

Morphometric analysis and clinical significance of the os sacrum

 Ayşe Gül Kabakçı¹,  Gamze Taşkın Şenol²

¹Department of Anatomy, Faculty of Medicine, Çukurova University, Adana, Turkey

²Department of Anatomy, Faculty of Medicine, Bolu Abant İzzet Baysal University, Bolu, Turkey

Cite this article as: Kabakçı AG, Taşkın Şenol G. Morphometric analysis and clinical significance of the os sacrum. *J Med Palliat Care.* 2023;4(3):211-218.

Received: 03.04.2023

Accepted: 24.05.2023

Published: 28.06.2023

ABSTRACT

Aims: The purpose of this study is to assess the architecture and clinical importance of the sacrum, which features the dorsal and pelvic nerves.

Methods: 32 os sacrum of adult Anatolians of undetermined gender were measured for this investigation. Sacrum maximum length, os sacrum maximum width, sacrum I vertebral body antero-posterior width, sacrum I vertebral body transverse width, sacral index, Auricular surface short arm, auricular surface long arm and auricular surface oblique arm, the measurements of pelvic surface linea transverse length and, the measurements of dorsal surface linea transverse length and the sacrum height from the dorsal surface are evaluated.

Results: Sacrum maximum length 103.30±10.03 mm, sacrum maximum width 108.40±6.10 mm, sacrum I vertebral body transverse width 47.00±5.00 mm, sacrum I vertebral body antero-posterior width 28.30±3.50 mm, sacral index 104.00±9.00, Auricular surface short arm 31.90±4.20 mm, Auricular surface long arm 39.40±4.80 mm, Auricular surface oblique arm 49.10±6.00 mm, the length measurements of dorsal surface distance respectively as mm; 36.72±0.37, 29.75±0.31, 26.53±0.33, 26.56±0.39, the length measurements of dorsal surface distance respectively as mm; 29.16±0.36, 27.16±0.33, 24.50±0.26, 24.38±0.24 and the sacrum height from the dorsal surface as 103.4±9.70 mm were calculated.

Conclusion: Clinically stated, understanding the architecture of the sacrum and taking morphometric measures of it are crucial to avoiding difficulties and the surgical intervention that will be used to treat disorders associated to the sacrum.

Keywords: Anatomy, morphometry, sacrum

This study was presented as a poster presentation at the "Anthropology, Radiology & Anatomy Congress" held in Ankara University, Ankara between 12-13 November 2015.

INTRODUCTION

The five sacral vertebrae come together to form the huge triangular bone known as the os sacrum, which is located in the posterior upper portion of the pelvic cavity (cavitas pelvis). Above is its base (basis ossis sacri), and below is its apex (apex ossis sacri). Facies pelvica and facies dorsalis are the names of the sacrum's anterior and rear surfaces, respectively.¹⁻⁵ The lateral side of the os sacrum forms a "L"-shaped joint with the facies auricularis of the ilium. The promontorium, or base of the sacrum, protrudes anteriorly. The union of the processus transversus additionally forms the crista sacralis lateralis. The ala ossis sacri, which resembles a pair of wings, is visible on the upper portion of the crista sacralis lateralis. Additionally, the sacrum's posterior surface is convex and its anterior surface is concave. There are four transverse lines, or linea transversae, on the face of the os sacrum, also known as the facies pelvica, which connect the corpus vertebrae. The foramina sacralia pelvica, eight holes on the right and left sides of these lines contain the anterior branches of

the spinal nerves. Additionally, the aa. and vv. sacralis lateralis passes through these openings. The facies dorsalis refers to the dorsal surface of the os sacrum. There are eight foramina sacralia posteriora on the right and left posterior surfaces of the os sacrum, through which the posterior branches of the spinal nerves continue.^{4,6} Through the foramen intervertebrales, these holes join the canalis sacralis.⁷ In terms of protecting neural tissues during surgical interventions to this area and caudal anesthesia, foramina sacralia anteriora and foramina sacralia posteriora are clinically significant.⁸

The pelvic girdle has a solid joint system that allows weight to be transferred from the trunk to the lower extremities. The spine lumbalis transmits body weight to the os sacrum, which travels through the sacroiliac joint to the os coxae and os femoris.⁵ The number of bones that make up the sacrum can change in some circumstances.⁹ In the treatment of lumbosacral, sacral, and sacroiliac anomalies or injuries, the sacrum is a vital bone for

Corresponding Author: Gamze Taşkın Şenol, rumeysagamzetaskin@ibu.edu.tr



stability and fusion. Therefore, it is crucial to understand the complicated anatomical nature of the os sacrum before performing any surgery there. The architecture of the os sacrum must be understood to provide adequate fixation and prevent neurovascular damage.^{6,9-11}

This study, it is aimed to reveal the anatomical structure of the os sacrum with morphometric measurements and to emphasize its clinical importance. Thus, the results obtained in this study will guide clinical research and applications.

METHODS

Since the study was performed on dry bones, ethics committee approval is not required, institutional approval was obtained. All procedures were carried out in accordance with the ethical rules and the principles.

In this study, 32 pieces of dry bone os sacrum of unknown age and gender were measured. Partially broken, fragmented or damaged bones were excluded from the study. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. We measured maximum length of os sacrum, maximum width of os sacrum, anterior posterior width of os sacrum corpus vertebrae, transverse width of os sacrum corpus vertebrae, sacral index, facies auricularis short arm length, facies auricularis long arm length, facies auricularis oblique arm length, measurements of os sacrum facies pelvica, measurements of facies dorsalis and the height of the os sacrum on the dorsal (Figure 1-5). Measurements of os sacrum's includes facies pelvica length between foramina sacralia anteriora I, length between foramina sacralia anteriora II, length between foramina sacralia anteriora III, length between foramina sacralia anteriora IV parameters (Figure 5). In addition, the measurements of the facies dorsalis of the os sacrum are the length between foramina sacralia posteriora I, length between foramina sacralia posteriora II, length between foramina sacralia posteriora III, between foramina sacralia posteriora IV length parameters (Figure 1).

Measurement Design

Each bone was photographed from a distance of 100 cm under artificial light. The photographic system was set up by fixing the camera at a distance of 100 cm with an adjustable tripod. The tripod height was also positioned and fixed in accordance with the position of the bones. Photographs of dry bones were taken with a Digital SLR camera with fixed photo shooting settings (Canon EOS 80D; ISO 100 f/4.5) from the right-left, pelvic-dorsal side. The photos taken were transferred to the computer and uploaded to the Sketchup design program. The reference points of the parameters to be measured were determined and the length measurements were carried

out by drawing lines between the two reference points.

Measurements Parameters

Measurements of the dorsal surface (facies dorsalis) of the os sacrum (FDL1-4): The length between the right foramina sacralia posteriora and the left foramina sacralia posteriora was measured (Figure 1).¹¹

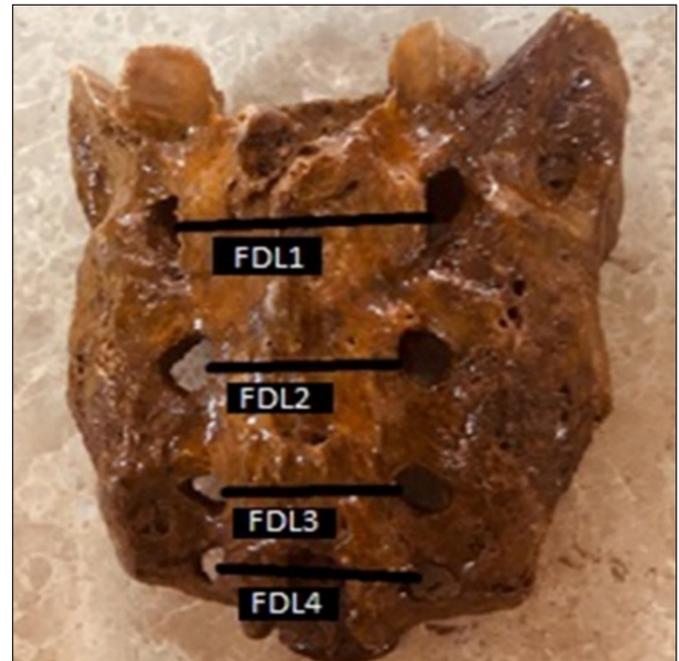


Figure 1. Measurements of os sacrum facies dorsalis (FDL1; length between foramina sacralia posteriora 1, FDL2; length between foramina sacralia posteriora 2, FDL3; length between foramina sacralia posteriora 3, FDL4; length between foramina sacralia posteriora 4).

Height of os sacrum (SH): The distance between the highest point of the crista sacralis media from the os sacrum facies dorsalis on the dorsal aspect and the cornu sacrale in the mid-sagittal plane was taken as reference.¹¹

Anterior-posterior width of the os sacrum corpus vertebrae (CVAPW): The anterior-posterior width of the corpus vertebrae of the os sacrum was measured (Figure 2).⁹

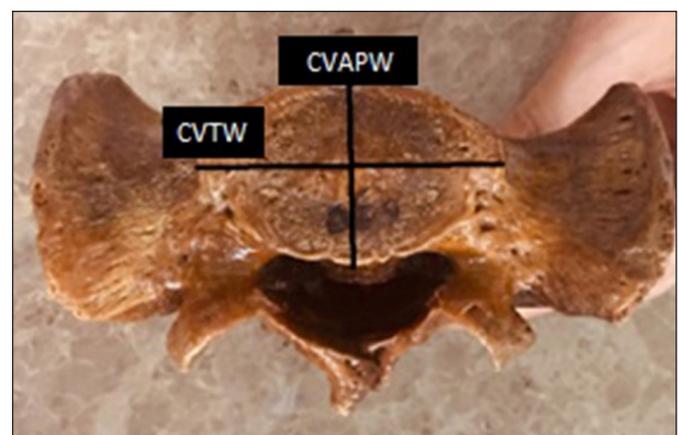


Figure 2. Measurements of os sacrum I corpus vertebrae (CVAPW; anterior posterior width of os sacrum corpus vertebrae, CVTW; transverse width of os sacrum corpus vertebrae).

Transverse width of the os sacrum corpus vertebrae (CVTW): The os sacrum corpus vertebrae was measured horizontally from right lateral to left lateral (Figure 2).⁹

Facies auricularis short arm length (SAL) of Os sacrum: Measurements were made from the right side and the distance from point A to point B was calculated (Figure 3).¹¹

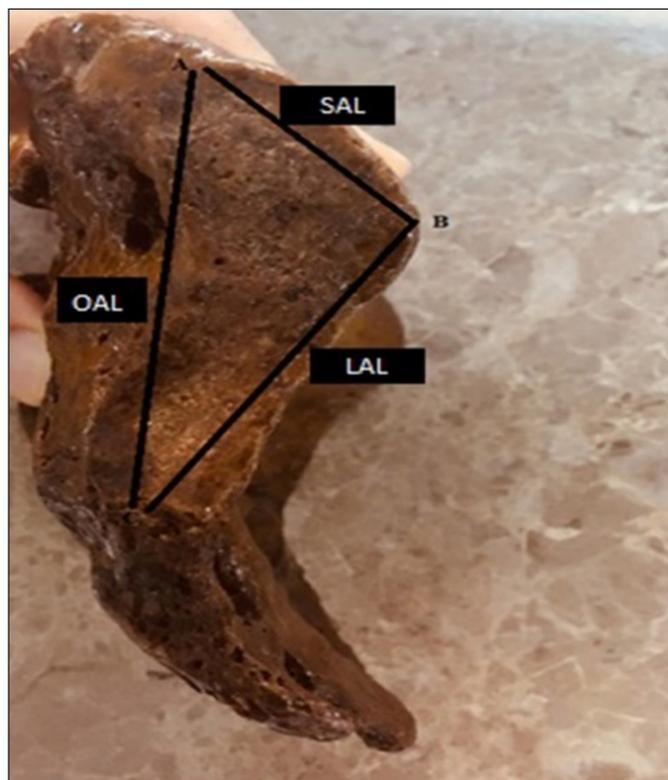


Figure 3. Measurements of facies auricularis of os sacrum (SAL; facies auricularis short arm length, LAL; facies auricularis long arm length, OAL; facies auricularis oblique arm length).

Facies auricularis long arm length (LAL) of Os sacrum: Measurements were taken from the right side and the distance from point B to point C was measured (Figure 3).¹¹

Os sacrum’s facies auricularis oblique arm length (OAL): Measurements were made from the right side and the distance from point A to point C was measured (Figure 3).¹¹

Maximum length of the os sacrum (SL): The distance between the promontorium and the lowest point of the anterior edge of the os sacrum was calculated in the mid-sagittal plane (Figure 4).¹²⁻¹⁴

Maximum width of os sacrum (SW): The distance between the most lateral right and left parts of the ala ossis sacri on the most upper part of the os sacrum facies auricularis from the anterior facies was measured (Figure 4).¹²⁻¹⁶



Figure 4. Length and width measurements of the os sacrum (SL; maximum length of os sacrum, SW; maximum width of os sacrum).



Figure 5. Measurements of os sacrum facies pelvica (FPL1; length between foramina sacralia anteriora 1, FPL2; length between foramina sacralia anteriora 2, FPL3; length between foramina sacralia anteriora 3, FPL4; length between foramina sacralia anteriora)

Sacral index (SI):¹²⁻¹⁴ Maximum width of os sacrum × 100

Maximum length of the os sacrum

Measurements of the os sacrum facies pelvica (FPL1-4): The length of the linea transversa between the right foramina sacralia anteriora and the left foramina sacralia anteriora was measured (Figure 4).¹¹

Statistical Analysis

The SPSS 22 package program was used for statistical analysis and statistically significant degree were considered as $p < 0.05$. Also, the normal distribution of the data distribution were identified by Skewness and kurtosis statistics (between +1.5 and -1.5). After statistical evaluation of the measurement results, mean (μ), standard deviation (σ), minimum (min.) and maximum (max.) values were calculated.

RESULTS

Our study includes the following findings; width of os sacrum, length of os sacrum, transverse width of os sacrum corpus vertebrae, sacral index, anterior posterior width of os sacrum corpus vertebrae, facies auricularis short arm length, facies auricularis long arm length, facies auricularis oblique arm length, length between foramina sacralia posteriora 1, 2, 3, 4, length between foramina sacralia anteriora 1, 2, 3, 4 and facies dorsalis height of os sacrum. The minimum, maximum, mean and standard deviation values of the linear measurements of 32 dry bone os sacrum are shown in **Table 1**. In addition, we compared the results of these parameters in our study with the literature findings (**Table 2**, **Table 3** and **Table 4**).

Table 1. Mean (μ), standard deviation (σ), minimum (min.) and maximum (max.) values of the measurements of os sacrum

Parameters (mm)	μ	σ	Minimum	Maximum
SW	108.40	6.10	91.50	120.00
SL	103.30	10.03	80.00	125.00
CVTW	47.00	5.00	37.00	56.00
CVAPW	28.30	3.50	21.50	35.00
SI	104.00	9.00	78.00	133.00
SAL	31.90	4.20	21.00	42.00
LAL	39.40	4.80	31.00	49.00
OAL	49.10	6.00	38.00	58.00
FDL1	36.72	0.37	28.0	40.3
FDL2	29.75	0.31	24.0	30.6
FDL3	26.53	0.33	22.0	30.3
FDL4	26.56	0.39	20.0	30.5
FPL1	29.16	0.36	23.0	30.6
FPL2	27.16	0.33	19.0	30.3
FPL3	24.50	0.26	20.0	30.0
FPL4	24.38	0.24	20.0	30.1
SH	103.40	9.70	82.0	126.0

SW; maximum width of os sacrum, SL; maximum length of os sacrum, CVTW; transverse width of os sacrum corpus vertebrae, CVAPW; anterior posterior width of os sacrum corpus vertebrae, SI; sacral index, SAL; facies auricularis short arm length, LAL; facies auricularis long arm length, OAL; facies auricularis oblique arm length, FDL1; length between foramina sacralia posteriora 1, FDL2; length between foramina sacralia posteriora 2, FDL3; length between foramina sacralia posteriora 3, FDL4; length between foramina sacralia posteriora 4, FPL1; length between foramina sacralia anteriora 1, FPL2; length between foramina sacralia anteriora 2, FPL3; length between foramina sacralia anteriora 3, FPL4; length between foramina sacralia anteriora 4, SH; Facies dorsalis height of os sacrum. μ ; mean, σ ; Standard deviation.

Table 2. Comparison of anterior and posterior surface measurements of the os sacrum with the literature

Parameters	$\mu \pm \sigma$	Literature	Measurement type	Population/Year
FDL1	38.68 \pm 4.03 mm	Koç et al. ¹¹	Dry os	Turkey/2014
FDL2	31.45 \pm 4.13 mm			
FDL3	26.10 \pm 3.68 mm			
FDL4	26.04 \pm 3.31 mm			
FPL1	30.01 \pm 5.03 mm			
FPL2	28.33 \pm 4.48 mm			
FPL3	26.51 \pm 4.82 mm			
FPL4	24.81 \pm 3.93 mm			
FPL1	Erkek 31.1 \pm 3.6 mm Kadın 28.0 \pm 3.1 mm	Duman. ⁶	Computed Tomography	Turkey/2009
FPL2	28.8 \pm 3.4 mm 26.1 \pm 2 mm			
FPL3	26.5 \pm 2.3 mm 24.6 \pm 2.4 mm			
FPL4	24.6 \pm 2.4 mm 23.2 \pm 2.4 mm			
FDL1	36.72 \pm 0.37 mm	This study	Dry os	Turkey/2018
FDL2	29.75 \pm 0.31 mm			
FDL3	26.53 \pm 0.33 mm			
FDL4	26.56 \pm 0.39 mm			
FPL1	29.16 \pm 0.36 mm			
FPL2	27.16 \pm 0.33 mm			
FPL3	24.50 \pm 0.26 mm			
FPL4	24.38 \pm 0.24 mm			

FDL1; length between foramina sacralia posteriora 1, FDL2; length between foramina sacralia posteriora 2, FDL3; length between foramina sacralia posteriora 3, FDL4; length between foramina sacralia posteriora 4, FPL1; length between foramina sacralia anteriora 1, FPL2; length between foramina sacralia anteriora 2, FPL3; length between foramina sacralia anteriora 3, FPL4; length between foramina sacralia anteriora 4, μ ; mean, σ ; Standard deviation.

Table 3. Comparison of measurements of corpus vertebrae and facies auricularis of os sacrum with literature

Parameters (mm)	μ	Literature	Population/Year
CVAPW	29.71 mm	Koç et al. ¹¹	Turkey/2004
	31.10 mm (female) 29.50 mm (male)	Kothapalli et al. ¹²	India/2012
	28.50 mm (female) 31.50 mm (male)	Sachdeva et al. ¹⁵	India/2011
	29.40 mm	Singh et al. ¹⁶	India/2017
	30.50 mm (female) 30.60 mm (male)	Kumar and Wishwakarma ¹⁷	Oman /2015
	28.30 mm	This study	Turkey/2018
CVTW	49.33 mm	Koç et al. ¹¹	Turkey/2004
	47.20 mm (female) 44.60 mm (male)	Kothapalli et al. ¹²	India/2012
	45.50 mm (female) 47.60 mm (male)	Sachdeva et al. ¹⁵	India/2011
	48.00 mm	Singh et al. ¹⁶	India/2017
	51.40 mm (female) 53.00 mm (male)	Kumar and Wishwakarma ¹⁷	Oman/2015
	47.00 mm	This study	Turkey/2018
Facies auricularis lengths	32.08 mm (short arm) 52.47 mm (long arm) 59.60 mm (oblique arm)	Koç et al. ¹¹	Turkey/2004
	31.9 mm (short arm) 39.4 mm (long arm) 49.1 mm (oblique arm)	This study	Turkey/2018

CVAPW; Anterior-posterior width of the corpus vertebrae, CVTW: Transverse width of the corpus vertebrae, μ;mean

Table 4. Comparison of os sacrum length, width and index results with the literature...

Parameters (mm)	μ	Literature	Population/Year
SL	93.49 mm	Koç et al. ¹¹	Turkey/2014
	100.10 mm (female) 98.50 mm (male)	Kothapalli et al. ¹²	India/2012
	100.10 mm (female) 98.50 mm (male)	Janipati et al. ¹³	India/2014
	94.46 mm (female) 109.47 mm (male)	Patel et al. ¹⁴	India/2014
	106.10 mm	Singh et al. ¹⁶	India/2017
	91.80 mm (female) 104.10 mm (male)	Sachdeva et al. ¹⁵	India/2011
	93.50 mm (female) 102.70 mm (male)	Kumar and Wishwakarma ¹⁷	Oman/2015
	92.50 mm (female) 115.40 mm (male)	Mustafa et al. ¹⁸	Egypt/2012
	90.58 mm (female) 107.53 mm (male)	Mishra et al. ¹⁹	India/2003
	101.80 mm (female) 103.10 mm (male)	Sinha et al. ²⁰	India/2013
	103.30 mm	This study	Turkey/2018
	108.40 mm (female) 102.20 mm (male)	Başaoğlu et al. ⁹	Turkey/2005
	111.67 mm	Koç et al. ¹¹	Turkey/2004
	108.20 (female) 101.10 (male)	Janipati et al. ¹³	India/2014
SW	106.45 mm (female) 106.42 mm (male)	Patel et al. ¹⁴	India/2014
	101.70 mm (female) 103.10 mm (male)	Sachdeva et al. ¹⁵	India/2011
	103.10 mm	Singh et al. ¹⁶	India/2017
	109.50 mm (female) 99.90 mm (male)	Kumar and Wishwakarma ¹⁷	Oman/2015
	115.00 mm (female) 113.60 mm (male)	Mustafa et al. ¹⁸	Egypt/2012
	105.79 mm (female) 105.34 mm (male)	Mishra et al. ¹⁹	India/2003
	108.40 mm	This study	Turkey/2018
	108.20 mm (female) 101.10 mm (male)	Kothapalli et al. ¹²	India/2012

Table 4. Comparison of os sacrum length, width and index results with the literature...(cont.)

Parameters (mm)	μ	Literature	Population/Year
SI	115.72 (female) 104.08 (male)	Kothapalli et al. ¹²	India/2012
	115.72 (female) 104.08 (male)	Janipati et al. ¹³	India/2014
	113.40 (female) 97.61 (male)	Patel et al. ¹⁴	India/2014
	111.74 (female) 100.24 (male)	Sachdeva et al. ¹⁵	India/2011
	117.35 (female) 97.51 (male)	Kumar and Wishwakarma ¹⁷	Oman/2015
	121.70 (female) 100.20 (male)	Mustafa et al. ¹⁸	Egypt/2012
	104	This study	Turkey/2018
	SW; maximum width of os sacrum, SL; maximum length of os sacrum, SI; sacral index, μ : mean		

DISCUSSION

The five sacral vertebrae fuse to form the triangle-shaped sacrum, which functions as the anterior border of the pelvic cavity.^{1-5,21,22} The sacral vertebrae begin connecting after puberty. The development of the sacral canal and laminae is incomplete in the presence of any recognized formational defect. Spina bifida and cystitis are co-occurring conditions with this illness, and neurological issues might be seen in this scenario.²¹ The median sacral crest is created when the spinous processes unite at the midline. On either side of the median sacral crest lies the sacral groove. The sacral groove is made up of sacral laminae. The sacral groove serves as the origin of back muscles such as the multifidi, sacrospinal muscle, and erector spinae. Without the formation of the second sacral lamina, these muscles won't be able to properly insert to the dorsal surface of the sacrum. Dorsal agenesis is brought on by the sacral lamina's failure to fuse, and hidden spina bifida is brought on by a defect in the sacral canal's posterior wall at the level of the second sacral vertebra.²¹ Caudal anesthesia refers to the injection of the anesthetic into the sacral canal through the sacral hiatus during surgical procedures to be done to the uterine cervix and perineum after birth. Surgery can be done while under anesthesia if an anesthetic solution is applied to the roots of the sacral and coccygeal segments in the sacral canal. Knowing the sacrum morphometry inside and out is crucial in this regard.⁷ Accordingly, it is claimed that effective caudal epidural anesthesia and analgesia require knowledge of the usual anatomical structure, morphometric values, and variations of the sacrum.^{6,21,22} Additionally, the sacrum and coccyx are the vertebrae most frequently affected by malformations of the vertebrae connected to the number. A sixth lumbar vertebra, known as lumbarization, can be formed when the S1 vertebra separates from the sacrum and combines with the L5. On the other hand, sacralization and the fusion of L5 with the sacrum are both possible.^{4,5,7,23} Spina bifida or concealed spina bifida, which emerge as a result of

failure to fuse or develop that can be seen in the lamina vertebral arch of one or more vertebrae, may occur, as well as sacral hiatus variants, caudal agenesis, or developmental abnormalities.^{7,23} On the other hand, since it is situated close to where the common iliac is divided into its terminal branches, the promontorium is a crucial point of reference in laparoscopic surgery.⁷

Clinicians such as anesthesiologists, radiologists, orthopaedists, and obstetricians should have an extensive knowledge of normal anatomy, morphometric measures, and variations of the sacrum. A structural difference in the sacrum helps in the analysis of sacral spina radiography by radiologists, the estimation of age, gender, and height by forensic scientists, the diagnosis of low back pain by orthopaedists, and the detection of spondylolisthesis by obstetricians.^{6,21,22} Additionally, accurate diagnosis and administration of treatment in clinical disorders affecting the lumbosacral and sacrococcygeal regions depend on a detailed understanding of sacrum variations.²²

Measurement results of the sacrum have been observed to vary between males and women in the literature.^{6,15,23-25} In terms of gender, it is stated that the bones of men are heavier and larger. The reason why the SI value obtained as a result of dividing the width of the SW is lower in men is due to the fact that the sacrum is longer in men than in women. It has been reported that the sacrum is wider and shorter in women, while promontorium is smaller.^{5,26} Differences in age, climatic conditions, race, and gender are thought to be the root causes of these sacral variations.^{15,23,24} The fact that the ala of sacrum is wider in women is due to the increased pelvic volume and the need for a wider pelvic outlet during pregnancy, in addition to an increased sacrovertebral angle and the shifting of apex of sacrum to the posterior at delivery.²³ In addition, measurements such as sacral index and subpubic angle were found to be very useful measurements in determining gender differences due to the effect of sex hormones.^{24,25} One of the bones

that is most frequently utilized to determine gender and that best demonstrates gender differences is the sacrum.¹⁵ The sacrum morphometric data, according to Kumar and Viscwakarma, are valuable metrics for predicting gender in broken, incomplete, and damaged dry human bones.¹⁷

In our study, it was found that the FPL1-4 were higher than the FPL1-4. These values were found to be lower than the data in Koç et al.'s¹¹ study in all parameters, except for FDL3 and FDL4 parameters. When our FPL1-4 measurement values were compared with the results found in the study conducted by Duman T⁶ by using computed tomography, it was found that all parameters except for FPL3 parameter were among the mean values found in female and male population. In our study, mean vertebral body anterior posterior diameter of the sacrum was found to be lower than that of Indian,^{12,15,16} Oman¹⁷ and Turkish¹¹ population. Mean of the CVTW was found to be lower than those found in studies by Koç et al.¹¹ Kumar and Viscwakarma¹⁷ and Singh et al.¹⁶

Our mean auricular surface of the sacrum length measurements were found to be lower than those found in studies conducted in Turkey. On the other hand, the SL was found to be higher than the measurements in Turkish,¹¹ Oman¹⁷ and Indian^{12,13,20} populations. When the parameter of the SW was compared with the literature, it was found to be higher than the results found in studies conducted by Patel et al.¹⁴ Mishra et al.¹⁹, Sachdeva et al.¹⁵ and Singh et al.¹⁶; similar to the results found in studies conducted by Janipati et al.¹³ and Başaoglu et al.⁹ and lower than the results found in studies conducted by Mustafa et al.¹⁸ and Koç et al.¹¹

In addition, when we examine the current studies comparing CT and osteometry, Dubory et al. found that the thickness of the lower part of the Sacral 1 vertebrae body increased in male patients ($p < 0.001$). While no significant difference was found between vertebral body width in men and women in this study, they found a significant difference ($p < 0.001$) in both sexes in terms of vertebral body median diameter and vertebral body height parameters in both osteometry and CT scans.²⁷ In another study, the transverse and vertical diameters of the auricular surface had significant differences ($p < 0.001$) in males and females in both osteometry and CT scans.²⁸

The limitations of our study were the fact that 32 dry sacrum were used in the study since partly broken, fragmented and damaged bones were not included in the study and the study was conducted with only one department. We recommend such studies to be conducted by bringing together many departments or by using more sacrum.

CONCLUSION

It is thought that factors such as race, gender, age, nutritional status, geographical conditions and the measurement methods used are effective in differences between the data obtained from studies conducted in literature. In the present study, the relationship between vertebral column and pelvis and the sacrum and morphometric values of the sacrum were determined. It can be said that a good knowledge of the variations related with the sacrum, which is at a critical point, will increase the success of surgical interventions in this region in the future and prevent the emergence of future clinical complications. It is also clear that the data obtained as a result of the study will contribute to basic and clinical research that will be conducted on sacrum in the future.

ETHICAL DECLARATIONS

Ethics Committee Approval: Since the study was performed on dry bones, ethics committee approval is not required, institutional approval was obtained.

Informed Consent: Since the study was performed on dry bones, no written informed consent was obtained.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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