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CUT-OFF VALUES FOR SEX DETERMINATION VIA FORAMEN MAGNUM AREA: AN ANTHROPOMETRIC PILOT STUDY

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Abstract: The foramen magnum is an important landmark and it is the largest and 3-dimensional aperture of the base of the skull, has been used in sex determination in many studies. The aim of this study is to examine the foramen magnum area (FMA) using statistical evaluations and to generate cut-off values for sex determination by using automatic CT area calculation, area calculations of Teixeira and Radinsky. The study was conducted on CT images of 493 (248 male, 245 female) individuals. The effects of FMAs calculated according to 3 different FMA calculation methods on estimating sex were examined using logistic regression analysis. Hosmer-Lemeshow test was used for regression model fit in logistic regression analysis. ROC curve analysis was used to determine whether the FMA variable, which contributed significantly to the model as a result of the logistic regression analysis, has a diagnostic value in the estimation of sex. According to the ROC analysis results, the cut-off values obtained in all three FMA calculation methods are effective in sex determination. The cut-off values for automatic CT area calculation and for area calculations of Teixeira and Radinsky were 688.5 mm^2, 767.8 mm^2 and 755.3 mm^2 respectively. The data of the present study will be of use in forensic science and anthropology and for further studies on population data and serve as a future framework for sex determination using craniometric parameters.

Keywords: foramen magnum, morphology, cut-off point, sex determination.

INTRODUCTION

In living humans, sex is a separate trait determined by the genetic makeup of the individual. Therefore, there are easily identifiable characteristics that can be used to classify any individual into only one of two categories (male or female). Unfortunately, this is much more difficult in the human skeleton, as all shape- and size-based features form a continuum that overlaps a lot. This difficulty in estimating sex is compounded by the fact that residues are often fragmentary, populations can vary in expression of certain traits, and the identification of some traits is dependent on observers' experience [1].

The entire skeleton is necessary for accurate results for sex determination, it is rarely found complete and in good condition. Therefore, it is important to apply appropriate methods for sex determination from skeletal remains [2, 3]. In forensic context, sexual determination is directly related to the quantity and quality of bone remains. The more bones available, the better opportunity will be for reliable sex assessment results [4]. Krogman [5] sexed a sample of 750 adult skeletons from the Hamann-Todd Collection. The success rates were as follows: whole skeleton present (100%), pelvis alone (95%), skull alone (92%), pelvis plus skull (98%), long bones alone (80%), long bones plus pelvis (98%). In many studies [6-8], sex determination using the morphological features of the pelvis has the highest accuracy. However, in most cases, the skull is easily preserved because it consists of hard tissue compared to the whole skeleton. Therefore, sex identification through the skull has become a core content of forensic anthropology [9]. Stewart reported that sex estimation can be made with an accuracy of 90% using the skull [10].

Morphological or morphometric methods are used for sex prediction from skull bones. Sex estimation

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in the human skull is often based on size differences and robustness. Physical anthropologists and medical forensic experts traditionally study sites of sexual dimorphism, including the skull's general appearance, nuchal crest, orbita, glabella, mastoid process, and mandible [11,12].

The basal region of the occipital bone is covered with a larger volume of soft tissue. Because of its thickness and relatively well-preserved anatomical location, the basal region of the occipital bone is more likely to withstand physical impacts than other parts of the skull. Therefore, studies on sex estimation using the occipital bone may be useful if significantly impaired residues are identified [12, 13]. The foramen magnum (FM) is an important landmark and it is the largest and 3-dimensional aperture of the base of the skull, has been used in sex determination in many studies [2, 4, 12-20]. Teixeira conducted an initial study of sex estimation based on FM size and created a formula for area calculation of FM [14]. Radinsky [21] reported that the area of the FM is significantly associated with total skeletal weight through its relationship with cranial capacity from five different orders of mammals.

The main purpose of this study is to examine the foramen magnum area in the Turkish population using statistical evaluations and to generate cut-off values for sex determination by using automatic CT area calculation, area calculations of Texeira and Radinsky.

MATERIAL AND METHOD

In the present study, the area measurements obtained from CT images of 493 randomly selected patients who applied to Kırşehir Ahi Evran University Training and Research Hospital with headache complaints and did not have any pathology were used as retrospective data between 2020-2021. This study was approved by the Kırşehir Ahi Evran University Ethical Board (2021-07/69).

CT Image Acquisition

The CT images were obtained from the Kırşehir Ahi Evran University PACS (Kardelen Software, 2014) system, length and area measurements were made using the same system. FML, FMW, FMA were measured from the axial plane. The FML was measured from the end of the anterior border (basion) to the end of the posterior border (opisthion). The FMW was measured from the point of maximum concave on the right edge to the maximum concave on the left edge. The axial plane images were created by multiplaner reconstruction from sagittal plane T1 weighted 3D volume rendering images. The FMA were automatically given after tracing the bony margin of the FM on the CT image using a 3D program on the CT workstation with a resolution of 1280*1042 full screen format (Fig. 1).

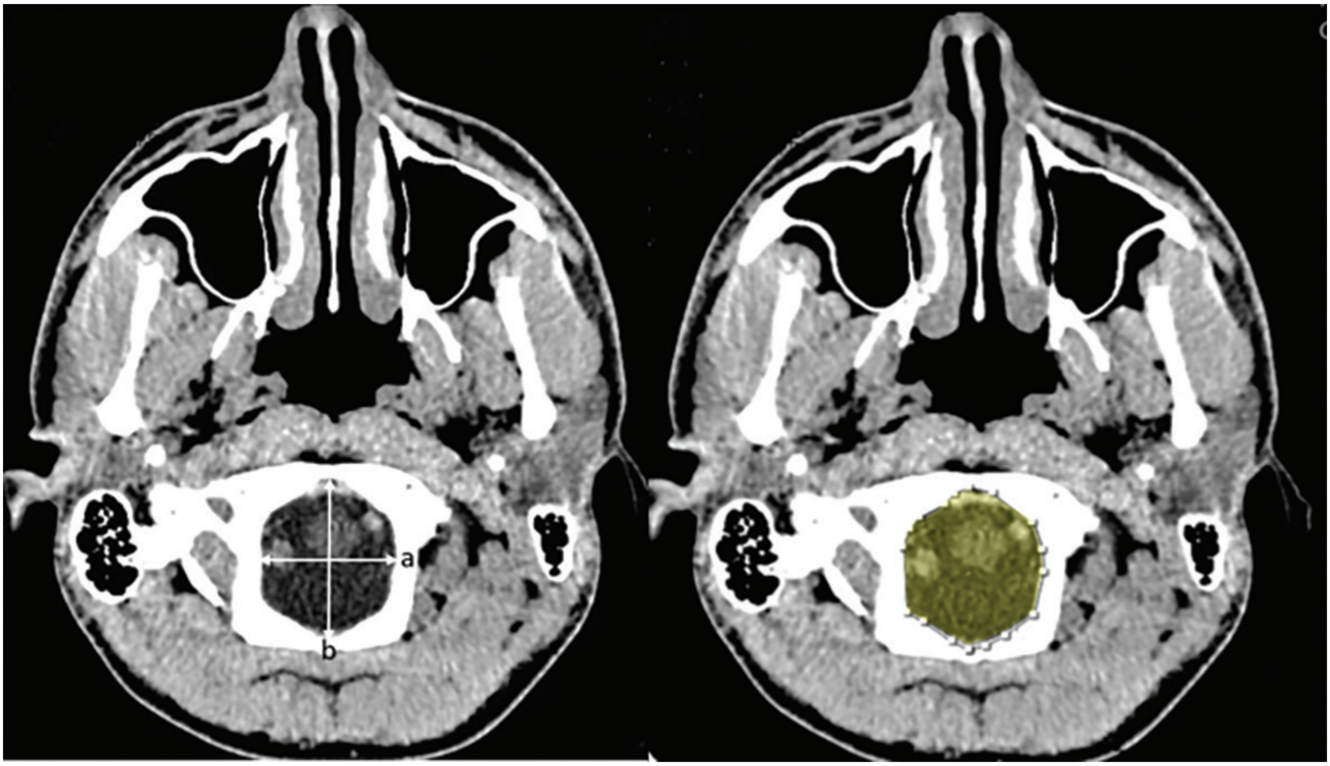

Figure 1. Transverse diameter or width (a), sagittal diameter or length (b) and area of FM.

Calculation of FM Area

In the equations of Teixeira and Radinsky methods used in FM area calculation in the literature (Teixeira's formula: $A= \pi*\{(a+b)/4\}^2$ Radinsky's formula: $A= (1/4*\pi*a*b)$ the area formula of the circle (πr^2) was used.

FM Shapes

The different shapes of the FM were macroscopically noted and classified as two semicircle, oval, round, egg, tetragonal, pentagonal, hexagonal, drop, and irregular shapes. The shapes were determined after the discussion with team of three members in order to avoid observational bias. The number and incidence of each shape type in the studied skull was registered and tabulated according to the sex (Table 3).

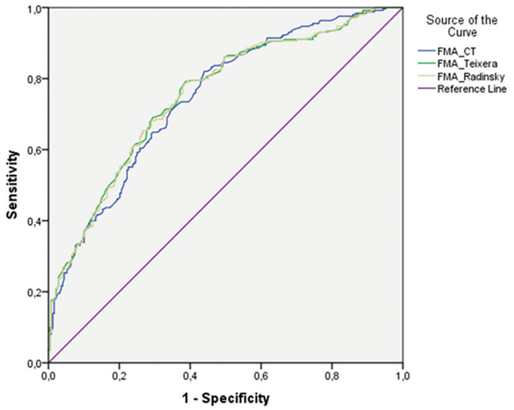

Figure 1. ROC curve of FMA in sex determination.

Table 1. FMA of the three methods

	Mean±SD
FMA^{CT}	716.50±110.15
FMA^{T}	777.89±101.95
FMA^{R}	772.46±101.80
P^{CT-T}	*0.000*
P^{CT-R}	*0.000*
P^{T-R}	*0.000*

FMA: Foramen magnum area, CT: computed tomography, T: Teixeira, R: Radinsky.

Statistical Analysis

Statistical analyzes of the study were performed using the Statistical Package for Social Sciences version 25.0 for Windows software (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp., USA). Normality assumption for quantitative variables was tested with Kolmogorov-Smirnov and Shapiro-Wilk tests. The effects of FMAs calculated according to 3 different FMA calculation methods, which are the subject of the study, on estimating sex were examined using logistic regression analysis. Hosmer-Lemeshow test was used for regression model fit in logistic regression analysis. ROC curve analysis was used to determine whether the FMA variable, which contributed significantly to the model as a result of the logistic regression analysis, has a diagnostic value in the estimation of sex. In all statistical analyzes, cases with a P value below 0.05 were interpreted as statistically significant.

RESULTS

The study was conducted on CT images of 493 patients. 248(50.3%) of the patients were female and 245(49.7%) were male. The mean age of the patients was 45.83±17.50 (18.0-82.0) years. Values of FMAs calculated with three different methods are given in

Table 2. FMA by Sex

Sex	n	FMA^{CT}	FMA^{T}	FMA^{R}	P^{CT-T}	P^{CT-R}	P^{T-R}
Female	248	670.27±91.53	733.48±83.54	728.40±83.66	0.000	0.000	0.000
Male	245	763.28±107.76	822.84±99.30	817.05±99.20	0.000	0.000	0.000
P		0.000	0.000	0.000			

FMA: Foramen magnum area, CT: computed tomography, T: Teixeira, R: Radinsky.

Table 3. Distribution of FM shapes by sex

FM Shapes	N(%)	Female, n(%)	Male, n(%)	*P*
Drop Shaped	30 (6.1)	14 (46.7)	16 (53.3)	0.020
Egg Shaped	20 (4.1)	11 (55.0)	9 (45.0)	
Hexagonal	72 (14.6)	33 (45.8)	39 (54.2)	
Irregular	70 (14.2)	33 (47.1)	37 (52.9)	
Oval	39 (7.9)	19 (48.7)	20 (51.3)	
Pentagonal	24 (4.9)	17 (70.8)	7 (29.2)	
Round	48 (9.7)	20 (41.7)	28 (58.3)	
Tetragonal	68 (13.8)	47 (69.1)	21 (30.9)	
Two Semicircle	122 (24.7)	54 (44.3)	68 (55.7)	

Table 1. According to Table 1, statistically significant differences were found between FMA measured by CT, FMA calculated with Teixeira and Radinsky formulae ($P<0.01$). The area measured by CT was smaller than the areas calculated by Teixeira and Radinsky methods ($P<0.01$). The FMA calculated with the Teixeira method was found to be larger than the FMA calculated with the Radinsky method ($P<0.01$). The results of the effect of the sex factor on FMA are given in Table 2. According to these results, the difference between the sexes in terms of FMA calculated by CT, Teixeira and Radinsky methods is statistically significant ($P<0.01$). In all three FMA calculation methods, male FMAs were calculated larger than females. FMA is an effective factor that can be used in sex determination in anthropological and forensic medical studies.

When the areas given by 3 different methods used in the calculation of FMA are compared within each sex, the difference between the areas calculated by 3 different methods in both males and females is statistically significant ($P<0.01$). In both sexes, the smallest area is calculated by CT, while the largest area is calculated by the Teixeira method.

A significant relationship was found between FM shapes and sex ($P<0.05$). In Table 3, the number of observations regarding the sex and FM shapes are given. According to these results, egg-shaped, pentagonal and tetragonal shapes are more common in female, and drop, hexagonal, irregular, oval, round and two semicircle FM shapes are more common in male (Table 3).

The results of the logistic regression analysis are given in Table 4. The percentage correct values of the logistic regression models were calculated as CT=89.4%, T=78.8, R=79.2, respectively. According to the Hosmer and Lemeshow test score, the value of correctly predicting sex is quite good in all three logistic regression models ($X\_CT^2=9.759, P>0.05; X\_T^2=12.335, P>0.05; X\_R^2=7.519, P>0.05$). When the odds ratios (OR) are examined, 1 mm^2 increase in FMA calculated by CT increases the probability of the skull to belong to a male 1.010 times (OR: 1.010, CI: 1.007-1.012, $P<0.01$). The 1 mm^2 increase in FMA calculated by Teixeira increases the probability that the skull belongs to a male 1.011 times (OR: 1.01, CI: 1.008-1.013, $P<0.01$). Similarly, a 1 mm^2 increase in FMA calculated by the Radinsky method increases the probability that the skull belongs to a male 1.011 times (OR: 1.011, CI: 1.009-1.012, $P<0.01$). According to logistic regression analysis results, FMA values were found to be statistically significant in estimation of sex in all three calculation methods ($p<0.05$).

As a result of the logistic regression analysis with FMA values calculated by all three FMA calculation techniques, it was determined that FMA values are an important predictor in estimating sex. In order to determine whether FMA has a diagnostic cut-off value in sex determination, ROC analysis was performed for three FMA calculation methods. As a result of the evaluation with ROC analysis, it was determined that FMA obtained by three methods has diagnostic value in sex determination. When the ROC curve given in Figure 2 is examined, it is seen that the area under the curve is statistically significant for all three FMA calculation methods. As seen in Figure 2 and Table 5, when 688.5 mm^2 is taken as the cut-off point among the FMA values determined by CT (sensitivity: 71.4% and specificity: 65.0%), it is understood that the FMA variable has a diagnostic value in sex determination. The cut-off point value for Teixeira's FMA formula is 767.8 mm^2. The sensitivity (71.0%) and specificity (68.0%) values of this cut-off value also show that the area value obtained from

Table 4. Results of logistic regression analysis

VARIABLES	β	Sig.	Odds Ratio	95% C.I. for Exp (β) Lower	Upper	Percentage Correct	Hosmer and Lemeshow	*P*
FMA^{CT}	0.009	0.000	1.010	1.007	1.012	89.4	9.759	0.282
FMA^{T}	0.011	0.000	1.011	1.008	1.013	78.8	12.335	0.137
FMA^{R}	0.012	0.000	1.011	1.009	1.012	79.2	7.519	0.486

FMA: Foramen magnum area, CT: computed tomography, T: Teixeira, R: Radinsky, Sig: Significant.

Table 5. Diagnostic performance assessment of FMA to predicts sex determination

Sex (ref: Male)	AUC±SE	95% CI	Sensitivity	Specificity	p	Cut-off value
FMA^{CT}	0.746±0.02	0.703-0.788	71.4	65.0	**<0.001**	>688.5
FMA^{T}	0.753±0.02	0.711-0.796	71.0	68.0	**<0.001**	>767.8
FMA^{R}	0.752±0,02	0.710-0.795	72.0	66.0	**<0.001**	>755.3

AUC: Area under the curve; SE: Standart Error; CI: Confidence Interval; CT: computed tomography, T: Teixeira, R: Radinsky.

the FMA formula of Teixeira has a diagnostic value in determining sex. The cut-off point value for the area value obtained from Radinsky's FMA formula is 755.3 mm^2. The sensitivity (72.0%) and specificity (66.0%) values of this cut-off value also show that the area value obtained from the Radinsky FMA formula has a diagnostic value in determining sex. According to the ROC analysis results, the cut-off values obtained in all three FMA calculation methods are effective in sex determination.

DISCUSSION

Biological sex determination is an important aspect of forensic research in identifying unknown skeletal remains. Where remains are missing or compromised by damage or fragmentation, this can affect the accuracy of sex determination and requires the development of reliable techniques using isolated bone elements. The FM is ideal for use in the development of sex criteria due to the increased probability of survival of the region resulting from the robustness of the occipital bone and the protective anatomical position of this feature [22].

This study utilized CT scanning data acquired to analyze the FMA and shape in a sample population of 493 adult individuals. Sexual dimorphism was assessed calculating cut-off values in the area measurements using binary logistic regression and ROC analysis. Visual observations were made of the morphological shape of FM.

Variability in the size and shape of FM and their relation to sex have been described by many studies in the literature [2-4, 11-20, 22]. In a recent study of sex estimation from foramen magnum sizes in an eighteenth - and nineteenth-century British sample, Gapert *et al.* [13] showed statistically significant differences between male and female skulls using discriminant function and regression analysis. However, the discriminant functions developed in the study predicted the correct sex in 70.3% of all cases. Gapert *et al.* [13] thus concluded that the expression of sexual dimorphism in the FM region, though statistically significant, is limited. Günay and Altınkök [16] observed that the mean FMA in females was significantly lower than in males. Their findings on this subject are similar to our observation in our study. However, based on the correlation coefficient analysis, they concluded that domain is not a useful indicator for sex estimation and can only be used as a supporting finding. In a study of Uthman *et al.* [23] FM dimensions, area and circumference were statistically analyzed using discriminant analysis and multiple regression analysis. They were stated that the FMA was the best discriminating parameter for sex determination with an overall accuracy of 69.3%. In another study, Kanchan *et al.* reported that the FMAs calculated by Radinsky's and Teixeria's formulae are better predictors of sex than the sagittal and transverse dimensions using *t*-test to analyze the significance [24]. Edwards *et al.* [22] analyzed CT scans of 250 Swiss ethnic group adults to determine the value of foramen magnum dimensions in sex determination. Statistical analysis revealed 66% accuracy in determining cranial sex by discriminant function analysis, and the Binary Logistic Regression (BLR) showed an overall classification rate of 66.4%.

A study similar to the present one in Indian population by Raghavendra Babu *et al.* [12], BLR analysis was performed to derive models for estimation of sex from the different measurements of FM and Receiver Operating Characteristic (ROC) curve was drawn for the predicted probabilities obtained from BLR analysis. They stated that the predictability of FM measurements in sexing of crania was 65.4% for transverse diameter and 86.5% for the anteroposterior diameter. For FMA that was calculated using the formula derived by Radinsky and Teixeira, the area under curve were observed to be 0.816 and 0.822 respectively. However, despite such a possibility, the authors conclude that the potential for sexing is limited due to significant overlapping of male and female values. Their findings show that statistically significant differences exist between the areas estimated using formulae derived by Radinsky and Teixeira, area calculated from the formula used by Teixeria being significantly larger than that estimated using Radinsky's formula. Our findings in this regard are similar to that shown in the study of Raghavendra Babu *et al.* [12]. In a study of Kamath *et al.* [17] in 2015, area estimation was made using two formulae, Radinsky's and Teixeira. In the study, although the area values obtained with the Teixeira formula were higher than those obtained with the Radinsky formula, the area under the curve was observed as 0.703 for both areas in the statistical analyzes made with ROC. In the current study the area under curve obtained from ROC analysis of FMA measurements in sexing of crania to be CT=0.746, Teixeira=0.753 and Radinsky=0.752.

In some studies, morphological variations of the FM have also been investigated in sex determination [25, 26]. Natsis *et al.* [25] documented a statistical difference between males and females. They observed the egg-shape as most common in males (23.4 %) whilst the two-semicircle shape was most common in females (33.3 %). Similar research was reported by

Burdan *et al.* [26] in Poland as the wide-oval shape was most common in both males and females. In the present study, the morphology of the FM was classified by visual assessment into nine shape types. Egg-shaped, pentagonal and tetragonal shapes are more common in female, and drop, hexagonal, irregular, oval, round and two semicircle FM shapes are more common in male.

In the present study, unlike the studies in the literature, cut-off values were created for sex determination, and these values were created both for the areas obtained from the formulae of Radinsky and Teixeira and for the automatic CT area calculation method. In addition, sex determination by automatic CT area measurement method for FM was applied for the first time in our study in the literature. The current study performed a large-scale analysis of 493 adult individuals, increasing the reliability of the cut-off values we created. Percentage classification of high accuracies were obtained from our study population indicating high level of sexual dimorphism in the crania, setting specific cut-off values for the sex determination in Turkish population.

Since the sex determination using morphometric analysis depends on numerical values, in case of any unidentified skull the first and foremost step will be to identify the source population of the skull and cut-off values specific for that population group only should be used in sex determination. The data of the present study will be of use in forensic science and anthropology and for further studies on population data and serve as a future framework for sex determination using craniometric parameters in Turkish population.

Conflict of interest

The authors declare that they have no conflict of interest.

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