial-Axis (ρ=-0.833, P < 0.01), and PFH/AFH ratio (ρ=-0.695, P < 0.05), and a positive correlation with Sagittal Wits appraisal (ρ = 0.700, P < 0.05), NL-ML angle (ρ = 0.733, P < 0.05),, and ML - NSL angle (ρ = 0.700, P < 0.05).

Principal Component Analysis (PCA)

The PCA investigated all of the cephalometric parameters to determine the most relevant ones for classifying the skeletal class of a single patient accurately classified into class II or III and was performed after standardization of the data. The results of the PCA are shown in Tables 4A-B. According to the findings in Table 4A, 43% of the variance in classifying the skeletal class of an individual can be explained by the first component, whereas components 2, 3, and 4 contribute another 25%, 15%, and 9%, respectively, resulting in a cumulative percentage of 92%.

Since the first two components already explained 68% of the total variance, the interpretation of the loading matrix focused on the loadings of the first two components. (Table 4B) presents the loadings of the first four components. In the first component, high positive values were noticed for the following parameters: ANB angle and Calculated_ANB. While negative values were presented for the parameters

SNB, and SN-Pg angles. In the second component, the results showed that NL-ML, and ML-NSL angle were with high positive values, PFH/AFH ratio, and interincisal angle were with the most negative values.

Figures 6 and 7 illustrate the contribution of each cephalometric parameter to the PCA's first, second, third, and fourth components. According to the cosine squared function (Figure. 6), the main variables contributing to PCA components are SN - Pg, SN - ML, ML - NSL, SNB angular measurements, and PFH / AFH proportion. Similarly, in (Fig. 7), we presented a PCA biplot displays the connections between variables and the initial two principal components, where PC1 represents 43.8% and PC2 represents 22.7% of the dataset's variability.

Finally, we've repeated the PCA analysis while including the covariates gender and age, and the results revealed the low contribution of gender and age to the PCA analysis. For example, these two covariates were not powerful in any of the first four components and were the last to appear in the cosine squared function.

Discussion

By applying multiple comparison techniques, this study analyzed cephalometric differences associated with age, sex, and skeletal malocclusion. It additionally investigated parameter relationships within demographic subgroups and performed PCA to isolate the variables most relevant to skeletal class prediction.

Differences in cephalometric parameters

Statistical analysis revealed significant differences in cephalometric variables between skeletal class II and III subjects. The difference in the Calculated_ANB is evident because it reflects the definition of the two separate classes [25]. Similarly, the Wits index was more negative in class III cohort, which also matches the meaning of the parameter. In line with this finding, class III patients also showed a markedly forward-positioned mandible (SNB) than class II subjects, which explains the sagittal discrepancy of the jaw bases between patients with class II and class III. Concerning the effects of age and gender, the most significant differences for Calculated_ANB, SNB angle, and Wits appraisal were found in adults (age > 21) and male patients in the case of Wits, this might reflect that the extent of dysgnathia increases during growth. However, there might have been a selection bias in our study sample since we included only patients with an orthodontic treatment need. In Germany, public health insurance only pays for orthodontic treatment for adult patients if a combined therapy, including maxillofacial surgery, is necessary due to severe skeletal discrepancies. Thus, the adult study collective might have predominantly consisted of such severe surgery cases, leading to bigger cephalometric differences. In literature, similar cephalometric differences are described too. For example, Jacobson defined the Wits appraisal such that it was more negative in class III and more positive in class II patients [10]. The Calculated_ANB, which was used in our study to distinguish between skeletal classes II and III, was applied in the form suggested by Panagiotidis and Witt appraisal [15]. Patients presenting skeletal class

III showed a greater vertical openness compared with class II subjects, as evident from the increased values of NL/ML angle and Gonion angle and the decreased value of NL / NSL angle, which indicate hyperdivergent jaw bases, vertical growth pattern as well as maxillary rotation in a counterclockwise direction, respectively. Partly, the differences were biggest in males (NL/NSL, NL/ML) and in adults (NL/NSL). However, concerning the Gonion angle, the comparison with children (0 < age < 13) resulted in the highest contrast. Contradictory to the above-mentioned findings, the values of the facial axis were higher in class III than in class II patients, indicating an overall flatter growth trajectory in class III patients, especially in female adults.

Concerning the effect of age and gender, Gianelly reported for children between 8 and 13 years with normal occlusion and class II division 1 malocclusion comparable cephalometric parameters [26]. In contrast to this observation, we found significant differences among class II patients, but they were present between different age groups and hence these results are not directly comparable. Stahl et al. reported similar growth patterns between class II and class I patients other than the smaller gains in mandibular length among class II cases, resulting in a worsening of the class II during growth and hence a more considerable extent of dysgnathia after growth [27], which is consistent with our finding. Regarding the comparison between different age groups, we found the highest differences, if adult patients were part of the comparison. This result is confirmed by other authors, who described an increase in the jaw bases' sagittal discrepancy in class III patients [28]. Gender alone did not result in significant differences within each of the malocclusion classes. A contradictory finding was reported by Taner et al. who identified significant cephalometric differences in adolescent Caucasian Turkish class I and II subjects but barely in class III [29]. A possible explanation for this contrast may be methodological differences since the study consisted of patients with a small age range (10–11.5 years) and applied another method (ANB) to classify patients.

Concerning the dental parameters, the measurements indicated dental compensation for the skeletal discrepancies in the sagittal direction. Hence, compared to class II patients, class III subjects presented a higher degree of proclination (+ 1/NL angle, + 1/SN angle, + 1/NA angle) and a more anterior position (1i/NA mm) of the upper and retroinclination of the lower incisors (-1/Me-Go angle). This difference became especially obvious if adult class II patients were part of the comparison, which might be explained by the more extensive extent of dental compensation occurring after the completion of the growth. Our observations are consistent with those already described in the literature: Alexander et al. reported an increasing dental compensation in skeletal class III patients at higher age [28].

Correlations between cephalometric variables

Within the various cephalometric variables, many of the dental parameters were (almost) perfectly correlated with each other: for example, in the lower jaw, -1 / ML angle and − 1 / NB mm presented strong negative correlation, which is plausible since both parameters indicate the inclination of the lower front teeth.

As indicated by Panagiotidis and Witt's regression equation [15], specific skeletal cephalometric variables are correlated with each other, too. According to our results, vertical parameters, which intend to measure similar directions, presented strong correlations, such as the negative one between ML-NSL angle and PFH/AFH ratio and the positive one between gonion angle and ML - NSL angular measurement. In these cases, the correlations illustrate that the inclination of the mandible affects the growth pattern, and that the Gonion angle positively influences the inclination of the jaw basses. In terms of sagittal direction, a strong direct correlation existed between SNA angle on the one hand and SNB angle, and SN-Pg angular value on the other. Furthermore, SNB angle showed a perfect positive correlation with SN-Pg angle in both classess. Class II and III subjects presented comparable cephalometric parameter correlations besides minor differences. Interestingly, vertical and sagittal skeletal parameters were also associated with each other, such as PFH/AFH ratio that presented a positive significant correlation with SN-Pg angle, and SNB angle, or PFH/AFH ratio with ML-NSL negative correlation.

Analyzing the influence of sex and age by building corresponding subdivisions revealed that more correlations were observed in older age groups and that this was reinforced in adult males. The Calculated_ANB did not present significant correlations in the youngest subgroup (age < 13), but showed increasing correlations at higher age groups, especially in male subjects. The results demonstrated that the extent of skeletal class II, the more horizontal and deep the growth pattern. Similar correlations were found in class III male adults too. The results showed a positive correlation between NL-ML angle and ML-NSL angle, which indicates that a higher degree of skeletal class III is correlated with a more open configuration. In contrast, the negative correlation with Facial-Axis and PFH/AFH suggest the opposite.

In line with our observations, our previous study that examined skeletal class I, and II German patients, demonstrated that several correlations between cephalometric parameters in the same and between different planes for class I and class II patients were available, and showed that in the vertical plane, the divergence of the jaw bases (NL-ML) was positively associated with the inclination of the mandible (ML-NSL) but negatively with the growth pattern (PFH/AFH) [30]. Besides, Midlej et al. [24], that examined skeletal class II and III Arab patients, found that in both skeletal classes, the results revealed many correlations between Calculated_ANB and other parameters. For example, among skeletal class II patients, Calculated_ANB presented significant positive correlations with ANB angle, and Wits appraisal, and negative significant correlation with SN-Pg angle. Regarding skeletal class III, Calculated_ANB was associated positively with ANB angle, and Wits appraisal, and negatively correlated with facial axis, SNB, and SN-Pg angles. Plaza et al. reported a higher odds ratio (OR) to develop a skeletal class II and III, in case of a retrognathic and prognathic mandible, respectively [31]. However, they found a higher risk to develop a SCII in highly divergent basal jaw structures, whereas we observed a negative correlation between Calculated_ANB and NL-ML angle. This contradiction may stem from study-specific variations in the population with respect to ethnicity (Hispanic patients).

PCA

The PCA analysis revealed that two principal components explain already 68% of the variance when classifying a patient as SCIIMO or SCIIIMO. Adding two subsequent principal components contributes to an overall cumulative share of 92%. In the first component, high positive values were noticed for the following parameters: ANB angle and Calculated_ANB, with a bit higher contribution of the Calculated_ANB. While negative values were presented for the parameters SNB, and SN-Pg angles. In the second component, the results showed that NL-ML, and ML-NSL angle were with high positive values, PFH/AFH ratio, and interincisal angles were with the most negative values. These results suggest that the Calculated_ANB was the most powerful variable to contribute to skeletal class II and III variations. The skeletal parameters are primarily similar to those identified to show strong correlations with Calculated_ANB within the heatmap correlation matrices. Furthermore, the cosine squared function revealed that the most critical parameters for PCA are SN-Pg angle, SN-ML angle, SNB angle, and PFH/AFH. This finding reflects that both sagittal and vertical cephalometric variables affect the actual skeletal class of an individual and that the consideration of the degree of prognathism of the maxilla and mandible alone is not sufficient. Furthermore, these results indicate that especially the mandible affects the classification of skeletal malocclusion.

PCA is increasingly applied in orthodontics. For example, a study in which PCA was performed to sub-classify skeletal class III patients according to their cephalometric phenotype revealed that 66.7% is clarified by the variance captured within the first four principal components [32]. The first PC was based on vertical linear measurements, but the second PC was based on vertical angular parameters. In another study, the PCA-method, which was performed on cephalometric analyses to describe the patients' shape variability, could explain 63.2% of the total variance with the first four principal components [33]. Whereas the first PC was mainly based on vertical, the second one consisted of sagittal cephalometric parameters. These studies show, as ours, that both the anteroposterior and vertical dimensions must be considered during the classification of individuals. In this study we included 24 parameters, however, our results demonstrated the need to mainly focus on specific parameters when diagnosing the patient as skeletal class II or III, which mainly contribute to the variations. Finally, the PCA results showed the low impact of gender and age covariates to contribute to the PCA analysis results and thus confirmed the approach of the individualized ANB of Panagiotidis and Witt that don't include these covariates in their equation.

Limitations

The present research relied on a subgroup of German orthodontic subjects without age specific restrictions. A possible limiting factor of our study is that the ethnicity of the individual patients was not tested. Therefore, the study collective might include other ethnic groups too, although this is rather unlikely owing to the fact that every study site was based in Germany. Furthermore, a disadvantage considering the study collective is the limited number of patients in the adult and adolescent subgroups, so that subsequent investigations should seek to equalize the number of participants across subgroups. Finally, the cephalometric analysis, which was conducted before the PCA, might be a possible source of

error. However, the statistical analysis revealed high reliability of the cephalometric analysis and the input data.

Conclusions

The results of this research shed light on variations in cephalometric measurements across malocclusion categories and demographic subgroups defined by sex and age, emphasizing the potential impact of these variables. Furthermore, correlations between different cephalometric parameters describing sagittal, vertical, and dental dimensions were found – especially for the Calculated_ANB, which emphasizes the need to consider the craniofacial skeleton's complexity when diagnosing an individual's skeletal class. Based on further analysis, PCA was identified as an effective method to determine an individual's skeletal class, including only a few sagittal and vertical skeletal cephalometric parameters. Overall, our study might be helpful in the practical and precise diagnosis and treatment, by considering the gender and age as critical factors, in addition to the correlations between the different cephalometric parameters, when analyzing the patient's cephalometric parameters.

Declarations

Author Contributions: Conceptualization. F.A.I.. P.P. and N.W.; methodology. E.P.S., K.M., O.Z., and S.K.; validation. F.A.I.; investigation. O.Z., K.M., and S.K.; resources. F.A.I., P.P., and N.W.; data curation. E.P.S., S.K., O.Z., and K.M.; writing—original draft preparation. E.P.S., K.M., and F.A.I.; writing—review and editing. P.P., N.W., and F.A.I.; supervision. F.A.I., P.P., and N.W.; project administration. F.A.I..

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Institutional Review Board Statement: According to current guidelines and following the Ethics Committee of the University of Regensburg, ethics and regulations. The committee reviewed and approved this research project and study design with approval number 19-1596-101 (dated 13.11.2019)

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest: The authors declare no conflict of interest.

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Tables

Tables 1 to 4 are available in the Supplementary Files section.

Figures

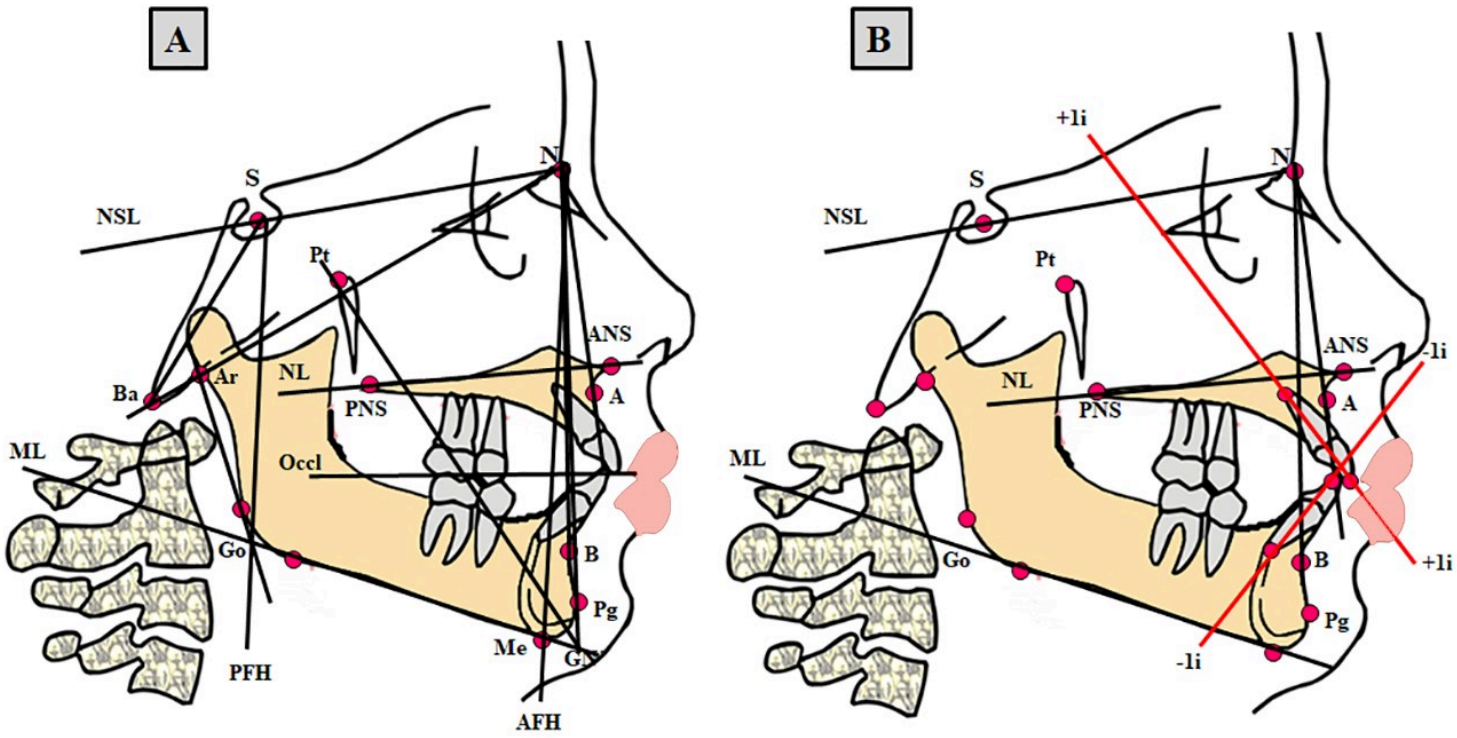


Figure 1

Relevant skeletal (A) and dental (B) cephalometric variables analyzed. Details are described in Table 1.

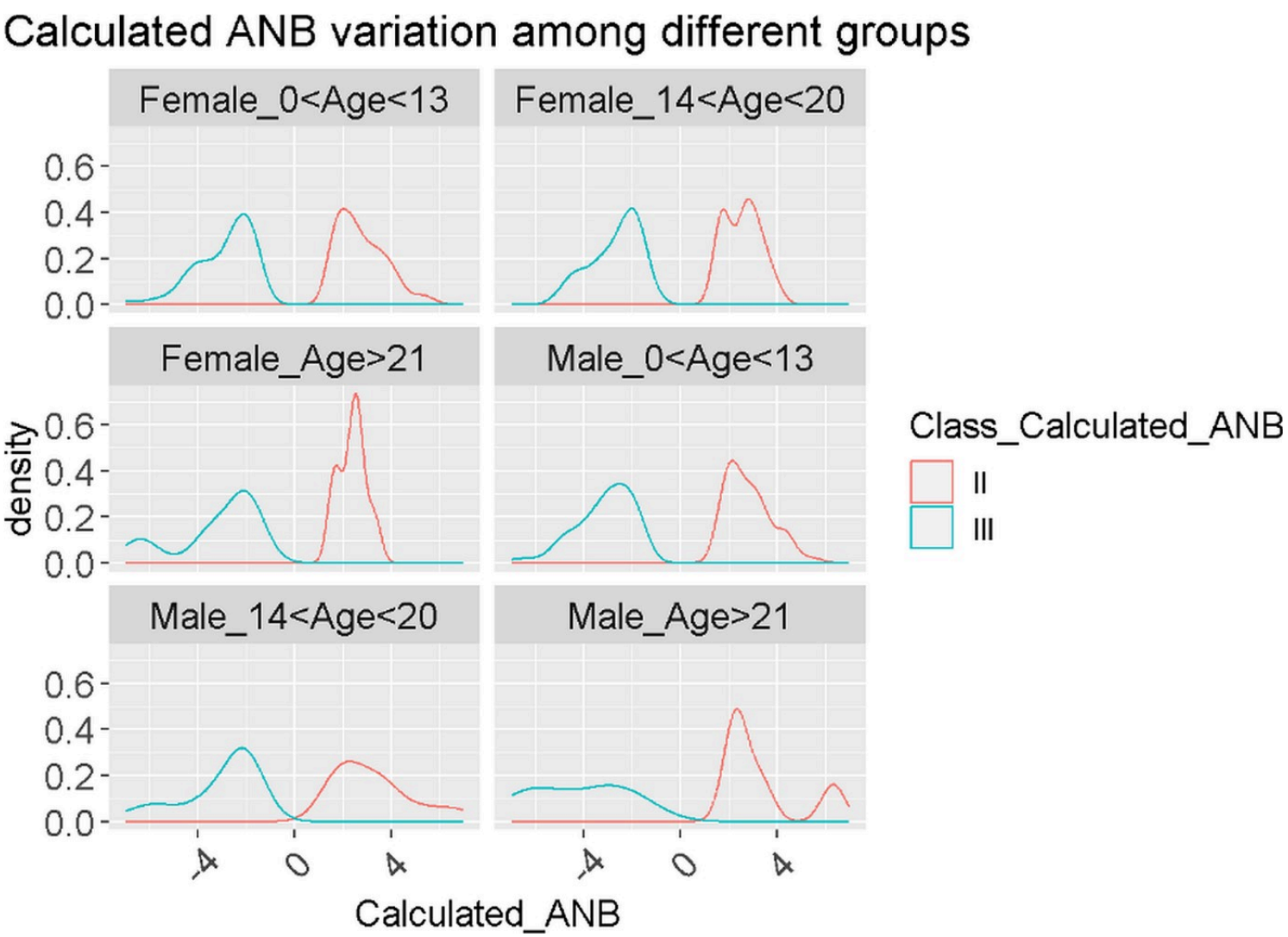


Figure 2

Distribution of the subgroups (age, gender) with respect to skeletal classes II and III as diagnosed by the individualized ANB of Panagiotidis and Witt.

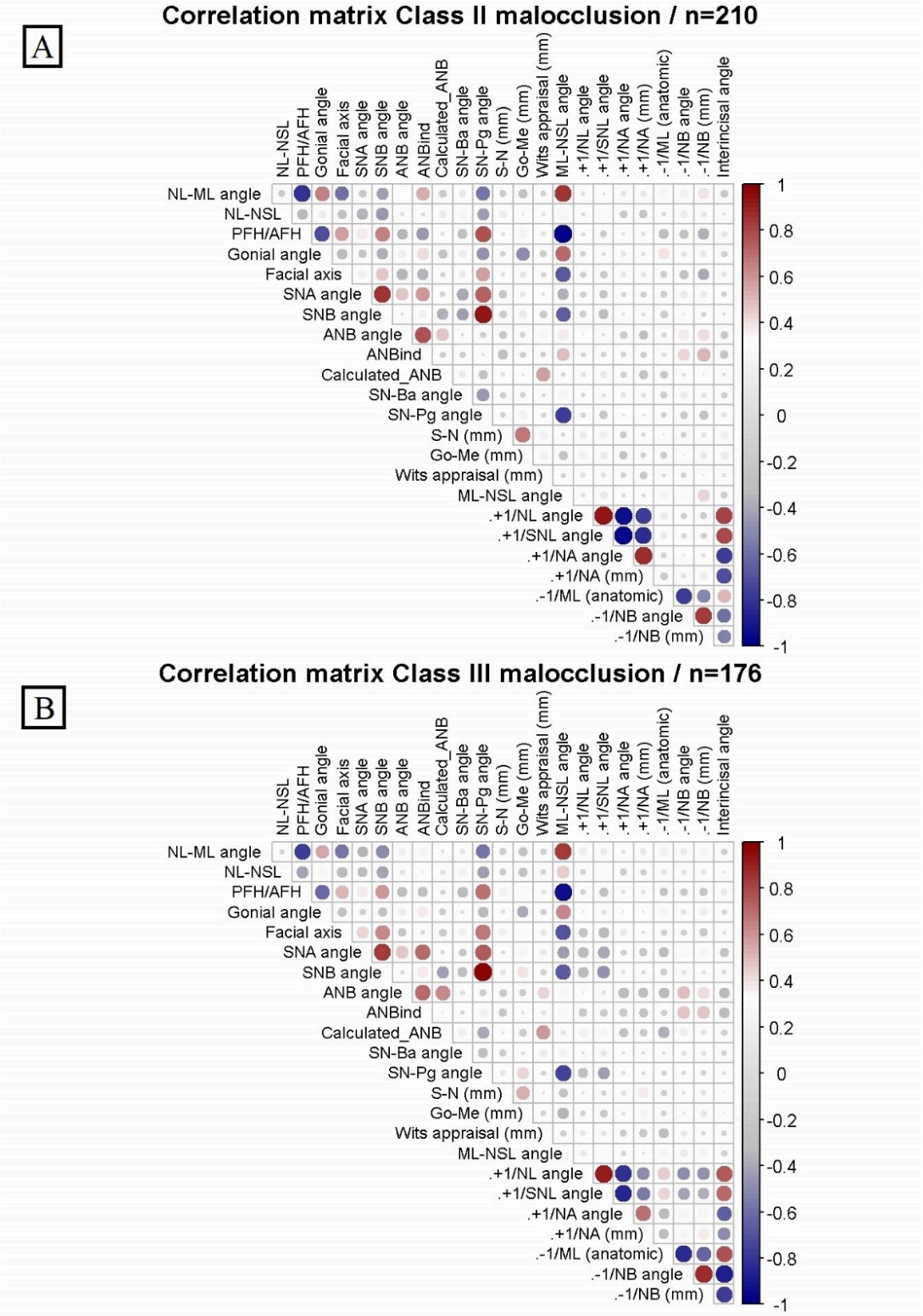


Figure 3

Heatmap Correlation Matrix between cephalometric parameters, separated by patients with skeletal class II (Figure 3A) and III (Figure 3B).

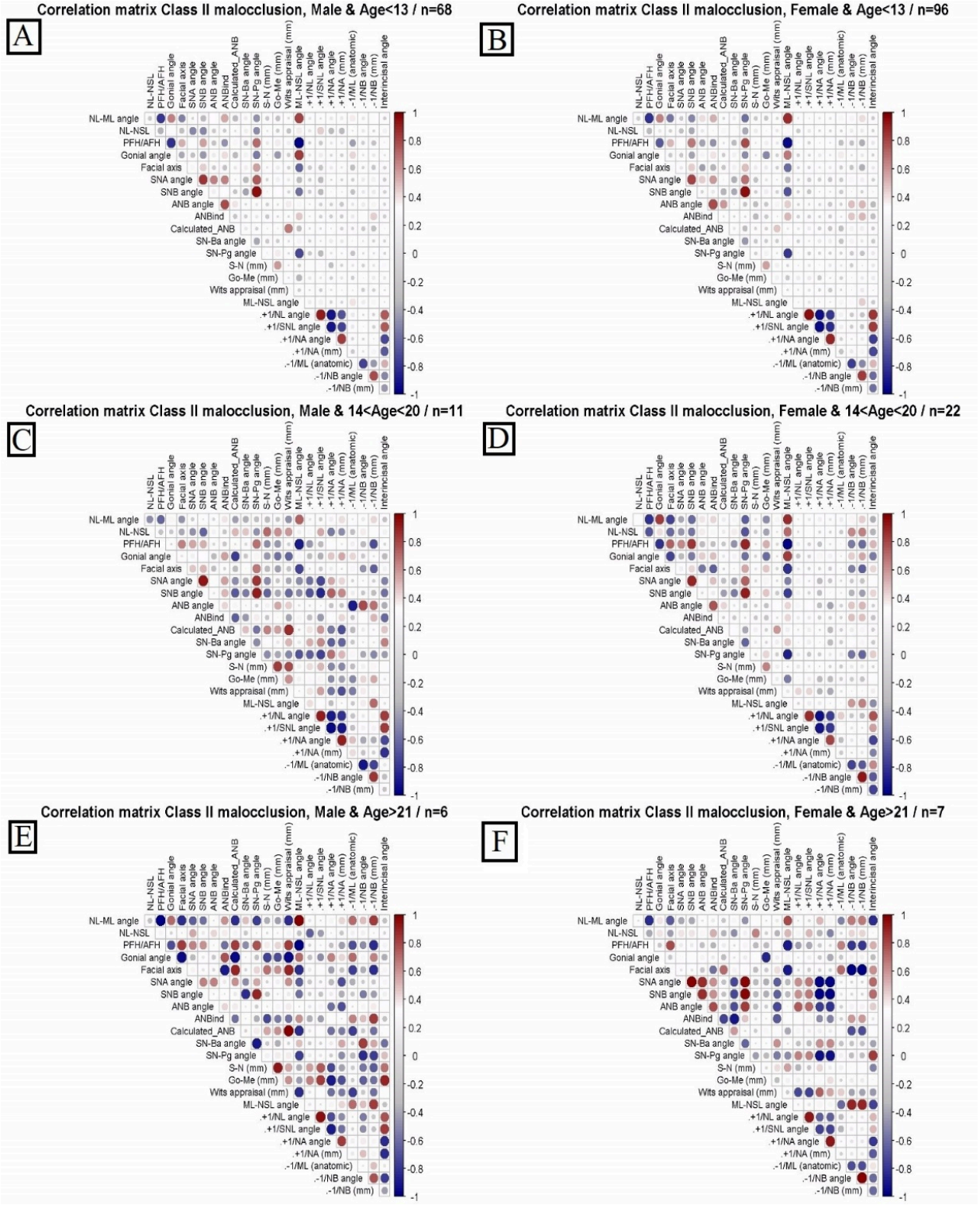


Figure 4

Heatmap Correlation Matrix between cephalometric parameters of patients with skeletal class II, separated by gender and age into six subgroups, A-F, respectively.

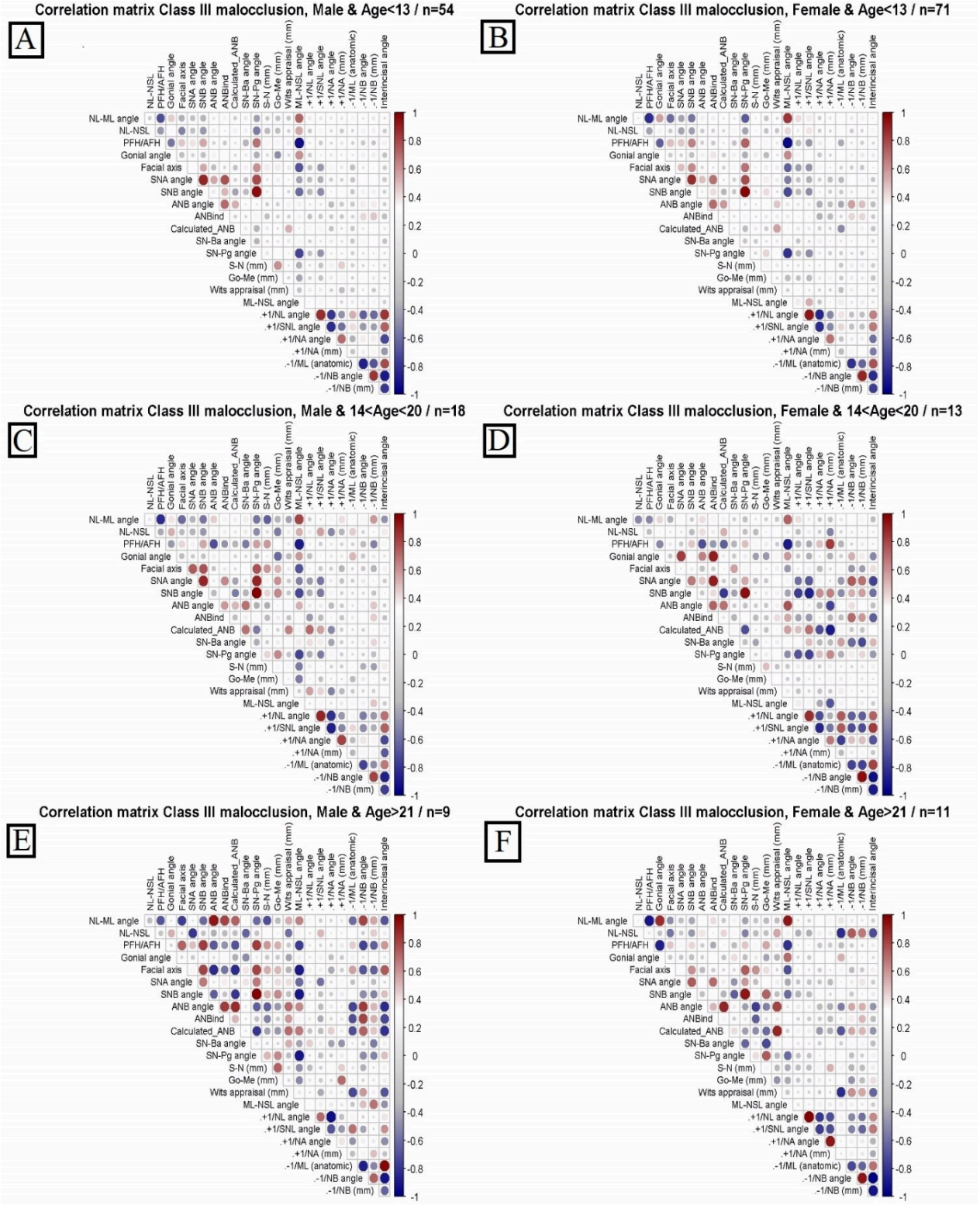


Figure 5

Heatmap Correlation Matrix between cephalometric parameters of patients with skeletal class III, separated by gender and age into six subgroups, A-F, respectively.

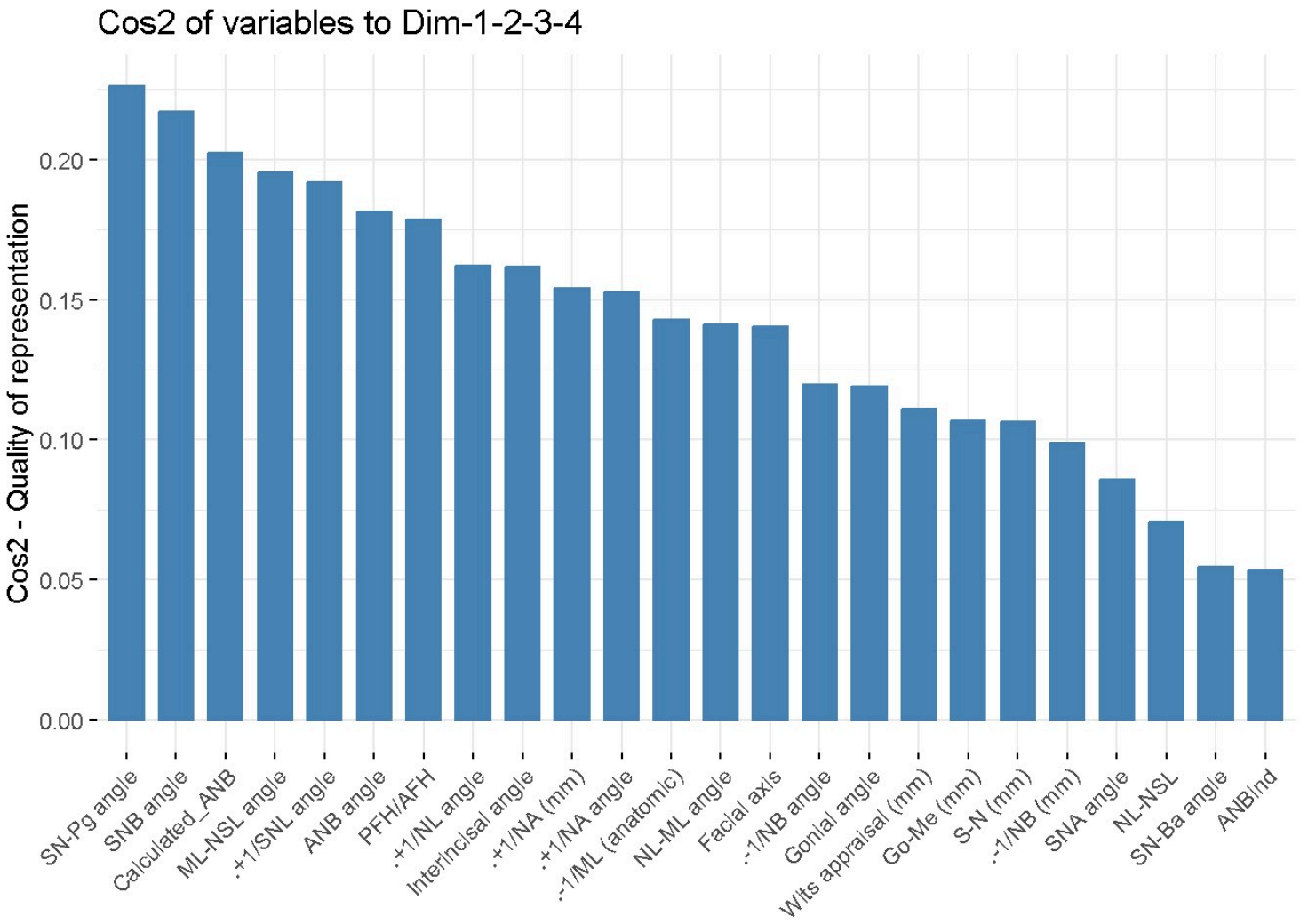


Figure 6

Cosine squared function to analyze the contribution of the cephalometric parameters to the first four components of PCA conducted.

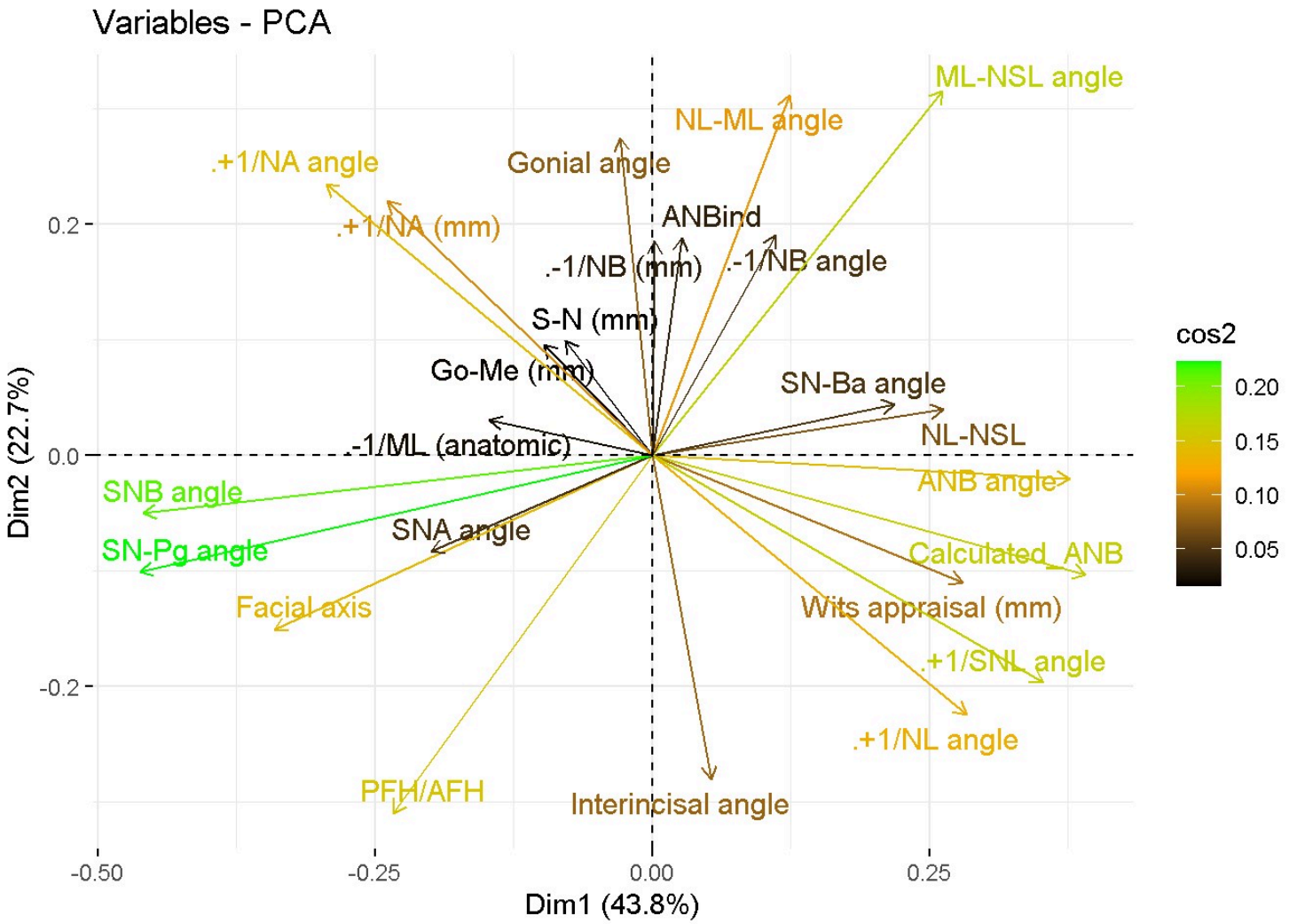


Figure 7

This figure presents a PCA biplot that visualizes the relationships between the variables and the first two PCs (PC1 and PC2). PC1 captures 43.8% and PC2 captures 22.7% of the data variance. The X and Y axes represent PC1 and PC2, respectively. High-contributing variables are colored green, while variables with lower contributions are shown in black.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Tables.docx