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The cranio-orbital foramen: a meta-analysis with a review of the literature

P. Ostrowski et al., The cranio-orbital foramen

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ABSTRACT

Background: The goal of the present study was to provide accurate data on the prevalence and morphometrical aspects of the cranio-orbital foramen (COF), which can surely be of use by surgeons performing procedures on the lateral orbit. Furthermore, the embryology and the clinical significance of this osseous structure were thoroughly discussed.

Materials and methods: Major online medical databases such as PubMed, Scopus, Embase, Web of Science, and Google Scholar were searched to find all relevant studies regarding COF.

Results: Eventually, a total of 25 studies that matched the required criteria and contained complete and relevant data were included in this meta-analysis. The pooled prevalence of COF was found to be 48.37% (95% CI: 41.67% - 55.10%). The occurrence of the COF unilaterally was set to be 71.92% (95% CI: 41.87% - 96.97%). The occurrence of the COF bilaterally was set at 26.08% (95% CI: 3.03% - 58.13%).

Conclusions: In conclusion, we believe that this is the most accurate and up-to-date study regarding the anatomy of the COF. The COF is prevalent in 48.37% of the cases, and it is most frequently unilateral (73.92%). Furthermore, the prevalence of accessory COFs was found to be 16.72 percent. The presence of these foramina may represent a source of hemorrhage that ophthalmic surgeons should be aware of when performing procedures in the lateral part of the orbit.

Key words: cranio-orbital foramen, lateral orbit, whitnall tubercle, frontozygomatic suture

INTRODUCTION

The orbits are bilateral bony cavities in the facial skeleton housing numerous canals and foramina, which form connections with other neighboring cavities of the skull. Oftentimes, these osteological structures are used as surgical landmarks by ophthalmic surgeons to define operating margins and locate nearby vulnerable neurovascular structures [15].

The cranio-orbital foramen (COF) is an ostial opening in the lateral wall of the orbit, adjacent to the superior orbital fissure. The COF is known by different names, such as the meningo-orbital foramen, lacrimal foramen, foramen of Hyrtl, spheno-frontal foramen, sinus canal foramen, and anastomotic foramen [6, 14, 16]. The foramen is said to contain an arterial anastomosis between the orbital branch of the middle meningeal artery and the lacrimal artery [17]. Its prevalence, which has been widely discussed in the available literature and across all studies, ranges from 28 to 82.9 % [6]. Moreover, the morphometrical aspects of this osseous opening have also been a topic of discussion. These parameters include the distance between the supraorbital notch/foramen and the COF [1, 3, 12]. Furthermore, many studies have reported double or even triple accessory cranio-orbital foramina in cadaveric specimens [3, 12].

Knowledge about the prevalence and morphometrical aspects of the COF may be of great importance for ophthalmic surgeons involved in orbital reconstructions, anterior skull base procedures, orbital tumor resection, and decompression surgery for thyroid eye disease [1, 8]. During deep dissection of the lateral orbital wall, unexpected hemorrhage may complicate surgery if the COF is present.

Therefore, the goal of the present study was to provide accurate data on the prevalence and morphometrical aspects of the COF, which can surely be of use by surgeons performing procedures on the lateral orbit. Furthermore, the embryology and the clinical significance of this osseous structure were thoroughly discussed.

MATERIALS AND METHODS

Search strategy

Major online medical databases such as PubMed, Scopus, Embase, Web of Science, and Google Scholar were searched to find all relevant studies regarding COF. The search was conducted in July 2022. The following search terms were used: ((cranio-orbital) OR (cranio orbital) OR (meningo-orbital) OR (meningo orbital) OR (lacrimal foramen) OR (Hyrtl foramen) OR (spheno-frontal foramen) OR (sinus canal foramen) OR (anastomotic foramen)). The search terms were adjusted to each of the databases in order to maximize the number of results. No dates, language, article type, and/or text availability conditions were applied. Subsequently, an additional search was carried out for references from the screened studies. During this study, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed. In addition, the Critical Assessment Tool for Anatomical Meta-analysis (CATAM) was used to provide the highest quality findings [4].

Eligibility assessment

The database search and the manual search identified a total of 3621 studies and were initially evaluated by two independent reviewers. After removing duplicates and irrelevant records, a total of 956 articles were qualified for full-text evaluation. To minimize potential bias and maintain an accurate statistical methodology, articles such as case reports, case series, conference reports, reviews, letters to the editors, and studies that provided incomplete or irrelevant data were excluded. The inclusion criteria involved original studies with extractable numerical data on the prevalence, morphology, and anatomical relations of the COF. Finally, a total of 25 studies were included in this meta-analysis. The AQUA Tool, which was specifically designed for anatomical meta-analyses, was used to minimize the potential bias of included studies [9]. The flow chart presenting the study inclusion process is shown in Figure 1.

Data extraction

Data from qualified studies were extracted by two independent reviewers. Qualitative data, such as year of publication, country, and continent, were gathered. Quantitative data, such as sample size, numerical data regarding the prevalence of the COF, its morphology, and the distances between the COF and other anatomical structures, were gathered. Studies containing mean results but without SD or interquartile range or unclear or unspecified variations were excluded. Any discrepancies between the studies identified by the two reviewers were resolved by contacting the authors of the original studies wherever possible or by consensus with a third reviewer.

Statistical analysis

To perform statistical analysis, STATISTICA version 13.1 software (StatSoft Inc., Tulsa, OK, USA), MetaXL version 5.3 software (EpiGear International Pty Ltd, Wilston, Queensland, Australia), and Comprehensive Meta-analysis version 3.0 software (Biostat Inc., Englewood, NJ, USA) were used. A random-effects model was performed in all analyses. The Chi-square test and I-square statistics were used to assess heterogeneity among the studies (Higgins et al., 2019). A p-value and confidence intervals were used to determine statistical significance between studies. A p-value less than 0.05 was considered statistically significant. In the case of overlapping confidence intervals, differences were considered statistically insignificant. The statistics of squares were interpreted as follows: values of 0–40% were considered 'may not be important', values of 30–60% were considered 'may indicate moderate heterogeneity', values of 50–90% were considered 'may indicate substantial heterogeneity', and values of 75% to 100% were considered 'may indicate substantial heterogeneity'.

RESULTS

Eventually, a total of 25 studies that matched the required criteria and contained complete and relevant data were included in this meta-analysis. The characteristics of each study submitted are shown in Table 1.

The pooled prevalence of COF (n=5649) was found to be 48.37% (95% CI: 41.67% - 55.10%). The occurrence of the COF unilaterally (n=926) was set to be 73.92% (95% CI:

41.87% - 96.97%). The occurrence of the COF bilaterally (n=926) was set at 26.08% (95% CI: 3.03% - 58.13%).

The pooled prevalence of COF in men (n=1061) was found to be 50.52% (95% CI: 40.38% - 60.64%). The pooled prevalence of COF in women (n=1061) was 51.91% (95% CI 28.75% - 74.68%). Overall, there are no statistically significant differences in the occurrence of COF between men and women (p = 0.93).

The pooled prevalence of the COF on the left side (n=773) was found to be 51.42% (95% CI: 34.85% - 67.83%), as on the right side (n=773) it was established at 47.63% (95% CI: 28.11% - 67.51%).

The pooled prevalence of the accessory COF (n=257) was set to 16.72% (95% CI: 11.09% - 23.22%). All the results mentioned above and the more detailed ones can be found in Table 2.

The mean maximal diameter (n=944) of the COF was set at 0.969 mm (SE = 0.140). For more detailed results, see Table 3.

The mean distance between the COF and the frontozygomatic suture (n=1347) was set to 26.89 mm (SE = 0.62). The mean distance between the COF and the supraorbital notch (n=1347) was established at 34.95 mm (SE = 0.74). The mean distance between the COF and the Whitnall tubercle (n=1347) was established to be 27.56 mm (SE = 0.62). The mean distance between the COF and the lateral angle (n=1347) was established at 7.18 mm (SE = 0.76). For more detailed results and the analysis of distances on the sex and side of the patients, see Table 4.

DISCUSSION

Numerous anatomical studies have discussed the location, prevalence, and morphometric properties of the COF [1, 6, 17]. O'Brien et al. conducted an anatomical study on the prevalence and the location of the COFs [17]. In the study, the prevalence of this foramen was stated to be 73%. However, the location of the COF varied significantly, being found predominately where the frontosphenoidal suture had fused. This raised the question of whether the COF could create connections with the frontal rather than the middle cranial fossa. This communication was proved to exist in the aforementioned study, where 2 out of

16 specimens contained this connection. Pankaj et al. reported a significantly lower prevalence of this structure (36.02%) in their cadaveric study [18]. However, they also reported an orbit- anterior cranial fossa communication. Our results show that the COF is present in 48.37% of the cases and occurs more frequently unilaterally (73.92%), than bilaterally (26.08%). Furthermore, the location of the COF within the orbit was proven to be quite variable. The COF was located most frequently in the greater wing of the sphenoid bone (26.28%) and the orbital surface of the frontal bone (25.69%). Other intraorbital locations of the COF were within the frontosphenoidal suture (15.06%) and where the frontosphenoidal suture had fused (18.87%). Interestingly, no statistically significant differences in prevalence were observed with respect to the sex of the subject.

Many studies have also reported the presence of accessory COFs [6, 17, 18, 21]. The present study shows that the prevalence of any accessory COFs is 16.72%.
However, Abed et al. stated that these accessory cranio-orbital foramina are unlikely to be a source of significant hemorrhage because of their small caliber [1]. However, bleeding at these locations can serve as a warning that a potential COF may be present, with a significantly larger vessel passing through it.

Georgiou and Cassell presented a study about the relationship between the COF and the development of the ophthalmic artery [7]. They described that the initial vascular supply of the orbit arises from the internal carotid artery and then by the supraorbital division of the stapedial artery, which is an embryonic artery that disappears during the tenth week in utero and is the precursor of some orbital, dural, and maxillary branches [2]. Furthermore, they describe the formation of an anastomosis between the ophthalmic artery and the supraorbital branch of the stapedial artery which forms a “ring” around the optic nerve. The stapedial artery is represented as the orbital branch of the middle meningeal artery in adulthood. It is thought that the COF represents the point at which the supraorbital division of the stapedial artery passes through the greater wing of the sphenoid bone which has not been ossified yet [1, 7].

The orbital branch of the middle meningeal artery (OB) enters the orbit through the superior orbital fissure or the COF and it forms an anastomosis with the lacrimal artery [5]. The anatomic features of the COF and the course of the OB were thoroughly described by Erturk et al. in a cadaveric study [6]. In the study, the OB was most frequently observed to pass through the COF (43.2%). However, the vessel was also running through the superior orbital fissure in 16.2 percent of the cases. Shimada et al. presented similar results, with the OB coursing most commonly through the COF rather than the superior orbital fissure [20].

This vessel is said to contribute to the arterial supply of the anterior part of the dura of the middle cranial fossa and form anastomoses between the ophthalmic artery and middle meningeal artery. Furthermore, Stiernberg et al. and Price et al. showed that the aforementioned branch might provide accessory blood supply to the orbital contents [19, 22]. Therefore, great care has to be taken by the surgeon performing reconstructions of the anterior base of the skull and the orbit because the OB can get damaged and a large part of the blood supply to the orbital contents may be lost [6].

In order to provide an effective method for surgeons to localize the COF, morphometric values from the frontozygomatic suture and the supraorbital notch to the foramen have been measured and reported by previous studies [1, 10, 13]. The results of the present meta-analysis show that the average distance between the COF and the frontozygomatic suture and the supraorbital notch is 26.89 mm and 34.95 mm, respectively. McQueen et al. presented a method of defining a safe operating zone with respect to the COF, where the shortest aforementioned measurements were subtracted by 5 mm [13]. When using this method and taking advantage of the frontozygomatic suture and the supraorbital notch as surgical landmarks, operating beyond a distance of 29.95 mm and 21.89 mm from the COF, respectively, may increase the risk of damaging the contents of the foramen [1].
Other landmarks may also be used by the ophthalmic surgeon in order to establish a safe zone for the COF. These include the Whitnall's tubercle and the lateral angle, and the mean distance between these landmarks and the COF was set as 27.56 mm and 7.18 mm, respectively. All of the aforementioned measurements give the ophthalmic surgeon flexibility in choosing the technique of locating the COF in the orbit.

This study is not without limitations. It may be burdened with potential bias, as the results of this meta-analysis are limited by the accuracy of the studies submitted. The authors of the present study were unable to perform some of the morphological analyses due to the lack of consistent data in the literature. Additionally, most of the evaluated studies come from Asia, therefore, the results of this study may be burdened, as they may reflect the anatomical features of Asian people rather than the global population.

CONCLUSIONS

In conclusion, we believe that this is the most accurate and up-to-date study regarding the anatomy of the COF. The COF is prevalent in 48.37% of the cases, and it is most frequently unilateral (73.92%). Furthermore, the prevalence of accessory COFs was found to be 16.72 percent. The presence of these foramina may represent a source of hemorrhage that ophthalmic surgeons should be aware of when performing procedures in the lateral part of the orbit.

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Conflict of interest: None declared

REFERENCES

1. Abed SF, Shams P, Shen S, et al. A Cadaveric Study of the Cranio-orbital Foramen and Its Significance in Orbital Surgery. Plastic and Reconstructive Surgery. 2012; 129(2): 307e–311e, doi: 10.1097/PRS.0b013e31821b6382.
2. Bonasia S, Smajda S, Ciccio G, et al. Stapedial Artery: From Embryology to Different Possible Adult Configurations. American Journal of Neuroradiology. 2020; 41(10): 1768–1776, doi: 10.3174/ajnr.A6738.
3. Celik S, Kazak Z, Ozer MA, et al. Navigational area of the cranio-orbital foramen and its significance in orbital surgery. Surgical and Radiologic Anatomy. 2014; 36(10): 981–988, doi: 10.1007/s00276-014-1293-7.
4. D’Antoni A v., Tubbs RS, Patti AC, et al. The Critical Appraisal Tool for Anatomical Meta-analysis: A framework for critically appraising anatomical meta-analyses. Clinical Anatomy. 2022; 35(3): 323–331, doi: 10.1002/ca.23833.
5. Diamond MK. Homologies of the meningeal-orbital arteries of humans: a reappraisal. J Anat. 1991; 178: 223–41.
6. Erturk M, Kayalioglu G, Govsa F, et al. The cranio-orbital foramen, the groove on the lateral wall of the human orbit, and the orbital branch of the middle meningeal artery. Clinical Anatomy. 2005; 18(1): 10–14, doi: 10.1002/ca.20020.
7. Georgiou C, Cassell MD. The foramen meningo-orbitale and its relationship to the development of the ophthalmic artery. J Anat. 1992; 180 (Pt 1): 119–25.
8. Ghosh SK, Narayan RK. Fractures involving bony orbit: A comprehensive review of relevant clinical anatomy. Translational Research in Anatomy. 2021; 24: 100125, doi: 10.1016/j.tria.2021.100125.
9. Henry BM, Tomaszewski KA, Ramakrishnan PK, et al. Development of the Anatomical Quality Assessment (AQUA) Tool for the quality assessment of anatomical studies included

in meta-analyses and systematic reviews. Clinical Anatomy. 2017; 30(1): 6–13, doi: 10.1002/ca.22799.

10. Huanmanop T, Agthong S, Chentanez V. Surgical anatomy of fissures and foramina in the orbits of Thai adults. J Med Assoc Thai. 2007; 90(11): 2383–91.
11. Iwanaga J, Singh V, Ohtsuka A, et al. Acknowledging the use of human cadaveric tissues in research papers: Recommendations from anatomical journal editors. Clinical Anatomy. 2021; 34(1): 2–4, doi: 10.1002/ca.23671.
12. Kwiatkowski J, Wysocki J, Nitek S. The morphology and morphometry of the so-called “meningo-orbital foramen” in humans. Folia Morphol (Warsz). 2003; 62(4): 323–5.
13. Mcqueen CT, Diruggiero DC, Campbell JP, et al. Orbital osteology: A study of the surgical landmarks. Laryngoscope. 1995; 105(8): 783–788, doi: 10.1288/00005537-199508000-00003.
14. Moore KL, Dalley AF, Agur A. Clinically oriented anatomy (8th ed.). Lippincott Williams and Wilkins. 2017.
15. Mpolokeng KS, Louw GJ. An unusual arrangement of the neurovascular structures in one ethmoidal foramen of the human orbit. Translational Research in Anatomy. 2020; 18: 100058, doi: 10.1016/j.tria.2019.100058.
16. Narayan RK, Ghosh SK. Analysis of variations in morphological characteristics of orbito-meningeal foramen: An anatomical study with clinical implications. Translational Research in Anatomy. 2021; 24: 100108, doi: 10.1016/j.tria.2020.100108.
17. O’Brien A, McDonald SW. The meningo-orbital foramen in a Scottish population. Clinical Anatomy. 2007; 20(8): 880–885, doi: 10.1002/ca.20558.
18. Pankaj AK, Kumar N, Verma RK. Incidence of Meningo Orbital foramen In Dry Skull and Its Clinical Relevance. Indian Journal of Basic & Applied Medical Research. 2013; 2(6): 514–517.
19. Price JC, Loury M, Carson B, et al. THE PERICRANIAL FLAP FOR RECONSTRUCTION OF ANTERIOR SKULL BASE DEFECTS. Laryngoscope. 1988; 98(11): 1159???1164, doi: 10.1288/00005537-198811000-00002.
20. Shimada K, Kaneko Y, Sato I, et al. Classification of the Ophthalmic Artery that Arises from the Middle Meningeal Artery in Japanese Adults. Okajimas Folia Anatomica Japonica. 1995; 72(2–3): 163–176, doi: 10.2535/ofaj1936.72.2-3_163.
21. Simão-Parreira B, Cunha-Cabral D, Alves H, et al. Morphology and Navigational Landmarks of the Cranio-orbital Foramen in a Portuguese Population. Ophthalmic Plastic & Reconstructive Surgery. 2019; 35(2): 141–147, doi: 10.1097/IOP.0000000000001188.
22. Stiernberg CM, Bailey BJ, Weiner RL, et al. Reconstruction of the Anterior Skull Base Following Craniofacial Resection. Archives of Otolaryngology - Head and Neck Surgery. 1987; 113(7): 710–712, doi: 10.1001/archotol.1987.01860070024009.

Table 1. Characteristics of published studies

First Author	Year	Continent	Country
Mahajan, MV	2020	Asia	India
Simao-Parreira, B	2019	Europe	Portugal
Modasiya, UP	2018	Asia	India
Silva, J	2017	South America	Chile
Garapati, S	2016	Asia	India
Macchi, V	2016	Europe	Italy
Pratha, AA	2016	Asia	India
Agarwal, C	2015	Asia	India
Celik, S	2014	Asia	Turkey
Tomaszewskia, A	2014	Europe	Poland
Chauhan, R	2013	Asia	India
Gopalakrishna, K	2013	Asia	India
Pankaj, AK	2013	Asia	India
Abed, SF	2012	Europe	Unitek Kingdom
Jadhav, S	2012	Asia	India
Yuvaraj Babu, K	2011	Asia	India
Krishnamurthy, A	2008	Asia	India
O'Brien, A	2007	Europe	Unitek Kingdom
Erturk, M	2005	Asia	India
Jovanovic, I	2003	Europe	Serbia
Kwiatkowski, J	2003	Europe	Poland
Lee, HY	2000	Asia	Korea
Georgiou, C	1991	North America	USA
Mysorekar, VR	1987	Asia	India
Santo, N	1984	South America	Brazil

Table 2. Statistical results of this meta-analysis regarding the prevalence of the cranio-orbital foramen (COF). LCI – lower confidence interval. HCI – higher confidence interval. Q – Cochran's Q

Category	**Pooled Prevalence**	**N**	**LCI**	**HCI**	**Q**	**I^2**	**P value**
Pooled prevalence of the COF	48.37%	5649	41.67%	55.10%	540.50	95.56	-
Pooled prevalence of occurance of the COF in different locations							
COF in the sphenoid bone	26.28%	793	17.29%	36.37%	15.21	80.28	-
COF in the frontal bone	25.69%	793	14.21%	39.09%	26.51	88.68	
COF at the frontosphenoidal suture	15.06%	793	12.19%	18.17%	1.29	0.00	
COF at the ossified	18.87%	793	0.00%	57.32%	224.57	98.66	

frontosphenoidal suture							
COF at different locations	9.85%	793	0.00%	47.79%	282.18	98.94	
Occurrence of Unilateral or Bilateral COF							
Pooled prevalence of the unilateral COF	73.92%	926	41.87%	96.97%	25.74	92.23	0.36
Pooled prevalence of the bilateral COF	26.08%	926	3.03%	58.13%	25.74	92.23	
Occurrence of COF regarding sex							
Pooled prevalence of the COF in Females	50.52%	1061	40.38%	60.64%	18.99	78.94	0.93
Pooled prevalence of the COF in Males	51.91%	1061	28.75%	74.68%	105.24	96.20	
Occurrence of COF regarding patients' side							
Pooled prevalence of the COF on the Left side	51.42%	773	34.85%	67.83%	50.97	90.19	0.82
Pooled prevalence of the COF on the Right side	47.63%	773	28.11%	67.51%	72.64	93.12	
Occurrence of an additional COF							
Pooled prevalence of the aCOF	16.72%	257	11.09%	23.22%	3.10	35.56	-

Table 3. Statistical results of this meta-analysis regarding the diameter of the cranio-orbital foramen (COF). LCI – lower confidence interval. HCI – higher confidence interval.

Category	**N**	**Mean**	**Standard Error**	**Variance**	**LCI**	**HCI**	**Z-Value**	**p-Value**
Mean maximal diameter of the COF [mm]	944	0.969	0.140	0.019	0.695	1.242	6.943	0.00

Table 4. Statistical results of this meta-analysis regarding the location of the cranio-orbital foramen (COF). LCI – lower confidence interval. HCI – higher confidence interval.

Category	**N**	**Mean**	**Standard Error**	**Variance**	**LCI**	**HCI**	**Z-Value**	**p-Value**
Overall results								
Distance between COF and the Frontozygomatic Suture [mm]	1347	26.89	0.62	0.39	25.68	28.11	43.32	0.00
Distance between COF and the Supraorbital Notch [mm]	1347	34.95	0.74	0.54	33.50	36.39	47.37	0.00

Distance between COF and the Whitnall's Tubercle [mm]	1347	27.56	0.62	0.39	26.34	28.78	44.19	0.00
Distance between COF and the Lateral angle [mm]	1347	7.18	0.76	0.58	5.68	8.67	9.43	0.00
	Results regarding sex							
Distance between COF and the Frontozygomatic Suture in Females [mm]	248	25.92	0.93	0.87	24.09	27.75	27.72	0.00
Distance between COF and the Frontozygomatic Suture in Males [mm]	248	26.03	0.36	0.13	25.32	26.73	72.24	0.00
Distance between COF and the Supraorbital Notch in Females [mm]	248	34.52	0.66	0.44	33.22	35.82	52.06	0.00
Distance between COF and the Supraorbital Notch in Males [mm]	248	34.33	0.41	0.17	33.52	35.14	83.09	0.00
	Results regarding the patients' side							
Distance between COF and the Frontozygomatic Suture on the Left side [mm]	192	24.78	1.92	3.69	21.01	28.54	12.90	0.00
Distance between COF and the Frontozygomatic Suture on the Right side [mm]	176	25.62	2.30	5.27	21.12	30.12	11.16	0.00
Distance between COF and the Supraorbital Notch on the Left side [mm]	192	35.19	1.58	2.50	32.09	38.29	22.24	0.00
Distance	176	35.12	1.83	3.37	31.53	38.72	19.14	0.00

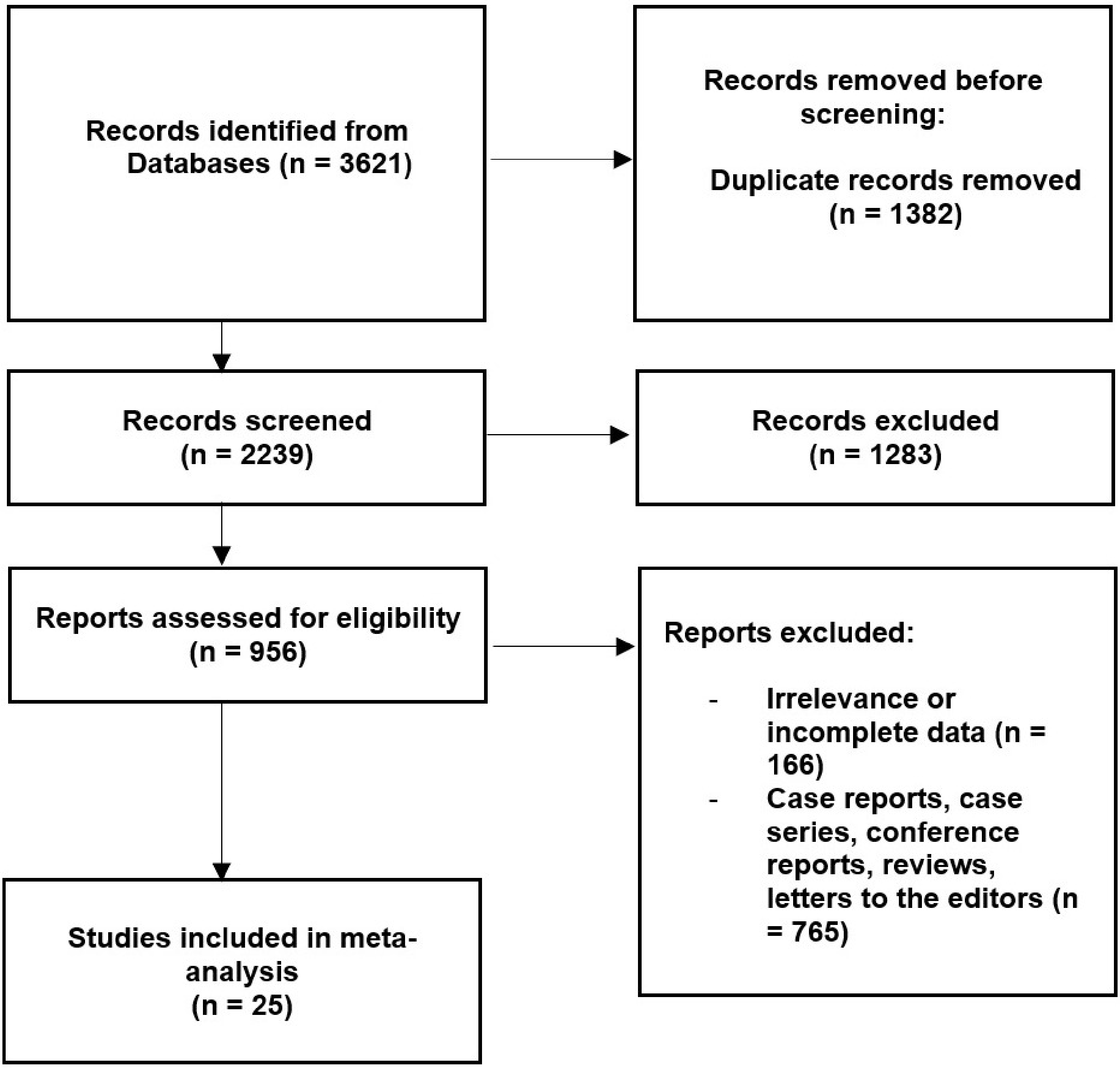
between COF and the Supraorbital Notch on the Right side [mm]								
Distance between COF and the Superior Orbital Fissure on the Left side [mm]	192	10.28	1.35	1.83	7.63	12.94	7.60	0.00
Distance between COF and the Superior Orbital Fissure on the Right side [mm]	176	11.10	2.29	5.25	6.61	15.59	4.84	0.00

Figure 1. Flow-chart presenting the inclusion process in this meta-analysis.

Figure 2. Scheme illustrating the cranio-orbital foramen and its anatomical area. A - cranio-orbital foramen; B - frontozygomatic suture; C - superior orbital fissure; D - supraorbital notch; E - inferior orbital fissure; F - Whitnall's tubercle.

Figure 3. A photograph depicting the right orbit. A - cranio-orbital foramen; B - frontozygomatic suture; C - Superior orbital fissure; D - Supraorbital notch

Figure 4. A photograph depicting the left orbit. A - cranio-orbital foramen; B - frontozygomatic suture; C - Superior orbital fissure; D - Supraorbital notch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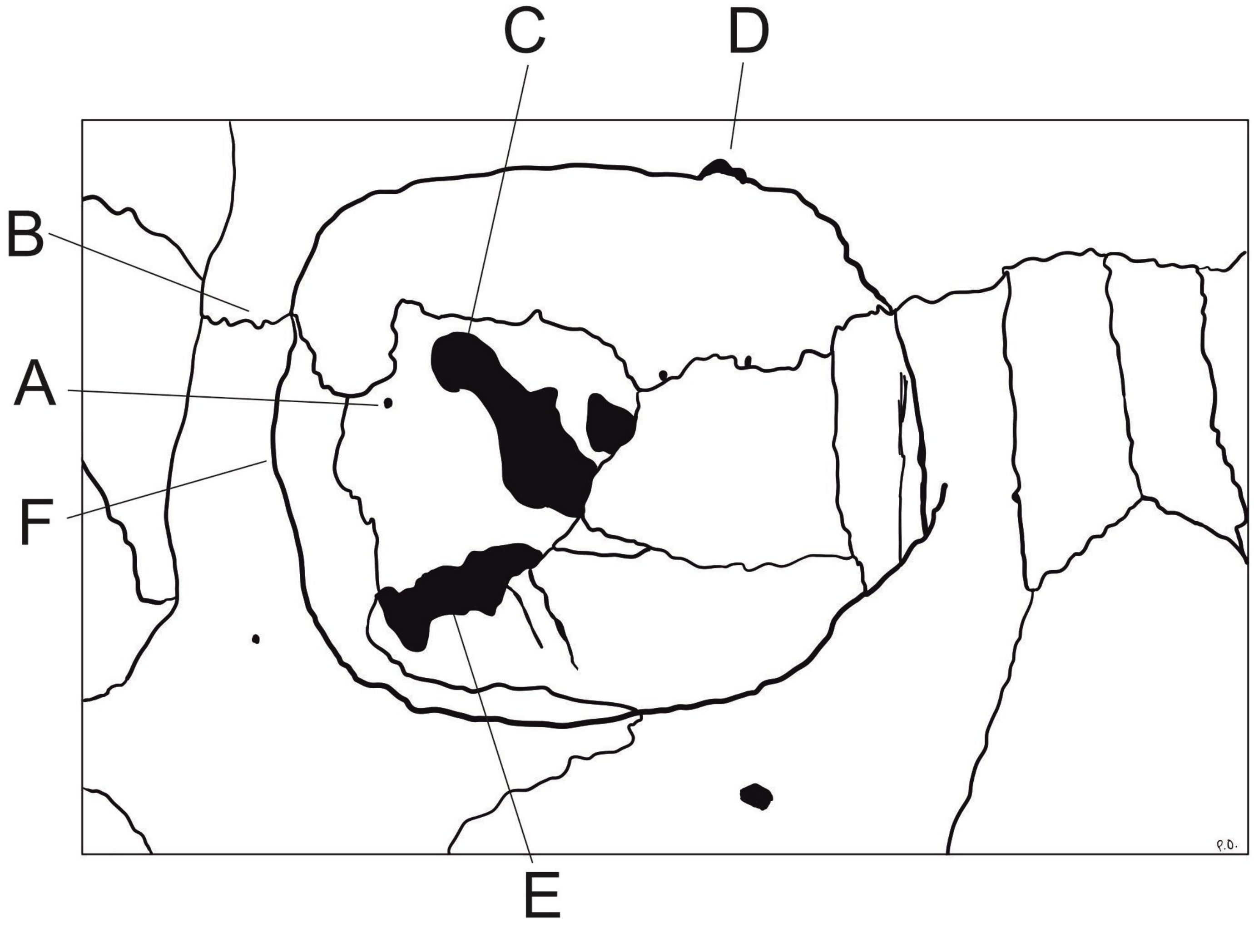
Records removed before screening:
Duplicate records removed (n = 1382)
Records screened (n = 2239)
Records excluded (n = 1283)
Reports assessed for eligibility (n = 956)
Reports excluded:
- Irrelevance or incomplete data (n = 166)
- Case reports, case series, conference reports, reviews, letters to the editors (n = 765)
Studies included in meta-analysis (n = 25)



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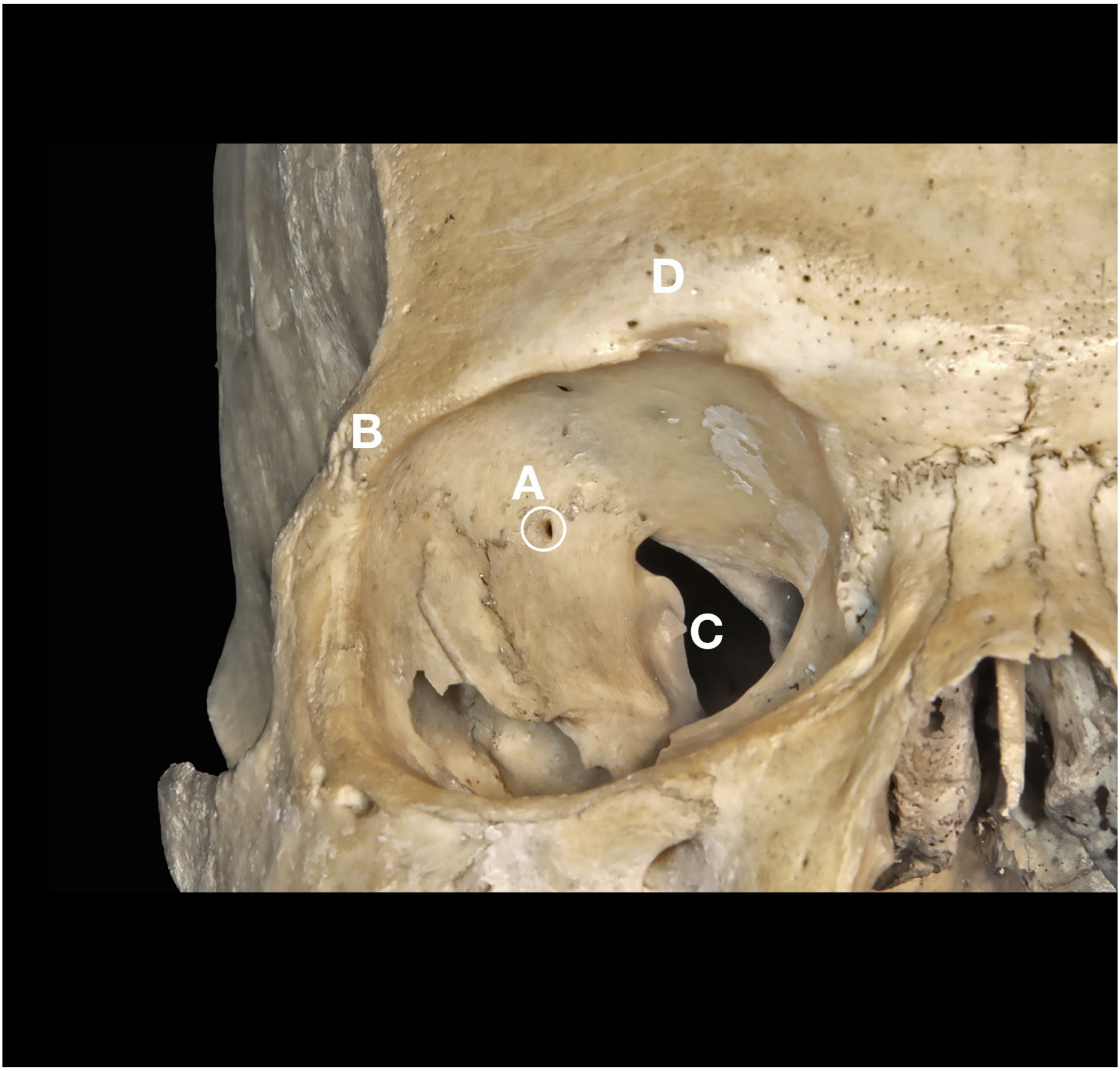
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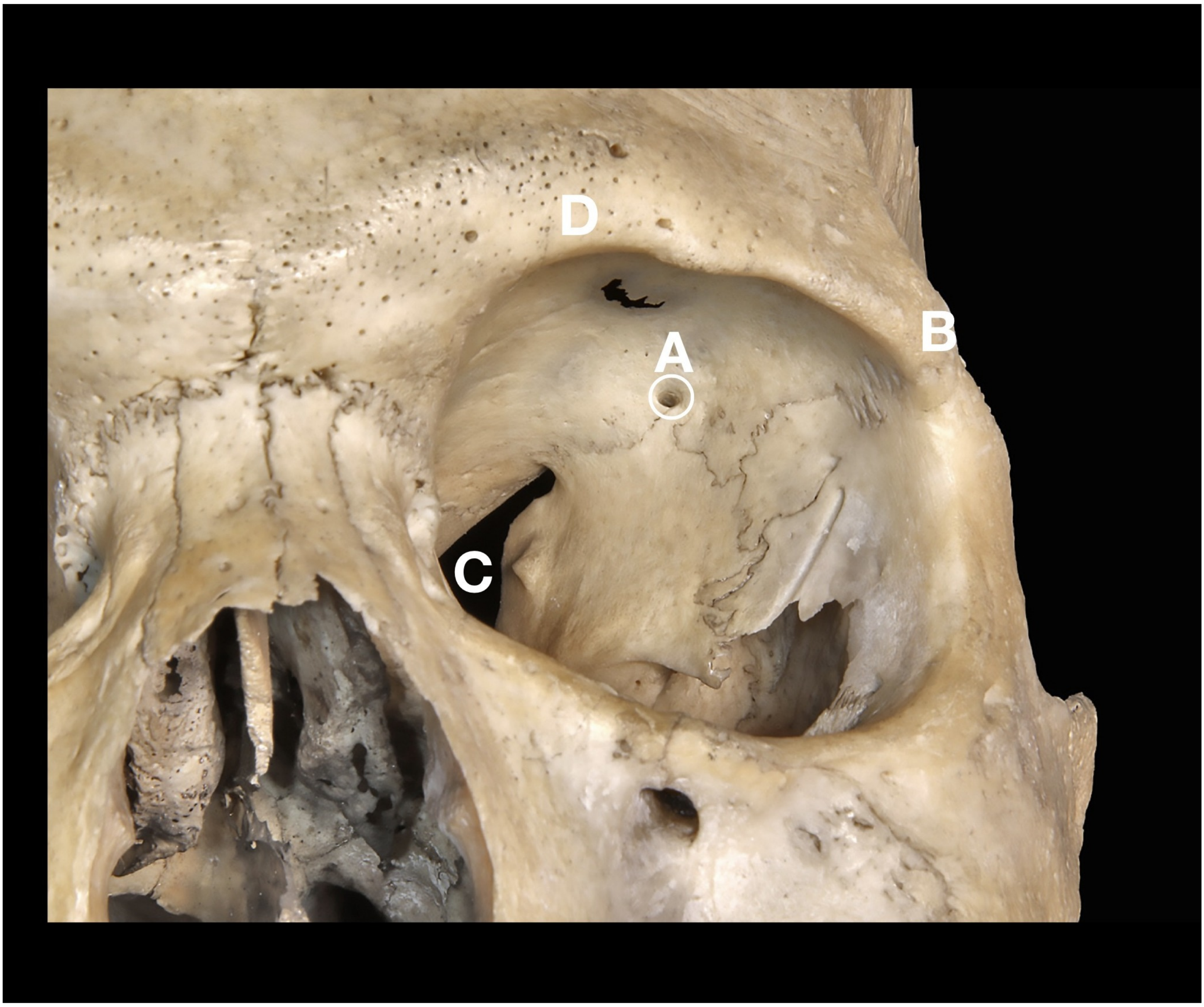
D
A
B
C