The caroticoclinoid foramen in fetal and infantile orbitosphenoid, presphenoid, and sphenoid bones: developmental and neurosurgical considerations

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OBJECTIVE The presence of a caroticoclinoid foramen may increase the likelihood of adverse neurosurgical events. Despite the clinical importance of the caroticoclinoid foramen, its study has been mostly limited to adult populations. Therefore, the object of this study was to describe the prevalence, morphology, and development of the caroticoclinoid foramen among varied sexes and races in early life.

METHODS The study analyzed caroticoclinoid foramina in dry orbitosphenoid, presphenoid, and sphenoid bones from a population of 101 fetal and infantile crania of varied sex and race.

RESULTS A caroticoclinoid foramen, whether complete, near complete, or partial, was found in 36 of 199 sides (18.1%). Of the 98 crania with bilaterally intact sides, 21 (21.4%) had the presence of at least one caroticoclinoid foramen. Caroticoclinoid foramina were found unilaterally and bilaterally, in both female and male crania (9/41, 22.0%; 12/57, 21.1%, respectively) and, likewise, in crania of both black and white races (9/54, 16.7%; 12/44, 27.3%, respectively). Caroticoclinoid foramina were formed from cornuate bony projections from the anterior clinoid process, middle clinoid process, or both anterior and middle clinoid processes. Caroticoclinoid foramina were also found in isolated orbitosphenoid bones from individuals as young as 4 months' fetal age.

CONCLUSIONS The caroticoclinoid foramen occurs in approximately one of every 5 sides and in one in every 5 individuals of perinatal age and should, therefore, be considered a common finding in both fetuses and infants. It is common in both females and males as well as in both black and white races, alike. Furthermore, the caroticoclinoid foramen can be found in individuals as young as 4 months of fetal age. Failure to anticipate the presence of a caroticoclinoid foramen will place important neurovascular structures, including the internal carotid artery, at risk of injury. Neurosurgeons should, therefore, anticipate the caroticoclinoid foramen even in their youngest patients.

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KEYWORDS anatomy; internal carotid artery; anterior clinoid process; middle clinoid process; neurosurgery; surgical technique

ANATOMICAL variations in the sphenoid may complicate operative procedures and increase the likelihood of adverse surgical events. Such a noteworthy variation is that of the caroticoclinoid foramen (of Monro) (CCF), a foramen formed by an ossified caroticoclinoid ligament between the anterior and middle clinoid processes.^{18,25,26} The CCF has been categorized as “complete,” “contact,” “almost complete,” “kissing-clinoids,” “incomplete,” or “partial” based on the extent of ligamentous ossification.^{5,9–11,21}

When present, the CCF encompasses the internal carotid artery (ICA) in such close contact that the CCF has been measured to have a smaller diameter than the ICA and, as a result, causes morphological changes to the artery in almost all cases.^{3,20} Due to the intimate relationship between the foramen and the ICA, the artery is predisposed to damage.^{16,20}

Despite the clinical importance of the CCF, reports have largely been limited to studies in adults. Little is known about the prevalence or morphology of the CCF in

ABBREVIATIONS CCF = caroticoclinoid foramen; ICA = internal carotid artery.

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FIG. 1. Superior view of a sphenoid bone from an 8-month-old black female fetus. A complete CCF is found on the left, and a partial CCF, formed by a cornuate bony projection from the anterior clinoid process, is found on the right. Figure is available in color online only.

FIG. 2. Superior view of the left- and right-sided orbitosphenoid bones from a 6-month-old white male fetus. Near-complete CCFs are seen bilaterally. The posterior and posterolateral boundaries of the near-complete foramina are formed by bony extensions from the anterior clinoid processes found bilaterally. Figure is available in color online only.

fetuses and infants. In the fetal and infant population, most reports are limited to descriptions of isolated cases.^{10,15} Accordingly, little is known about the development of the CCF. Therefore, this report analyses fetal and infantile orbitosphenoid, presphenoid, and sphenoid bones in order to elucidate the prevalence, morphology, and development of the CCF among varied sexes and races in early life.

Methods

The study analyzed dry orbitosphenoid, presphenoid, and sphenoid bones from the Johns Hopkins collection of perinatal crania with approval from the Department of Physical Anthropology at the Cleveland Museum of Natural History. Bones came from a population of 101 fetal and infantile crania of varied sexes and races. The bones originated from individuals who died between the years 1916 and 1951 in Baltimore, Maryland—gathered by Johns Hopkins University anatomist Adolph H. Schultz, prior to their transfer to the Cleveland Museum of Natural History in 1973. Demographic information from archival records regarding race was limited to “black” and “white.” Data regarding age, which was documented in month increments, was also taken from the archival records.

There were a total of 42 female and 59 male crania included in the study. Of these crania, 57 were from black individuals and 44 were from white individuals. Likewise, crania were from individuals of varied age. There were a total of 59 fetal crania and 42 infantile crania. Of the latter, 12 were identified as newborns. Of the 101 crania, 3 had either been unilaterally damaged or had absent sides (one left-sided and two right-sided, respectively).

A total of 199 sides (100 left sides and 99 right sides) were assessed for the presence of CCF. When present, the morphology of each CCF was categorized as “complete,” “near complete,” or “partial,” consistent with descriptions from prior reports.^{9,10} A “complete” CCF was defined as one in which bone formed a complete ring. A “near-complete” CCF was defined as one in which extensions from the anterior and middle clinoid processes formed an extremely small gap between one another, akin to that of

a suture joint. A “partial” CCF was defined as an incomplete foramen in which extensions from the anterior and/or middle clinoid process projected toward one another but not to the extent of a “near-complete” CCF.

In accord with prior studies of the CCF, Fisher’s exact test was performed to assess differences in subpopulations.¹⁰ Fisher’s exact tests were performed among races and sexes. Likewise, Fisher’s exact tests were performed among samples grouped by both race and sex combined. Statistical analysis was performed with GraphPad Prism statistical software, version 6.00 (GraphPad Software).

Results

Examples of complete, near-complete, and partial CCF can be seen in Figs. 1 and 2. Among specimens with a near-complete or partial CCF, the cornuate projections forming the posterior boundaries of the foramen could arise from the anterior clinoid process, such as those seen in Figs. 1 and 2, or from the middle clinoid process, such as those seen in Fig. 3.

Most sides were unremarkable (163/199; 81.9%); however, a CCF, whether complete, near complete, or partial, was found in 36 of 199 sides (18.1%). A complete CCF was found in 3.5% of sides (7/199). The complete CCF was found on the right side (5/99; 5.1%) more often than the left side (2/100; 2.0%). Among sides with a complete CCF, 100% (7/7) were found to have either a partial CCF (6/7, 85.7%) or a near-complete CCF (1/7; 14.3%) on the contralateral side. The CCF was more commonly found on the right side than the left side (20.2% vs 16.0%, respectively). The prevalence of CCF morphological types, according to side, can be found in Table 1.

With regard to age, the youngest individual with a partial CCF was a black male fetus of 5 months’ gestational age. The youngest individual with a near-complete CCF was a white male fetus of 6 months’ gestational age (Fig. 2). The youngest individuals with a complete CCF were one black male and two black female fetuses of 8 months’ gestational age (Fig. 1). A heat map of variation frequency according to age can be found in Fig. 4.

Of the 98 crania with bilaterally intact sides, 77 (78.6%) were unremarkable and 21 (21.4%) had the presence of at

FIG. 3. Superior view of the sphenoid bone from a newborn white male infant. Partial CCFs are seen bilaterally. In this case, extensions from the anterior clinoid processes are forming the posterolateral boundaries of the incomplete foramina, and bony projections arising from the presphenoid region of the sphenoid (i.e., the middle clinoid processes) are extending posterolaterally to form the posteromedial boundaries of the incomplete foramina. The bony processes arising from the middle clinoid processes are asymmetrical—the left-sided projection is marked, while the right-sided projection is relatively small. Figure is available in color online only.

least one CCF variant. Of the 21 crania with caroticoclinoid variations, the most common bilateral presentation was that of a unilateral unremarkable side paired with a unilateral partial CCF (7/21; 33.3%; 2 left-sided and 5 right-sided partial CCFs, respectively). The prevalence of morphological combinations of CCF can be found in Table 2.

With regard to sex, CCF variation prevalence was 22.0% (9/41) among female crania and 21.1% (12/57) among male crania. Fisher's exact probability did not show a significant difference between sexes ($p = 0.9999$). With regard to race, CCF variation prevalence was 16.7% (9/54) and 27.3% (12/44) among black and white crania, respectively. Fisher's exact probability did not show a significant difference between races ($p = 0.2250$).

In consideration of CCF prevalence with respect to sex and race together, white males had a prevalence of CCF variation in 28.6% of the crania (8/28), followed by 25% (4/16) of white female crania, 20% (5/25) of black female crania, and 13.8% of black male crania (4/29). Complete and partial CCFs were found in both males and females of both races. Near-complete CCFs were only seen in white individuals, both male and female. Fisher's exact probability did not show a significant difference between any combination of sex and race with any other combination of sex and race (Table 3).

Discussion

Though the prevalence and morphology of the CCF has been studied in adults, there is a paucity of study on the development of the CCF and its prevalence in the fetal and infantile populations. This report provides insight into CCF development and prevalence in the perinatal population. Also, the report establishes that the presence of the CCF should be anticipated even among patients as young as 4 months of fetal age.

TABLE 1. The prevalence of the CCF and foraminal variations among fetal and infant cranial sides

Morphology	Side(s)	Ratio*	%
Unremarkable			
	Lt	84:100	84.0
	Rt	79:99	79.8
	Lt + rt	163:199	81.9
Variant			
Complete foramen	Lt	2:100	2.0
	Rt	5:99	5.1
	Lt + rt	7:199	3.5
Near-complete foramen	Lt	4:100	4.0
	Rt	1:99	1.0
	Lt + rt	5:199	2.5
Partial foramen	Lt	10:100	10.0
	Rt	14:99	14.1
	Lt + rt	24:199	12.1
All variant types	Lt	16:100	16.0
	Rt	20:99	20.2
	Lt + rt	36:199	18.1

* The ratio is variations/sides.

Prevalence and Demographics

The results of this study are consistent with many of the studies performed among adults. For example, studies by Ertürk et al.,⁴ Gupta et al.,⁵ and Kapur & Mehic⁹ observed the CCF in 16.75% (67/400), 23.68% (81/342), and 20% (14/70) of sides, respectively. Similarly, the present study found the CCF present in 18.1% (36/199) of sides. Likewise, a meta-analysis by Ertürk et al.⁴ found the CCF in 20.51% (104/507) of crania. Jha et al.⁸ found the CCF in 22.22% of crania (24/108). Likewise, the present study found the CCF in 21.4% (21/98) of crania. This study, therefore, demonstrates that adult prevalence of the CCF is established in a perinatal population. Indeed, this report documents that an adult prevalence is seen even among the fetal population (Fig. 4). Among newborns, the prevalence of the CCF was as high as 45.8% (11/24) of sides and 50% (6/12) of crania, a prevalence higher than what is typically reported among adults.

With regard to CCF types (i.e., complete, near-complete, and partial types), in adult populations the most common form of CCF is that of an incomplete or partial type.^{4,8,9,11,16,23}

There is general agreement among reports studying the CCF in adults that the CCF is most often found unilaterally.^{4,7-9,16} Conversely, this study found a unilateral CCF in one-third of instances (33.33%; 7/21); otherwise, the CCF was found bilaterally (66.66%; 14/21). With striking similarity, the study performed by Keyes,¹¹ which analyzed a similar racial demographic, black and white individuals, found the CCF (what he referred to as the clinocarotid canal or anterior interclinoid canal) unilaterally in approximately one-third of instances (250/762; 32.8%) and bilaterally in approximately two-thirds of instances (512/762; 67.2%). A comparison between this study and that of

FIG. 4. Heat map relating the relative frequency (expressed as a percentage) of CCF types to age in fetal and infant populations.

TABLE 2. The prevalence of CCF combinations in crania

Morphological Type		Ratio of Total (ratio of variants)	% of Total (% of variants)
Major Type/Subtype	Details		
Unremarkable	—	77:98 (—)	78.6 (—)
Variant			
Unilateral partial	Lt partial	2:98 (2:21)	2.0 (9.5)
	Rt partial	5:98 (5:21)	5.1 (23.8)
	Lt + rt partial	7:98 (7:21)	7.1 (33.3)
Partial & complete	Lt partial w/ rt complete	4:98 (4:21)	4.1 (19.0)
	Rt partial w/ lt complete	2:98 (2:21)	2.0 (9.5)
	Total partial w/ complete	6:98 (6:21)	6.1 (28.6)
Bilateral partial	—	4:98 (4:21)	4.1 (19.0)
Partial & near complete	Lt partial w/ rt near-complete	0:98 (0:21)	0.0 (0.0)
	Rt partial w/ lt near-complete	2:98 (2:21)	2.0 (9.5)
	Total partial w/ near-complete	2:98 (2:21)	2.0 (9.5)
Bilaterally near complete	—	1:98 (1:21)	1.0 (4.8)
Near-complete & complete	Lt near-complete w/ rt complete	1:98 (1:21)	1.0 (4.8)
	Rt near-complete w/ lt complete	0:98 (0:21)	0.0 (0.0)
	Total near-complete w/ complete	1:98 (1:21)	1.0 (4.8)
Other variant combinations*	—	0:98 (0:21)	0.0 (0.0)
All variant types	—	21:98 (21:21)	21.4 (100.0)

— = not applicable.

* Other variant combinations include unilateral complete, unilateral near complete, bilateral complete.

TABLE 3. Results of Fisher's exact test among the fetal and infant population based upon race and sex

Race & Sex	p Value			
	Black Females	Black Males	White Females	White Males
Black females	—	0.7175	0.7169	0.5355
Black males	0.7175	—	0.4270	0.2070
White females	0.7169	0.4270	—	0.9999
White males	0.5355	0.2070	0.9999	—

Keyes¹¹ suggests that race may influence the unilateral or bilateral presence of the CCF. Furthermore, both this study and that of Keyes¹¹ found the unilateral CCF to be more common on the right side (5/98 [5.1%] and 142/2187 [6.49%], respectively) than the left side (2/98 [2.0%] and 108/2187 [4.93%], respectively).

Aside from the study by Keyes,¹¹ reports generally agree that unilateral occurrence of the CCF is more common than that of bilateral occurrence. The relationship between the increased prevalence of bilateral CCFs among the perinatal population relative to the adult population suggests that CCFs found in the adult population could be in a process of bony resorption rather than accretion. This point is further underscored by the similarity in overall prevalence of crania possessing CCFs between the perinatal population and the general adult population.

Another noteworthy similarity between this study and that of the large-scale study of adult crania by Keyes¹¹ is in regard to the prevalence of the CCF in females and males of different races. The studies agree that the CCF is more prevalent in white males than black males and in white females than black females (Table 4). Similarly, the studies agree that the CCF is more prevalent among white individuals than black individuals, in general (Table 4). Still, Keyes¹¹ reported the CCF in 34.84% (762/2187) of crania, whereas this report found the CCF in 21.4% (21/98). The study by Keyes,¹¹ however, was predominantly of white male crania (1146 white males compared to 208 white females, 599 black males, and 234 black females), and therefore, the overall prevalence of the CCF was skewed in a manner that would give the most weight to the prevalence in white males. Furthermore, several reports have also noted differences between races with regard to the prevalence of the CCF.¹⁶

As an aside, caution must be exercised when interpreting the prevalence data among CCF studies. For example, reports have frequently cited the lowest reported prevalence of the CCF from the study by Azeredo et al.¹ as 6.3% (17/270);^{4,22} however, these studies have not emphasized that this prevalence only documents complete-type CCFs and does not take into consideration other variations of the CCF such as partial-type foramina, which are the most prevalent type of CCF. Indeed, the 6.3% prevalence of the complete-type CCF is higher than the prevalence reported in many other studies documenting the prevalence of the complete CCF, including the present study, which documented a complete CCF in 3.5% (7/199) of sides.^{9,16}

Some reports have erroneously described the preva-

TABLE 4. A comparison of CCF prevalence results between this study and that of Keyes

Race & Sex	Keyes, 1935		Present Study	
	Ratio	%	Ratio	%
Black females	52:234	22.22	5:25	20.0
Black males	156:599	26.04	4:29	13.8
Black females & males	208:833	24.96	9:54	16.7
White females	81:208	38.94	4:16	25.0
White males	473:1146	41.27	8:28	28.6
White females & males	554:1354	40.91	12:44	27.3

lence of the CCF as the same as the prevalence of the middle clinoid process, bundling all CCF variations together as middle clinoid process variations.²¹ Indeed, as can be seen in this report, CCF variants may be formed by processes from the anterior clinoid process (see, for example, Figs. 1 and 2) and/or the middle clinoid process (Fig. 3).

Developmental Considerations

With regard to the development of the sphenoid, endochondral ossification centers have been reported to appear in the orbitosphenoid cartilage at about the ninth week of fetal life²⁴; however, some have noted that the orbitosphenoid ossification centers appear at approximately the twelfth week.^{13,17} Nemzek et al.¹⁹ performed a study of formalin-fixed fetuses with mammographic plain radiography, CT, and MR imaging that documented evidence of orbitosphenoid ossification as early as 16 weeks of development.

The arrival of the main ossific centers of the presphenoid differs among individuals. Also, from fetus to fetus, differences in size may be appreciated; as Kodama¹⁴ described, "the size is that of a grain of rice in one case, while miliary in size in another case." Similarly, the left and right side may differ in size in a similar way. A pair of posterior accessory centers may appear at the posterolateral end of the main presphenoid ossification centers. Kodama¹⁴ noted that the posterior accessory centers were observed in only 2 of 15 skulls (13.33%), in embryos of a length between 29.0 and 31.50 cm.¹⁴ In both crania, they occurred bilaterally.¹⁴ The author suggests that the asymmetrical development of the presphenoid may influence the development of the CCF. Also, inconsistent posterior accessory ossification centers may have some role in the formation of the CCF, perhaps contributing to the growth of the middle clinoid process.

Hochstetter⁶ assessed 113 fetuses, noting that 12 (10.6%) had bilateral CCF completed by tissue slings and three (2.7%) had unilateral partially completed foramina (two left-sided and one right-sided) formed as a result of elongated middle clinoid processes. The results of this study are somewhat difficult to compare to those of Hochstetter⁶ due to differences in the nature of the specimens (wet vs dry, respectively). Furthermore, the report by Hochstetter⁶ is nondescript with regard to the nature of the tissues forming the complete CCF (e.g., bone, cartilage, ligament, dura, etc.), whereas the present study was limited to only the assessment of dry bone.

Aside from the aforementioned study by Hochstetter,⁶ reports of fetal crania have been largely limited to cases. For example, Kier¹² noted a CCF in conjunction with a posterior interclinoid foramen in a fetus of 30 weeks' development. Kawakubo et al.¹⁰ demonstrated a near-complete and complete CCF in Japanese fetuses of 7 and 10 months' gestation, respectively. The posterior margin of the near-complete CCF was formed by a bony projection arising from the middle clinoid process. In comparison, this report shows a bilateral near-complete CCF in the orbitosphenoid bones of a 6-month-old white male fetus that are formed by extensions of the anterior clinoid process (Fig. 2).

This study documents a partial CCF occurring in the orbitosphenoid of a fetus of 5 months' gestational age. However, since the orbitosphenoid was an independent bone in this case, as well as the aforementioned 6-month-old fetus shown in Fig. 2, it draws attention to the accuracy of the documented fetal age. Kodama¹⁴ observed that the main body of the presphenoid first unites with the orbitosphenoid at the beginning of the 5th fetal month. The postsphenoid begins fusing with the orbitosphenoid in the beginning of the 6th fetal month (26.5 cm).² Therefore, the independent orbitosphenoid bones reported here, though recorded as 5 or 6 months' fetal age, were likely from fetuses in their 4th month. This notion is congruent with the report of Kier,¹³ who shows an image of a dissected sphenoid specimen from a 20-week-old fetus that shows the orbitosphenoid bones already joined with the bone encompassing the large olive-shaped presphenoid cartilage. Of special note, the report of the 20-week-old fetus shows a near-complete or complete left-sided CCF formed with the main body of the presphenoid.¹³

This report documents the earliest developmental occurrence of a CCF. With regard to the development from a partial to a complete CCF, the earliest partial, near-complete, and complete CCFs were found among individuals of 5, 6, and 8 months' fetal age, respectively. Therefore, the growth from 5–8 months' fetal age may represent the earliest growth stage from a partial to a complete CCF. This notion is in accord with the findings of the near-complete CCF in a fetus of 7 months age, and the complete CCF in a fetus of 10 months of age reported by Kawakubo et al.¹⁰ Still, a limitation to the study is that the earliest osteological specimens available were from individuals of 5 months' fetal age. However, the orbitosphenoid bones studied here are probably less than 20 weeks of fetal age, as evidenced by the independence of the orbitosphenoid bones from the body of presphenoid. Therefore, this report demonstrates that the CCF may begin to develop in the 4th fetal month, before the orbitosphenoid bones merge with the presphenoid portion of the sphenoid.

Conclusions

This report documents that the CCF may be found in fetuses and infants—black and white—female and male. With regard to development, the CCF occurs even in isolated orbitosphenoid bones. Therefore, the CCF must be anticipated in patients at least as young as 4 months of fetal age. This study identified a CCF in approximately 1

of 5 sides and in approximately 1 of 5 crania among the perinatal population and should, therefore, be considered a common finding. Special care should be taken to anticipate and identify the CCF in even the youngest of patients.

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Disclosures

The author reports no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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