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Volumetric assessment of the sella turcica: a reevaluation

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**Both authors participated equally in the study and are both in the position of first author.*

ABSTRACT

Background: The sella turcica volume is widely measured by the Di Chiro-Nelson method. The purpose is to compare the fidelity of a proposed volumetry method versus the Di Chiro-Nelson method, using Computed Tomography (CT) images.

Materials and methods: Morphometric examination of 173 CT were included, of which 52.6% were female. The mean age was 53.2 ± 17.6 years. Considering the Di Chiro-Nelson method, two measurements were added for each axis in the CT evaluation: Length (Central,

Left, and Right), Width (Central, Anterior, and Posterior), and Height (Central, Left, and Right).

Results: The mean measurements were Length: Central 10.11 ± 1.44, Left 7.45 ± 1.67, Right 7.53 ± 1.59; Width: Central 12.27 ± 2.11, Anterior 10.99 ± 1.92, Posterior 10.10 ± 1.74; Height: Central 7.68 ± 1.38, Left 7.16 ± 1.35, Right 7.40 ± 1.41. A statistically significant difference between sex was found only in the anterior width (p=0.01). Using the proposed method, the volume was 342.2 ± 88.5 and 378. 6 ± 113.9 mm3 respectively between females and males (p=0.02) versus 476.1 ± 132.4 and 523.8 ± 186.0 mm3 (p=0.05) using the Di Chiro-Nelson's method.

Conclusions: Women had significantly smaller sella turcica volume than men. This proposed method considers the sella turcica as a not strictly symmetrical structure and indicates reduced variation between the maximum and minimum values, compared to the Di Chiro-Nelson's. Our findings may be useful to reassess the volume of the sella turcica as the measurements indicate a higher precision.

Key words: Sella turcica, Computed Tomography, Volumetry, Di Chiro-Nelson

INTRODUCTION

The sella turcica is a bony structure located in the middle cranial fossa [14]. Its anatomy consists of anterior and posterior clinoid processes and central hypophyseal fossa. The latter is a space formed at the upper surface of the body of the sphenoid bone between the tuberculum sellae and the dorsum sellae (16,30). The pituitary gland is a structure with important endocrinological function, as is the central regulator of the endocrine system, located in the deepest point of the sella turcica (15).

There are pathologies and deviations in its development that increase or decrease the size of the pituitary gland. Likewise, these pituitary gland alterations may modify the size and morphometry of the sella turcica, as their development is closely related (26,34). The sella turcica abnormalities are caused by individual variations, shape, and asymmetry in normal subjects, pituitary adenomas, hypothyroidism, empty sella syndrome, acromegaly,

tumors, and Sheehan syndrome (2,12,14,26). It also plays a role in craniofacial abnormalities and the decision making and application of surgical interventions (1,26,31,33), as anatomical knowledge is essential during the procedure to avoid damage (34).

Determining the volume of the sella turcica by image studies has been used to infer the pituitary gland volume(7,27) and helps to recognize the normal and anomalous morphology (26). One of the most widely used volumetry methods is the Di Chiro-Nelson method, in which the length, height, and width are multiplied together and divided in half (7). However, they utilized radiograph images, and with the improvement of imaging technology, the existing methods have been re-evaluated (18,26,34). We provide a straightforward method, considering the sella turcica as a not strictly 3D symmetrical structure. These measurements play an advantage where Magnetic Resonance Imaging (MRI) is not readily available or contraindicated.

Our objective is to validate a proposed method to determine the volume of the sella turcica and compare it to the Di Chiro-Nelson method using computed tomography [CT] scans. Thus, standardizing the sella turcica volume adds clinical suspicion of pathologies that alter the pituitary gland's size.

MATERIALS AND METHODS

Research design

An observational, retrospective and comparative study was performed. Images were obtained in a case consecutive method from the database of the Radiology and Imaging Department of the University Hospital “José Eleuterio González” of the Universidad Autónoma de Nuevo León. Studies were obtained from adult patients without discrimination for age or gender. Those with a history of fractures, tumors, surgical interventions in the skull base, cancer, craniofacial syndromes, congenital structural abnormalities, or conditions that could affect bone metabolism were excluded. This study adheres to the STROBE guidelines for the report of observational studies (29).

Study technique

All images were acquired using a 64-slice tomograph (General Electric CT99 Light Speed VCT) Software 2978195VCT, with a rotation of 0.4s helical acquisition, detector coverage of 20mm, Kv of 120 mAs and 400; thickness of cut of 0.625mm, pitch of 0.53: 1 mm / rot, FOV of 22 to 33 cm. The data obtained was transferred and analyzed in a Work Station AW Volume Share2 workstation using multiplanar reformatting with maximum projection intensity and rendering volume. During the measurements, a window range of WW: 4000 and WL: 1000 was used in a standardized manner in all subjects. The images and measurements were assessed independently by two radiologists with experience in neuroradiology.

The CT scans were measured with Di Chiro-Nelson [0.5 x (length x width x depth)] and our proposed method (Table I). In our proposed method, we added two measurements parallel to each of the three axes (length, height, and width) (Figure 1). The volume, according to our method, is obtained by the mean of the three measurements of each axis [0.5 x [(mean length distances) x (mean height distances) x (mean width distances)]. All authors agreed on the bone landmarks, as anatomical variations on the sella turcica shape have been determined.

Ethics approval

This study was previously reviewed and approved by the ethics and research committees Hospital Universitario “Dr. Jose Eleuterio Gonzalez” of the Universidad Autónoma de Nuevo León under the registration number AH17-00004, certifying that it adheres to the guidelines of the General Health Law on Health Research in Human Beings of our country, as well as international guidelines and the Declaration of Helsinki. Research and Ethics committees waived the need for further written consent.

Statistical analysis

The sample size calculation was made with a formula for estimating a mean in an infinite population resulting in a sample size of 173 studies. Normality tests were performed using the Kolmogorov-Smirnov test. Central tendency and dispersion data were

obtained, expressed as mean and standard deviation for parametric data, and as median and minimum and maximum in nonparametric data. The comparisons between the different groups for the categorical variables were made by Pearson's Chi-Square test and for the numerical variables by the two-tailed Student T test for the parametric data, and Mann Whitney U for the non-parametric data. Parametric (Pearson's) and non-parametric (Spearman's) correlations were performed to evaluate the linear relationship between the numerical variables. A p-value of <0.05 was considered statistically significant. Furthermore, for categorical observations, the inter-observer agreement was assessed by the Cohen's Kappa statistic. A p value of <0.05 was considered statistically significant. All the statistical analyses were performed in IBM SPSS Statistics for Mac, version 25 (IBM Corp., Armonk, N.Y., USA).

RESULTS

A total of 173 CT scans were included, and 52.6% of the participants were female. The mean age was 53.22 ± 17.62 years (*p=0.73)*. All sets of inter-observer reliability analyses resulted in substantial reliability (ICC>0.85 and k >0.85). The measurements and volume of the sella turcica as means and stratified by sex are shown in Table II.

Statistically significant differences between sex were found only in the anterior width (p=0.01). The comparison of mean volume between sex was not statistically different using the Di Chiro-Nelson method (p=0.05) but it was when using the proposed method (p=0.02) (Table II). We then compared the mean measurements of both methods and we found a significant difference (p<0.001).

The differences in standard deviations of the volume were also higher in the Di Chiro-Nelson method (132.41 mm^3 in females and 186 mm^3 in males) versus the proposed method (88.53 mm^3 and 113.89 mm^3). Likewise, the box plot diagram indicates a greater consistency by reducing the variation between the maximum and minimum values, as well as a decrease in the range of the distribution (Figure 2).

The subjects were stratified according to the age in younger and older than 25 years. A statistically significant correlation is seen between age and the proposed method (r=.195) p=0.01*, but not between the Di Chiro-Nelson method (r=.130) p= 0.08, in both groups separated by age.

DISCUSSION

Main findings

This study is not the first to use CT to determine the volumetry of the sella turcica. However, we determined the volume considering it as an asymmetrical structure, in an adult population without pituitary pathology. Our three-dimensional assessment method demonstrates greater consistency and statistically significant differences between sex. It reports higher fidelity measurements and lower standard deviations than by the Di Chiro-Nelson method, with two-dimensional radiographs (at the publication time, radiographs were one of the standard techniques for pituitary diseases (5).)

Comparison with previous anatomical studies

Other authors have proposed modifications to the Di Chiro-Nelson method (Table III). Hasan *et al.* (2016) described the morphology and measurements of the sella turcica in CT images stratified by sex, age, and with global data. No significant differences were found for all linear and area measurements of sella turcica between sex, however, a gradual increase in the size of sella turcica was observed as age advances (9).

Venieratos *et al.* (2005) (30) utilized dry skulls and focused on the hypophyseal fossa with a geometrical method as they determined the dimensions of the fossa are smaller than those of the sella, and direct measurement of its volume and depth could lead to errors. However, they measured the total volume of the sella with the Di Chiro-Nelson method, obtaining a range between 460 and 1570mm^3. Hlaing *et al.* (2012) (10) examined adult crania to observe the bony landmarks and to determine the location of a fossa that may occur in the sellar floor. They described four variations and reported a smooth surface in eight of the 205 crania. A single posterior fossa was the most common feature, which they

described for the first time. We consider these findings to support the reason to measure depth in three different points to have a closer real volume of the sella turcica by taken the anatomical variations into consideration.

Yasa *et al.* (2017) (34) established the mean distances of length, depth, diameter, and the interclinoid distance of the sella turcica in 177 subjects. No statistically significant difference was found between sex, but statistically significant differences between ages. Our proposed method also identified similar central measurements and a statistically significant correlation between age.

Taner *et al.* (2019) (26) assessed the volume of sella turcica by cone-beam CT in healthy adults. They did not find statistically significant differences between sex for any Di Chiro-Nelson's method measurements, however significant difference was established in volume (*p=0.003),* which was higher in men. Our proposed method showed statistically significant differences between sex in the Anterior Width (*p=0.01)* and in the volume between sex (*p=0.02).*

Pittayapat *et al.* (2015) developed high precision system for the sella turcica identification using Maxilim® software in 32 subjects. They also focused on orthodontics as the sella point is a reference for the evaluation of the longitudinal growth of patients and their treatment (18). Our method does not include high precision technology, yet an advantage is that it could be easily replicated with CT images.

Comparison with previous clinical studies

Ugurlu *et al.* (2019) performed a three-dimensional morphometric analysis of the pituitary fossa with cone-beam CT studies with 19 measurements in subjects with maxillary impacted canines and controls. Only the right sella length differed among the three groups ($p<0.05$) (28).

Studies have also determined the volume of the sella turcica in endocrinological diseases. Yamada *et al.* (1976) compared the size of the sella turcica in normal subjects and patients with primary hypothyroidism and hyperthyroidism. They determined the volume increased with age, and after 25 years of age, remained constant (32).

A small sella turcica size is one predisposing factor that restricts the pituitary blood supply, contributing to Sheehan syndrome (11). There are studies that compared the volume between patients and controls (4,25), reporting significantly smaller measurements ($p<0.001$) in the patients than in the control subjects (4). Therefore, it is worthy to establish mean volumes (Table III), to clinically orient with pituitary disease.

A systematic review by Roomaney and Chetty (2020) (22) determined that the craniofacial morphometry affected by genetic syndromes is likely to be associated with abnormal variations of the sella turcica. Clinicians should be aware of the abnormalities and considering the underlying signs and symptoms for medical referral. They also conclude more high-quality studies are needed, with standardized and objective methods to determine the morphology of the sella turcica.

Di Chiro-Nelson's method was the first used to evaluate pituitary pathology indirectly. Undoubtedly, we can now assess it with MRI and laboratory tests. However, in pathologies where there is a change in the pituitary gland's volume, it is relevant to have a reference for the volume of the sella turcica. Our work could be used to establish a relationship between measurements by CT images and the ones obtained by MRI to standardize an index that supports these diseases' diagnosis.

Limitations of the study

Our method may present inherent imprecision as it has not been validated by other studies or compared to segmentation software methods. Besides, this model attempts to standardize a structure, representing a simplification, given the intrinsic anatomical variability (35). Further studies are needed to confirm these as there are variations of normal subjects (1,26), and other abnormal sellar variants, altering sellar volume, such as sellar bridging (8), and variations and morphological types in genetic syndromes (e.g. Williams syndrome) (3). Also, subjects with dental anomalies and either complete or partial calcification of interclinoid ligament, are highly suggestive of a genetic condition (19,20). Although there is evidence the sella turcica linear measurements can be used to estimate the pituitary gland size (24) , we cannot translate our method. Our results' morphometric differences with other studies may be due to the demographic characteristics and imaging

methods. We did not performed intraobserver measurements. MRI grants a better understanding of the patient's anatomy and endocrinological diseases (21). However, it is not always easy to distinguish tumors from hemorrhage and fat packing (13). CT is less expensive, has a broader distribution, better bone assessment, and it is useful in patients where MRI is contraindicated (23).

Relevance for the clinical practice

The diseases that alter the size of the pituitary are not uncommon (21). Our results indicate smaller volumes compared to the Di Chiro-Nelson method, and they should be taken cautiously, as a small sella turcica may show upward bulging of the sellar content (one adenomas' indirect sign), leading to potential misinterpretation (17), as well as other normal and abnormal variants that may modify the volume (1,8,26).

This study has established a new volume assessment regarding the sella turcica as a variable shape structure enclosing anatomical landmarks. The success in diagnosis and treatment depends on a multicentered management with the integration of internal medicine experts (6). Nonetheless, the assessment with an anatomical approach provides the clinicians a thorough analysis and better understanding of the related diseases' physiopathology. This is why it is essential to renew the previous methods and consider the sella turcica as a not strictly symmetrical structure. Our findings may be useful to identify the volume of the sella turcica as a component of the integral management of pituitary diseases.

CONCLUSIONS

We determined a volume method with greater consistency among measurements and a narrow standard deviation. The Di Chiro-Nelson method has been used for several years. With the new technologies, it was possible to obtain a three-dimensional view of anatomical structures. This is why it is essential to renew the previous methods and consider the sella turcica as a not strictly symmetrical structure. Our findings may be useful to identify the volume of the sella turcica as a component of the integral management of pituitary diseases.

Conflict of interest: None declared

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Table I. Comparison of the measurements

Di Chiro-Nelson method	Description	Current study, [2021] method	Description
Length	The distance on the anteroposterior axis of the sella turcica from the back to the tuberculum.	Central Length	The distance on the anteroposterior axis of the sella turcica from the dorsum to the tubercle.
		Left and Right Length	The distance from each lateral end of the tubercle to the lateral end of the posterior clinoid processes.
Height	The line perpendicular to the line that measures the length and that coincides with the deepest portion of the sella turcica.	Central Height	The line perpendicular to the Center Length of the sella to the deepest point of the hypophyseal fossa.
		Left and Right Height	The perpendicular distance of the midpoint of the Left and Right lengths, respectively to the deepest point of the sella turcica.
Width	The lateral-lateral distance of the highest point of the tubercle of the sella turcica.	Central Width	The lateral-lateral distance of the highest point of the tubercle of the sella turcica
		Anterior Width and Posterior Width	The width of the tubercle and the width of the dorsum of the sella, respectively.

Table II. Measurements for both sexes and comparison by methods

Measurement		Mean ± SD	Median (Min – Max)	Females (Mean ± SD)	Males (Mean ± SD)	P value
Length	Central	10.11±1.44	10.30 (4.3–14.2)	10.11±1.36	10.11±1.54	0.99
	Right	7.53±1.59	7.70 (2.9–11.8)	7.32±1.62	7.68±1.53	0.06
	Left	7.45±1.67	7.40 (2.8–12.2)	7.35±1.77	7.56±1.55	0.42
Width	Central	12.27±2.11	12.30 (7.4–17.5)	12.02±2.12	12.55±2.07	0.09
	Anterior	10.99±1.92	11.00 (5.8–16.2)	10.66±1.87	11.36±1.92	0.01*
	Posterior	10.10±1.74	9.90 (6.0–14.8)	9.95±1.77	10.27±1.70	0.22
Height	Central	7.68±1.38	7.50 (3.4–11.9)	7.50±1.23	7.77±1.51	0.19
	Right	7.40±1.41	7.30 (3.4–11.1)	7.36±1.29	7.44±1.54	0.71
	Left	7.16±1.35	7.10 (3.0–10.6)	7.12±1.34	7.19±1.38	0.72
Volume	Di Chiro's	**498.7 ± 161.4**	**499.6 (90.3–1254.7)**	**476.1 ± 132.4**	**523.8 ± 186.0**	**0.05**
	Proposed	**359.4 ± 102.7**	**348.5 (85.6–776.2)**	**342.2 ± 88.5**	**378.6 ± 113.9**	**0.02***

SD: Standard deviation; All measurements in millimeters. Volume in cubic millimeters, *: statistical difference between sex.

Table III. Comparison with previous studies

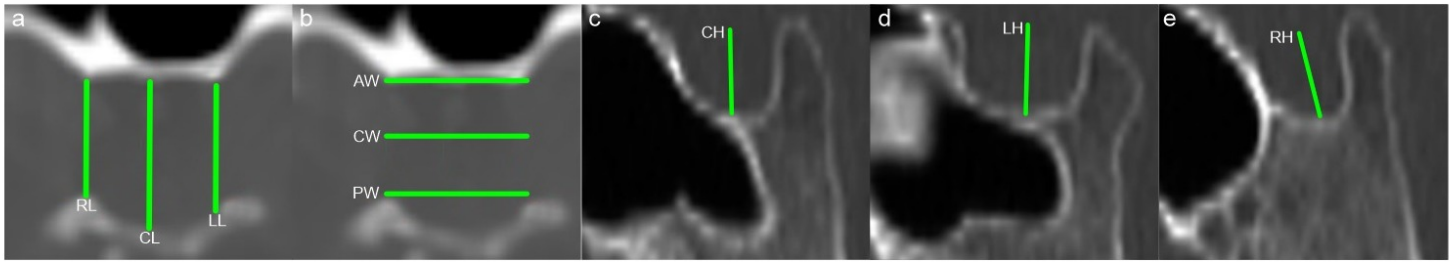
Author, Year, Country	**Sample**	**Mean age [years]**	**Method**	**Mean Volume [mm^3]**
Yamada *et al.*, 1976 Japan	570 controls 26 primary hypothyroid patients 34 thyrotoxic patients	Controls: 1-60	Di Chiro-Nelson	Age 1: 206 ± 19 Age 1-25: 530 ± 23 Age >25: 554 ± 8 Hypothyroid: 1,334.4 ± 101.0 Thyrotoxic: 558.3 ± 24.7
Parks *et al.*, 1978 USA	Patients with hypopituitarism: 3	Case 1: 18.6 Case 2: 10.4 Case 3: 6.7	Di Chiro-Nelson	1560 1008 840
Sherif *et al.*, 1989 Libya	Control: 17 Sheehan's: 57	41 ± 8	Statistics volume software and resistor matrix	922±155 565±292
Bakiri *et al.*, 1991 Algeria	Control: 12 Sheehan's: 54	38.3 ± 3.6 40.21 ± 1.22	Height and length on their greatest axis	796±5.6 55.7±2.7
Venieratos *et al.*, 2005 Greece	Dry skulls: 20	NR	Di Chiro-Nelson	835
Pittayapat *et al.*, 2015 Belgium	32 Cone-Beam CT Scans	26.0 ± 21.6	Maxilim® software	NR
Hasan *et al., 2016 Iraq*	71 CT images	33.9	Di Chiro Nelson and three different heights of the sella turcica	65.3
Yasa *et al.*, 2017 Turkey	177 Cone-Beam CT Scans	11–73	NR	NR
Taner *et al.*, 2019 Turkey	80	F: 26.6 ± 8.6 M: 27.5 ± 9.0	Di Chiro-Nelson	951.3±278.5 1102.0±285.3
Ugurlu et	Control: 15	20.01 ±	Own method	NR

al., 2020 Turkey	Patients with maxillary impacted canines: 73	6.53	[19 measurements]	
Current study, 2021 Mexico	Control: 173 CT scans	F: 52.8 ± 18.3 M: 53.6 ± 17.0	Proposed method [9 measurements]	F: 342.2±88.5 M: 378.6±113.9

M: Male; F: Female; NR: not reported; CT: Computed tomography

Figure 1. Representation of the measurement variables in the proposed method. Measurements represent the variables described in Table I. Axial slice of CT. a: [CL] Central, [RL] right, and [LL] left length. b: [CW] Central, [AW] anterior, and [PW] posterior width. Sagittal slice of CT. c: [CH] central height. d. [LH] left height. e: [RH] right height

Figure 2. Box plot demonstrating the values obtained by the Di Chiro-Nelson and the Proposed method. The proposed method shows a decrease in the range of the distribution indicating a higher precision of the measurements


a
RL
CL
LL
b
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CW
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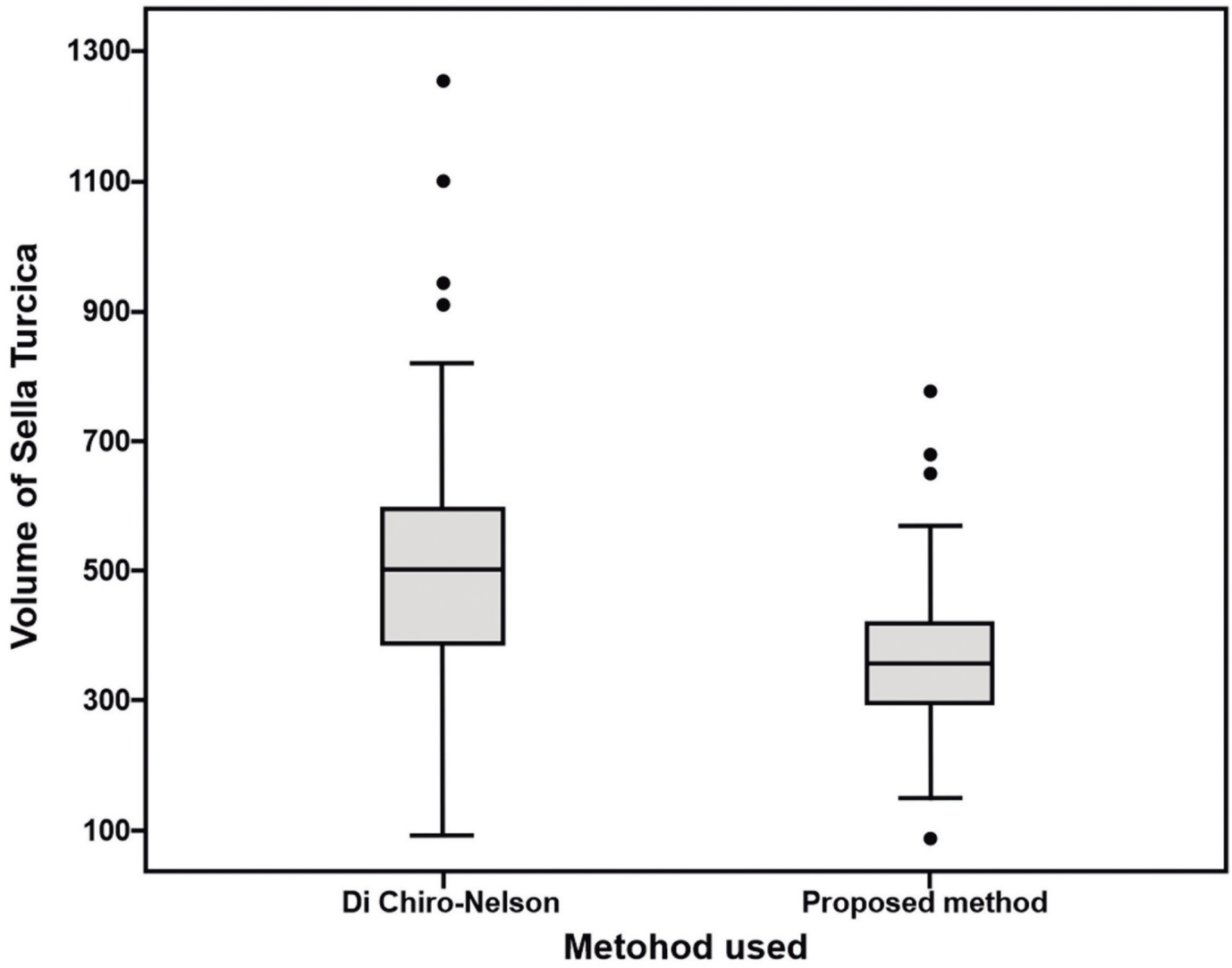
1300
1100
900
700
500
300
100
Volume of Sella Turcica
Di Chiro-Nelson
Proposed method
Metohod used