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Title: Sex estimation by morphometric analysis of the intracranial volume and foramen magnum on three-dimensional volume rendering computed tomography.

Short title: Intracranial volume and foramen magnum analysis for sex estimation: 3D modelling.

Abstract

Purpose: Identification of decomposed human bodies and bone remains is very important in medicolegal examinations. The cranium has an important place in sex estimation due to its dimorphic features. Recent studies in this field have used radiological methods. The present study aimed to examine sexual dimorphism through morphometric analysis of the intracranial volume and Foramen Magnum on Three-Dimensional (3D) Volume Rendering Computed Tomography (CT) images.

Materials and methods: For this purpose, 3D images were generated after the reconstruction of CT Angiography scans of 87 female and 107 male cases. The length, width, circumference, area, and intracranial volume of the foramen magnum were measured on these 3D images.

Results: All measurements except foramen magnum index were greater in males than in females ($p < 0.05$). The single best sex-discriminatory measurement was intracranial volume, with an accuracy rate of 84.5%. The best sex-discriminatory parameter in foramen magnum measurements was the length of the foramen magnum, with a rate of 74.2%. Intracranial volume was positively correlated with foramen magnum parameters in males ($p < 0.05$).

Conclusion: Three-dimensional volume rendering CT images showed sexual dimorphism in the intracranial volume and foramen magnum. The use of radiological methods in forensic investigations may allow for examinations of decomposed human bodies without the need for maceration procedures. It may also help create databases by examining population-specific differences in today's societies.

Keywords: Volume rendering CT, 3D modeling, foramen magnum, intracranial volume, sex estimation.

Makale başlığı: Volume rendered bilgisayarlı tomografi görüntülerinde intrakranial hacim ve foramen magnum morfometrik analizinden cinsiyetin değerlendirilmesi.

Kısa başlık: Cinsiyet tahmini için intrakranial hacim ve foramen magnum analizi: 3B modelleme.

Öz

Amaç: Medikolegal incelemelerde çürümüş cesetlerde ve kemik kalıntılarında kimliklendirme çok önemlidir. Kranium dimorfik özelliklere sahip olduğu için cinsiyet tahmininde önemli yer tutar. Son zamanlarda bu alandaki araştırmalarda radyolojik yöntemlerin kullanıldığı görülmektedir. Bu çalışmada Volume Rendered Bilgisayarlı Tomografi 3B görüntülerinde intrakranial hacim ve Foramen Magnum morfometrik analizinden seksüel dimorfizmin araştırılması amaçlanmıştır.

Gereç ve yöntem: Bu amaçla 87 kadın ve 107 erkek olguya ait BT Anjiyografi görüntülerinden rekonstrüksiyon sonrası üç boyutlu (3B) görüntüler elde edilmiştir. Elde edilen görüntülerde foramen magnum uzunluğu, genişliği, çevresi, alanı ve intrakranial hacim ölçülmüştür.

Bulgular: Foramen magnum indeksi dışındaki tüm ölçümlerin erkeklerde kadınlarda daha büyük olduğu görülmüştür ($p<0,05$). Cinsiyeti tek başına en iyi ayırt eden ölçüm %84,5 doğruluk oranı ile intrakranial hacimdi. Foramen magnum ölçümlerinde cinsiyeti en iyi ayırt eden parametre ise %74,2 oranı ile foramen magnum uzunluğuydu. İntrakraniyal hacim erkeklerde foramen magnum parametreleri ile pozitif bir korelasyon gösterdi ($p<0,05$).

Sonuç: Volume rendered BT 3B görüntülerinde intrakranial hacim ve foramen magnumda cinsel dimorfizm olduğu görülmüştür. Radyolojik yöntemlerin adli incelemelerde kullanılması çürümüş cesetlerde maserasyon işlemlerine gerek kalmadan incelemelerin yapılmasına olanak sağlayabilir. Ayrıca günümüz toplumlarındaki popülasyona özgü farklılıkların araştırılarak veri tabanlarının oluşturulmasına yardımcı olabilir.

Anahtar kelimeler: Volume rendering BT, 3B modelleme, foramen magnum, intrakranial hacim, cinsiyet tahmini.

Introduction

Sex estimation in human skeletal remains in forensic anthropology studies is extremely important for identification and medicolegal studies. Since body and bone fragments with lost integrity will be encountered especially in mass disasters and explosions, identification of these bone fragments will be required. The assessment of the skull, which has dimorphic features, using morphometric and morphological methods has an important place in sex estimation. The skull base of the cranial skeleton in the occipital bones is the most resistant to physical and environmental factors due to its anatomically preserved localization. The Foramen Magnum (FM) in this region is a suitable anatomical region for forensic anthropological studies [1-3]. It was first reported by Teixeira in 1982 [4] that FM could be used for sex estimation. Several studies found FM dimensions to differ significantly in sex estimation [5-8].

Since the intracranial volume shows sexual dimorphism, it is an important parameter used in identification [9-11]. It also helps in the assessment of growth and development and the examination of cranial pathologies [12]. The intracranial volume is assessed using anthropological methods such as linear dimensions and packing method or radiological methods [12-14].

In forensic anthropology, imaging methods such as computed tomography (CT) may be useful, especially in decomposed human bodies, as it allows for the examination of bone tissues without the need for maceration. Three-dimensional (3D) reconstruction of bony structures can be made, especially on volume-rendering CT images. This enables 1:1 landmark measurements and other morphometric and morphological examinations in bony structures [15-19]. A comparative study by Franklin et al. [20] demonstrated that direct bone measurements and 3D volume rendering CT imaging-derived measurements were concordant and there was no statistically significant difference.

A limited number of studies evaluated foramen magnum measurements and intracranial volume on 3D volume rendering CT images [21-23]. The present study aimed to examine sexual dimorphism through morphometric analysis of the intracranial volume and FM on 3D volume-rendering CT images.

Materials and methods

This study was initiated following the granting of approval by the ethics committee for non-interventional clinical research. All patients who had cranial CT angiography at the Radiology Department of the Medical Faculty between January 2017 and December 2018 were evaluated in our study. Among these cases, after excluding those under the

age of 18, with motion artefacts, head traumas and bone pathologies, 194 cases remained were included in the study.

CT angiography scans were acquired by a 16-detector MSCT device (Brilliance CT 16 V2.00 Philips Medical Systems, Cleveland, OH) with 1 mm thickness. These images in the archive were reuploaded to the standard workstation (MxViewexp; release 4.01; Philips Medical Systems) and three-dimensional images were generated after reconstruction.

On the three-dimensional images, the skull was rotated horizontally to get an en face view of the foramen magnum, and the maximum length (anteroposterior diameter) and the maximum width of the foramen magnum (transverse diameter) were measured. The distance between the basion and the opisthion was used for the maximum length of the foramen magnum (LFM). The largest distance between the lateral margins of the foramen magnum was measured for the maximum width of the foramen magnum (WFM) (Figure 1). In the same imaging plane, the entire contour of the foramen magnum was drawn using the manual segmentation method in such a way that it would not protrude into the surrounding bone tissue and be the widest, and the area (FMA) and circumference (FMC) of the foramen magnum were determined. The maximum length, maximum width, circumference, and area of the foramen magnum were expressed in millimeters.

The following formula was used to calculate the Foramen Magnum Index (FMI): $FMI = (\text{Width} / \text{Length}) \times 100$

Volumetric measurement was made using IntelliSpace Portal 8.0 software on the workstation. The region of interest (ROI) was selected via the semi-automatic segmentation method, mainly using axial CT images, and then the entire intracranial volume was included using the region augmentation method (Figure 2). After observing that the ROI did not protrude into the bone tissue and completely filled the intracranial area in each axial section, a visual assessment was also performed in the sagittal and coronal planes, and improvements were made to the ROI contour when necessary. Following this process, the software automatically gave us the volume in cubic centimeters (cc).

All statistical analyses were conducted with SPSS 25.0 (IBM SPSS Statistics 25 software (Armonk, NY: IBM Corp.)). Continuous variables were defined by the mean \pm standard deviation, median (minimum – maximum values) and categorical variables were defined by frequencies and percent. Normal distribution was determined using the Kolmogorov-Smirnov test. For independent groups comparisons, Independent samples t test was used when parametric test assumptions were provided and Mann Whitney U

test was used when parametric test assumptions were not provided. Pearson correlation coefficient was used for investigating the relationships between continuous variables. We used Binary Logistic Regression Analysis and Linear Discriminant Analysis to test the power of predicting sex classification. Statistical significance was determined as $p < 0.05$.

Results

This study evaluated the foramen magnum morphometric parameters and intracranial volume on 194 “volume-rendering” CT scans from 87 females and 107 males. The mean values, minimum and maximum values, and standard deviation for the length, width, circumference, and area of the foramen magnum, the foramen magnum index, and the intracranial volume are presented in Table 1. The examinations revealed statistically significant differences in all variables between the sexes. In all measurements except the FMI, the values were statistically significantly higher in males than in females ($p < 0.01$). The FMI, in turn, was significantly higher in females than in males ($p < 0.05$).

In females, there was no statistically significant association between intracranial volumes and other study variables. In males, in turn, intracranial volumes had a statistically significant moderate positive correlation with all variables, except for the FMI (Table 2).

In both females and males, the LFM had a statistically significant positive correlation with the WFM, FMA, and circumference and a statistically significant negative correlation with the FMI (Table 2).

In both females and males, the WFM had a statistically significant positive correlation with the FMA, circumference, and FMI (Table 2).

In both females and males, the FMA had a statistically significant positive correlation with the circumference. While the FMA had a statistically significant positive correlation with FMI in females, such correlation was not statistically significant in males (Table 2).

The results of the discriminant analysis for the intracranial volume and the parameters of the foramen magnum showed that the variable with the highest success in sex discrimination was intracranial volume. It was followed by LFM, circumference, FMA, and WFM, respectively. The FMI had the lowest rate of accuracy (Table 3).

The results of the classification according to the logistic regression model using intracranial volume and foramen magnum measurements revealed that the most effective variable in sex estimation was intracranial volume, with a rate of 84.5%. It was followed by LFM (74.2%), circumference (70.1%), FMA (68%), and WFM (64.9%), respectively, while the least effective variable was FMI, with a rate of 61.3% (Table 4).

Discussion

In cases where the entire skeleton is not available, sex can be estimated using dimorphic features of the cranial bones. The sexual dimorphism-associated features of bones are affected by genetic, social, and environmental factors and are population-specific [24]. With new technologies, radiological methods are quite commonly used in skeletal sex estimation studies. Radiological methods are useful tools in detecting population-specific differences in modern societies, as they also allow research in living populations with known variables such as gender, age, geographical origin, and diseases [24]. Moreover, it allows morphometric measurements on radiological images without the need for maceration procedures in decomposed human bodies in forensic medicine and forensic anthropology practice [24, 25]. Since three-dimensional images of bones can be generated from reconstructed images in volume-rendering CT, measurements can be made as if working on real bones.

The present study determined that all parameters of the foramen magnum differed significantly between the two sexes at the measurements on 3D volume-rendering CT scans of the cranium. In all measurements except the FMI, the values were statistically significantly higher in males than in females. This finding is consistent with most of the previous studies [7, 22, 25-32]. However, some authors reported no sexual dimorphism in FML and FMW [6]. The studies by Meral et al. [29] and Chovalopoulou and Bertsatos [30] did not observe sexual dimorphism in the FM index.

Our study found that the length, circumference, area, and width of the foramen magnum estimated sex with an accuracy rate of 74.2%, 70.1%, 68%, and 64.9%, respectively. The study by Uysal et al. [33] using 3D CT reported that the foramen magnum estimated sex with an accuracy rate of 81%. The study by Tambawala et al. [34] using cone-beam CT (CBCT) established that the sex discriminatory power of FM measurements was 70.3% in males and 62.6% in females, with a mean of 66.4%. In an Iraqi population, Uthman et al. [26] reported an accuracy rate of 81.8% for foramen magnum parameters in sex estimation. Meral et al. [29] reported that the best sex-discriminatory parameter was the FM area (calculated by Radinsk'y formula) with a rate of 74.5% and the rate of accurate sex estimation was 75% when multiple parameters were used.

In this study, the mean FML and FMW were 35.69 mm and 30.12 mm in males, and 32.81 mm and 28.27 mm in females, respectively. A CT study by Toneva et al. [28] in a Bulgarian population reported that the mean FML and FMW were 36.63 mm and 31.47 mm in males, and 35.19 mm and 29.25 mm in females, respectively. A CBCT study by

Akay et al. [25] in a Turkish population found the sagittal and transverse diameters and FMC to be statistically significantly higher in males than in females. The reported mean FML and FMW were 36.43 mm and 31.26 mm in males, and 34.66 mm and 29.78 mm in females, respectively [25]. A CT study by Meral et al. [29] in a Turkish population reported that the mean FML and FMW were 37.54 mm and 32.75 mm in males, and 34.76 mm and 29.98 mm in females, respectively. A 3D volume rendering CT study by Abdel Karim et al. [22] reported that the mean FML and FMW were 42.17 mm and 33.98 mm in males, and 38.75 mm and 31.38 mm in females, respectively. The study by Jain et al. [32] in an Indian population, reported that the length and width were 31.3 mm and 36.2 mm in males, and 28.3 mm and 34 mm in females. The study by Gapert et al. [31] in a British population found the length and width of the FM to be 35.91 mm and 30.51 mm in males, and 34.71 and 29.36 mm in females, which is consistent with our study. The study by Uthman et al. [26] found the length and width to be 34.9 mm and 29.5 mm in males, and 32.9 and 27.3 mm in females, which is consistent with our study.

In our study, FMA and FMC were calculated automatically. The mean FMC was 113.63 mm in males and 105.98 mm in females, respectively and the FM area was 808.4 mm² in males and 705.83 mm² in females. The study by Akay et al. [25] reported the mean FMC as 107.94 mm in males and 102.67 mm in females. The study by Ilguy et al. [35] found the mean FMC to be 108.10 mm in males and 102.21 mm in females. The study by Bayrak and Goller Bulut [36] reported the mean FMA as 906.05 mm² in males and 850.07 mm² in females. Meral et al. [29] found that the mean FMA, which was calculated by the Radinsk'y formula, was 967.66 mm² in males and 820.49 mm² in females. Toneva et al. [28] in turn, found the FMA to be 851.60 mm² in males and 763.64 mm² in females. Our results for FMA and FMC are lower than those reported in the literature. These differences in mean foramen magnum dimensions may be due to population-specific differences and/or different anatomical and radiological methods used in studies.

Meral et al. [29] identified the strongest correlations between LFM and FMA and between WFM and FMA in males and females. Tambawala et al. [34] found the strongest correlations between Area 1 (Routal formula) and Area 2 (Teixerra formula). Uthman et al. [26] established the strongest correlations between FMC and FMA in males and females. In our study, on the other hand, the length and width of the foramen magnum were strongly correlated with both area and circumference in males and females.

There are studies in the literature reporting the measurement of intracranial volume on CT scans [21, 37]. Our study measured intracranial volume on 3D volume-rendering CT scans and found a higher mean intracranial volume in males than in females. These

results are consistent with those reported by other studies in the literature [9-11, 38-41]. The sex estimation rate of intracranial volume alone was 84.5%. A comparison of our results on intracranial volume with various studies is presented in Table 5. It is believed that the differences in the mean values may result from the methods used and the population-specific differences. The present study identified a statistically significant positive correlation between intracranial volume and foramen magnum parameters (except FMI) in males. Gapert and Last [42] demonstrated that endocranial capacity was significantly correlated with LFM, FMA, and FMC. Shepur et al. [43] and Acer et al. [10] reported a significantly positive correlation between endocranial capacity and the area of the foramen magnum.

In conclusion, according to the findings of our study, 3D volume-rendering CT images allow the measurement of foramen magnum parameters and intracranial volume. The foramen magnum parameters, except for FMI, had higher values in males than in females and may be useful in sex estimation since they show sexual dimorphism. Intracranial volume was higher in males than in females and was positively correlated with foramen magnum parameters. The use of radiological methods in medicolegal examinations will provide advantages such as the examinations of decomposed human bodies without the need for time-consuming maceration procedures. Due to the archival storage of the DICOM digital data, examinations can be performed easily when re-assessment is required. The transfer of 3D volume-rendering CT images or the transfer of DICOM digital data will enable performing morphometric analyses after the 3D modeling of these data. Thereby, cases where the skulls cannot be transferred to other centers or where the experts in the field cannot be immediately available will be easily resolved. Furthermore, it will help to create databases by examining population-specific differences in today's societies and to use such data for sex estimation in forensic investigations, as it allows studying in the cranium of living people with known gender, age, and medical history.

Conflict of interest: No conflict of interest was declared by the authors.

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Ethical approval: Permission was obtained from xxxxxxxx University xxxxxxxxxxxx Ethics Committee for the study (27.10.2020- E-60116787-020-3505). All procedures performed in studies were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Authors' contributions to the article

A.K.D. and K.A. constructed the main idea and hypothesis of the study. E.S. and A.H.Ö. developed the theory and arranged/edited the material and method section. A.K.D, H.Ş. and A.A. have done the evaluation of the data in the Results section. Discussion section of the article written by A.K.D. K.A. reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.

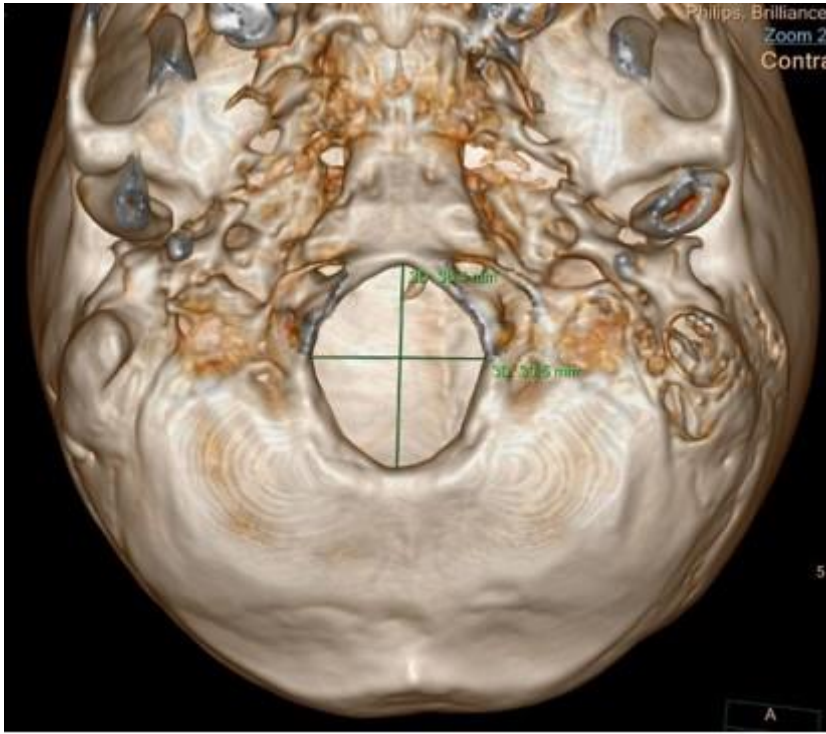


Figure 1. Measurement of foramen magnum dimensions on a three-dimensional volume rendering CT image of the skull base

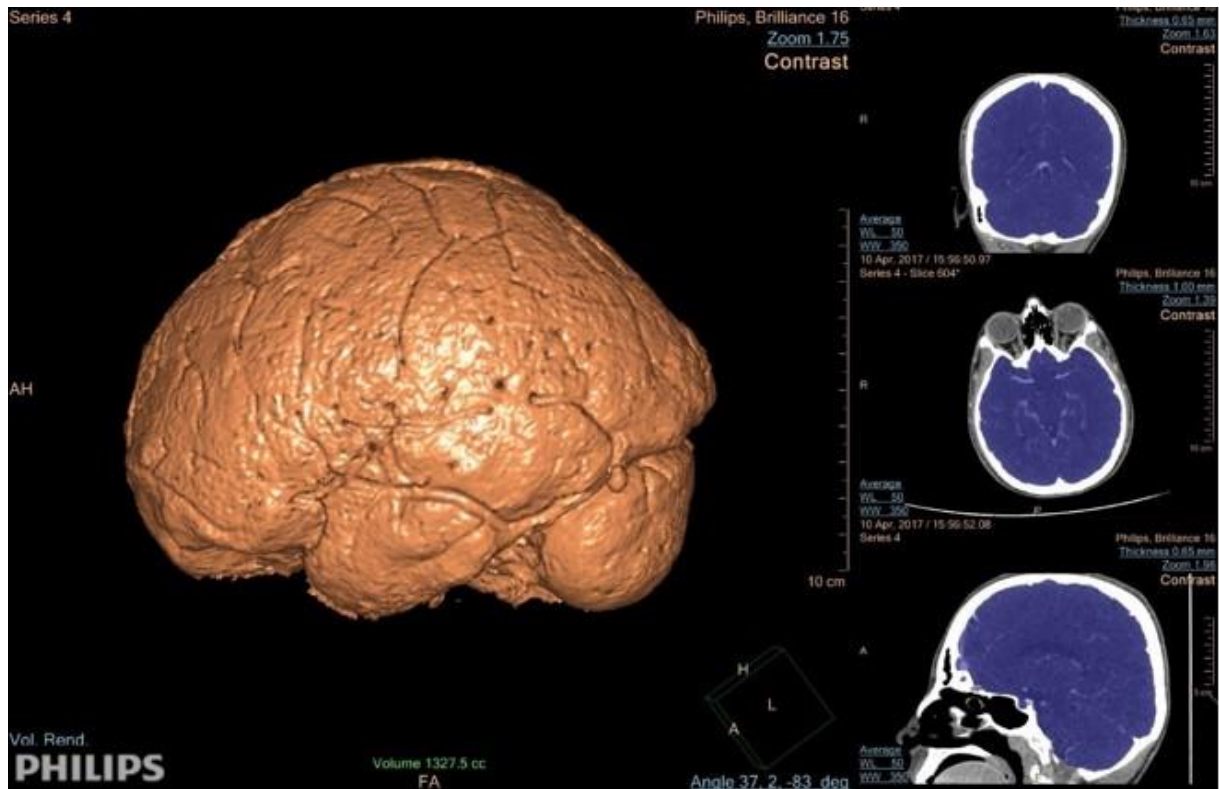


Figure 2. The entire intracranial space is marked in purple on coronal, axial, and sagittal CT images from top to bottom on the right, through the semi-automatic segmentation method. The measurement data and the three-dimensional image of the selected volume are displayed on the left

Table 1. Comparison of foramen magnum parameters and intracranial volume by sex

		Total (n=194)	Female (n=87)	Male (n=107)	<i>p</i>
Intracranial volume	Mean±S.D.	1374.71±159.09	1263.77±110.26	1464.91±133.8	0.0001*
	Med (min-max)	1371.3 (937.2-2025.5)	1263.2 (1000.9-1504.6)	1460.8 (937.2-2025,5)	(z=-9.54)
LFM	Mean±S.D.	34.4±2.69	32.81±2.19	35.69±2.35	0.0001*
	Med (min-max)	34.15 (28.5-42)	32.8 (28.5-37.8)	35.9 (29-42)	(t=-8.73)
WFM	Mean±S.D.	29.29±2.52	28.27±2.36	30.12±2.34	0.0001*
	Med (min-max)	29.15 (23.3-37.5)	28.4 (23.3-35)	30.1 (24.3-37.5)	(t=-5.46)
FMA	Mean±S.D.	762.64±123.99	705.83±109.85	808.84±115.76	0.0001*
	Med (min-max)	767.95 (468.4-1170.4)	712.6 (468.4-951.5)	799 (519-1170.4)	(t=-6.30)
FMC	Mean±S.D.	110.2±9.26	105.98±8.82	113.63±8.16	0.0001*
	Med (min-max)	110.1 (87.3-141.9)	106.2 (87.3-128.4)	114.3 (93-141.9)	(t=-6.25)
FMI	Mean±S.D.	85.3±5.86	86.26±6.07	84.51±5.58	0.038*
	Med (min-max)	85.27 (69.33-98.84)	85.76 (74.6-97.61)	84.51 (69.33-98.84)	(t=2.087)

LFM, maximum length of foramen magnum; WFM, maximum breadth of foramen magnum; FMA, foramen magnum area; FMC, foramen magnum circumference; FMI, foramen magnum index; SD, standart deviation

**p*<0.05. t: Independent samples t test; z: Mann Whitney U test

Table 2. Correlations between the intracranial volume and the parameters of the foramen magnum

		Female					Male				
		LFM	WFM	FMA	FMC	FMI	LFM	WFM	FMA	FMC	FMI
Intracranial volume	<i>r</i>	0.068	0.180	0.178	0.042	0.151	0.411*	0.372*	0.363*	0.357*	0.032
	<i>p</i>	0.529	0.096	0.099	0.696	0.163	0.000	0.000	0.000	0.000	0.747
LFM	<i>r</i>	1	0.576*	0.743*	0.694*	-0.267*	1	0.585*	0.827*	0.681*	-0.320*
	<i>p</i>		0.000	0.000	0.000	0.013		0.000	0.000	0.000	0.001
WFM	<i>r</i>		1	0.851*	0.792*	0.632*		1	0.756*	0.733*	0.580*
	<i>p</i>			0.000	0.000	0.000			0.000	0.000	0.000
FMA	<i>r</i>			1	0.856*	0.296*			1	0.788*	0.050
	<i>p</i>				0.000	0.005				0.000	0.609
FMC	<i>r</i>				1	0.274*				1	0.163
	<i>p</i>					0.010					0.094

**p*<0.05 statistically significant correlation; *r*: Pearson Correlation Coefficient. LFM, maximum length of foramen magnum; WFM, maximum breadth of foramen magnum; FMA, foramen magnum area; FMC, foramen magnum circumference; FMI, foramen magnum index

Table 3. Results of the discriminant analysis for the intracranial volume and the parameters of the foramen magnum

	CCC	Wilks' Lambda	Predicted Group Membership (F/M)%	Total
Intracranial volume	0.63	0.603	80.5 / 87.9	164 (84.5%)
LFM	0.533	0.716	69 / 78.5	144 (74.2%)
WFM	0.367	0.866	54 / 73.8	126 (64.9%)
FMA	0.414	0.828	60.9 / 73.8	132 (68%)
FMC	0.412	0.831	59.8 / 77.6	135 (69.6%)
FMI	0.149	0.978	35.6 / 82.2	119 (61.3%)

CCC: Canonical Correlation Coefficient; Discriminant Analysis

Table 4. Logistic regression models using intracranial volume and parameters of the foramen magnum

		Wald	<i>p</i>	O.R.	95% C.I. for O.R.		CCP (%)
					Lower	Upper	
Univariate models	Intracranial_volume	47.483	0.0001*	1.015	1.011	1.019	84.5
	LFM	40.753	0.0001*	1.74	1.468	2.062	74.2
	WFM	22.694	0.0001*	1.412	1.225	1.627	64.9
	FMA	28.214	0.0001*	1.008	1.005	1.011	68
	FMC	27.807	0.0001*	1.116	1.072	1.163	70.1
	FMI	4.223	0.04*	0.949	0.903	0.998	61.3

**p*<0.05 statistically significant; O.R: Odds Ratio; C.I: Confidence Interval; CCP: Correct Classification Percent; Logistic Regression Analysis. LFM, maximum length of foramen magnum; WFM, maximum breadth of foramen magnum; FMA, foramen magnum area; FMC, foramen magnum circumference; FMI, foramen magnum index

Table 5. Comparison of the intracranial volume determined in our study with those reported by various studies

Population	Male (cm ³)	Female (cm ³)	Method	Reference
Nigerian Ibo	1298.44±90.67	1186.73±79.05	CT (Stereology)	Onwuzu
South India	1030.050±35.648	850.24±40.944	Skull	Rasidi
India	1367.3±127.8	1255.2±113.3	Skull	Shepur
	1347.1±90.7	1130±111.9	CT	
Korea	1470±107	1317±117	Skull	Hwang
Turkey	1474±93	1252±72	CT (point-counting)	Acer 2007
Turkey	1389.50±96.50	1134.5±94.30	Skull (Water filling)	Sahin 2007
Turkey	1382.5±104.5	1165.5±111.6	Skull (Water filling)	Emirzeoğlu M 2011
Turkey	1464.91±133.8	1263.77±110.26	CT	Present study

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