

## Prevalence of the sphenoid emissary foramen and its clinical relevance in a selected South African population

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### Abstract

**Background:** The sphenoid bone is an intricate bone with several features, such as sphenoid emissary foramen (SEF). The SEF serves as a passage for the veins of Vesalius that connects the pterygoid plexus to the cavernous sinus, which acts as a means of transferring extracranial thrombosis to the cavernous sinus. SEF and its content are usually absent in individuals, and it mainly varies in morphology, laterality, and age if present. Notably, the prevalence of SEF regarding sex, laterality, and age remains underexplored. Therefore, this study aims to document the prevalence of SEF about sex, age, and laterality in a selected South African (SA) population.

**Materials and Methods:** 137 skulls were bilaterally analysed. The middle cranial fossa of each skull was observed for the presence and absence of the SEF. The patency of the SEF was confirmed by inserting a bristle through each probable foramen, and only patent foramina was used for this study.

**Results:** Out of 137 skulls that were analysed, the SEF was found present in 48 (35.8%) skulls, with a high incidence in the White SA population and the lowest incidence amongst the Black SA population. 29.2% were unilateral (right 17.5%; left 11.7%), while 6.6% were bilateral. A high prevalence of the SEF was noted in males on the right side. A statistically significant association was obtained between laterality and absence of the foramen about age,  $p = 0.02$ . In addition to age, a fluctuating trend was noted in the occurrence of the SEF, where the prevalence was very high in the <29 years age group and decreased from 30-39 years to 60-69 years age group. It then increased again during age advancement. The incidence of SEF is associated with a pathway of the sphenoid emissary veins as it sometimes travels along the mandibular division of the trigeminal nerve through the foramen ovale. Thus, making the trigeminal rhizotomy procedure problematic.

**Conclusion:** SEF was highly prevalent in the SA population, particularly the White SA sample, and on the right side in males. Knowledge of the SEF variations is important during trigeminal rhizotomy procedures to avoid damage to sphenoid emissary veins.

**Keywords:** Sphenoid emissary foramen, sphenoid emissary veins, foramen Vesalius, middle cranial fossa, cavernous sinus

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## Introduction

Identifying skull base foramina is of clinical importance as it permits neurovascular structures to move in and out of the skull (Mistry *et al.*, 2021, Jadhav *et al.*, 2016). Sphenoid emissary foramina (SEF), also known as foramen of Vesalius, are sometimes found on the greater wing of the sphenoid bone along with foramen rotundum, foramen ovale and foramen spinosum (Cochinski *et al.*, 2022a). The SEF is a small, variable, and inconsistent foramen that is located between the foramen ovale posteriorly and the scaphoid fossa anteriorly (Jadhav *et al.*, 2016). Several pieces of literature have shown that SEF is often absent in some individuals or present on either side of the greater wing of the sphenoid (Leonel *et al.*, 2020, Jadhav *et al.*, 2016). Acquired or hereditary diseases, including neurofibromatosis, osteopetrosis, and osteoporosis may cause the absence of the SEF (Cochinski *et al.*, 2022b).

The content of the SEF includes the lateral sphenoidal nerve, accessory meningeal artery as well as the small sphenoid emissary veins (Leonel *et al.*, 2020, Jadhav *et al.*, 2016). Notwithstanding, several authors have documented variations in the content of this foramen in cases where the sphenoid emissary veins were found absent in the SEF, and they traversed the skull using the foramen ovale only (Piagkou *et al.*, 2023, Cochinski *et al.*, 2022b, Leonel *et al.*, 2020). The sphenoid emissary veins are tiny veins that connect the cavernous sinus to the pterygoid plexus of veins, and they serve as a means by which an infected thrombus may travel from the extracranial plexus of veins to reach the cavernous sinus (Dolapsakis *et al.*, 2019, Bayrak *et al.*, 2018).

The absence of the SEF signifies that the sphenoid emissary veins will travel through the foramen ovale together with the mandibular division of the trigeminal nerve (Jadhav *et al.*, 2016, Kale *et al.*, 2009). Furthermore, a study by Kale *et al.* (2009) revealed that if present, the sphenoid emissary veins may divide and drain via the foramen ovale and the SEF. This variation remains a clinical concern for surgeons as treating trigeminal neuroglia requires the percutaneous intervention of the needle targeting the foramen ovale. During this surgical operation, sphenoid emissary veins may be exposed to severe damage in the cranium, which may cause intracranial bleeding (Kale *et al.*, 2009).

Previous literature has reported that SEF on the sphenoid bone is more common in females than males (Gupta *et al.*, 2005). The absence of SEF on both sides of the sphenoid was found to be very common compared to the bilaterality presence of the SEF, with unilaterality of the SEF being the least frequently recorded (Kale *et al.*, 2009). However, the study by Boyd (1930) differed from these observations as they recorded a high unilaterality frequency compared to the SEF's bilaterality.

The SEF variations in sex and age compared with laterality have not been extensively explored in the literature. More so, the SEF variations regarding sex, age, and laterality remain unexplored in the SA population, which is a multi-ethnic country. Anatomically, if SEF presents, it transverses the Sphenoid emissary vein. Thus, the variation is of clinical importance during trigeminal rhizotomy procedures in a diverse population like South Africa, which has reported a prevalence of 6-8% cases of trigeminal neuralgia per annum. Hence, the study aims to investigate the prevalence and variation of SEF concerning laterality, sex, and age in the South African population.

## Materials and Methods

### Study design and population

This is a retrospective bilateral observational analysis of 137 dry skulls, age  $\geq 13$  years (89 males & 48 females). The starting age was considered because the venous sinuses of the skull demonstrate their most significant growth between the ages of 0 to 7 years and typically reach adult size around 5 to 10 years of age (Larson *et al.*, 2020). This implies that the venous foramina

are typically fully developed by these ages. The diseases affecting the dural venous sinuses were also found to affect women in their reproductive ages (age  $\geq$  13 years) (Coutinho *et al.*, 2009). The skulls were obtained from the Discipline of Clinical Anatomy, School of Laboratory Medicine and Medical Science, College of Health Sciences at the University of KwaZulu Natal in the Westville and Medical school campuses and the Durban University of Technology, Department of Medical Sciences. The demographics (age, sex, and population) of the skulls were obtained from the cadaver records book, but the patients' identities were anonymised.

The age categories were classified according to Biwasaka *et al.*, 2019: <29, 30-39, 40-49, 50-59, 60-69, 70-79, 80-89, and >89 years. Regarding population, due to the scarcity of the Indian population skulls, only two of the South African population groups were included in the study-Black South Africans (82; 60.0%) and White South Africans (55; 40.0%). (Note: In the distribution of the South African population, Black South Africans make up about 79.8% and White South Africans make up about 8,7%) (Khalfani and Zuberi, 2001; L'Abbé *et al.*, 2011; Aladeyelu *et al.*, 2024).

### **Inclusion and Exclusion criteria**

Bones broken due to osteoporosis, bones with skeletal asymmetries or trauma, congenital disorders, and a history of surgery were excluded from the study. Due to the paucity of population diversity, only the Black and White SA population groups were considered for this study.

### **Approval**

The ethical clearance for this study was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu Natal (**BREC/00005683/2023**).

### **Study procedure**

The middle cranial fossa of each skull was observed for the presence and absence of the SEF. The patency of the SEF was confirmed by inserting a 1mm bristle through each probable foramen, and only patent foramina were used for this study following the procedure of Jadhav *et al.* (2016). A bristle with a diameter of 1 mm was used because most studies found the diameter of the SEF to range from 1 to 2 mm (Chaisuksunt *et al.*, 2012). The incidence of unilaterality and bilaterality of the SEF was observed and recorded. The principal investigator inserted a 1 mm bristle three times, and the intra-observer error was determined if the bristle entered intracranially and came out extracranially. A second observer repeated the observations from 10% of the skulls three times to determine the inter-observer error.

### **Statistical Analysis**

Descriptive statistics were used to summarise the data, while frequencies and percentages were also used for categorical data. Chi-square tests were used to identify demographic characteristics like age, sex and population associated with the SEF. Non-parametric tests such as Mann Whitney (2 variables) and Kruskal Wallis (more than 2 variables) were used to find the association between the prevalence of the SEF compared to population (Black SA and White SA), age and sex (male and female). SPSS version 28 software was used to analyse the data, and the significant level was set at  $p < 0.05$ .

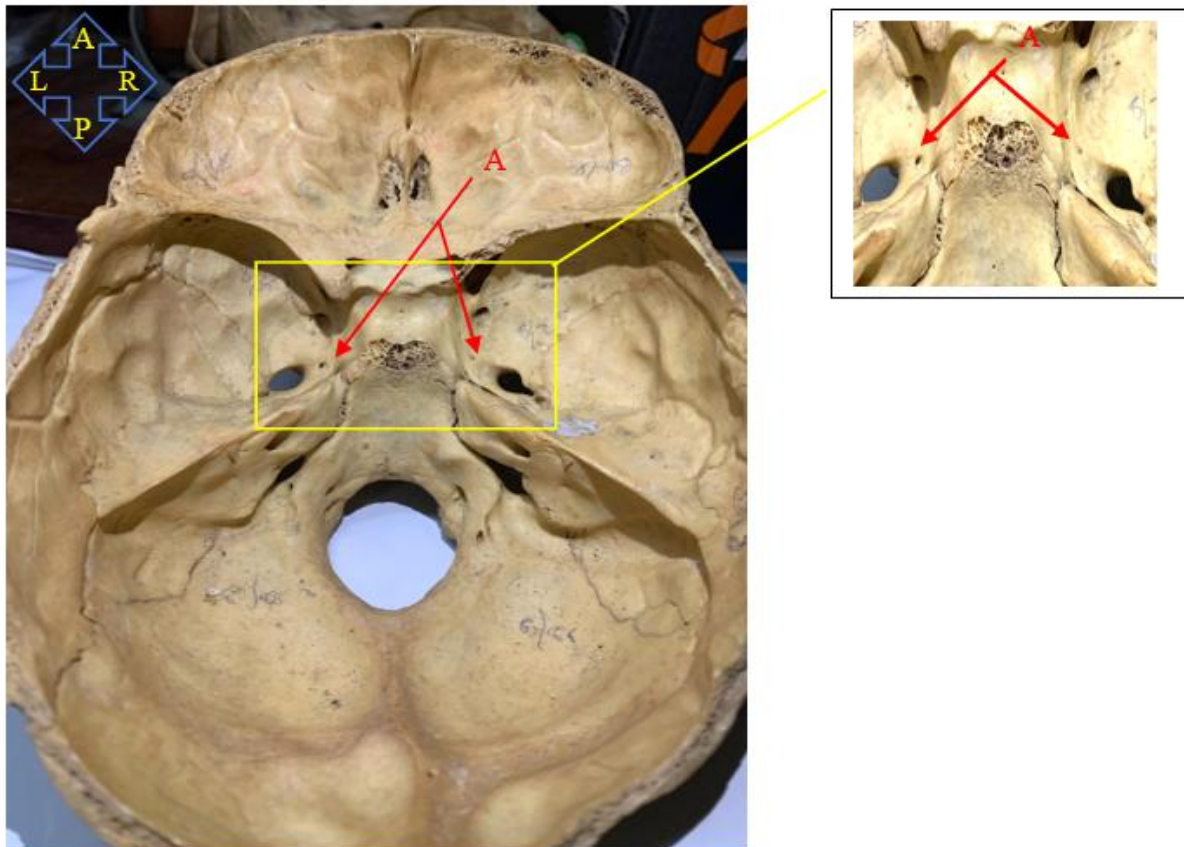
### **Results**

Out of 137 analysed skulls, the SEF was present in 48 (35.8%) skulls [Table 1]. Out of 82 Black SA population, the SEF was found present in 22 (26.8%), and White (55) accounted for 27 (49.1%) of the SEF. Regarding sex, 28 SEF were found to be present in 89 male skulls examined, which accounted for 31.5%, and out of 48 female skulls that were examined, the SEF was found in 21 (43.8%) skulls [Table 1].

**Table 1. Distribution of the sphenoid emissary foramen (SEF) according to population, sex and age**

	Absent n (%)	Present n (%)	p-value
Population			0.008
Black (82)	60 (73.2%)	22 (26.8%)	
White (55)	28 (50.9%)	27 (49.1%)	
Total (135)	87 (64.2%)	48 (35.8%)	
Sex			0.15
Male (89)	61 (68.5%)	28 (31.5%)	
Female (48)	27 (56.3%)	21 (43.8%)	
Age group			0.15
<29 (13)	5 (38.5%)	8 (61.5%)	
30-39 (18)	15 (83.3%)	3 (16.7%)	
40-49 (20)	14 (70.0%)	6 (30.0%)	
50-59 (23)	17 (73.9%)	6 (26.1%)	
60-69 (18)	14 (77.8%)	4 (22.2%)	
70-79 (20)	9 (45.0%)	11 (55.0%)	
80-89 (16)	8 (50.0%)	8 (50.0%)	
>89 (9)	6 (66.7%)	3 (33.3%)	

*n* = sample number, % = percentage, *p* < 0.05



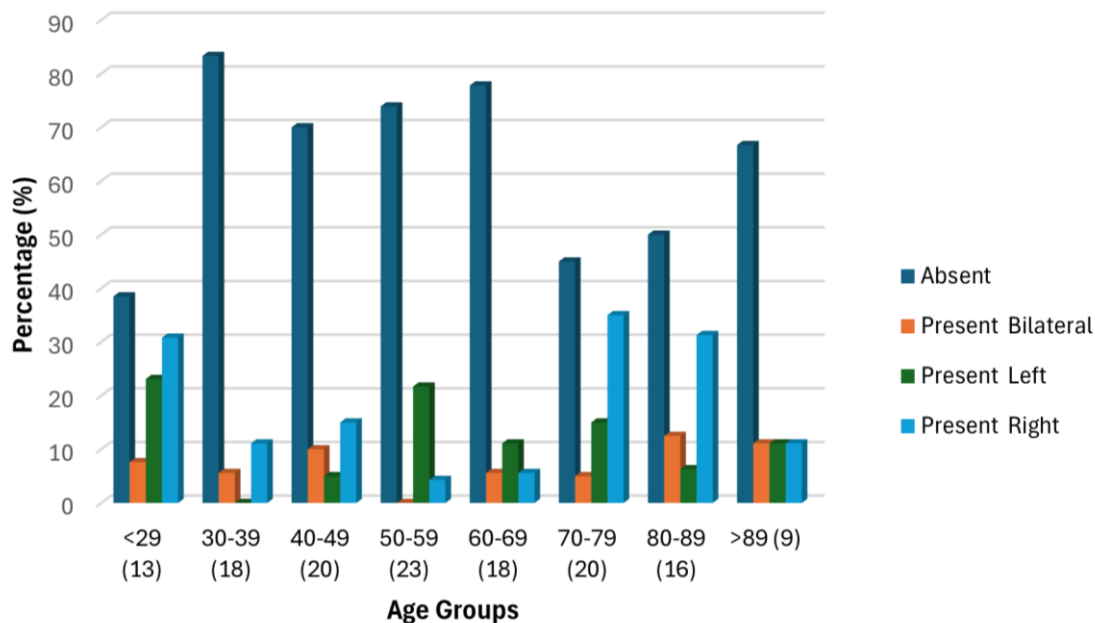
**Fig.1: Showing the skull's interior which presents the bilateral sphenoid emissary foramen (SEF). Key: red arrow (A) = SEF, Orientation of the skull; L - left, R- Right, A- Anterior, P- Posterior**

**Table 2. Distribution of the SEF according to population, sex, and age in comparison to laterality**

	Absent n (%)	Present n (%)			p-value
		Bilateral	Left	Right	
<b>Population</b>					
Black (82)	60 (73.2%)	4 (4.9%)	10 (12.2%)	8 (9.8%)	0.06
White (55)	28 (50.9%)	5 (9.4%)	14 (25.5%)	8 (14.5%)	
Total (137)	88 (64.2%)	9 (6.6%)	24 (17.5%)	16 (11.7%)	
<b>Sex</b>					
Male (89)	61 (68.5%)	4 (4.5%)	8 (9.0%)	16 (18.0%)	0.26
Female (48)	27 (56.3%)	5 (10.4%)	8 (16.7%)	8 (16.7%)	

Age group					
<29 (13)	5 (38.5%)	1 (7.6%)	3 (23.1%)	4 (30.8%)	0.02
30-39 (18)	15 (83.3%)	1 (5.6%)	0 (0.0%)	2 (11.1%)	
40-49 (20)	14 (70.0%)	2 (10.0%)	1 (5.0%)	3 (15.0%)	
50-59 (23)	17 (73.9%)	0 (0.0%)	5 (21.7%)	1 (4.3%)	
60-69 (18)	14 (77.8%)	1 (5.6%)	2 (11.1%)	1 (5.6%)	
70-79 (20)	9 (45.0%)	1 (5.0%)	3 (15.0%)	7 (35%)	
80-89 (16)	8 (50.0%)	2 (12.5%)	1 (6.3%)	5 (31.3%)	
>89 (9)	6 (66.7%)	1 (11.1%)	1 (11.1%)	1 (11.1%)	

*n* = sample number, % = percentage, *p* < 0.05



**Fig. 2: Distribution of the Sphenoid emissary foramen according to age**

In terms of population, no significant statistical correlation was found between the absence of the SEF and laterality. Among all the parameters considered for the study, only age was found to affect the absence, bilaterality, and unilaterality of the SEF [Table 2], [Fig. 2]. Overall, the absence

of the SEF is common across all the parameters; however, in sex, males had the highest prevalence of the SEF compared to females.

### Population

In terms of population, in the Black SA sample, 82 skulls were analysed, and 4 out of these skulls presented bilaterality of the foramen. Eight (8) skulls had the foramen on the right side only, and 10 had the foramen on the left. Furthermore, in this study, out of 55 skulls present in the White SA population, only five skulls presented with bilaterality of the SEF, while eight skulls had the foramen on the right side only, and 14 skulls had the foramen on the left side only, [Table 2]. A statistically significant association was obtained between the presence and absence of the SEF when compared to population,  $p = 0.008$ , [Table 1]. However, no significant association was found between the bilaterality, unilaterality, and absence of the SEF compared to the population [Table 2].

### Laterality

Regarding laterality, the SEF was found bilaterally in 9 (6.6%) out of 137 analysed skulls. The foramen was found unilaterally in some individuals, where 16 individuals presented with the SEF on the left and 24 skulls had the SEF on the right side only [Table 2]. There was no significant association between the bilaterality and unilaterality of the SEF when compared to the absence of the SEF.

### Sex

The incidence of the SEF was high in males compared to females. In addition, the incidence of unilaterality was high in males, especially on the right side, compared to females, with females presenting with equal amounts of SEF on the left and right sides. No significant association was found between bilaterality, unilaterality, and the absence of SEF about sex.

### Age

In terms of laterality compared to age, the prevalence of the SEF was higher on the right side than on the left. The 70-79 age group had the highest prevalence (35%) on the right side compared to all age groups, with the 50-59 age group (4.3%) having the least frequency recorded. Furthermore, on the left side, the 50-59 age group (21.7%) had the highest SEF recorded, while the 30-39 age group had 0.0% recorded for SEF presence. Bilaterality of the SEF was high in the 80-89 years age group (12.5%), and there was no SEF recorded for the 50-59 years age group (0.0%). These results showed that unilaterality of the SEF was more common than bilaterality. A statistically significant association ( $p = 0.02$ ) indicated a strong statistical association between the absence and presence (laterality) of the SEF when compared to age [Table 1 & 2], [Fig. 2].

### Discussion

The sphenoid emissary foramen (SEF) is an inconsistent foramen that is believed to be a variation of cranial venous outlets that only occurs in human beings (Kale *et al.*, 2009, Wood-Jones, 1931). This foramen has been thought to be caused by different pathological processes (Lanzieri *et al.*, 1988). These processes include invasion by nasopharyngeal melanoma, angiofibroma and neurofibromatosis (Lanzieri *et al.*, 1988). However, Kale *et al.* (2009) their study found a ratio high enough to represent a specific type of disorder but rather a normal variation. These findings were supported by recent literature that the presence of this foramen does not indicate any pathological process but rather a normal variation (Berge and Bergman, 2001, Ginsberg *et al.*, 1994).

### Laterality

The variability in the presence and absence of the SEF has been reported in earlier literature (Cochinski *et al.*, 2022b). In the present study, unilaterality of the foramen was found to be more common than bilaterality. These results agree with Bayrak *et al.* (2018), who found unilaterality more common than bilaterality. The high incidence of SEF was recorded on the right side compared to the left side by most literature, including the current study (Leonel *et al.*, 2020, Bayrak *et al.*, 2018, Jadhav *et al.*, 2016, Gupta *et al.*, 2005, Reymond *et al.*, 2005, Boyd, 1930). These results could mean most patients would find the inconsistent foramina on the right side. It is also important to emphasise that Gupta *et al.* (2005) found the foramen dominant on the right side only, as they did not observe any SEF on the left side in their study. Most previous reports, including the present study, are summarised in Table 3.

**Table 3. Reports on the prevalence of the sphenoid emissary foramen (SEF) from different studies**

Authors	Specimen examined	Total distribution	Bilateral	Unilateral	
				Right	Left
Boyd (1930)	1500 skulls	26.5%	14.7%	10.6%	11.2%
Gupta <i>et al.</i> , 2005	35 skulls	42.83%	22.85%	20%	-
Reymond <i>et al.</i> , 2005	100 skulls	17%	5%	7%	5%
Kale <i>et al.</i> , 2009	347 skulls	45%	25.1%	9.5%	10.4%
Lazarus <i>et al.</i> , 2015	100 skulls	5%	-	-	-
Jadhav <i>et al.</i> , 2016	250 skulls	28.8%	11.2%	10%	7.6%
Bayrak <i>et al.</i> , 2018	317 cone-beam CT scans	28%	6.9%	53.7%	46.3%
Natsis <i>et al.</i> , 2018	195 skulls	40%	21.5%	7%	11%
Leonel <i>et al.</i> , 2020	1000 CT images	46.8%	25.4%	11.8%	9.6%
	170 skulls	45.25%	18.8%	11.7%	14.7%
*Present study	137 skulls	35.8%	6.6%	17.5%	11.7%

### Sex

Based on previous literature about the prevalence of the SEF about sex, this is the first study to describe the prevalence of the SEF according to sex. In this study, males presented with a high incidence of unilaterality for the foramen compared to females, where 16 males had the foramen on the right side only, and eight males had the foramen on the left side. Only four males were found to possess bilaterality of the SEF. Furthermore, the incidence of the SEF in females was found to be much lower. This could mean that in most females, the sphenoid emissary veins will course with the mandibular division of the trigeminal nerve in the foramen ovale, making the



trigeminal rhizotomy procedure and various microsurgical and microvascular approaches at the base of the skull more complicated in females compared to males (Rossi *et al.*, 2010, Sindou *et al.*, 1987).

### Population

The prevalence of the SEF was found to be higher on the left side compared to the right side in both population groups. These results disagree with previous investigations, which found the SEF to be more prevalent on the right side (Leonel *et al.*, 2020, Bayrak *et al.*, 2018, Jadhav *et al.*, 2016, Gupta *et al.*, 2005, Reymond *et al.*, 2005, Boyd, 1930). SEF is a developmental variation; the differences between the current and the previous studies may be due to embryological and hereditary factors and geographical location.

Overall, in the SA population, there is a high incidence of SEF (35.6%) when compared to studies by Reymond *et al.* (2005) and Lazarus *et al.* (2015) which was also done in the SA population. The study by Lazarus *et al.* (2015) the SEF (Foramen Vesalius) was 5% of the SA population. However, the current study found the incidence to be 35.6%. This difference could bring a new insight into the occurrence of this foramen, which could be evolutionary as it shows that the incidence of this foramen increased over time.

Other factors contributing to these differences could be the sample size used in these studies, the site where bones were collected, and the methodologies used. This could also mean that the SA population is becoming less susceptible to intracranial bleeding during the treatment of the trigeminal neuroglia. This speculation is because it will become easier for surgeons to inject the mandibular nerve without injuring the adjacent vessels.

### Age

Age has been a contributing factor in the diseases affecting the trigeminal nerve (trigeminal neuroglia) that travels with the emissary vein (Mistry *et al.*, 2021). Thus, this study is the first to describe the prevalence of the SEF according to age. A very high incidence was noted in the occurrence of SEF in <29 years (61.5%), 70-79 years (55.0%), and 80-89 years (50.0%) age groups. A fluctuating trend was noted in the occurrence of the SEF, where the prevalence was very high in the <29 years age group and decreased from 30-39 years to 60-69 years age group; it then increased again during age advancement and decreased in the >89 years age group.

Notably, the 30-39 age group were the least recorded, with the left side having 0.0% SEF recorded. This incident of the SEF could mean that the sphenoid emissary veins in the 30-39 years to 60-69 years age groups will be travelling with the mandibular division of the trigeminal nerve in the foramen ovale (Leonel *et al.*, 2020, Chaisuksunt *et al.*, 2012). Furthermore, these age groups are likely to be admitted for the treatment of cranial base diseases, as it is suggested that they affect women in their reproductive ages (Coutinho *et al.*, 2009). Hence, this study is of great clinical importance in identifying suitable treatment for these age groups (30-39 years to 60-69 years).

The prevalence of trigeminal neuralgia is very high in South Africa compared to other countries (Chetty *et al.*, 2012). This may be due to the diverse population and SEF variations. The SEF showed variations in presence and absence, with a high incidence of unilaterality across age, population, and sex. Clinicians working with the South African population for trigeminal rhizotomy procedures should pay attention to the Black SA population, as the current study showed the absence of SEF, which determines the pathways for sphenoid emissary veins. The sphenoid emissary veins are likely to be punctured during the trigeminal rhizotomy procedure while travelling via the foramen ovale, along with trigeminal nerves in the absence of SEF.

Most South African population presented with unilaterality of the SEF (R: 11.7%; L: 17.5%). The SA black population have less SEF compared to White population. Notably, SEF was high in <29 years of age, meaning the older population may contribute to a higher prevalence of

trigeminal neuralgia due to the absence of SEF. Future research will investigate the prevalence of SEF over time and correspond it to the incidence of trigeminal neuralgia. More so, finding new ways to perform the trigeminal rhizotomy procedure in patients without the sphenoid emissary foramen may be explored to minimize the risk of sphenoid emissary vein puncture.

### Conclusion

The prevalence of the sphenoid emissary foramen is higher in the SA population than in previous literature, particularly in the White SA population. Notably, SEF was found to be more prevalent on the left side in both population groups studied, with males having the highest SEF recorded on the right side. Age was found to be statistically associated with the prevalence of the SEF. Knowledge of the SEF variations is important during trigeminal rhizotomy procedures to avoid damage to sphenoid emissary veins, leading to neurosurgical complications.

### Limitations and Recommendations

A small sample size and little population diversity limited this study. Future studies can be done on CT images and bones to increase population diversity and avoid bias. Future studies may also focus on finding new surgical methods to perform trigeminal rhizotomy in patients without the SEF.

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### Author contribution

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T and CO designed the experiments; T performed experiments and collected data; T, CO, OS, SK, and SO discussed the results and strategy; CO Supervised, directed and managed the study; CO, OS, SK, and SO assisted in structuring and writing of the manuscript; T, CO, OS, SO and SK Final approved of the version to be published.

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