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REVIEW ARTICLE

Zygomaticofacial foramen and its surgical anatomy in plastic and maxillofacial surgery — a systematic review with a meta-analysis

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ABSTRACT

A comprehensive understanding of the ZFF is essential in clinical and surgical settings, particularly in procedures involving facial trauma repair, reconstructive and plastic surgery.

The aim of this meta-analysis was to obtain anatomical data on ZFF and its variations, in order to emphasize its physiological, as well as clinical implications.

A large-scale search was conducted in all major databases (PubMed, Embase, Science Direct, Scopus and Web of Science) in order to determine and pool all available and relevant ZFF data.

A total of 22 studies (5438 skull sides) was included. The analysis revealed that in the majority of skull sides, the number of ZFF is one (45.34%, 95% CI: 41.56–49.12), followed by two (25.83%, 95% CI: 18.27–33.39), and then zero (14.11%, 95% CI: 10.15–18.07). The

mean diameter of ZFF was 1.23 mm (95% CI: 0.33–2.13). The mean distance from the ZFF to the zygomatic angle was 12.02 mm (95% CI: 10.06–13.98), to the closest point of the orbital rim — 6.71 mm (95% CI: 5.98–7.43), to the midpoint of frontozygomatic suture — 25.50 mm (95% CI: 24.91–26.10), and to the lowest point of the zygomaticomaxillary suture — 19.00 mm (95% CI: 18.39–19.61).

Understanding the precise anatomy and variability of the ZFF's prevalence, number and spatial relationships is critical in surgical and clinical practices involving the midfacial region.

Keywords: zygomaticofacial foramen, zygomaticofacial nerve, surgical anatomy, maxillofacial surgery

INTRODUCTION

The zygomaticofacial foramen (ZFF) is an opening located on the facial aspect of the zygomatic bone which serves as an exit site for the terminal branch of the maxillary nerve, namely the zygomaticofacial nerve (ZFN), as well as the corresponding zygomaticofacial vessels, which together form a neurovascular bundle. According to the existing studies, multiple foramina may be present, although in some individuals they may be completely absent [1]. Such variance may result from the embryonic development of the zygomatic nerve (ZN). As the nerve divides, it may become trapped in mesenchyme on its way to the division point within the orbit, causing causing the entry (ZO) and exit foramina [ZFF and zygomaticotemporal foramina (ZTF)] to be either equal or unequal [19].

Therefore, the number of ZFF can range from a single opening to multiple foramina on the zygomatic bone, with their precise localization differing among individuals and populations [6]. Variations in shape and diameter further add to the complexity. Additionally, the ZFF often demonstrates anatomical connections with other foramina and neurovascular structures, such as the ZTF and infraorbital foramina, underscoring its role in the intricate network of midfacial innervation and vascularization [23].

Understanding its precise location, morphology, and clinical relevance is essential for both anatomical study and surgical applications, since ZFF serves as a key landmark for various interventions, including reconstructive, aesthetic, and trauma-related procedures. In surgeries such as maxillary osteotomies, repair of midface fractures, and cosmetic interventions damage to the neurovascular bundle exiting the ZFF can lead to complications like hematomas and prolonged recovery [6].

Clinical applications of the anatomy and the variability in ZFF frequency and localization are diverse. Interestingly enough, these structures have been utilized as anthropological markers for discerning populations and ethnic groups, contributing to the accumulation of anthropological data and providing valuable insights for practitioners to improve performance in the periorbital region [4].

This meta-analysis delves into the detailed anatomy of the ZFF, including its variations, relationships with surrounding structures and its significance in clinical practice. By exploring this structure, we aim to provide a comprehensive resource for surgeons and anatomists seeking to deepen their understanding of craniofacial anatomy.

MATERIALS AND METHODS

This systematic review and meta-analysis was prospectively registered in PROSPERO (CRD42024570748).

Search strategy

In October 2024 an extensive search of the main online databases (Pubmed, Embase and Web of Science Core Collection, Scopus, SciElo) was performed to extract all the studies that included relevant information regarding ZFF and its anatomy. In addition to database searching, we reviewed all the major anatomical journals (e.g. Annals of Anatomy, Journal of Anatomy, Anatomical Record, Clinical Anatomy, Surgical and Radiologic Anatomy, Anatomical Science International, Folia Morphologica, etc.), as well as the suitable clinical journals, related to the anatomical structure of the study. Finally, the authors searched the references of all incorporated studies for additional articles eligible for inclusion in the meta-analysis. Search terms used in this systematic review and meta-analysis included: ‘zygomaticofacial foramen’ OR ‘zygomatic foramina’ OR ‘zygomaticofacial foramina’ OR ‘foramen zygomaticofaciale’ OR [(‘zygomaticofacial foramen’ OR ‘zygomatic foramina’ OR ‘zygomaticofacial foramina’ OR ‘foramen zygomaticofaciale’) AND (‘accessory’ OR ‘anatomy’ OR ‘variant’ OR ‘variation’ OR ‘morphometry’)]. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were strictly adhered to, throughout all of the analysis [25]. Additionally, guidelines for writing evidenced based anatomical meta-analysis were followed [10].

Eligibility assessment

Eligible articles that were included in our study were assessed by five independent reviewers: GF, KM, TT, JW and JO. All studies describing any extractable data regarding anatomical characteristics and prevalence on zygomaticofacial foramen were included. The following exclusion criteria were used: (1) animal studies, conference abstracts, case studies, letters to editors and reviews; (2) studies with incomplete or irrelevant data (i.e., when the distance measurements were given without signifying specific projection in which measurements of ZFF were made or when they lacked mean values). There were no language or date restrictions. Publications in languages other than English were included and collected in order to be assessed by medical professionals fluent in the original language and English.

Any lack of agreement about eligibility of provided studies was solved by a consensus agreement among reviewers, in some cases after consulting with authors of original study, if possible and needed.

Data extraction

Five independent reviewers: TT, GF, KM, RC and JO extracted data regarding: prevalence, number of foramina, localization within zygomatic bone, shape, diameter, connection with other foraminas and finally distance measured (Table 1) related to the ZFF (Fig. 1). In the case of the localization of the foramina, for the purpose of uniformity, we have distinguished 4 points/planes: A (inferior-medial), B (inferior-lateral), C (superior-lateral) and D (superior-medial).

Quality assessment

To assess possible risk of bias the Anatomical Quality Assurance (AQUA) Checklist and the Anatomical Quality Assessment Tool were used, results are presented in Supplementary materials. The aforementioned AQUA guidelines have been validated by the Federative International Committee for Scientific Publications of the International Federations of Associations of Anatomists [9].

Statistical analysis

To test the variability of ZFF, the statistical analysis was performed by MO using MetaXL 5.3 by EpiGear International Pty LtD (Wilston, Queensland, Australia). The random effects model was implemented to calculate the pooled prevalence approximation. The I^2 statistic and Chi^2 tests were used to determine the heterogeneity of the included studies. The I^2 statistics were interpreted in terms of four intervals: 0–40% (‘might not be important’), 30–60%

(‘might indicate moderate heterogeneity’), 50–90% (‘might indicate substantial heterogeneity’), and 75–100% (‘might represent considerable heterogeneity’) [Cochrane Handbook]. Cochran’s Q p-value < 0.10 was used to define significant heterogeneity among studies in the X^2 test [Cochrane Handbook]. Sensitivity analysis was carried out by comparing subgroups and, when possible, using the leave-one-out method to further look into possible sources of heterogeneity. The evaluation of the number of ZFF per skull side was subjected to a subgroup analysis with regard to geographic origin and type of imaging studies employed to investigate potential factors that might have influenced the observed heterogeneity.

RESULTS

Study selection

Process of identification and inclusion of the studies used in this article is presented on the PRISMA flow chart (Fig. 2). An extensive search was conducted through major online databases to reveal a total of 205 studies. While searching through the references of the included articles, additional 2 articles were found. After removing 63 duplicates, 144 records remained. We evaluated the rest of the 144 full text articles to determine their eligibility. 102 articles were excluded on the basis of article type or for being animal studies. 20 articles were excluded due to either lack of the data or irrelevance. Finally, 22 articles were included into our meta-analysis.

Study characteristics

A total of 22 studies (n = 5438 skull sides) were included and consisted of cadaveric dissections and CT studies. Characteristics of incorporated data are displayed in Table 2. The geographic origin of studies included 5 continents (Asia, Africa, Europe, North and South Americas), with the majority being from Asia (8 studies, n = 1029 skull sides).

Due to the fact that data on the ethnicity of the specimens was not available in certain studies included in our meta-analysis, we decided to group studies from the same countries and continents into separate sub-groups and subsequently pool data to achieve specified results. Below we present the results in the general population, the sub-group results are shown in the respective tables.

Prevalence and number of the ZFF

Majority of the zygomatic bones presented with 1 ZFF per skull side — 45.34% (95% CI: 41.56–49.12) (Fig. 3); 2, 3 or 4 ZFF per zygomatic bone were less prevalent — they were found in 25.83% (95% CI: 18.27–33.39), 7.71% (95% CI: 5.66–9.75) and 1.06% (95% CI: 0.57–1.54), respectively. Incidence of 5 or 6 was also confirmed in incidental cases — 0.06% (95% CI: 0.00–0.13) and 0.05% (95% CI: 0.00–0.12). Absence of ZFF was pooled in 14.11% (95% CI: 10.15–18.07).

For the analysis of ZFF's prevalence in right or left skull sides, regional subpopulations and separately in cadaveric and radiographic studies see Table 3.

Localization of the ZFF in the zygomatic bone

We were able to distinguish 4 possible localizations within the zygomatic bone where ZFF may be present. Localization C was the most frequent, with ZFF being present there in 40.42% (95% CI: 28.86–51.98) of skull sides, whereas in B and A ZFF was observed in 32.35% (95% CI: 20.71–43.78) and 27.03% (95% CI: 23.88–30.18), respectively. The least common localization was D with the ZFF's occurrence of 0.25% (95% CI: 0.00–0.72). Details are provided in Table 4.

Connections between ZFF and other cranial foramina

Table 5 provides detailed information about ZFF's connections with other foramina. The estimated prevalence of ZFF with no connection to any foramina was 31.18% (95% CI: 0.00–67.11; $p < 0.001$). We found ZFF to be connected to ZTF in 23.19% (95% CI: 0.00–53.20; $p < 0.001$) and to ZOF in 59.73% (95% CI: 27.21–92.25; $p < 0.001$), respectively. ZFF connected to both ZTF and ZOF occurred in 29.28% (95% CI: 23.51–35.05; $p = 0.797$).

Distances from the ZFF to other anatomical structures

Distance between several cranial landmarks and ZFF were pooled, mean distance from ZFF to zygomatic angle equaled 12.02 mm (95% CI: 10.06–13.98). In total skull sides, distance from ZFF to the closest point of the orbital rim was 6.71 mm (95% CI: 5.98–7.43) with 6.78 mm (95% CI: 5.75–7.81) and 6.83 mm (95% CI: 5.79–7.87) on the left and right sides, respectively. Distance from ZFF to the midpoint of frontozygomatic suture equaled 25.50 mm (95% CI: 24.91–26.10) — overall, 26.56 mm (95% CI: 25.84–27.28) on the right and 26.60 mm (95% CI: 25.89–27.30) on the left. Distance from ZFF to the lowest point of the zygomaticomaxillary suture was found to be 19.00 mm (95% CI:18.39–19.61), on the right

this value equaled 19.31 mm (95% CI:18.39–20.23) and on the left — 19.51 mm (95% CI:18.63–20.39).
More details are included in Table 6.

Foramen diameter

Details about diameter of the ZFF are present in Table 7, mean was pooled to be 1.23 mm (95% CI: 0.33–2.13).

Shape of the ZFF

We have assessed the data on ZFF shapes and found 4 main types with respective overall prevalence: circular — 41.77% (95% CI: 11.24–72.31; $p < 0.001$), oval — 54.78% (95% CI: 30.90–78.66; $p < 0.001$), semilunar — 1.99% (95% CI: 0.00–6.61; $p = 0.024$) and irregular — 0.52% (95% CI: 0.00–2.12; $p = 0.169$). Left and right sides were also evaluated and are presented in Table 8, along with the aforementioned results.
The laterality of the most common shape, oval, was reported in two studies with a total number of 121 foramina, present in 54.58% (95% CI: 45.72–63.43; $p = 0.545$) on the left side and in 45.42% (95% CI: 36.57–54.28; $p = 0.545$) on the right side. Data regarding the circular shape was described in two studies in a total of 97 foramina — 44.33% (95% CI: 34.44–54.22; $p = 0.989$) on the left and 55.67% (95% CI: 45.78–65.56; $p = 0.989$) on the right. Laterality of semilunar and irregular foramina were not commonly reported, therefore due to the lack of data their analysis was not possible.

DISCUSSION

To the authors' knowledge, this is the first meta-analysis regarding the clinical anatomy of ZFF. Variations in prevalence, localization and shape have deep roots in embryological development of the zygomatic bone. The zygomatic bone has either one or three ossification centers, they form in the eighth week of pregnancy and fuse in the twenty second. Many authors point towards the diversity of ossification centers as the possible source of variation of the number and localization of ZFF [23].
Our results may be useful in various fields, including neurosurgery, in which some authors suggest using the ZFF as a guide in orbitozygomatic craniotomies [20].
The orbitozygomatic craniotomy is a skull base approach that provides wide access to the superior and lateral surfaces of the orbit as well as the anterior and middle cranial fossa; it needs elevation of the lateral orbital rim and zygomatic arch, which requires a bone cut across

the zygomatic bone. To avoid damaging the frontal branch of the facial nerve, the ZFF, when present alone, can be used as a landmark to perform the inferior cut of the zygoma and identify the inferior orbital fissure, thereby preventing overstretching of the cutaneogaleal flap and damage to the nerve. Unfortunately, we found that 1 ZFF occurs only in 45.34% (95% CI: 41.56–49.12; $p < 0.001$) of skull sides. In case of absence or multiple foramina, ZFF becomes an unreliable landmark [20]. Melchenko et al. [21] also suggested that the orbitozygomatic approach among others offers better access to important anatomical sites including the anterior, middle, posterior fossae and sellar region.

This subject is especially relevant in the treatment of bone loss, performed with the help of special dental implants known as zygomatic implants. These implants are anchored in the second premolar region in a way that enables them to bypass the maxillary sinus and embed within the body of the zygoma [13]. The intervention may damage the infraorbital nerve along with the ZFN, which courses through ZFF. Sensory disturbance, including paresthesia, anesthesia and dysesthesia in the cheek region have been reported as postoperative complications, potentially resulting from damage to the ZFN.

Anatomical knowledge of possible ZFF variations is useful in orbit restoration, which is performed in order to treat deformities in the region caused by various etiologies, including congenital hypoplasia, trauma, iatrogenic deformities and others [8]. Similarly to the zygomatic implants, all kinds of sensory impairment may follow operations in this area due, among other reasons, to variations in the number and/or location of the ZFF and the associated nerves.

Reduction malarplasty, also known as malar reduction, is a surgical procedure of face contour improvement. Conventional L-shaped incisions used in these operations extend from the lower lateral margin of the zygomaticofacial foramen to the upper medial aspect of the frontal process of the zygomatic bone [26]. Given this approach, it would be valid to state that the ZFF anatomy and its variability could serve as landmarks for preventing complications such as paresthesia and for influencing surgical outcomes.

Moreover, clinical applications of the ZFF anatomy may include considering it in aesthetic augmentation of the face, management of facial trauma, and craniofacial surgeries. However, the reliability of such an anatomical landmark remains controversial. The zygomaticofacial branch of the zygomatic nerve passes from the orbital cavity to the facial surface through a bony canal, which ends as zygomaticofacial foramen. Little attention is drawn to the orbital opening (ZFFin) of this canal, located within the lateral wall of the orbit, in studies describing its endpoint — the zygomaticofacial foramen (ZFFout) [12]. Only a few researchers

investigated this structure's diameter and its position in relation to other anatomical landmarks. Difficulties in visualising ZFFin either during dissection or imaging tests may contribute to the little amount of evidence present in the literature. Obtaining more detailed data concerning this structure might result in more awareness among surgeons during procedures performed on the orbitozygomatic area and therefore reduce the number of complications caused by zygomaticofacial branch injury [12].

Our analysis showed that the majority of the zygomatic bones had only 1 ZFF with prevalence equal to 45.34% (95% CI: 41.56–49.12; $p < 0.001$). Similar data was presented by Malakhov et al. and Ferro et al., on the other hand Chatzioglou et al. reported exactly the same frequency of 1 and 2 ZFF per skull side [6, 18, 23]. The incidence of 2 ZFF and complete absence of ZFF were less prevalent in our research — 5.83% (95% CI: 18.27–33.39; $p < 0.001$) and 14.11% (95% CI: 10.15–18.07; $p < 0.001$), respectively.

It has been reported that the absence of ZFF can sometimes be explained by the absence of the ZFN. In such instances other branches of the trigeminal nerve extend to the malar skin, anastomose with ZFN and provide sensory innervation of this area. This phenomenon could explain why, on some occasions, despite damaging the nerve during surgical procedures, active sensory innervation might still be present [18, 23].

In terms of choosing the most accurate imaging technique for visualizing the ZFF, according to the literature, the cone beam computed tomography (CBCT) seems to be the most reliable method. Del Neri et al. [5] evaluated this imaging method by comparing the number of ZFF detected by CBCT scans with physical inspection of zygomatic bones. CBCT showed excellent accuracy and even small foramina can be identified on the scans obtained with CBCT.

In the study by Malakhov et al. [18] the authors suggested that the diameter of ZFF might serve as a tool for the estimation of nerve damage risk during surgical procedures based on the associations between diameter of ZFF and the development of nerve paresthesia that were previously described; we found that the average diameter of ZFF was 1.23 mm (95% CI: 0.33–2.13; $p < 0.001$). In our analysis we found that region C presented the highest incidence of ZFF equal to 40.42% (95% CI: 28.86–51.98; $p < 0.001$). In studies by Aksu et al. [1], Lone et al. [16] and Deana et al. [4] all of the researchers reported that region C presented the highest frequency of ZFF with 46.9%, 51.82% and 58.5%, respectively. Therefore, procedures in this area should be performed with great caution as this region is at the highest risk of lesions concerning blood vessels and nerves exiting the ZFF among others [10].

Supplementary materials. Studies presented a 'high' risk of bias in 2 categories mostly —

objectives and characteristics of the studies and methodology characterization. The first issue arises from the lack of clearly stated sex or ethnicity of the specimens, while the second reflects the omission of data by the authors regarding the number of scientists performing dissections or assessing the radiological images, as well as their level of experience.

The significant degree of variability among the included studies limited our investigation. It stayed constant throughout the analysis, despite the efforts taken to investigate the potential source of heterogeneity through the use of multiple subgroup analyses. However, given the inherent heterogeneity of anatomical investigations, considerable heterogeneity is anticipated in this kind of meta-analysis [10]. We suspect that several factors might have influenced the observed values. Firstly, although most of the included articles were based on cadaveric dissections, some of them employed imaging studies or mixed approaches of data collection methods. Secondly, the sample sizes differed considerably between all of the included research, which is visible while comparing the study with the lowest number of the analyzed skull sides (14) to the study that included the largest number of the analyzed skull sides (858). Thirdly, the data provided for the synthesis of estimated outcomes come from studies with various geographic origins, genetic and ethnic predispositions, and thus intrinsically implement the differences noted in the anatomical features reported among the included articles. Moreover, it is worth mentioning that the ethnicity of the body donors was not known or clarified; hence, classification into ethnic categories was based on the countries where the programs or institutions conducting the original studies were located. The information mentioned above should be taken into consideration when interpreting the data, as the ethnicities of donors within the included programs or institutions may vary. Lastly, the generalizability of our findings may be constricted by the lack or limited number of studies conducted in the Australian, African, and South American populations.

CONCLUSIONS

ZFF's variations in location, size, and connections with other foramina can complicate maxillofacial surgeries and aesthetic treatments like fillers or implants. Accurate preoperative imaging is critical for avoiding nerve injury, sensory deficits, or asymmetry. Knowledge of ZFF anatomy is essential for surgeons and clinicians to minimize complications and ensure successful outcomes in both functional and cosmetic procedures.

ARTICLE INFORMATION AND DECLARATIONS

Authors’ contribution

Project leadership: GF. Conception of the study: JAW, PP. Literature search: KM, RC, JO, TT, JT, JW. Data extraction: GF, KM, RC, JO, TT, JT, JW. Statistical analysis: MO, AO. Writing: GF, KM, RC, JO, TT, JT, JW, MO, AO. Figures: TK. Review process: AF, MR, KG, JAW, PP.

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Conflict of interest

The authors confirm that there are no known conflicts of interest and that no significant financial funding is associated with this publication.

Supplementary material

Supplementary material is available on Journal's website. This includes:

Supplementary Figure 1. Risk of bias of included studies assessed using AQUA checklist tool.

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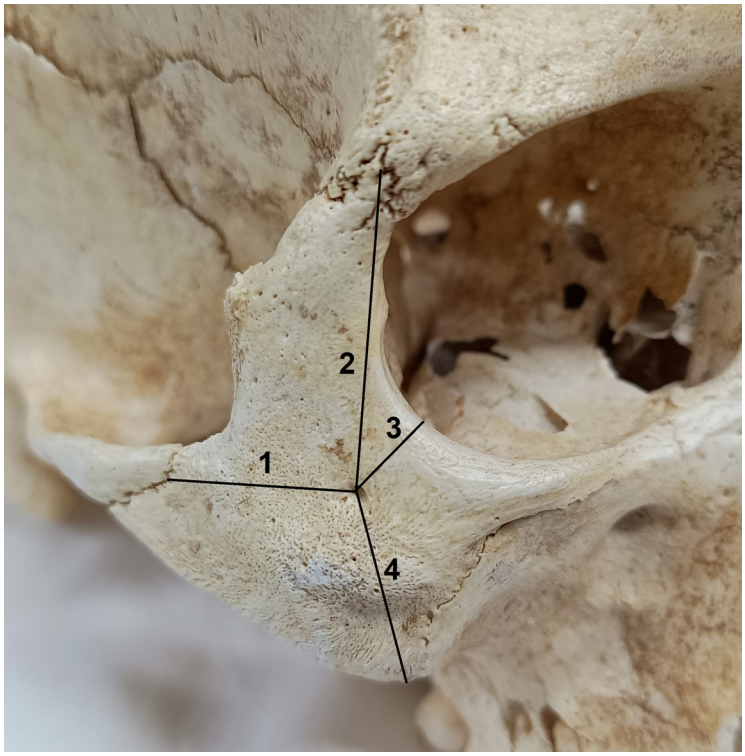
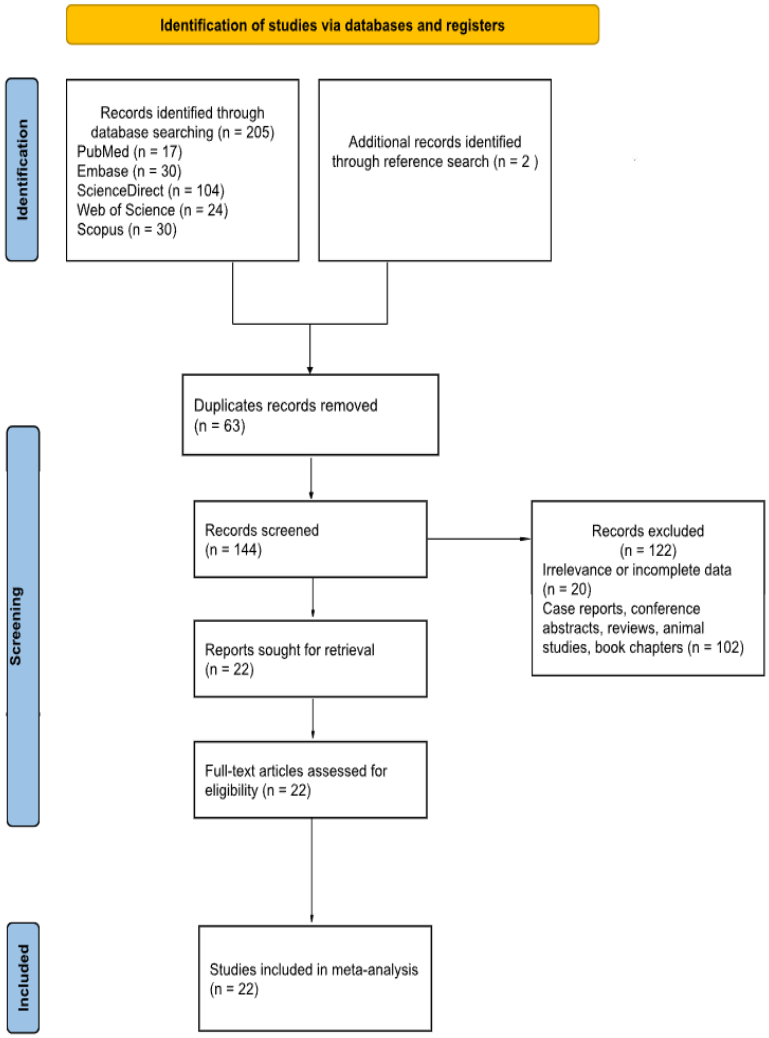


Figure 1. Measured distances on the skull: 1 — zygomaticofacial foramen (ZFF) to the zygomatic angle, 2 — ZFF to the midpoint of fronto-zygomatic suture, 3 — ZFF to the closest point of orbital rim, 4 — ZFF the lowest point of zygomatico-maxillar suture.



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Figure 2. PRISMA flow chart for study identification, evaluation, and inclusion in the meta-analysis [25].

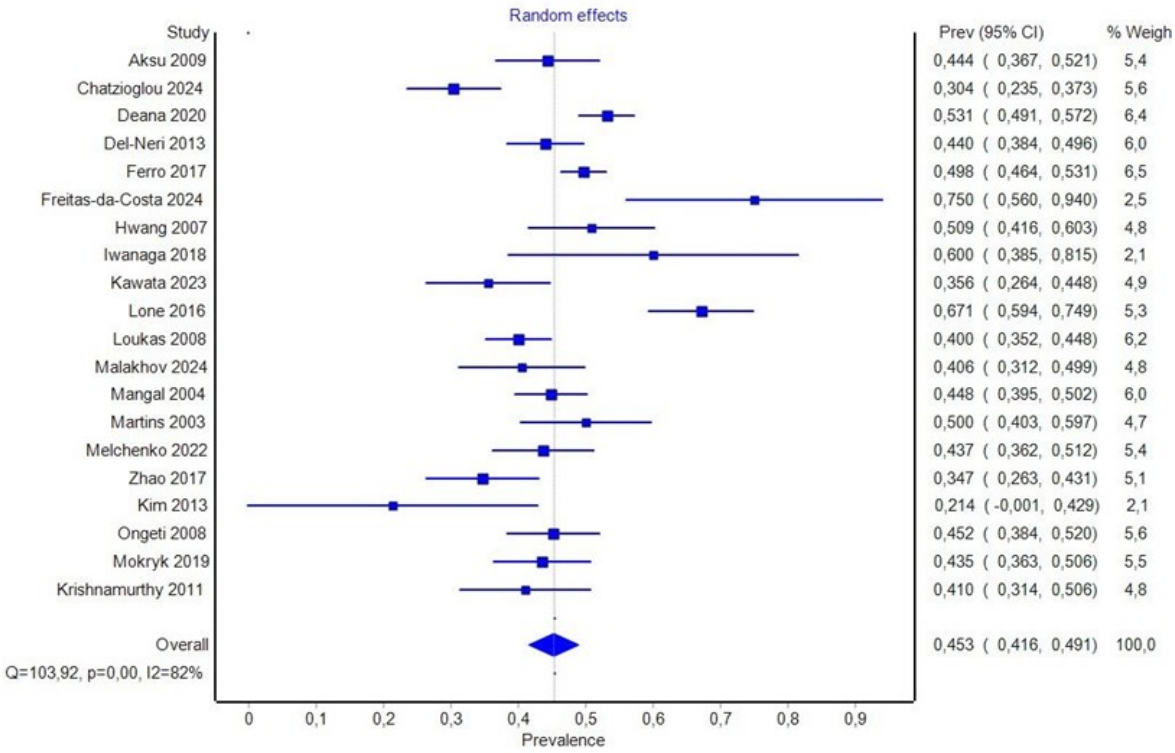


Figure 3. Forest plot presenting the pooled prevalence estimate of one zygomaticofacial foramen per skull side.

Table 1. List of measured distances.

Distance measured:	
1) Distance between the ZFF and the lowest point of zygomatico-maxillar suture	2) Distance between the ZFF and zygomatic angle
3) Distance between the ZFF and closest point of orbital rim	4) Distance between the ZFF and fronto-zygomatic suture

Table 2. List of included studies.

Study ID	Country, Continent	Type of study	Number of skull sides
Aksu 2009 [1]	Türkiye, Asia	Cadaveric	160

Carvalho 2022 [2]	Brazil, South America	Imaging	1126
Chatzioglou 2023 [23]	Türkiye, Asia	Cadaveric	171
Couthino 2018 [3]	Brazil, South America	Cadaveric	122
Deana 2020 [4]	Chile, South America	Cadaveric	574
Del Neri 2014 [5]	Brazil, South America	Cadaveric	302
Ferro 2017 [6]	UK, Europe	Cadaveric	858
Freitas-da-Costa 2024 [7]	Portugal, Europe	Cadaveric	20
Hwang 2007 [11]	South Korea, Asia	Cadaveric	110
Iwanaga 2018 [12]	USA, North America	Cadaveric	20
Kawata 2024 [13]	Japan, Asia	Imaging	104
Kim 2013 [14]	South Korea, Asia	Imaging	14
Krishnamurthy 2011 [15]	India, Asia	Cadaveric	100
Londhe 2016 [16]	India, Asia	Cadaveric	140
Loukas 2008 [17]	USA, North Amercia	Cadaveric	400
Malakhov 2024 [18]	Slovakia, Europe	Cadaveric	106
Mangal 2004 [19]	India, Asia	Cadaveric	330
Martins 2003 [20]	USA, North America	Cadaveric	102

Melechenko 2022 [21]	Russia, Europe	Cadaveric	166
Mokryk 2019 [22]	Ukraine, Europe	Mixed	184
Ongeti 2008 [24]	Kenya, Africa	Cadaveric	208
Zhao 2018 [27]	USA, North America	Cadaveric	121

Table 3. Total number of foramina per skull side.

Subgroup	Number of ZFF per skull side	Number of skull sides analyzed (number of studies)	PPE (95%CI)	I^2	p-value
Overall	0 ZFF per side	5320 (21)	14.11% (10.15–18.07)	98.21%	< 0.001
	1 ZFF per side	4194 (20)	45.34% (41.56–49.12)	81.72%	< 0.001
	2 ZFF per side	4194 (20)	25.83% (18.27–33.39)	98.19%	< 0.001
	3 ZFF per side	4194 (20)	7.71% (5.66–9.75)	92.40%	< 0.001
	4 ZFF per side	4194 (20)	1.06% (0.57–1.54)	72.71%	< 0.001
	5 ZFF per side	4194 (20)	0.06% (0.00–0.13)	0.00%	0.962
	6 ZFF per side	4194 (20)	0.05% (0.00–0.12)	0.00%	1.00
Right	0 ZFF per side	957 (11)	13.36% (7.94–18.79)	94.63%	< 0.001
	1 ZFF per side	957 (11)	42.63% (37.04–48.23)	68.27%	< 0.001
	2 ZFF per side	957 (11)	27.74% (21.90–33.58)	77.10%	< 0.001
	3 ZFF per side	957 (11)	9.79% (5.97–13.60)	81.38%	< 0.001
	4 ZFF per side	957 (11)	0.14% (0.00–0.45)	46.02%	0.047
	5 ZFF per side	957 (11)	0.06% (0.00–0.22)	0.00%	0.898
	6 ZFF per side	957 (11)	0.05% (0.00–0.19)	0.00%	1.00
Left	0 ZFF per side	949 (11)	14.77% (8.31–21.23)	94.75%	< 0.001

	1 ZFF per side	949 (11)	45.66% (38.92–52.40)	78.02%	< 0.001
	2 ZFF per side	949 (11)	27.50% (20.84–34.17)	83.24%	< 0.001
	3 ZFF per side	949 (11)	5.66% (2.93–8.39)	85.82%	< 0.001
	4 ZFF per side	949 (11)	0.84% (0.12–1.56)	52.24%	0.022
	5 ZFF per side	949 (11)	0.06% (0.00–0.22)	0.00%	0.892
	6 ZFF per side	949 (11)	0.05% (0.00–0.20)	0.00%	1.00
Asia	0 ZFF per side	1129 (8)	15.74% (7.67–23.82)	97.04%	< 0.001
	1 ZFF per side	1129 (8)	43.08% (34.48–51.68)	88.12%	< 0.001
	2 ZFF per side	1129 (8)	24.15% (17.13–31.18)	87.18%	< 0.001
	3 ZFF per side	1129 (8)	8.55% (4.65–12.45)	86.59%	< 0.001
	4 ZFF per side	1129 (8)	1.41% (0.37–2.44)	74.62%	< 0.001
	5 ZFF per side	1129 (8)	0.07% (0.00–0.22)	0.00%	0.453
	6 ZFF per side	1129 (8)	0.06% (0.00–0.20)	0.00%	0.997
Europe	0 ZFF per side	1335 (5)	7.95% (0.23–15.67)	97.79%	< 0.001
	1 ZFF per side	1335 (5)	47.40% (41.05–53.76)	71.53%	0.007
	2 ZFF per side	1335 (5)	27.18% (8.06–46.31)	99.23%	< 0.001
	3 ZFF per side	1335 (5)	7.74% (3.52–11.97)	94.77%	< 0.001
	4 ZFF per side	1335 (5)	2.40% (0.72–4.08)	78.49%	< 0.001
	5 ZFF per side	1335 (5)	0.05% (0.00–0.18)	0.00%	0.749
	6 ZFF per side	1335 (5)	0.05% (0.00–0.17)	0.00%	1.00
North America	0 ZFF per side	646 (4)	18.36% (0.00–39.71)	98.30%	< 0.001
	1 ZFF per side	646 (4)	43.05% (35.25–50.84)	65.39%	0.034
	2 ZFF per side	646 (4)	24.97% (12.13–37.81)	90.39%	< 0.001
	3 ZFF per side	646 (4)	5.36% (0.77–9.95)	92.46%	< 0.001
	4 ZFF per side	646 (4)	0.94% (0.00–2.05)	55.55%	0.080
	5 ZFF per side	646 (4)	0.06% (0.00–0.25)	0.00%	0.832
	6 ZFF per side	646 (4)	0.05% (0.00–0.22)	0.00%	1.00
South	0 ZFF per side	2002 (3)	17.93% (16.25–19.61)	0.00%	0.901

America	1 ZFF per side	876 (2)	48.80% (39.89–57.70)	84.89%	0.010
	2 ZFF per side	876 (2)	25.32% (19.82–30.83)	69.31%	0.071
	3 ZFF per side	876 (2)	6.30% (3.69–8.91)	55.61%	0.133
	4 ZFF per side	876 (2)	0.87% (0.26–1.49)	0.00%	0.544
	5 ZFF per side	876 (2)	0.05% (0.00–0.20)	0.00%	1.00
	6 ZFF per side	876 (2)	0.05% (0.00–0.20)	0.00%	1.00
Cadavery	0 ZFF per side	3590 (16)	16.45% (11.21–21.70)	95.87%	< 0.001
	1 ZFF per side	3590 (16)	46.82% (42.48–51.15)	83.68%	< 0.001
	2 ZFF per side	3590 (16)	24.71% (16.37–33.05)	98.37%	< 0.001
	3 ZFF per side	3590 (16)	6.07% (4.17–7.97)	91.19%	< 0.001
	4 ZFF per side	3590 (16)	0.87% (0.40–1.33)	70.64%	< 0.001
	5 ZFF per side	3590 (16)	0.06% (0.00–0.14)	0.00%	0.843
	6 ZFF per side	3590 (16)	0.05% (0.00–0.13)	0.00%	1.00
Imaging	0 ZFF per side	1546 (4)	9.82% (0.00–20.28)	98.71%	< 0.001
	1 ZFF per side	420 (3)	37.39% (27.47–47.30)	64.57%	0.060
	2 ZFF per side	420 (3)	28.78% (24.45–33.11)	0.00%	0.858
	3 ZFF per side	420 (3)	20.04% (4.43–35.65)	89.02%	< 0.001
	4 ZFF per side	420 (3)	4.12% (0.00–10.02)	74.49%	0.020
	5 ZFF per side	420 (3)	0.05% (0.00–0.26)	0.00%	1.00
	6 ZFF per side	420 (3)	0.05% (0.00–0.26)	0.00%	1.00

CI — confidence interval; PPE — percent point estimate; ZFF — zygomaticofacial foramen.

Table 4. Localization of the zygomaticofacial foramen (ZFF) within the zygomatic bone.

Localization	Number of foramina analysed (number of studies)	PPE (95% CI)	I^2	p-value
A	763 (4)	27.03% (23.88–30.18)	0.00%	0.661
B	763 (4)	32.35% (20.71–43.78)	92.03%	< 0.001
C	763 (4)	40.42% (28.86–51.98)	90.87%	< 0.001
D	664 (3)	0.25% (0.00–0.72)	32.01%	0.230

CI — confidence interval; PPE — percent point estimate.

Table 5. Connection between zygomaticofacial foramen (ZFF) and other foramina.

Connection	#n of analysed foramina (number of studies)	PPE (95% CI)	I^2	p-value
No connection to any foramina	331 (2)	31.18% (0.00–67.11)	96.84%	< 0.001
Connection to ZTF	506 (2)	23.19% (0.00–53.20)	98.52%	< 0.001
Connection to ZOF	506 (2)	59.73% (27.21–92.25)	98.46%	< 0.001
Connection to both ZTF and ZOF	239 (2)	29.28% (23.51–35.05)	0.00%	0.797

CI — confidence interval; PPE — percent point estimate; ZOF — zygomaticoorbital foramen; ZTF — zygomaticotemporal foramina.

Table 6. Distance measurements between zygomaticofacial foramen (ZFF) and other cranial landmarks.

Distance measurements	Side	Number of foramina	Distance [mm] (95% CI)	I^2	p-value

		analysed (number of studies)			
Distance from ZFF to the zygomatic angle	Overall	215 (2)	12.02 (10.06–13.98)	90.21%	0.001
Distance from ZFF to the closest point of the orbital rim	Overall	817 (4)	6.71 (5.98–7.43)	96.17%	< 0.001
	Right	294 (3)	6.78 (5.75–7.81)	95.21%	< 0.001
	Left	261 (3)	6.83 (5.79–7.87)	94.60%	< 0.001
Distance from ZFF to the midpoint of Frontozygomatic suture	Overall	932 (5)	25.50 (24.91–26.10)	85.11%	< 0.001
	Right	294 (3)	26.56 (25.84–27.28)	74.26%	0.021
	Left	261 (3)	26.60 (25.89–27.30)	66.72%	0.050
Distance from ZFF to the lowest point of the zygomaticomaxillary suture	Overall	717 (3)	19.00 (18.39–19.61)	86.09%	< 0.001
	Right	294 (3)	19.31 (18.39–20.23)	84.28%	0.002
	Left	261 (3)	19.51 (18.63–20.39)	76.50%	0.014

CI — confidence interval.

Table 7. Foramen diameter.

Number of foramina analysed (number of studies)	Diameter of the ZFF [mm] (95% CI)	I^2	p-value
753 (3)	1.23 (0.33–2.13)	99.73%	< 0.001

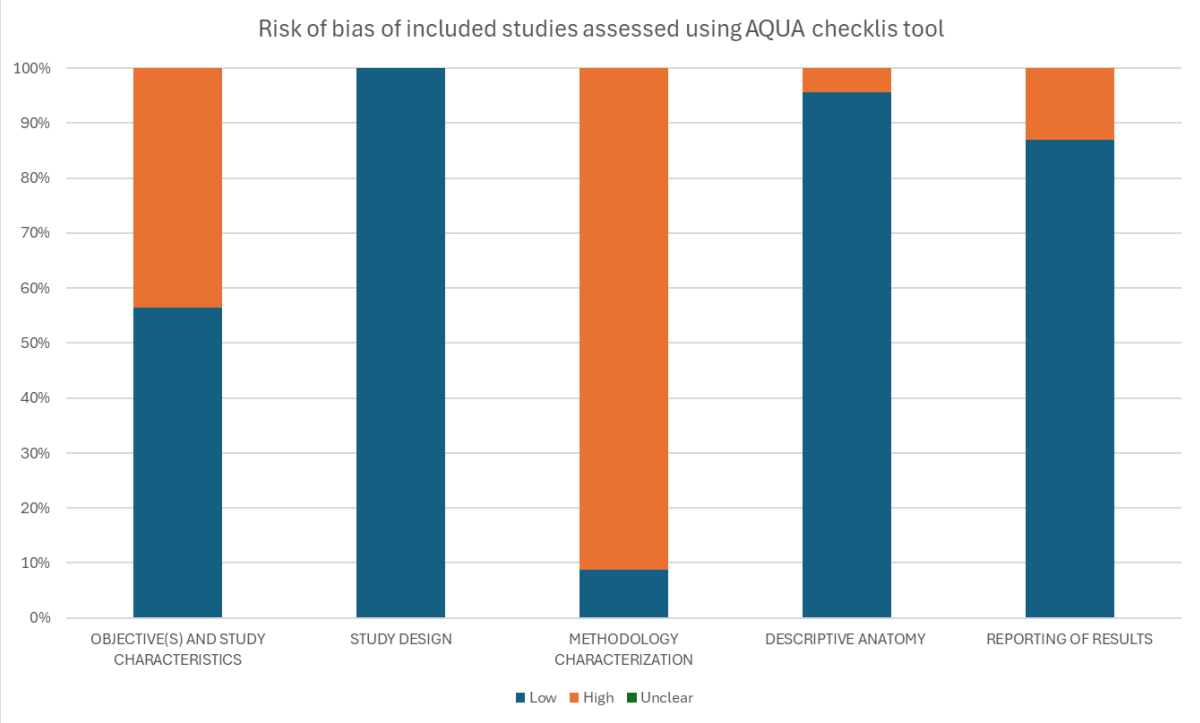
CI — confidence interval; ZFF — zygomaticofacial foramen.

Table 8. Shape of the zygomaticofacial foramen (ZFF).

Side	Shape	#n of analysed ZFF (number of studies)	PPE (95% CI)	I^2	p-value
Overall	Circular	225 (2)	41.77% (11.24–72.31)	96.00%	< 0.001
	Oval	225 (2)	54.78% (30.90–78.66)	93.01%	< 0.001
	Semilunar	225 (2) 113 (2) 112 (2)	1.99% (0.00–6.61)	80.40%	0.024
	Irregular	225 (2)	0.52% (0.00–2.12)	47.20%	0.169
Right	Circular	113 (2)	46.41% (12.03–80.80)	93.72%	< 0.001
	Oval	113 (2)	49.64% (22.79–76.49)	89.02%	0.003
	Semilunar	113 (2)	2.00% (0.00–7.32)	67.79%	0.078
	Irregular	113 (2)	0.09% (0.00–0.65)	0.00%	0.331
Left	Circular	112 (2)	37.07% (10.33–63.81)	89.76%	0.002
	Oval	112 (2)	59.89% (38.91–80.87)	82.18%	0.018

	Semilunar	112 (2)	1.04% (0.00–4.36)	50.17%	0.157
	Irregular	112 (2)	0.09% (0.00–0.65)	0.00%	0.330

CI — confidence interval; PPE — percent point estimate.



Supplementary Figure 1. Risk of bias of included studies assessed using AQUA checklist tool.