Forensic Sciences Research, 2024, Vol. 9, Issue 2
https://doi.org/10.1093/fsr/owad046
Review

Potential role of the sella turcica X-ray imaging aspects for sex estimation in the field of forensic anthropology: a systematic review and meta-analysis

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Abstract

Several studies have evaluated the parameters of normality of the sella turcica (ST), which is important to face different craniofacial syndromes that may affect this structure. Therefore, this research summarized the scientific evidence on the role of ST in the sex estimation of non-syndromic individuals. The research protocol was registered (Prospective International Registry of Systematic Reviews # CRD42021256469), followed by an electronic search in six databases (PubMed, LILACS, Web of Science, Scopus, EMBASE, and LIVIVO) and gray literature (Google Scholar and OpenGrey). Meta-analysis of linear (width, length, height, and diameter) and volumetric measurements, in addition to an assessment of risk of bias (RoB) and certainty of evidence, were performed. After the screening of 986 articles, 13 were evaluated by meta-analysis (1 307 males and 1 231 females). In subgroup analysis, females had lower values for width (lateral radiograph; −0.67 mm; $P = 0.040$), length (computed tomography; −0.23 mm; $P = 0.020$), and diameter (computed tomography; −0.27 mm; $P < 0.001$) compared to males. There was no statistically significant difference regarding height ($P = 0.95$), area ($P = 0.72$), and volume ($P = 0.21$). Most studies exhibited moderate RoB, and the certainty of evidence of the outcomes was very low. In this review, significant differences were observed between the sexes for the length and diameter of the ST; however, the heterogeneity of the studies must be considered.

Key points

- Studies from different geographic regions evaluated the morphology of ST according to sex and showed this anatomical structure as an important indicator of dimorphism.
- Meta-analysis showed shorter ST length and diameter in women.
- Subgroup analysis found lower ST width in women based on lateral skull radiographs.
- Subgroup analysis found smaller lengths and diameters in women based on CT scans.

Keywords: forensic medicine; sella turcica; sexual dimorphism; tomography; spiral computed; cone-beam computed tomography

Introduction

The sella turcica (ST) is a depression in the upper central portion of the sphenoid bone which houses the pituitary gland [1, 2]. Studies investigating the close relationship between these two structures have indicated that alterations in the pituitary gland may be related to alterations in the morphology of the ST, and, consequently, alterations in the ST have been linked to several syndromes (Downs's syndrome, William's syndrome, Cleidocranial dysplasia, velocardial-facial syndrome, Sotos syndrome, among others) [1–3].

Several investigations have been carried out with non-syndromic individuals in different populations aiming at evaluating the morphology and parameters of normality of the ST [4–31]. For this purpose, cephalometric radiographs (CR) [4–8, 16, 18–20, 22–24, 26, 27], as well as multislice computed tomography (MSCT) [10, 11, 13–15, 21, 25, 30] and cone beam computed tomography (CBCT) images have been employed [9, 12, 17, 27, 29, 31]. Local and regional validation of these methods are of great relevance because of possible variations in different populations, and some studies have already found significant differences in ST morphology among different ethnic groups [18, 19].

However, most of these studies did not focus on the ST analysis for sex estimation. Significant differences between the sexes observed in some parameters of the ST could set the path for its regular use in the analysis of sexual dimorphism. In a scenario where different researchers have been conducted in the field of forensic anthropology to investigate potential alternatives in the sex estimation process, the study by De Donno et al. [10] evaluated the ST measurements in an Italian European sample. They found males showing higher ST length values compared to females. These authors considered the

Received: October 14, 2022. **Accepted:** December 13, 2023

results useful for forensic purposes and reinforced the need to combine several methods for more accurate sex estimation. It is assumed that the association of forensic analysis methods can enhance the estimate of sex, raising the accuracy values [32].

The use of imaging examinations to carry out forensic examinations has been proposed as an important means of forensic analysis, being an integral part of the virtual necropsy, known as virtopsy. This method can take advantage of surface scanning with an optical scanner, CT, or magnetic resonance imaging in the performance of autopsies. It helps clarify the manner and cause of death and the human identification process, in which several cranial and/or dental parameters validated in the literature are used [33].

This type of expertise can avoid contamination of the professional with biological agents, as in the case of the SARS-CoV-2 disease. During the COVID-19 pandemic, manipulating bodies victimized by this disease was considered a high-risk procedure, and a virtopsy is recommended for this purpose [34]. In this process, the analysis of bone structures such as the ST, commonly visible in imaging examinations, may contain useful information for human identification [10, 35].

A recent systematic review found associations between genetic syndromes and changes in ST morphology [3]. It reinforces the importance of evaluating normative parameters of this structure in non-syndromic individuals, in addition to the possibility of its use for sex estimation. Thus, this research aimed to summarize the scientific evidence available in observational studies on normal ST parameters according to sex in different populations.

Materials and methods

Registration protocol

The research protocol was registered on the Prospective International Registry of Systematic Reviews (PROSPERO, https://www.crd.york.ac.uk/PROSPERO/) platform before the data collection. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA 2020) was used as a guide for reporting this review [36].

Eligibility criteria

Observational studies that performed linear, angular, volumetric measurements, and/or evaluated the morphology of the ST with CR, MSCT, and CBCT in humans were included in this research. There were no restrictions on the publication period.

Studies on samples of individuals with any type of anomalies, pathologies, syndromes, trauma, surgery in the ST region (which may generate changes in the normal shape and dimensions of the ST), and articles that did not compare the sex of individuals were excluded. Studies that only included $\leq$15-year-old individuals were also excluded from this review. Considering that the average period of pubertal development is around 15 years of age in females and that the skull base anatomy tends to remain stable after the age of 12 years in males [37], several articles included these age groups [5, 13, 14, 16, 22, 27]. Subsequently, the references of the included articles were also consulted to identify potential studies for this systematic review. Experts were also consulted to identify potential additional studies.

Information sources

A simultaneous search was carried out in the literature in June 2021 on the main virtual health databases listed below:

- PubMed—(https://pubmed.ncbi.nlm.nih.gov/—hosted by the National Center for Biotechnology Information—NCBI).
- LILACS—(https://lilacs.bvsalud.org/en/—Latin American and Caribbean Health Science Literature).
- Web of Science—(www.webofknowledge.com—hosted by Clarivate Analytics).
- Scopus—(https://www.scopus.com/—hosted by Elsevier and consulted through the institutional access of the Federal University of Ceará).
- EMBASE (http://www.elsevier.com/online-tools/embase/—Excerpta Medica dataBASE hosted by Elsevier, Netherlands).
- LIVIVO—(https://www.livivo.de/—The Search Portal for Life Sciences).

Grey literature was also consulted, with same-day access:

- Google Scholar—(https://scholar.google.com/). The search was limited to the first 300 most relevant articles.
- OpenGrey (http://www.opengrey.eu/—System for Information on Gray Literature in Europe).

Search strategy

The research question to be elucidated in this review was: Do the morphometric aspects of the ST in non-syndromic individuals differ between the sexes? This research question was based on the PECOS framework:

1. Population (P): non-syndromic individuals.
2. Exposure (E): morphometric aspects of the ST in CR, MSCT, and CBCT.
3. Comparison (C): not applicable.
4. Outcome (O): differences in ST measurements in relation to sex.
5. Study design (S): observational studies.

Based on this acronym, a search strategy was initially developed for the PubMed database. This search was conducted with keywords and synonyms related to the ST and the imaging examinations (CR, MSCT and CBCT) (Supplementary Table S1). Adaptations were made according to the controlled vocabulary of each database.

Study selection

The studies included through the search strategies were initially inserted into the EndNote X8 software (Clarivate, London, UK) for the identification and removal of duplicate articles using the find duplicates tool.

Then, titles and abstracts were screened for eligibility. This step was performed by two evaluators (ECR and DSM), independently, using the Rayyan® software (Rayyan® Qatar Computing Research Institute, Doha, Qatar) [38]. These reviewers were blinded to the authors and institution of the studies. In this systematic review process, we ensured the integrity of the blind review by implementing several measures. The two authors of the text conducted the article analysis independently and in different locations. For the initial stage (reading titles and abstracts), we used Rayyan® software, which facilitates this process and allows for the inclusion of an additional author for analysis. Each author logged in with their credentials to access their respective reviews. Within the software, titles and abstracts were presented clearly to the evaluators without disclosing the authors' institutional affiliations. Articles with only the title available and whose exclusion was not possible through title screening were considered for full-text reading. A third researcher (FWGC) was responsible for supervising the study, as well as for making the final decision in case of divergences in the selection process.

Next, the same researchers independently performed the full-text reading of the selected articles. In this step, the references of the included articles were consulted to identify studies not found in the previous phases. The articles considered eligible were then methodologically analyzed to plan the statistical evaluation of the data.

Data collection process

Data extraction was performed by two authors, independently and using a pre-established standard form and all descriptive and quantitative data from the selected studies were manually categorized in electronic spreadsheets in Microsoft Excel® (Redmond, Washington, DC, USA).

Data items

When available in the studies, the following data were extracted for analysis: (i) year of publication; (ii) journal/JCR (Journal Citation Reports); (iii) country/continent of origin; (iv) study design; (v) type of imaging exam; (vi) inclusion/exclusion criteria; (vii) sex; (viii) age groups; (ix) general age (mean/SD); (x) male age (mean/SD); (xi) female age (mean/SD); (xii) device used for image acquisition; (xiii) image analysis software; (xiv) number of evaluators; (xv) was there a calibration of the evaluators? (xvi) anonymization of examinations? (xvii) sample calculation? (xviii) reproducibility error analysis? (xiv) morphology; (xx) linear, angular, and volumetric measurements; (xxi) correlation with skeletal classes? (xxii) type of analysis (manual *versus* digital); (xxiii) main outcomes; (xxiv) limitations.

Risk of bias in individual studies

Based on the methodological design of the included studies, two evaluators (ECR and DSM) assessed the risk of bias using the Joanna Briggs Institute Critical Appraisal Tool for Analytical Cross-Sectional Studies (JBI) [39], which poses the following questions:

1. Were the criteria for inclusion in the sample clearly defined?
2. Were the study subjects and the setting described in detail?
3. Was the exposure measured in a valid and reliable way?
4. Were objective, standard criteria used for the measurement of the condition?
5. Were confounding factors identified?
6. Were strategies to deal with confounding factors stated?
7. Were the outcomes measured in a valid and reliable way?
8. Was appropriate statistical analysis used?

In case of disagreement, FWGC was the reviewer responsible for the final decision. The risk of bias was classified as high, moderate, or low based on the percentage of "yes" scores obtained after the final judgment of the item-related checklist ($\leq$49%, 50%–69%, and $\geq$ 70%, respectively) [39].

Effect measures and data synthesis methods

Data were exported to the Revman software (Review Manager, version 5.4.1, Cochrane Collaboration, Copenhagen, Denmark) for meta-analysis of mean differences (linear and volume measurements) and prevalence ratio (morphological findings), both by inverse variance and random-effects methods. The I^2 heterogeneity coefficients were calculated, as well as Egger's and Begg's tests to analyze the risk of publication bias. Additionally, leave-one-out analysis was performed by removing each study to verify their weight on the meta-analysis, and subgroup testing was carried out whenever possible.

Certainty of evidence

The quality of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [40], in relation to study design, sample size, risk of bias, inconsistency, indirectness, population heterogeneity, imprecision, reliability, study power, statistical analysis, conflict of interest, and other relevant aspects.

Results

Study selection

After applying all the criteria in the established phases described in the Materials and methods section, 16 studies were selected [5, 8, 9, 11, 12, 20–22, 25–30]. Of these, three [5, 22, 27] were excluded from the meta-analysis as they did not present enough data for statistical comparisons. All phases concerning the selection of studies are described in Figure 1.

Study characterization

Most studies included in this review ($n = 11$) were from the Asian continent [8, 9, 12, 16, 20, 25, 26, 29, 30], with sample sizes ranging from 36 to 509 individuals. Of the articles included, six performed correlations with the skeletal class [5, 9, 17, 22, 26, 28] (Table 1). Regarding the type of examination, seven articles used lateral view radiographs [5, 8, 16, 20, 22, 26, 28]; and nine CT scans [9, 11, 12, 17, 21, 25, 27, 29, 30], five of which were CBCTs [9, 12, 17, 27, 29]. Most studies digitally analyzed the images [8, 9, 11, 12, 17, 20, 21, 25, 29, 30] ($n = 12$). Results regarding the tests performed and types of analysis are described in Table 2.

Supplementary Table S2 summarizes the inclusion and exclusion criteria of the articles, as well as the delimited points, morphometric and morphological analyses performed, main outcomes, and limitations reported in the studies. The most frequently performed linear measurements were length, diameter, height, and width. Volumetric analysis was performed in three articles [17, 27, 29], two of which were included in the meta-analysis [17, 29].

Regarding the limitations of the studies, the most frequently mentioned was the need for larger sample sizes for greater statistical significance. Two studies mentioned the need to assess different ethnic subgroups [12, 26].

Meta-analysis of linear and volumetric measurements

To carry out the meta-analysis, considering the differences inherent in the types of imaging examinations investigated in this research (two- and three-dimensional), the sample was divided into two subgroups: lateral radiograph (LR) and CT.

Considering the total sample included in the meta-analysis, there was a statistically significant difference between the

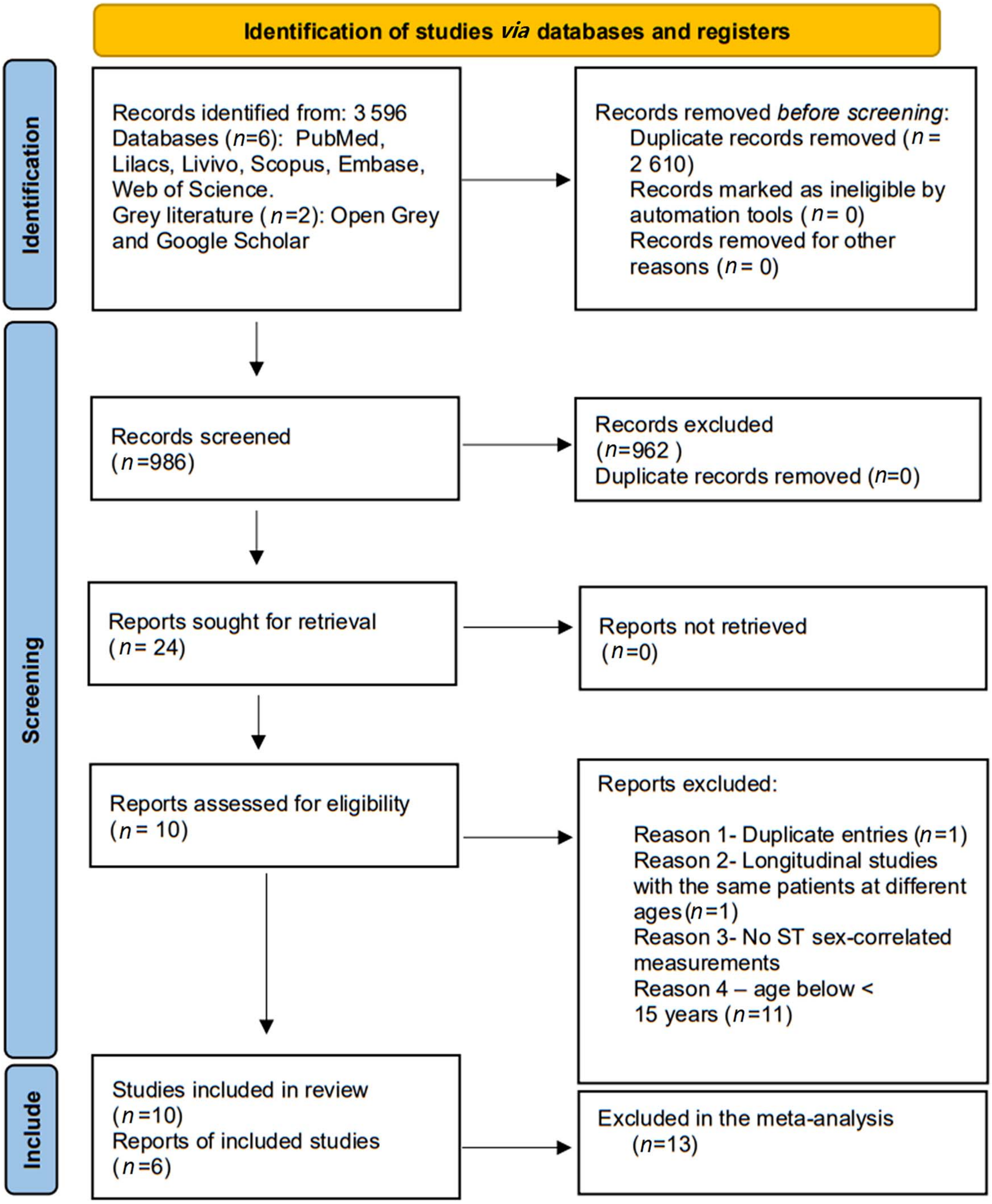


Figure 1 Flow diagram of the study selection process (adapted from PRISMA 2020) [36]. ST: sella turcica.

sexes for the length of the ST ($P = 0.020$). This parameter in females was 0.21 mm (95%CI: 0.03 to 0.38) (Cohen'*d*: − 0.21 (95%CI: −0.44, 0.03)) lower than in males ($P = 0.020$). In a subgroup analysis, the group analyzed through LR showed no significant difference between females and males ($P = 0.170$), while the group analyzed with CT scans showed that females had a length of 0.23 mm (95%CI: 0.04 to −0.42) smaller than males ($P = 0.020$). There was no significant heterogeneity ($P = 0.200$, $I^2 = 23\%$), and the leave-one-out analysis did not change the outcomes evaluated ($P > 0.05$). Egger's ($P = 0.1243$) and Begg's ($P = 0.5470$) tests did not demonstrate significant publication bias (Figure 2).

ST diameter was also statistically reduced in females ($P < 0.01$). The studies that evaluated LR did not show a significant difference between the sexes ($P = 0.610$), while the investigations assessing CT images showed that females exhibited a 0.27 mm (95%CI: 0.24 to 0.31) lower ST diameter than males ($P < 0.001$). There was no significant heterogeneity in the two subgroups, even considering all the studies ($I^2 = 0\%$), and the leave-one-out analysis did not change the outcomes investigated ($P < 0.05$). Egger's ($P = 0.0735$) and Begg's ($P = 0.6547$) tests did not demonstrate significant publication bias (Figure 3).

No significant difference in width was observed between males and females ($P = 0.340$) once all data were grouped. There was significant heterogeneity ($P = 0.001$, $I^2 = 67\%$) and a significant difference ($P = 0.040$) between the subgroups using LR (in which females exhibited a lower mean width

Table 1. Study characterization according to year and journal of publication, country and continent of origin, sex, age, and correlation with skeletal class.

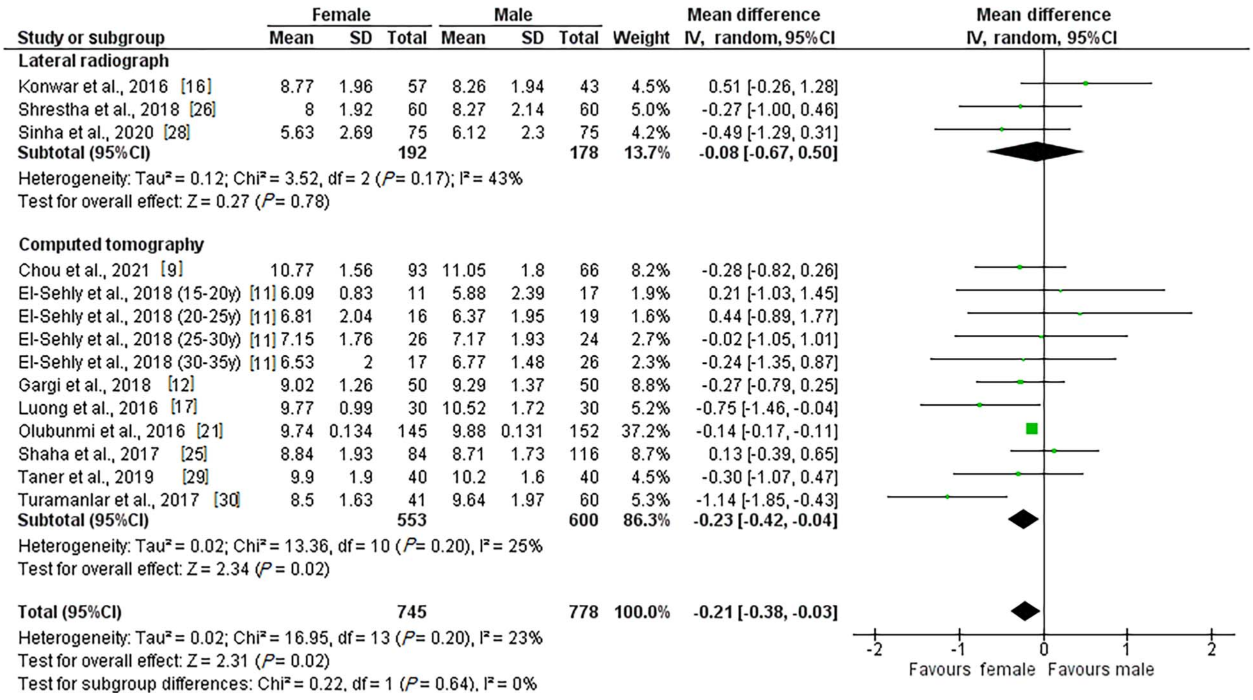
Reference	Publication year	Journal/ JCR 2020 IF	Country or region/ continent	*n* (male/female)	Male:female ratio	Age groups	Age (mean ± SD)			Correlation with skeletal class?
							Overall	Male	Female	
[8]	2012	Int J Recent Trends Sci Technol/NI	India/Asia	447 (237/210)	1.13	13–25; 26–40; 41–55	NI	NI	NI	No
[9]	2021	BioMed Res Int/3.411	Taiwan, China/Asia	159 (66/93)	0.71	18–40	NI	25.20 ± 4.88	25.68 ± 5.79	Yes
[11]	2018	Hum Biol/0.553	Egypt/Africa	215 (126/89)	1.42	0–5; 5–10; 10–15; 15–20; 20–25; 25–30; 30–35	20.35 ± 9.66	19.73 ± 10.23	21.67 ± 8.71	No
[12]	2018	Oral Radiol/1.852	India/Asia	100 (50/50)	1	20–60	40	NI	NI	No
[16]	2016	Int J Dent Med Specialty/NI	India/Asia	100 (43/57)	0.75	15–19; 20–38	NI	NI	NI	No
[17]	2016	J Dent Oral Biol/NI	USA/North America	60 (30/30)	1	>18	NI	37.06 ± 10.64	32.78 ± 10.09	Yes
[5]	2021	Oral Radiol/1.852	Iemen/Asia	234 (67/167)	0.40	8–14; 15–28	NI	NI	NI	Yes
[20]	2018	Ital J Anat Embryol/NI	Jordan/Asia	509 (252/257)	0.98	10–19; 20–40	NI	NI	NI	No
[21]	2016	Int J Med Imaging/NI	Nigeria/Africa	297 (152/145)	1.05	20–89	NI	NI	NI	No
[22]	2016	J Craniofac Surg/1.046	India/Asia	36 (18/18)	1	12–14; 16–18	NI	NI	NI	No
[25]	2017	J Pharm Sci Res/NI	India/Asia	200 (116/84)	1.38	25–70	NI	NI	NI	No
[26]	2018	BMC Oral Health/2.757	Nepal/Asia	120 (60/60)	1	18–30	NI	NI	NI	Yes
[27]	2020	Surg Radiol Anat/NI	Brazil/South America	95 (35/60)	0.58	16–57	NI	NI	NI	Yes
[28]	2020	Transl Res Anat/NI	NI	150 (75/75)	1	18–30	NI	NI	NI	Yes
[29]	2019	Folia Morphol/1.183	Turkey/Asia	80 (40/40)	1	18–45	NI	27.49 ± 8.96	26.57 ± 8.58	No
[30]	2017	Anatomy/NI	Turkey/Asia	101 (60/41)	1.46	17–70	40	NI	NI	No

NI: not informed; JCR: Journal Citation Reports; IF: impact factor; SD: standard deviation.

Table 2. Sample characterization according to the imaging examination and method of analysis

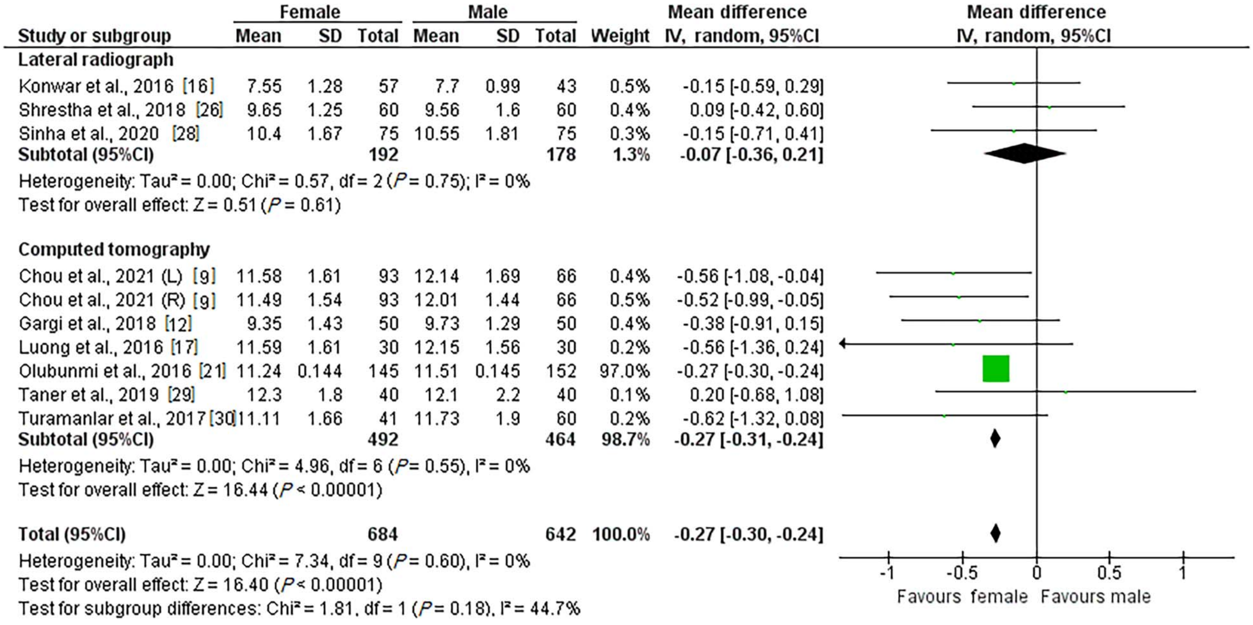
Reference	Imaging examination	Acquisition device	Acquisition parameters	Imaging software	Analysis type	Number of evaluators	Calibration (Kappa or ICC)?	Blind evaluation?	Sample size calculation or *power test?*	Error analysis?
[8]	Lateral skull radiograph	NI	50–90 kV; 100 cm distance	NI	Digital	NI	NI	NI	NI	NI
[9]	CBCT	NewTom VGi evo CBCT machine	110 kV, 4.59 Ma, 3.5 s, voxel 0.03 mm	Soteria DcmRecons (v0.7.0; Soteria Biotech, Ltd, Taipei, China)	Digital	1	NI	NI	Yes	Yes
[11]	MSCT	SOMATOM Defijinition AS, Siemens, Germany	NI	Siemens Syngo 3D	Digital	1	NI	NI	NI	NI
[12]	CBCT	Orthophos SL 3D (Sirona Dental Systems GmbH, Bensheim, Germany	Radiation dose: 68–1 073 μSv	NI	Digital	NI	Yes	NI	NI	NI
[16]	Lateral cephalometric radiography	Rotograph Plus	80 kVp, 10 mA, 0.8 s	NI	Manual	NI	NI	NI	NI	NI
[17]	CBCT	i-CAT® Cone Beam 3D	23 cm × 17 cm, 17.8 s, 0.3 voxels, 120 kVP and 37.10 mA	Dolphin Imaging™ (Dolphin, Chatswort, CA, USA)/ Check point™	Digital	NI	NI	NI	NI	Yes
[5]	Lateral cephalometric radiography	Vatech, Paxi3D Smart™	50–90 KVp and 4–16 mA for 12.9 s	Uceph versão 4.2.1, Chengdu Yaxun Technology Co., Ltd, Chengdu, China)	Digital	1	NI	NI	NI	Yes
[20]	Lateral cephalometric radiography	NI	NI	Viewbox 3 (dHAL Software, Kifissia, Greece)	Digital	NI	NI	Yes	NI	Yes
[21]	Cranial CT Scan	NI	NI	Radiology Information System Software	Digital	NI	NI	NI	NI	NI
[22]	Lateral cephalometric radiography	NI	NI	NI	Manual	2	NI	NI	NI	NI
[25]	Cranial CT Scan	NI	NI	Radiant dicom viewer software	Digital	NI	NI	NI	NI	NI
[26]	Lateral cephalometric radiography	Gendex Orthoralix 9200 DDE	NI	NI	Manual	1	NI	NI	Yes	Yes
[27]	CBCT	i-Cat (Hatfeld, PA, USA)	120 kV, 1–11 mA, FOV 25 × 17 cm, 3.6 s, voxel 0.2 mm^3	ITK-SNAP version 3.6	Digital	NI	NI	NI	NI	NI
[28]	Lateral cephalometric radiography	Planmeca Promax (Helsinki, Finland)	68 kV, 5 mA, 18.7 s	NI	Manual	1	NI	NI	NI	NI
[29]	CBCT	Planmeca Promax 3D unit (Helsinki, Finland)	84 kVp, 9–14 mA, 0.16 mm voxel size, expo 12 s, FOV 8 × 8 cm	Planmeca, Romexis viewer 2.9.2.R	Digital	1	NI	Yes	Yes	Yes
[30]	Cranial CT Scan	NI	NI	NI	Digital	NI	NI	NI	NI	NI

NI: not informed. CBCT: cone beam computed tomography; MSCT: multislice computed tomography.



Study or subgroup	Female Mean	Female SD	Female Total	Male Mean	Male SD	Male Total	Weight	Mean difference IV, random, 95%CI
Lateral radiograph								
Konwar et al., 2016 [16]	8.77	1.96	57	8.26	1.94	43	4.5%	0.51 [-0.26, 1.28]
Shrestha et al., 2018 [26]	8	1.92	60	8.27	2.14	60	5.0%	-0.27 [-1.00, 0.46]
Sinha et al., 2020 [28]	5.63	2.69	75	6.12	2.3	75	4.2%	-0.49 [-1.29, 0.31]
Subtotal (95%CI)			**192**			**178**	**13.7%**	**-0.08 [-0.67, 0.50]**
Heterogeneity: Tau² = 0.12; Chi² = 3.52, df = 2 (*P* = 0.17); I² = 43%								
Test for overall effect: Z = 0.27 (*P* = 0.78)								
Computed tomography								
Chou et al., 2021 [9]	10.77	1.56	93	11.05	1.8	66	8.2%	-0.28 [-0.82, 0.26]
El-Sehly et al., 2018 (15-20y) [11]	6.09	0.83	11	5.88	2.39	17	1.9%	0.21 [-1.03, 1.45]
El-Sehly et al., 2018 (20-25y) [11]	6.81	2.04	16	6.37	1.95	19	1.6%	0.44 [-0.89, 1.77]
El-Sehly et al., 2018 (25-30y) [11]	7.15	1.76	26	7.17	1.93	24	2.7%	-0.02 [-1.05, 1.01]
El-Sehly et al., 2018 (30-35y) [11]	6.53	2	17	6.77	1.48	26	2.3%	-0.24 [-1.35, 0.87]
Gargi et al., 2018 [12]	9.02	1.26	50	9.29	1.37	50	8.8%	-0.27 [-0.79, 0.25]
Luong et al., 2016 [17]	9.77	0.99	30	10.52	1.72	30	5.2%	-0.75 [-1.46, -0.04]
Olubunmi et al., 2016 [21]	9.74	0.134	145	9.88	0.131	152	37.2%	-0.14 [-0.17, -0.11]
Shaha et al., 2017 [25]	8.84	1.93	84	8.71	1.73	116	8.7%	0.13 [-0.39, 0.65]
Taner et al., 2019 [29]	9.9	1.9	40	10.2	1.6	40	4.5%	-0.30 [-1.07, 0.47]
Turamanlar et al., 2017 [30]	8.5	1.63	41	9.64	1.97	60	5.3%	-1.14 [-1.85, -0.43]
Subtotal (95%CI)			**553**			**600**	**86.3%**	**-0.23 [-0.42, -0.04]**
Heterogeneity: Tau² = 0.02; Chi² = 13.36, df = 10 (*P* = 0.20), I² = 25%								
Test for overall effect: Z = 2.34 (*P* = 0.02)								
Total (95%CI)			**745**			**778**	**100.0%**	**-0.21 [-0.38, -0.03]**
Heterogeneity: Tau² = 0.02; Chi² = 16.95, df = 13 (*P* = 0.20), I² = 23%								
Test for overall effect: Z = 2.31 (*P* = 0.02)								
Test for subgroup differences: Chi² = 0.22, df = 1 (*P* = 0.64), I² = 0%								

Figure 2 Meta-analysis of the sella turcica length parameter according to the type of imaging examination. CI: confidence interval. Cohen's *d*: – 0.21 ((95%CI: –0.44, 0.03).



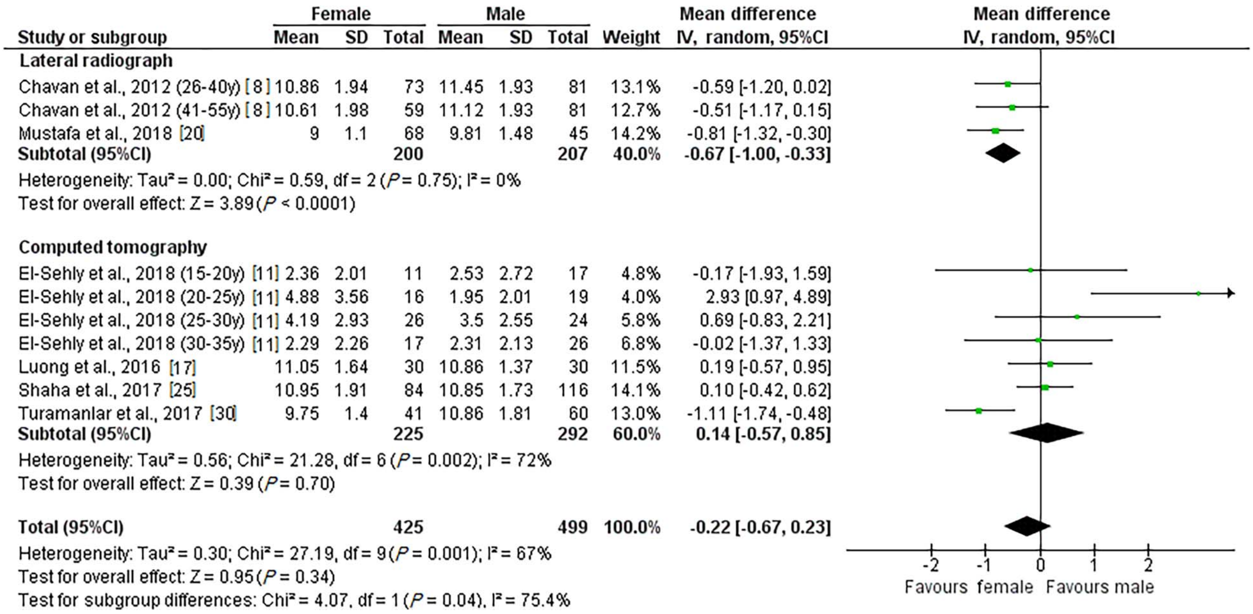
Study or subgroup	Female Mean	Female SD	Female Total	Male Mean	Male SD	Male Total	Weight	Mean difference IV, random, 95%CI
Lateral radiograph								
Konwar et al., 2016 [16]	7.55	1.28	57	7.7	0.99	43	0.5%	-0.15 [-0.59, 0.29]
Shrestha et al., 2018 [26]	9.65	1.25	60	9.56	1.6	60	0.4%	0.09 [-0.42, 0.60]
Sinha et al., 2020 [28]	10.4	1.67	75	10.55	1.81	75	0.3%	-0.15 [-0.71, 0.41]
Subtotal (95%CI)			**192**			**178**	**1.3%**	**-0.07 [-0.36, 0.21]**
Heterogeneity: Tau² = 0.00; Chi² = 0.57, df = 2 (*P* = 0.75); I² = 0%								
Test for overall effect: Z = 0.51 (*P* = 0.61)								
Computed tomography								
Chou et al., 2021 (L) [9]	11.58	1.61	93	12.14	1.69	66	0.4%	-0.56 [-1.08, -0.04]
Chou et al., 2021 (R) [9]	11.49	1.54	93	12.01	1.44	66	0.5%	-0.52 [-0.99, -0.05]
Gargi et al., 2018 [12]	9.35	1.43	50	9.73	1.29	50	0.4%	-0.38 [-0.91, 0.15]
Luong et al., 2016 [17]	11.59	1.61	30	12.15	1.56	30	0.2%	-0.56 [-1.36, 0.24]
Olubunmi et al., 2016 [21]	11.24	0.144	145	11.51	0.145	152	97.0%	-0.27 [-0.30, -0.24]
Taner et al., 2019 [29]	12.3	1.8	40	12.1	2.2	40	0.1%	0.20 [-0.68, 1.08]
Turamanlar et al., 2017 [30]	11.11	1.66	41	11.73	1.9	60	0.2%	-0.62 [-1.32, 0.08]
Subtotal (95%CI)			**492**			**464**	**98.7%**	**-0.27 [-0.31, -0.24]**
Heterogeneity: Tau² = 0.00; Chi² = 4.96, df = 6 (*P* = 0.55), I² = 0%								
Test for overall effect: Z = 16.44 (*P* < 0.00001)								
Total (95%CI)			**684**			**642**	**100.0%**	**-0.27 [-0.30, -0.24]**
Heterogeneity: Tau² = 0.00; Chi² = 7.34, df = 9 (*P* = 0.60), I² = 0%								
Test for overall effect: Z = 16.40 (*P* < 0.00001)								
Test for subgroup differences: Chi² = 1.81, df = 1 (*P* = 0.18), I² = 44.7%								

Figure 3 Meta-analysis of the sella turcica diameter parameter according to the type of imaging examination. CI: confidence interval. Cohen's *d*: – 0.36 (95%CI: –0.79, 0.06).

of 0.67 mm (95%CI: 0.33 to 1.00) compared to males ($P < 0.001$)) and the CT subgroup (which showed no difference between sexes ($P = 0.700$)). The leave-one-out analysis did not change the outcomes studied ($P > 0.05$), and Egger's ($P = 0.2549$) and Begg's ($P = 0.4208$) tests did not demonstrate significant publication bias (Figure 4).

The height analysis was also based on the same two subgroups. No difference between the two subgroups was observed ($P = 0.530$), and both showed no significant difference between females and males ($P = 0.660$ and $P = 0.650$, respectively). There was significant heterogeneity in the CT subgroup ($P = 0.030$, $I^2 = 51\%$), but not in the LR group ($P = 0.120$, $I^2 = 43\%$). The leave-one-out analysis did not change the outcomes studied ($P > 0.05$) and Egger's ($P = 0.1197$) and Begg's ($P = 0.5285$) tests did not demonstrate significant publication bias (Figure 5).

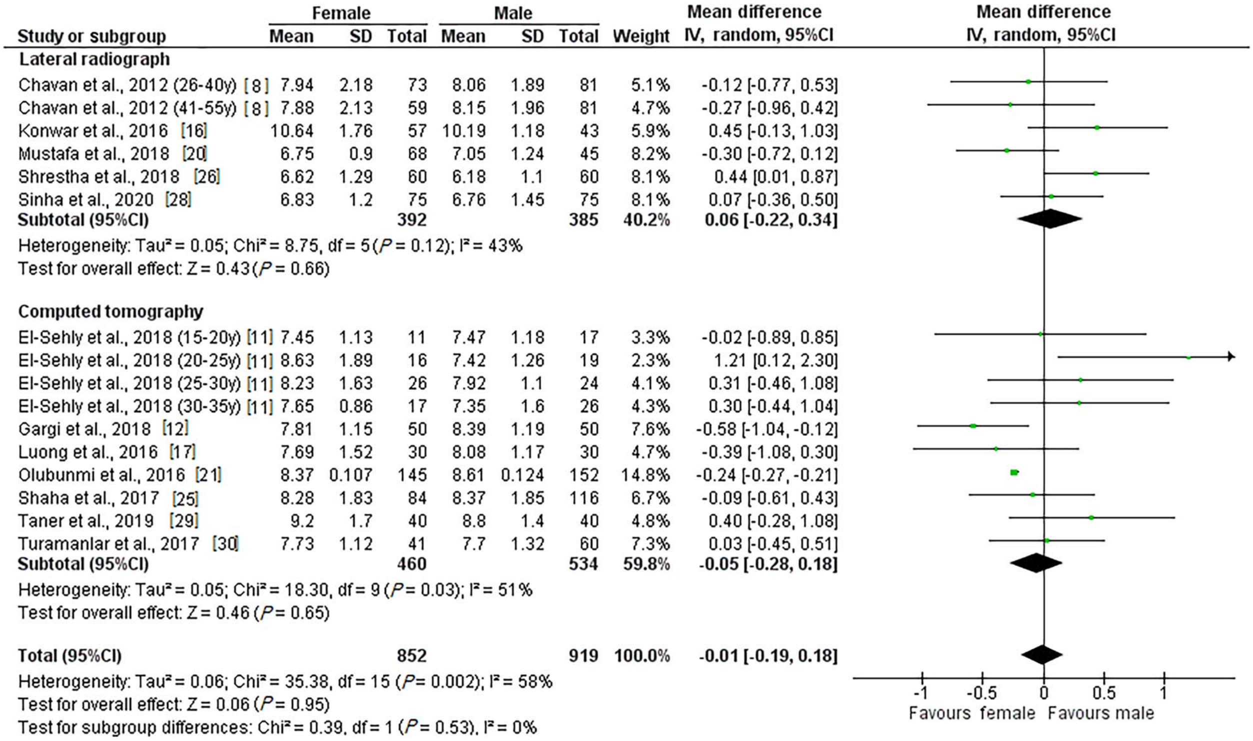
Only two studies evaluating CT scans measured ST volume [17, 29]. No significant difference between females and males ($P = 0.210$) nor significant heterogeneity ($P = 0.060$, $I^2 = 71\%$) was observed. Removing the findings by Luong et al. [17] favoured a significant difference between males and females as reported by Taner et al. [29] (Figure 6).



Study or subgroup	Female Mean	Female SD	Female Total	Male Mean	Male SD	Male Total	Weight	Mean difference IV, random, 95%CI
Lateral radiograph								
Chavan et al., 2012 (26-40y) [8]	10.86	1.94	73	11.45	1.93	81	13.1%	-0.59 [-1.20, 0.02]
Chavan et al., 2012 (41-55y) [8]	10.61	1.98	59	11.12	1.93	81	12.7%	-0.51 [-1.17, 0.15]
Mustafa et al., 2018 [20]	9	1.1	68	9.81	1.48	45	14.2%	-0.81 [-1.32, -0.30]
Subtotal (95%CI)			**200**			**207**	**40.0%**	**-0.67 [-1.00, -0.33]**
Heterogeneity: Tau² = 0.00; Chi² = 0.59, df = 2 (*P* = 0.75); I² = 0%								
Test for overall effect: Z = 3.89 (*P* < 0.0001)								
Computed tomography								
El-Sehly et al., 2018 (15-20y) [11]	2.36	2.01	11	2.53	2.72	17	4.8%	-0.17 [-1.93, 1.59]
El-Sehly et al., 2018 (20-25y) [11]	4.88	3.56	16	1.95	2.01	19	4.0%	2.93 [0.97, 4.89]
El-Sehly et al., 2018 (25-30y) [11]	4.19	2.93	26	3.5	2.55	24	5.8%	0.69 [-0.83, 2.21]
El-Sehly et al., 2018 (30-35y) [11]	2.29	2.26	17	2.31	2.13	26	6.8%	-0.02 [-1.37, 1.33]
Luong et al., 2016 [17]	11.05	1.64	30	10.86	1.37	30	11.5%	0.19 [-0.57, 0.95]
Shaha et al., 2017 [25]	10.95	1.91	84	10.85	1.73	116	14.1%	0.10 [-0.42, 0.62]
Turamanlar et al., 2017 [30]	9.75	1.4	41	10.86	1.81	60	13.0%	-1.11 [-1.74, -0.48]
Subtotal (95%CI)			**225**			**292**	**60.0%**	**0.14 [-0.57, 0.85]**
Heterogeneity: Tau² = 0.56; Chi² = 21.28, df = 6 (*P* = 0.002); I² = 72%								
Test for overall effect: Z = 0.39 (*P* = 0.70)								
Total (95%CI)			**425**			**499**	**100.0%**	**-0.22 [-0.67, 0.23]**

Heterogeneity: Tau² = 0.30; Chi² = 27.19, df = 9 (*P* = 0.001); I² = 67%
Test for overall effect: Z = 0.95 (*P* = 0.34)
Test for subgroup differences: Chi² = 4.07, df = 1 (*P* = 0.04), I² = 75.4%

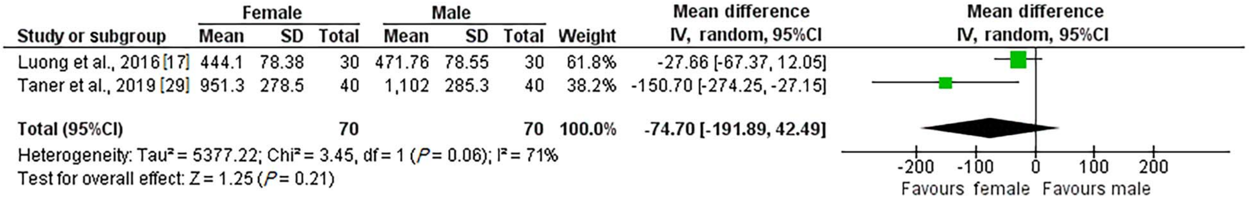
Figure 4 Meta-analysis of the sella turcica width parameter according to the type of imaging examination. CI: confidence interval. Cohen's *d*: – 0.11 (95%CI: –0.36, 0.14).



Study or subgroup	Female Mean	Female SD	Female Total	Male Mean	Male SD	Male Total	Weight	Mean difference IV, random, 95%CI
Lateral radiograph								
Chavan et al., 2012 (26-40y) [8]	7.94	2.18	73	8.06	1.89	81	5.1%	-0.12 [-0.77, 0.53]
Chavan et al., 2012 (41-55y) [8]	7.88	2.13	59	8.15	1.96	81	4.7%	-0.27 [-0.96, 0.42]
Konwar et al., 2016 [16]	10.64	1.76	57	10.19	1.18	43	5.9%	0.45 [-0.13, 1.03]
Mustafa et al., 2018 [20]	6.75	0.9	68	7.05	1.24	45	8.2%	-0.30 [-0.72, 0.12]
Shrestha et al., 2018 [26]	6.62	1.29	60	6.18	1.1	60	8.1%	0.44 [0.01, 0.87]
Sinha et al., 2020 [28]	6.83	1.2	75	6.76	1.45	75	8.1%	0.07 [-0.36, 0.50]
Subtotal (95%CI)			**392**			**385**	**40.2%**	**0.06 [-0.22, 0.34]**
Heterogeneity: Tau² = 0.05; Chi² = 8.75, df = 5 (*P* = 0.12); I² = 43%								
Test for overall effect: Z = 0.43 (*P* = 0.66)								
Computed tomography								
El-Sehly et al., 2018 (15-20y) [11]	7.45	1.13	11	7.47	1.18	17	3.3%	-0.02 [-0.89, 0.85]
El-Sehly et al., 2018 (20-25y) [11]	8.63	1.89	16	7.42	1.26	19	2.3%	1.21 [0.12, 2.30]
El-Sehly et al., 2018 (25-30y) [11]	8.23	1.63	26	7.92	1.1	24	4.1%	0.31 [-0.46, 1.08]
El-Sehly et al., 2018 (30-35y) [11]	7.65	0.86	17	7.35	1.6	26	4.3%	0.30 [-0.44, 1.04]
Gargi et al., 2018 [12]	7.81	1.15	50	8.39	1.19	50	7.6%	-0.58 [-1.04, -0.12]
Luong et al., 2016 [17]	7.69	1.52	30	8.08	1.17	30	4.7%	-0.39 [-1.08, 0.30]
Olubunmi et al., 2016 [21]	8.37	0.107	145	8.61	0.124	152	14.8%	-0.24 [-0.27, -0.21]
Shaha et al., 2017 [25]	8.28	1.83	84	8.37	1.85	116	6.7%	-0.09 [-0.61, 0.43]
Taner et al., 2019 [29]	9.2	1.7	40	8.8	1.4	40	4.8%	0.40 [-0.28, 1.08]
Turamanlar et al., 2017 [30]	7.73	1.12	41	7.7	1.32	60	7.3%	0.03 [-0.45, 0.51]
Subtotal (95%CI)			**460**			**534**	**59.8%**	**-0.05 [-0.28, 0.18]**
Heterogeneity: Tau² = 0.05; Chi² = 18.30, df = 9 (*P* = 0.03); I² = 51%								
Test for overall effect: Z = 0.46 (*P* = 0.65)								
Total (95%CI)			**852**			**919**	**100.0%**	**-0.01 [-0.19, 0.18]**

Heterogeneity: Tau² = 0.06; Chi² = 35.38, df = 15 (*P* = 0.002); I² = 58%
Test for overall effect: Z = 0.06 (*P* = 0.95)
Test for subgroup differences: Chi² = 0.39, df = 1 (*P* = 0.53), I² = 0%

Figure 5 Meta-analysis of the sella turcica height parameter according to the type of imaging examination. CI: confidence interval. Cohen's *d*: – 0.09 (95%CI: –0.46, 0.28).



Study or subgroup	Female Mean	Female SD	Female Total	Male Mean	Male SD	Male Total	Weight	Mean difference IV, random, 95%CI
Luong et al., 2016 [17]	444.1	78.38	30	471.76	78.55	30	61.8%	-27.66 [-67.37, 12.05]
Taner et al., 2019 [29]	951.3	278.5	40	1,102	285.3	40	38.2%	-150.70 [-274.25, -27.15]
Total (95%CI)			**70**			**70**	**100.0%**	**-74.70 [-191.89, 42.49]**

Heterogeneity: Tau² = 5377.22; Chi² = 3.45, df = 1 (*P* = 0.06); I² = 71%
Test for overall effect: Z = 1.25 (*P* = 0.21)

Figure 6 Meta-analysis of the sella turcica volume parameter according to the type of imaging examination. CI: confidence interval. Cohen's *d*: – 0.45 (95%CI: –0.79, –0.11).

Risk of bias and certainty of evidence analysis

Of the articles included in the meta-analysis of this review, four were at low risk of bias [9, 11, 12, 20] and only three studies were at low risk in less than 50% of the JBI tool items [21, 25, 30]. In most items, a low risk of bias was observed, except for Item 2 (Were the study subjects and the setting described in detail?), in which most studies did not present clear information on this topic; and in Item 3 (Was the exposure measured in a valid and reliable way?), in which most studies fell into the uncertain category, as they did not present information on the calibration of evaluators or reproducibility error analysis.

In the items referring to confounding factors, seven articles [8, 9, 11, 12, 16, 20, 28] performed subgroup analyses with possible confounding factors for the differentiation between the sexes—age group and skeletal classes (Supplementary Figure S1).

Table 3 presents the GRADE analysis, in which a very low certainty of evidence of the included articles was observed.

Discussion

In the field of forensic anthropology, the study of ST-related normality parameters in imaging examinations according to sex is relevant for Dentistry and Legal Medicine as a potential means for human identification [10, 35]. ST has been well-documented in anatomic and clinical-related literature; however, there are no synthesis of the evidence associated with meta-analysis and certainty evidence assessment focused on the utility of this structure in the process of sex-related personal identification. For this fact, anthropologists should be aware of the importance of ST in a forensic context [41], and the present study revealed a dysmorphic pattern associated with measurements from ST.

The general meta-analysis of the study measurements evidenced a significant difference between the sexes for the length and diameter parameters. When analyzed by examination type, these measurements were statistically significant only in the CT subgroup. CT scans present high-resolution sectional images in different orientation planes, enabling three-dimensional reconstructions [42]. Thus, several studies have been conducted with this three-dimensional imaging modality [9–15, 17, 21, 25, 27, 29–31]. In addition, CT allows for more detailed information, capable of elucidating minimal bone differences in the skull that may not be visible on radiographs because of inherent anatomical overlap [11]. Significantly larger linear measurements have been reported in lateral cephalograms compared to these measurements obtained more accurately through CBCT [43].

It is important to highlight that even considering all the studies and subgroups (cephalometric radiographs and CT), no significant heterogeneity ($I^2 = 0\%$) was observed for the ST diameter, and the leave-one-out analysis did not change the outcomes studied ($P < 0.05$). This indicates that the diameter parameter was very similar in all studies regardless of the samples. Even with the removal of papers with considerable weights, such as Olubunmi et al. [21], there were no changes in outcomes.

A trend for linear ST measurements with lower values in females was noted, which corroborates the studies by Chou et al. [9] and Olubunmi et al. [21]. Similarly, the study by Taner et al. [29] found ST volume to be lower in females. Discordant results were reported by Rai et al. [22], who evaluated a limited sample size in which the measurements of length and height were greater in females; and Silveira et al. [27] who evaluated a Brazilian population in which the diameter and volume were higher in females.

Two studies performed subgroup analyses by skeletal classes [9, 28]. In the investigation performed by Chou et al. [9], only one measurement significantly differed between skeletal classes in each sex group. However, the authors believe that these differences may have been related to discrepancies inherent in sex, and not in skeletal classes. Sinha et al. [28], however, demonstrated differences between the sexes in some skeletal classes, in which class II females presented greater depth and diameter values. Other studies reported higher measurements in males, except for depth in class I and length and depth in class III, in which there were no significant differences.

Morphological analysis was performed by eight authors [5, 12, 16, 20, 22, 26–28], most of them using the classification proposed by Axelsson et al. [7]. Nevertheless, in only three articles [16, 20, 26] discrimination of morphological findings according to sex was reported. As the purpose of this study was to perform ST evaluation for sexual dimorphism, the inclusion of a greater number of investigations was not feasible, which limited the strength of this research.

Interpreting variable data on ST dimensions may be challenging; therefore, the present results should be assessed with caution due to the potential presence of ethnic variations between the selected populations of the studies. It is seen that a relatively homogeneous body of literature does not exist on this topic, which reinforces the importance of this systematic review for future primary studies focused on this topic. Of the articles included in this review, there was a trend toward studies of this type in the Asian continent. It is important to ensure that these image assessment methods are validated in different populations because of the possibility of regional variations [18, 19, 44]. Some studies evaluating ST morphology in different ethnicities found significant differences among the populations [18, 19]. Similarly, some countries with continental dimensions may present different ethnic subgroups within the same population [45], which may be a confounding factor in the results of the studies. This fact was a limitation discussed by Gargi et al. [12] and Shresta et al. [26].

In this review, we sought to assess the normality parameters of ST focusing on sexual dimorphism. In sex estimation studies, a relevant aspect commonly addressed is the need to control confounding variables to increase the generalizability of the results. Confounding variables may reside in differences between the comparison groups beyond those initially intended to be investigated in the study, which may influence the direction of the results [39].

An important confounding factor for sex estimation is age. In studies comparing different age groups, significant differences between age groups were observed within the same sex [8, 11, 20]. In the study by El-Sehly' et al. [11], only in the age group from 20 to 25 years, a significant dimorphism for most measurements was detected. The literature reports a greater difficulty in estimating sex in prepubertal individuals because of different pubertal growth trajectories in males and females [33, 46]. Studies also suggest that there may be reductions in

Table 3. Analysis of the quality of the evidence of the included studies using the grading of recommendations assessment, development and evaluation (GRADE) approach.

Parameter	Certainty assessment							Number of patients		Effect		Certainty	Importance
	Number of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ST morphometry in females	ST morphometry in males	Relative (95%CI)	Absolute (95%CI)		
Sella width (mm)	10	Observational studies	Serious	Very serious[a]	Not serious	Not serious	Publication bias strongly suspected strong association[g]	425	499	NI	−0.11 (−0.36 to 0.14)	Very low	Important
Sella length (mm)	14	Observational studies	Serious	Very serious[b]	Not serious	Not serious	Publication bias strongly suspected strong association[g]	745	778	NI	−0.21 (−0.44 to 0.03)	Very low	Important
Sella height (mm)	16	Observational studies	Serious	Very serious[c]	Not serious	Not serious	Publication bias strongly suspected strong association[g]	852	919	NI	−0.09 (−0.46 to 0.28)	Very low	Important
Sella anterior height (mm)	6	Observational studies	Very serious	Serious[d]	Not serious	Not serious	None	195	262	NI	0.11 (−0.08 to 0.30)	Very low	Important
Sella posterior height (mm)	6	Observational studies	Very serious	Very serious[e]	Not serious	Not serious	None	195	262	NI	0.07 (−0.12 to 0.26)	Very low	Important
Sella diameter (mm)	10	Observational studies	Serious	Very serious[e]	Not serious	Not serious	Publication bias strongly suspected strong association[h]	684	642	NI	−0.36 (−0.79 to 0.06)	Very low	Important
Sella area (mm^2)	8	Observational studies	Serious	Very serious[e]	Not serious	Not serious	Publication bias strongly suspected strong association[h]	273	338	NI	−0.36 (−0.79 to 0.06)	Very low	Important
Sella volume (mm^3)	2	Observational studies	Very serious	Very serious[f]	Not serious	Serious	Publication bias strongly suspected strong association[h]	70	70	NI	−0.45 (−0.79 to −0.11)	Very low	Important

Confidence interval of individual studies and I^2: [a] 67%; [b] 23%; [c] 58%; [d] 7%; [e] 0%; [f] 71%. [g]Publication bias strongly suspected strong association. [h]Standardised mean difference values, expressed as mean±standard deviation. ST: sella turcica; NI: not informed.

cranial sexual dimorphism in elderly individuals [20, 47, 48]. These reductions may result from craniofacial changes related to hormonal variations that affect postmenopausal females [49, 50]. In this review, five studies performed subgroup analysis by age groups [8, 11, 12, 16, 20].

In the literature, normal values for the ST dimensions seem to be conflicting. Wide ranges of values can be seen in the previous studies. The varying results in those studies might be due to different landmarks representing the same dimensions and degrees of magnification in cephalometric radiographs. In this study, similar reference points were employed among most studies, with some authors proposing minor modifications for its delimitation (Figures 7 and 8). Furthermore, variations in the methodology used to demarcate and perform the ST measurements were observed. Regarding cephalometric images, some studies performed manual demarcation on acetate matte tracing paper under optimal illumination [16, 22, 26, 28], while

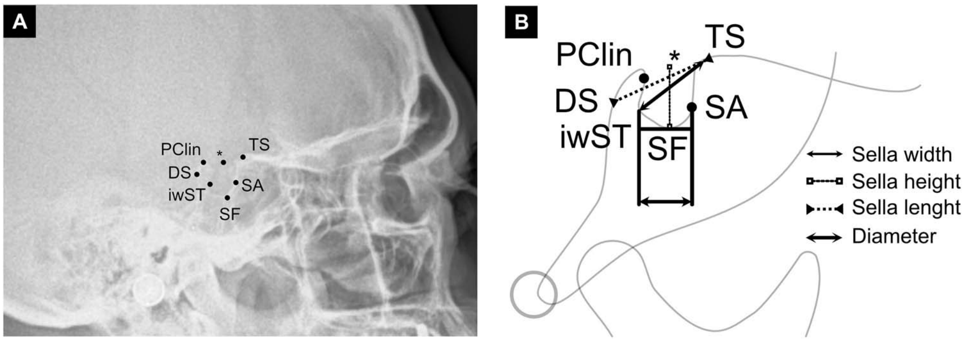


Figure 7 Summary of landmarks and sella turcica (ST) measurements on cephalometric radiographs [8, 16, 20, 26, 28]. Reference points: TS: tuberculum sellae; DS: dorsum sellae; SF: sella floor; SA: sella anterior; iwST: inner wall of the ST (most posterior point); PClin: posterior clinoid process; *Midpoint between TS and DS. The images were obtained from a database where images are anonymized to ensure patient privacy and confidentiality. This database originates from an ongoing observational study with images that was previously approved by the local ethical committee.

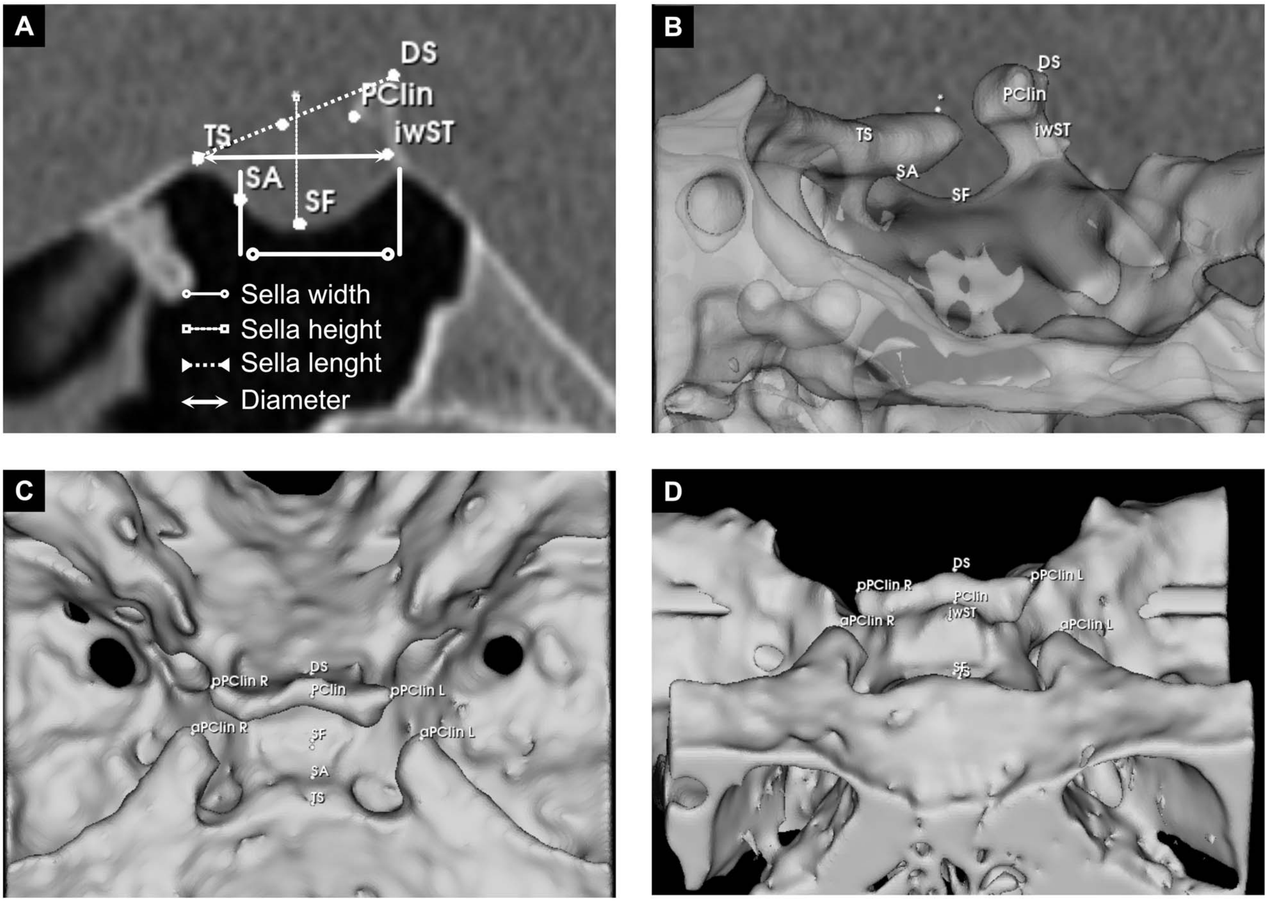


Figure 8 Sella turcica measurements in 2D (A) and 3D (B-D) CT images [9, 11, 12, 17, 21, 25, 29, 30]. Anteroposterior (A, B), craniocaudal (C), and oblique (D) views. Reference points: TS: tuberculum sellae; DS: dorsum sellae; SF: sella floor; SA: sella anterior; iwST: inner wall of the ST (most posterior point); PClin: posterior clinoid process; *Midpoint between TS and DS. The images were obtained from a database where images are anonymized to ensure patient privacy and confidentiality. This database originates from an ongoing observational study with images that was previously approved by the local ethical committee.

others performed the analysis on digital images [5, 8, 20]. It is reported that the magnification rate of different cephalometric devices can also generate differences in linear measurements [51]. Mustafa et al. [20] used a clear reference ruler to correct the magnification of the images, and Shrestha et al. [26] corrected all linear measurements according to the magnification rate of the device.

In studies that used CT, the problem of the magnification rate is eliminated, but there may still be some differences in the delimitation of the reference points. Most studies included in this systematic review analyzed a sagittal section of the image, performing measurements like those already published in cephalometric radiographs [11, 12, 17, 21, 25, 27, 29, 30]. The investigation by Chou et al. [9] carried out a three-dimensional analysis through image segmentation, with different measures for the right and left sides, representing a methodologically appropriate approach for future observational studies.

Based on the synthesis of evidence carried out in this systematic review with meta-analysis, we believe that the following aspects should be avoided to improve the design of future investigations: (i) lack of standardization regarding techniques for obtaining images and their analysis (manual *versus* digital methods); (ii) samples with an imbalance concerning the sex distribution; some studies included in the present systematic review did not equally match the number of men and women; (iii) unavailability of details regarding the protocol for obtaining X-ray images (i.e. devices and acquisition parameters); (iv) assessors not blind regarding the sex evaluation; (v) intra- and inter-examiner reproducibility tests not described in the methodology, which are recognized as helpful in confirming the calibration of the examiners; (vi) use of small samples and the ethnic variability. Methodologically, these limitations may impact the quality of the evidence related to sexual dimorphism assessment.

Conclusion

This study showed that the length and diameter of the ST were smaller in females; however, the certainty of evidence from this systematic review was graded to be “very low”. When compared by imaging examination type, females had lower values for width in the LR subgroup, and length and diameter only in the CT subgroup. There was no statistically significant difference regarding height, area, and volume. Considering the anatomical importance of the ST and its potential use for sex estimation, future research focusing on the evaluation of normality parameters of this structure in both sexes from different populations is needed.

Acknowledgements

The authors are grateful to the Brazilian National Council for Scientific and Technological Development (CNPq). Dr. Fábio W.G. Costa (PQ category 2) is fellow researcher. Miss Esther C. Ribeiro was supported by a research scholarship (CAPES—Brazilian Coordination for the Improvement of Higher Education Personnel).

Authors’ contributions

Esther C. Ribeiro, Francisco S. R. Carvalho, Diego S. de Mendonça and Fábio W. G. Costa contributed to the project development, data collection, data analysis and manuscript writing. Paulo G. de Barros Silva contributed to the data analysis and manuscript writing. Lúcio M. Kurita, Andréa S. W. de Aguiar, Fabrício M. Tuji and Frederico S. Neves participated in the project development and manuscript editing. All authors contributed to the final text and approved it.

Compliance with ethical standards

This research did not involve human participants and/or animals, therefore informed consent is not applicable.

Disclosure statement

The authors declare that they have no competing interests.

Funding

This study was funded by CAPES [grant number: 88887.641089/2021-00, Brazilian Government]. This research was also supported by PROAP/PRINT/CAPES and Portalde Periodicos CAPES - Finance Code 001.

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