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Summary

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Letter to the Editor

Inácio de Barros Melo Neto

When you read this letter, we will be celebrating the beginning of the Faculdade de Medicina de Olinda (FMO) internationalization Project - FMO Global. One of the axes is publishing our journal in a bilingual format to ensure that this letter can be read in Portuguese and English. This new format will increase the scope and quality of our journal by reaching other places and people. Also, the project will expand the dialogue between FMO teachers and students with other medical schools worldwide.

Along with the indexing and recognition process by the Qualis of the Coordenação de Aperfeiçoamento de Pessoal e Nível Superior (CAPES), the Annals of FMO Journal inaugurated its new layout this year and renewed its editorial board. In the articles presented in this issue, we can observe the solid integration of authors involving other educational institutions in Pernambuco and neighboring states. With a robust selection of articles, the journal is becoming a vehicle for publishing in Medicine for the internal community and other institutions, demonstrating its credibility.

However, our goal is to exchange with other people, seeking the universalization of knowledge. This goal is challenging, and our faculty and students have demonstrated their interest in providing answers to local health problems, but with global training based on contemporary assumptions. In this context, we will provide our community access to a platform that presents more than 25 languages and will be used to ensure linguistic training, initially focusing on English. By the end of 2023, we will complete the linguistic diagnosis, and the community will be developing their studies with in-person and virtual support.

In addition, we have structured the FMO Global Office, which initially aims to structure our language policy. In the medium term, the office will be the enucleator of multicultural integrative events in Medicine, our internationalized disciplines, and the structuring of international exchanges. Besides the physical structure with an area for web conferences, the space is equipped with a classroom headed by a master teacher qualified in language teaching. We also welcomed Dr. Dráuzio Varela, one of the greatest Brazilian authorities in Medicine, to the Doctor's Day celebrations. He gave the lecture "Perspectives for Medicine in the Face of a Global Village" to our teachers and students.

The Folha University Ranking (RUF), which annually evaluates higher education in Brazil, classifies universities, and establishes course rankings, was recently published. This evaluation began in 2012 and is conducted by Jornal Folha de São Paulo. In 2023, FMO had the best quality of education compared with other private higher education institutions in Pernambuco, demonstrating that our brand is our commitment to quality. Our journal is the result of this commitment.

Alsoin this semester, the Ministry of Education, through the Secretariat for Supervision and Regulation of Higher Education, determined the inclusion of

FMO in the list of higher education institutions that offer Medicine courses through the Educational Commission for Foreign Medical Graduates, which will guarantee the recognition of our diplomas in English-speaking countries. Last, I express my gratitude to the editorial board of the Annals of FMO Journal for their work so that we can reach even greater levels in disseminating scientific knowledge.

Anais da Faculdade de Medicina de Olinda
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Characterization of the quality of life of institutionalized older adults

Caracterização da qualidade de vida de idosos institucionalizados

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Abstract

Objective: To assess the quality of life of institutionalized older adults. **Methods:** A descriptive cross-sectional study was conducted with 20 older adults using a sociodemographic questionnaire for sample characterization and the WHOQOL-bref to assess the quality of life. Descriptive statistical analyses were performed. **Results:** Most participants were males (62.5%) aged between 70 and 80 years (43.7%), with income of up to one minimum wage (87.5%), no partner (87.5%), with children (75.0%), and some level of education (68.7%). The study revealed that the quality of life among participants was moderate across the physical, psychological, social relationships, and environment domains of the WHOQOL-bref. A statistically significant difference was observed in the environment and physical domains when dividing the sample according to age and presence of hypertension. **Conclusion:** In older adults, the higher the age, the lower the quality of life. Hypertension impacted the physical domain and quality of life. Developing and implementing strategies and interventions are important to improve the quality of life of institutionalized older adults.

Keywords: Aging; Older adults; Long-term care facilities; Quality of life.

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Resumo

Objetivo: Avaliar a qualidade de vida de idosos institucionalizados. **Métodos:** Estudo transversal descritivo, realizado com 20 idosos, a partir de um questionário de caracterização sociodemográfica e do instrumento WHOQOL-bref para avaliação da qualidade de vida. Os dados foram submetidos à análise estatística descritiva. **Resultados:** A maioria dos participantes do estudo referiram ser do sexo masculino (62,5%); com idade entre 70 e 80 anos (43,7%); com renda de até um salário mínimo (87,5%); sem companheiro(a) (87,5%); com filhos (75,0%); e com escolaridade (68,7%). O estudo evidenciou que a qualidade de vida dos participantes como moderada, segundo escores gerais do questionário WHOQOL-bref, nos domínios Físico, Psicológico, Relações Sociais e Meio Ambiente. Foi possível observar diferença estatisticamente significativa na variável Idade, em relação ao domínio Meio Ambiente e na variável Hipertensão Arterial Sistêmica referente ao domínio Físico. **Conclusão:** O estudo demonstrou que quanto maior a idade dos idosos institucionalizados, menor a qualidade de vida, assim como a presença de Doenças Crônicas Não Transmissíveis causa impacto no domínio físico e, consequentemente, na redução da qualidade de vida. Sendo importante o desenvolvimento e implementação de estratégias e ações para melhorar a qualidade de vida dos longevos institucionalizados.

Palavras-chaves: Envelhecimento; Idoso; Instituição de longa permanência para idosos; Qualidade de vida.

INTRODUCTION

In Brazil, the reduction in mortality and birth rates influenced the increase in the older adult population and the decrease in the number of children and young individuals. The population above 60 years represented 26.1 million in 2013, and it is estimated to increase to approximately 32 million by 2025[1]. In this context, demographic shifts lead to population aging, which is characterized by morphological, physiological, biochemical, psychological, social, and environmental changes that progressively impairs the adaptation of the individual to the environment[2,3].

The decline in functional capacity and inactivity of older adults are associated with aging and involve changes that impact the quality of life[3]. These alterations are common in senescence and result in progressive loss of physical vigor that may interfere with basic activities of daily living and instrumental activities of daily living. Both are needed to maintain an independent and autonomous life[4].

Despite the reduction in physical and cognitive capacities and the onset of comorbidities, it is crucial to maintain autonomy and independence among this population[5]. In this context, quality of life (QoL) does not solely refer to physical and psychological well-being and health. It is a broad concept fragmented into several aspects that predispose the perception, satisfaction with life and daily events, socio-cultural values, autonomy, and independence; thus, generating expectations and goals for each individual[6].

Functional limitations generate an increasing demand for health services by this population, accompanied by transformations in family, social, and economic dynamics. The growing trend in seeking long-term care facilities (LTCF) is also notable[4]. Although public policies in Brazil

prioritize family care for this population, LTCF becomes an important choice because it ensures the care of older adults and their families[7].

Placing older adults in a LTCF may result in a decline in physical capacity, function, and interpersonal relationships. The combination of these situations may also compromise the autonomy, independence, and QoL of older adults. Additionally, these individuals experience changes in societal roles and life spaces, increasing the risk of anxiety and depression[8].

QoL can be assessed in older adults using the World Health Organization Quality of Life (WHOQOL-bref) questionnaire, developed by the World Health Organization, as a tool to support the management and evaluation of public policies. This instrument was translated and validated for use in Brazil by a group of researchers of the Federal University of Rio Grande do Sul, which assessed the QoL of individuals across different contexts[9,10].

Therefore, the objective of this study was to assess the QoL of institutionalized older adults using the WHOQOL-bref and correlate the findings with sociodemographic variables.

METHODS

A descriptive cross-sectional study was conducted from April 2022 to April 2023 at a LTCF in Abreu e Lima, Pernambuco (Brazil). The study was a census involving 20 older adult residents in the LTCF; four did not participate: one declined, and three presented impaired cognition. Thus, the final sample was composed of 16 participants.

Inclusion criteria consisted of participants aged 60 or older, with preserved communication capacity, who resided in the studied city and the LTCF for more than three months and consented to participate in the study. Those diagnosed with cognitive diseases were excluded; refusal was considered when the individual did not consent to participate in the research.

Data were collected through interviews that lasted approximately 30 minutes. During these interviews, researchers individually read the questions in a room at the LTCF. A sociodemographic questionnaire was used to characterize social (age, gender, marital status, skin color, income, and education), lifestyle habits (smoking, alcohol, and other drug use), family network (number of children), and clinical data (pathologies and comorbidities).

Variables were stratified by age (60 to 70 years, 70 to 80 years, and older than 80 years), gender (male or female), marital status (with or without a partner), skin color (white and black or brown), income (up to one minimum wage or more than one minimum wage), education (with or without education), and non-communicable diseases (NCDs) (hypertension, diabetes mellitus, chronic obstructive pulmonary disease, or other diseases).

QoL was assessed using the WHOQOL-bref[11], which comprises 26 questions distributed into four domains: physical, psychological, social relationships, and environment. The scores of each domain range from 0 to 100 points. The mean score for each domain indicates the level of

satisfaction of individuals in each aspect of their lives. Since the final scale score ranges from 0 to 100, the higher the score, the higher the perceived satisfaction in the domain: 0 to 20 (very dissatisfied), 21 to 40 (dissatisfied), 41 to 60 (neither satisfied nor dissatisfied), 61 to 80 (satisfied), and 81 to 100 (very satisfied)[11].

Statistical analysis was performed using the Statistical Package for the Social Sciences, version 25.0 (SPSS, IBM Corp, USA) and Excel 365. Continuous variables were represented by central tendency and dispersion measures. The Mann-Whitney test was used to compare quantitative variables between two groups, whereas Kruskal-Wallis with Dunn's post-hoc compared more than two groups. All tests were conducted with a 95% confidence level.

The study was approved by the research ethics committee of the Faculdade de Medicina de Olinda (CAAE: 62254222.4.0000.8033) following Resolution 466/2012 of the National Health Council. All participants signed the informed consent form.

RESULTS

Most participants were male (62.5%), aged between 70 and 80 years (43.7%), and had an income of up to one minimum wage (87.5%), a partner (87.5%), children (75.0%), and some level of education (68.7%).

Table 1. Sociodemographic characteristics and family network of institutionalized older adults in Abreu e Lima - Pernambuco, 2022 to 2023. (n=16)

Variables	n	%
Age (years)		
60 - 70	5	31.3
70 - 80	7	43.7
≥ 80	4	25.0
Gender		
Male	10	62.5
Female	6	37.5
Skin Color		
White	4	25.0
Black or Brown	12	75.0
Education		
Without education	5	31.3
With education	11	68.7
Marital Status		
Without partner	14	87.5
With partner	2	12.5
Religion		
Catholic	7	43.8
Evangelical	7	43.8
Others	2	12.4
Children		
Without children	4	25.0
With children	12	75.0
Income		
Up to one minimum wage	14	87.5
More than one minimum wage	2	12.5

Table 2 presents the clinical characteristics and lifestyle habits of participants, indicating that most had hypertension (56.3%). All older adults were non-smokers, and none consumed alcoholic beverages during the study period. Most individuals had been at the LTCF for 3 to 12 months (62.5%).

Table 2. Clinical characteristics and lifestyle habits of institutionalized older adults in Abreu e Lima - Pernambuco, 2022 to 2023. (n=16)

Variables	n	%
Alcohol		
Yes	0	0.0
No	16	100.0
Smoking		
Yes	6	37.5
No	10	62.5
Illicit Drugs		
Yes	0	0.0
No	16	100.0
Hypertension		
Yes	9	56.3
No	7	43.8
DM		
Yes	1	6.3
No	15	93.8
COPD		
Yes	1	6.3
No	15	93.8
Other conditions		
Yes	4	25.0
No	12	75.0
Length of stay in the LTCF		
3 to 12 months	10	62.5
12 to 24 months	2	12.5
More than 36 months	4	25.0

DM: Diabetes mellitus; COPD: Chronic obstructive pulmonary disease; LTCF: Long-term care facility

Table 3 presents the QoL of older adults according to the WHOQOL-bref. A statistically significant difference was observed in the environment and physical domains between age and hypertension groups, respectively.

Table 3. Associations between WHOQOL-bref domain scores and sociodemographic variables, family network, and clinical aspects of older adults in Abreu e Lima - Pernambuco, 2022 to 2023. (n=16)

Variables	WHOQOL-Bref			
	Physical Mean ± SD	**Psychological Mean ± SD**	**Social Relationships Mean ± SD**	**Environment Mean ± SD**
Age (years)				
60 - 70	59.3 ± 23.8	68.3 ± 28.7	63.3 ± 26.7	60.0 ± 12.2
70 - 80	66.8 ± 28.8	54.8 ± 13.5	70.2 ± 15.1	66.1 ± 12.4
≥ 80	48.2 ± 22.3	33.3 ± 21.8	43.8 ± 12.5	32.0 ± 17.0
*p-value**	*0.581*	*0.121*	*0.129*	***0.040***
Gender				
Male	61.1 ± 26.5	46.7 ± 20.2	58.3 ± 20.0	52.5 ± 22.1
Female	57.7 ± 25.5	65.3 ± 26.7	66.7 ± 23.0	60.9 ± 12.6
*p-value***	*0.828*	*0.191*	*0.583*	*0.383*
Education				
Without education	59.3 ± 32.0	56.7 ± 27.7	71.7 ± 19.2	52.5 ± 18.5
With education	60.1 ± 23.5	52.3 ± 23.2	56.8 ± 20.7	57.1 ± 20.1
*p-value***	*1.000*	*0.864*	*0.229*	*0.609*
Children				
Without children	49.1 ± 34.9	52.1 ± 39.2	62.5 ± 32.3	49.2 ± 28.5
With children	63.4 ± 22.1	54.2 ± 18.9	61.1 ± 17.5	57.8 ± 16.0
*p-value***	*0.467*	*0.951*	*0.951*	*0.903*
Hypertension				
Yes	48.0 ± 24.0	45.8 ± 24.8	56.5 ± 18.5	49.7 ± 19.0
No	75.0 ± 18.9	63.7 ± 19.8	67.9 ± 23.3	63.4 ± 17.5
*p-value***	***0.034***	*0.099*	*0.284*	*0.137*
Length of stay in the LTCF				
Up to 12 months	54.3 ± 21.7	52.9 ± 20.2	57.5 ± 20.2	54.1 ± 17.8
More than 12 months	69.0 ± 30.2	54.9 ± 31.1	68.1 ± 22.0	58.3 ± 22.6
*p-value***	*0.329*	*0.785*	*0.227*	*0.785*

*Kruskal-Wallis; **Mann-Whitney; LTCF: Long-term care facility.

DISCUSSION

In this study, the perceived QoL was assessed among institutionalized older adults in Abreu e Lima (Pernambuco, Brazil). Among sociodemographic characteristics, most were male (62.5%), differing from the profile of older adults living in LTCFs[8,14]. Generally, females are pre-

dominant in LTCF due to a longer life expectancy than males, widowhood situations, and the presence of NCDs[6,15].

Most individuals had no partners, corroborating studies that showed a higher occurrence of widowed older adults[20,21]. The interviewed participants had some level of education and an average institutionalization period of approximately one year. In this sense, the level of education did not interfere with QoL. Also, education is an important factor that mediates the participation of older adults in society. Thus, it is expected that the lower the level of education, the greater the difficulties faced by individuals in seeking the rights; thus, impacting the QoL[15,22].

Although most participants had children (75%), QoL was not significantly different compared to those without children. Another study also conducted in Pernambuco[4,5] supported these data, emphasizing that family plays an important role in the lives of human beings. Nevertheless, most family members do not return to visit the institutionalized older adults, entrusting their care to LTCF professionals[5]; therefore, evidencing a breakdown in the bond between family and older adults.

The results of this study revealed a moderate QoL related to the physical, psychological, social relationships, and environmental domains. This corroborates similar studies conducted in São Paulo and Porto Alegre[4,21].

The environmental domain assesses the satisfaction of individuals based on aspects related to safety and protection, financial resources, availability and quality of healthcare, opportunities to acquire new information and skills, participation in recreational and leisure activities, and physical environment, including pollution, noise, traffic, climate, and transportation[15,22]. When assessing the QoL of older adults, significant differences in the environment domain were observed between age groups. Also, according to the environmental domain, older adults aged > 80 years (25%) had a lower quality of life. These data indicate that octogenarians feel more discomfort with the physical structure and healthcare in the LTCF environment; the environmental domain is also related to the safety and integrity of the individual[14,20].

Older adults with hypertension (53.1%) exhibited a low quality of life according to the physical domain, demonstrating that NCDs directly interfere with QoL of this population[13]. Studies showed that older adults engaging in regular physical activity presented a high QoL, favoring autonomy and independence for maintaining activities of daily living in this population[12,16,17,18]. A similar study conducted in an LTCF in Portugal demonstrated that older adults had low QoL scores, especially in the physical domain[5].

Differences in the remaining domains were not significant, possibly due to the moderate QoL pattern and relevant differences in most analyzed aspects. Additionally, the small sample size contributed to these findings.

Importantly, the profile of the older adult population is an important marker of quality of life. The better the socioeconomic status, lifestyle, and clinical characteristics, the higher the satisfac-

tion with life and aging.

The National Health Policy for the Elderly determines that care practices for these individuals must be based on a global, interdisciplinary, and multidimensional approach. Therefore, these care practices, especially for institutionalized older adults, should consider the interaction between physical, psychosocial, and spiritual factors since the primary purpose of this public policy is to restore, maintain, and promote the autonomy and independence of these individuals[5, 19, 20].

CONCLUSION

The QoL of older adults in the LTCF was moderate, according to the scores in the physical, psychological, social relationships, and environmental domains of the WHOQOL-bref. Also, the older the institutionalized individuals, the lower the QoL, while the presence of NCDs impacted the physical domain, consequently reducing the QoL.

The study had a limitation regarding the number of participants, emphasizing the importance of conducting further studies correlating data with other LTCFs in the region. These studies should also assess the factors associated with institutionalization of the older adult, expanding the capacity for analysis and the influence of the determinants of QoL, independence, autonomy, and functionality of this population.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

FSRB: conceptualization, data curation, methodology, project administration, supervision, validation, visualization, writing of original draft, and review and editing. **MLMI**: investigation, resources, visualization, writing of the original draft, and review and editing. **GCQJ**: investigation and resources. **LDPSP**: investigation and resources. **PAAP**: investigation and resources. **VSB:** visualization, writing of the original draft, and review and editing. All authors approved the final version.

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Supratrochlear foramen: morphology and clinical-surgical implications

Forame supratroclear: morfologia e implicações clínico-cirúrgicas

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Abstract

The supratrochlear foramen is an anatomical variation of the humerus bone that connects the olecranon fossa with the coronoid fossa. Considering the scarce data about this variation in the Brazilian population, its morphological and morphometric aspects may vary depending on the ethnic group. **Objective**: To investigate the morphology and frequency of the supratrochlear foramen in Brazilian human bones and its association with laterality and describe its clinical-surgical repercussions. **Methods**: This cross-sectional and prospective study analyzed a convenience sampling of 51 human humeri bones from a collection belonging to a higher education institution. **Results**: A total of 21.9% of the humeri presented supratrochlear foramen, and the oval shape was the most predominant. Although it was more frequent on the left side, no significant association was observed between the presence of the supratrochlear foramen and laterality.

Keywords: Surgery; Orthopedic procedures; Humerus; Anatomy variation.

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Resumo

O forame supratroclear é uma variação anatômica do osso úmero que comunica a fossa do olecrano com a fossa coronoide. Considerando o escasso número de dados desta variação na população brasileira, haja vista que seus aspectos morfológicos e morfométricos podem variar dependendo do grupo étnico. **Objetivo**: investigar a morfologia e frequência do forame supratroclear em ossos humanos brasileiros e sua associação com a antimeria, bem como descrever suas repercussões clínico-cirúrgicas. **Métodos**: Trata-se de um estudo do tipo transversal, observacional e prospectivo, com amostragem do tipo não probabilístico por conveniência, o qual analisou 51 úmeros humanos de um acervo pertencente a uma instituição de ensino superior. **Resultados**: Foi observado que 21,9% dos úmeros apresentaram o forame supratroclear, sendo a forma oval a mais predominante. Apesar de ter sido mais frequente no lado esquerdo, não foi observada associação estatística significante entre a presença do forame supratroclear e a antimeria.

Palavras-chaves: Cirurgia; Procedimentos ortopédicos; Úmero; Variação anatômica.

INTRODUCTION

The coronoid fossae and olecranons in the distal epiphysis of the humeri are separated by a thin bone plate called supratrochlear septum, whose thickness is between 0.5 mm and 1 cm[1,2]. In some cases, especially after seven years of age, this region can be perforated and generate the supratrochlear foramen (STF)[3].

The factors leading to the emergence of this anatomical variation have not been defined yet; however, the mechanical stress during flexion and extension at a high range of motion and genetic factors, mainly related to T-box genes, may be involved. This is possible because genes from the TBX family control the synthesis of T-box proteins, which are crucial for the development of limbs and affect postnatal development. Also, the supratrochlear septum remains intact and covered by synovial membrane until seven years of age; thus, perforations may occur only after this period[4].

Knowledge of the anatomical aspects of the STF is important in the preoperative period and during procedures to correct supracondylar fractures (e.g., intramedullary nail fixation), which are common in the pediatric group[1,5]. STF is relevant in this mechanism since it narrows the medullary canal in the distal epiphysis of the humerus and may lead to misinterpretations of radiographic examinations due to its radiolucency, which can be confused with osteolytic or cystic lesions[6,7].

Septal foramens have been observed in most mammalian species, with a slightly high prevalence among platyrrhine and pongid primates. Darwin considered the presence of this foramen in humans as one of the evolutionary characteristics of primates, and it was a source of study for anthropologists[8].

In this context, and considering that this anatomical variation can be confused with an

osteolytic lesion on radiographic images[9], the present study aimed to (1) investigate the morphology and frequency of the STF in Brazilian human bones and its association with laterality and (2) describe the clinical-surgical repercussions of this structure.

METHODS

This cross-sectional and prospective study was conducted at the Department of Anatomy of the Federal University of Pernambuco (Brazil) in February 2023. A convenience sampling of sixty-six human humeri from the collection of cadaveric parts of the department (32 were from the right and 34 from the left side) was analyzed without distinction of biological sex, age, population, and height. Bones could not be identified as belonging to the same individual.

The human humerus bones with anatomical variations of the distal epiphysis were included in the study since bone integrity could interfere with the evaluation. Fifteen human humeri were excluded because they were not in good condition (e.g., fragmentation and severe wear), which could affect the evaluation of anatomical variations.

Therefore, the study was divided into three stages: (1) selection of human humerus bones among bones in the collection, (2) morphological analysis of the distal epiphysis of the bones, and (3) identification of the STF in the distal epiphyses of the bones.

After analysis, 51 human humerus bones were included to study the frequency and morphology of the STF. Data were analyzed using the Predictive Analytics Software (PASW® Statistics), version 17.0. A descriptive analysis was conducted, and results were presented as absolute and relative values. The Chi-square test was applied to verify the associations between variables. Significance was set at 5%, and a confidence interval of 95% and maximum variability of 0.5 were used.

RESULTS

Of the 51 human humeri included in the study, 47.1% (n = 24) were from the right and 52.9% (n = 27) from the left side. A total of 21.6% (n = 11) of bones presented STF, whereas 78.4% (n = 40) did not. Regarding laterality, of the 24 bones from the right side, 9.8% (n = 5) presented STF, whereas 37.3% (n = 19) did not present this anatomical variation. Of the 27 left humerus bones, 11.8% (n = 6) presented STF, whereas 51.2% (n = 21) did not present the anatomical variation (Figure 1).

Figure 1. Right and left humerus bones with and without anatomical variation (supratrochlear foramen). **A:** Right humeri without supratrochlear foramen; **B:** Left humeri without supratrochlear foramen; **C:** Right humeri with supratrochlear foramen; **D:** Left humeri with supratrochlear foramen.

Regarding the morphological analysis, an opening was observed in the distal epiphysis of the humerus connecting the olecranon fossa with the coronoid fossa. The shape of the STF varied between the right and left humeri. Three types of shapes were observed: oval, round, and triangular (Figures 2 and 3). The oval shape was observed in 45.4% (n = 5) of humerus bones, with 36.4% (n = 4) on the left and 9.1% (n = 1) on the right side. The incidence of the round shape was 36.4% (n = 4), with 18.2% (n = 2) on the left and 18.2% (n = 2) on the right side. The incidence of the triangular shape was 18.2% (n = 2) and was present only on the right side (Table 1).

Table 1. Incidence of different forms of STF (n = 11)

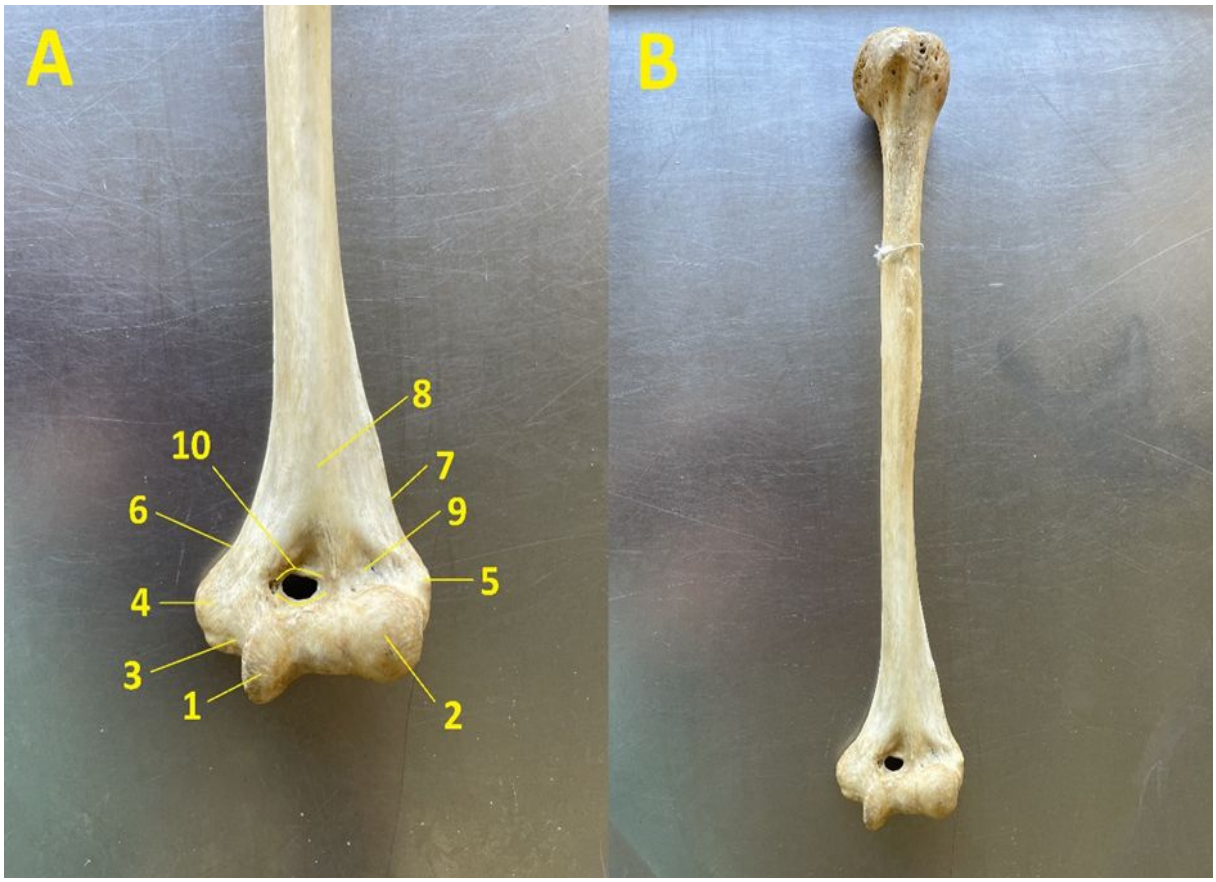
Shape	Right		Left		**Total**	
	N	%	N	%	N	%
Oval	1	9.1	4	36.4	5	45.4
Round	2	18.2	2	18.2	4	36.4
Triangular	2	18.2	0	0.00	2	18.2

STF: supratroclear foramen

Figure 2. Different shapes of the supratrochlear foramen

Anterior view. **A:** Triangular; **B:** Oval; **C:** Round

Figure 3. Supratrochlear foramen in the right humerus **A:** Distal epiphysis of the right humerus, anterior view; **B:** Right humerus, anterior view; **1:** Trochlea; **2:** Capitulum; **3:** Groove for ulnar nerve; **4:** Medial epicondyle; **5:** Lateral epicondyle; **6:** Medial supracondylar ridge; **7:** Lateral supracondylar ridge; **8:** Anteromedial face; **9.** Radial fossa; **10:** Supratrochlear foramen (in the center of the coronoid fossa).



A contingency table was constructed to assess the associations between laterality and the presence of STF. The Chi-square test was used to assess whether distributions were statistically different; assumptions were met, including the expected frequency of more than five in each cell of the contingency table. The Chi-square test value was 0.014, and the p-value was 0.904, demonstrating that differences regarding the presence of STF were not statistically significant between the right and left sides. Last, the Phi value approached zero, revealing that STF occurs independently of laterality (Table 2)

Table 2. Distribution of the supratrochlear foramen according to laterality (contingency table)

Anatomical variation	Laterality		Total
	Right	Left	
Without foramen			
Absolute frequency	19	21	40
Expected frequency	18.8	21.2	40.0
Total percentage	37.3%	41.2%	78.4%
Adjusted residuals	0.1	- 0.1	
With foramen			
Absolute frequency	5	6	
Expected frequency	5.2	5.8	11.0
Total percentage	9.8%	11.8%	21.6%
Adjusted residuals	- 0.1	0.1	
Total			
Absolute frequency	24	27	51
Expected frequency	24.0	27.0	51.0
Total percentage	47.1%	52.9%	100.0%

Chi-square test value = 0.014; p = 0.904;
Likelihood ratio = 0.015, and Phi = 0.017.

It is important to highlight that the statistical analysis of this study did not consider the biological sex, age, population, and height due to the absence of these data in the collection of cadaveric parts of the Department of Anatomy of the higher education institution.

DISCUSSION

The STF, also called intercondylar, olecranon, or epitrochlear foramen, is an anatomical variation located in the distal epiphysis of the humerus bone due to perforation and opening of the supratrochlear septum[8]. This anatomical variation is located above the humeral and intra-articular epiphyseal line in the olecranon fossa and below the reflex line of the synovial membrane[5].

The incidence of STF varies between 0.3% and 60% worldwide, with approximately 6.9% in the American population[1]. This anatomical variation is more common in black and female individuals and is present mostly in the left humerus. Nevertheless, bilaterality can also be observed, as demonstrated in a study conducted with 32 pairs of humeri from 32 individuals; 18.8% had STF in the left and right sides[6]. In a meta-analysis including 62 studies (n = 20,388 humeri), the overall prevalence of STF was 21.9% (95% confidence interval [CI]: 18.6% to 25.3%). STF was present in 26.6% (95% CI: 21.5% to 31.9%) of 6,866 left humeri and in 19.4% (95% CI: 15.3% to 23.8%) of 6,860 right humeri in 41 studies; analyses were statistically significant. Moreover, STF was present in 21.9% (95% CI: 13.5% to 31.8%) of the female sample and 12.1% (95% CI: 7.4% to 17.6%) of the male sample; this difference was also statistically significant[9]. This finding cor-

roborates with the present study, which found an incidence of 21.6%. However, no difference was observed regarding laterality, which could be explained by the sample size, the anthropological characteristics of the population, and the fact that bones were not from the same individual. In our study, associations with age, biological sex, population, and height were not performed.

This meta-analysis included only six studies from America (Brazil and the United States), whereas 28 were conducted in South Asia. STF is a common anatomical variation among the general population, although predisposition is higher in individuals from Africa[9]. These data reinforce the importance of the present study, given the scarce data on the Brazilian population and the existence of different prevalence rates according to ethnic groups.

During embryonic development, the supratrochlear septum is not perforated, but incomplete ossification of this structure during adolescence or early adulthood may lead to the formation of the STF[3]. Although its origin is not well clarified, two theories are present in the literature: (1) mechanical origin, which explains the perforation mechanism through movements of flexion and extension at high range of motion, weakness of triceps and biceps muscles, and laxity of the involved ligaments; and (2) genetic component, especially T-box genes, which are involved in the postnatal development of limbs[4,8,10].

Another important fact about STF is its association with other anatomical variations (e.g., supracondylar process and Struther's ligament), increasing the risk of neurovascular compression, affecting the median and radial nerves and the brachial artery, and leading to a clinical picture related to regions innervated and irrigated by these structures[8].

The supracondylar fractures represent approximately 17% of pediatric traumas, and retrograde intramedullary nailing is the basis of treatment. As STF is associated with a narrow medullary cavity, the antegrade route may be preferred. Thus, knowledge regarding its presence helps to decide the surgical approach[8,11]. The olecranon opening has also been reported to predispose low-energy fractures of the distal humerus[9].

We highlight the lack of epidemiological data about the individuals as a limitation of the study. Future studies should consider the inclusion of age, biological sex, population, and height and use the right and left humerus bones from the same individual so possible patterns of anatomical variation can be observed.

CONCLUSION

The present study analyzed the morphology and frequency of the STF in Brazilian human bones, its association with laterality, and its clinical-surgical implications. The data analyzed showed the presence of STF in 21.9% of the humeri studied, with the oval shape being the most predominant. Despite being more frequent on the left side, no significant associations were observed between the presence of STF and laterality.

Considering the clinical-surgical implications addressed, the study also provided a theoretical basis for assisting specialists (e.g., orthopedists and radiologists) in the preoperative period, during surgical procedures, or while interpreting images of the humerus. Therefore, in-depth knowledge about the topic is essential to improve the ability to perform differential diagnoses and provide appropriate treatments; thus, ensuring accurate and efficient decision-making and avoiding complications.

Last, we reinforce the lack of studies regarding the topic in the Brazilian population, given that the incidence of STF and morphological and morphometric aspects may vary according to population, ethnic group, and regions of the country. Future studies including age, biological sex, population, and height are needed to improve the understanding of anatomy and its variations in the Brazilian population.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

TJMBSV: writing of the original draft and review and editing; **IFGG**: writing of the original draft and review and editing; **ACCS**: writing (review and editing); **LLD**: writing (review and editing); **CBAM**: writing (review and editing); **RCFC**: resources, supervision, and writing (review and editing); **PFAP**: conceptualization, data curation, investigation, methodology, project administration, resources, supervision, writing of the original draft, and review and editing. All authors approved the final version.

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Characterization of primary health care professionals in a Pernambuco municipality during the COVID-19 pandemic

Caracterização dos profissionais da atenção primária à saúde de um município pernambucano durante a pandemia da COVID-19

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Abstract

Objective: To characterize the profile of primary healthcare professionals in a municipality of Pernambuco state during the coronavírus disease (COVID-19) pandemic. **Methods**: This cross-sectional study included 33 healthcare professionals from the family health strategies teams in Olinda, Pernambuco. Data were collected using a Google form after participants accepted and signed the informed consent form. Variables were expressed as absolute frequencies. **Results**: Most participants were community health agents, nurses, physicians, and nursing and pharmacy technicians. Of these, 84.8% were female, aged between 31 and 50, and possessed either technical or higher education. Half of the participants tested positive for COVID-19; 60% were diagnosed by PCR. Although all participants used personal protective equipment (PPE), only 14.3% reported no absence from work. **Conclusion**: Primary healthcare professionals were susceptible to COVID-19 despite not being on the front line. PPE was insufficient to prevent the disease, leading to absence from work.

Keywords: COVID-19; Health personnel; Primary health care.

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Resumo

Objetivo: Caracterizar o perfil dos profissionais da Atenção Primária à Saúde de um município pernambucano durante a pandemia da COVID-19. **Métodos**: Trata-se de uma pesquisa quantitativa, observacional do tipo transversal. Os participantes voluntários foram 33 profissionais de saúde das equipes de Estratégias de Saúde da Família do município de Olinda, Pernambuco. Os dados foram coletados por meio do Google formulário após o aceite e assinatura do Termo de Consentimento Livre e Esclarecido (TCLE) de todos os participantes. As variáveis foram expressas como frequência absoluta. **Resultados**: A maioria dos profissionais eram os Agentes Comunitários de Saúde (ACS), enfermeiros e os técnicos de enfermagem e farmácia. Destes profissionais, 84,8% eram do sexo feminino, idade variando entre 31 e 50 anos, e o grau de escolaridade reflete os profissionais que eram técnicos ou com formação superior. Houve uma prevalência de 50% testarem positivo para COVID-19, destes 60% diagnosticados pelo PCR. Todos os entrevistados relataram utilizar equipamento de proteção individual (EPI) e apenas 14,3% não relataram afastamento do trabalho. **Conclusão**: Percebe-se que os profissionais da atenção primária à saúde também estiveram susceptíveis ao coronavírus, mesmo não estando na linha de frente do combate à pandemia. O uso de EPIs pela totalidade dos entrevistados não foi suficiente para a prevenção da doença, refletindo no afastamento das atividades laborais destes profissionais.

Palavras-chave: COVID-19; Profissionais de saúde; Atenção primária à saúde.

INTRODUCTION

The World Health Organization (WHO) has been on alert since the first cases of the coronavirus disease (COVID-19) were identified by the end of 2019. This disease spread progressively worldwide, reaching more than 110 countries and creating great concern due to its high rate of transmissibility and severity in some cases. As a result, the WHO classified the disease as a pandemic on March 11, 2020. In Brazil, the first case of COVID-19 was diagnosed on February 26, 2020, and one year later, the country had more than nine million cases and more than 200 thousand deaths.[1-6]

Given the rapid progression of the pandemic, social distancing proved to be the most appropriate measure, following the experiences of other countries. This measure was essential to avoid overcrowding in the unified health system (SUS, Brazil) and ensure adequate access to the population, reducing the number of cases requiring care in intensive care units and ventilatory support.[3,7,8]

Despite widespread implementation of control measures, the COVID-19 pandemic is devastating. In addition, healthcare professionals working at the front line of the COVID-19 pandemic are one of the main risk groups because they directly deal with infected patients.

In this sense, the need for training and the proper use of personal protective equipment (PPE) was essential to prevent contamination. However, many healthcare professionals were infected due to the rapid spread of the COVID-19 pandemic, impairing their personal and professional lives and leading to death in the most serious cases.[9-12] This study aimed to characterize the

profile of primary health care professionals in a municipality of Pernambuco during the COVID-19 pandemic.

METHODOS

This cross-sectional study was conducted in the basic care units of a municipality in Pernambuco, and the participants were healthcare professionals from the family health strategies teams.

The non-probabilistic convenience sample included 33 professionals employed by the municipality or outsourced with a technical level or higher education. They had to be part of the team for at least one year before the COVID-19 pandemic. Those who were absent from work during the study were excluded.

Data were collected using a questionnaire (Google Forms®) after participants agreed to participate and signed the informed consent form. Participants spent about ten minutes responding to the questionnaire. The variables were expressed as absolute frequencies.

RESULTS AND DISCUSSION

During the COVID-19 pandemic, family health teams were the first contact for users suspected of having COVID-19. They contributed to the care network and community approach.[13,14] However, few reports on these professionals were found in the COVID-19 pandemic context.

In this study, most healthcare professionals were community health agents, nursing and pharmacy technicians, physicians, and nurses (Figure 1), corresponding to the family strategy team and others from the basic care unit. The reduced number of physicians was either because they were absent at the time of data collection or they were in attendance.

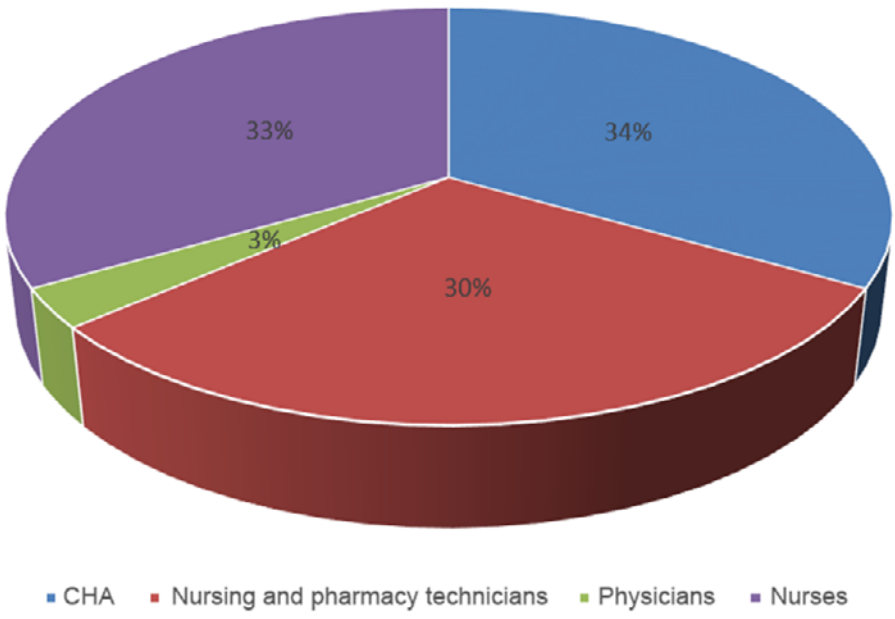

Figure 1. Occupation of the healthcare professionals

Sociodemographic data are presented in Table 1. Among these healthcare professionals, 84.8% were female, aged between 31 and 50 years, and the education level ranged from high school (technicians) to higher education.

Table 1. Sociodemographic data of healthcare professionals

Variables	Frequency
Gender	
Male	15.2%
Female	84.8%
Age (years)	
18 to 25	3.0%
25 to 30	0.0%
31 to 40	36.4%
41 to 50	36.4%
51 to 60	18.2%
> 60	6.1%
Education level	
High school	63.0%
Higher education	37.0%

A total of 50% of healthcare professionals tested positive for COVID-19; 60% were diagnosed by PCR. Moreover, only 14.3% did not report absences from work (Table 2). Although they reported using PPE, the equipment did not present a preventive effect. Healthcare professionals were three-fold more likely to contract COVID-19 than the general population[15,16], corroborating our results. According to Kowalski *et al.* (2020), healthcare professionals represented 3.8% to 20.0% of the infected population in Brazil, highlighting the significant impact of the disease on the workforce.[17] In addition, the state of Pernambuco had more than 1,353 healthcare professionals who tested positive for COVID-19.[15]

Table 2. Pattern of involvement of healthcare professionals by COVID-19

Variables	Frequency
Use of PPE	
Yes	100.0%
No	0.0%
COVID-19	
Yes	48.5%
No	51.5%
Diagnosis	
PCR	62.5%
Quick test	25.0%
Serological test	12.5%
Absence from work	
No	14.3%
7 days	28.6%
10 days	23.8%
14 days	33.3%

Source: PPE: personal protective equipment

CONCLUSION

Primary health care professionals were susceptible to the coronavirus, even though they were not on the front line of the COVID-19 pandemic. PPE was insufficient to prevent the disease, leading to absence from work.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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AUTHOR CONTRIBUTIONS

RMPMS: Investigation, data curation, visualization, and writing of the original draft. **DJAA:** Investigation, data curation, visualization, and writing of the original draft. **IFGG:** Investigation, data curation, visualization, and writing of the original draft. **SCSC:** Investigation, data curation, visualization, and writing of the original draft. **DMFS:** Investigation, data curation, and visualization. **CYM:** Conceptualization, formal analysis, project administration, supervision, and writing (review

and editing). **JLVS:** Conceptualization, formal analysis, project administration, supervision, and writing (review and editing). All authors approved the final version.

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Rare anatomical variation of the hypoglossal canal: morphology, morphometry, and clinical-surgical implications

Variação anatômica rara do canal do hipoglosso: morfologia, morfometria e implicações clínico-cirúrgicas

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Abstract

The hypoglossal nerve canal is a bony structure present above the occipital condyle that gives passage to important structures, such as the hypoglossal nerve, the meningeal branch of the ascending pharyngeal artery, and the emissary vein of the basilar plexus. As this structure may undergo variations, it is of particular interest to researchers, especially due to its clinical, radiological, and surgical implications. This study aimed to report a rare anatomical variation of the hypoglossal canal, describe the morphological and morphometric aspects and topographical relationships with the occipital condyle, and discuss the main clinical-surgical implications of this structure.

Keywords: Anatomy; Hypoglossal nerve; Neurosurgery; Measurement equipment; Anatomy variation.

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Resumo

O canal do nervo hipoglosso é uma estrutura óssea presente acima do côndilo occipital e dá passagem a importantes estruturas, tais como o nervo hipoglosso, o ramo meníngeo da artéria faríngea ascendente e a veia emissária do plexo basilar. Essa estrutura pode sofrer variações sendo um campo de estudo de particular interesse dos pesquisadores, especialmente devido às suas implicações clínicas, radiológicas e cirúrgicas. O presente estudo visou relatar uma variação anatômica rara do canal do nervo hipoglosso e descrever os aspectos morfológicos, morfométricos e sua relação topográfica com o côndilo occipital, além de discorrer sobre as principais implicações clínicas e cirúrgicas dessa estrutura.

Palavras chaves: Anatomia; Nervo hipoglosso; Neurocirurgia; Equipamentos de medição; Variação anatômica.

INTRODUCTION

The hypoglossal nerve canal (HC) is a bony structure located above the occipital condyle at its antero-posterior junction. This canal gives passage to vital structures, including the hypoglossal nerve responsible for innervating the intrinsic and extrinsic muscles of the tongue, the meningeal branch of the ascending pharyngeal artery, and the emissary vein that connects the basilar venous plexus to the internal jugular vein[1,2].

This structure may exhibit variations, such as when the HC is divided by a bony spur and results in a double HC. Other variations related to ancestry and biological sex have also been reported in the literature. Studies aimed at understanding these variations have been of particular interest to researchers, mainly due to their clinical, radiological, and surgical implications[1,3].

Several lesions have the potential to affect the HC, including tumors, abscesses, hematomas, aneurysms, arteriovenous malformations, cysts, and traumatic injuries. These conditions may impair the structures near the HC and lead to speech, swallowing, and chewing alterations. In the case of tumors in this region, the decision about the surgical intervention relies on its size, histological type, and anatomical variations of the HC. Thus, early identification of these lesions and a thorough understanding of anatomy and its variations are imperative for preventing neurological complications[1,2,4].

The present study aims to report an anatomical variation of the HC not documented in the literature, describe its morphological and morphometric aspects, explore topographical relationships with the occipital condyle, and address the primary clinical-surgical implications associated with this structure.

CASE REPORT

The current study was conducted at the Laboratory of Forensic Anthropology and Osteology of a higher education institution. The rare anatomical variation of the left HC was identified in a skull (Figure 1A) during a routine process of washing and drying the skeletons of the collection for subsequent storage.

Morphologically, the bilateral presence of the HC was observed. The HC traversed superiorly and positioned slightly on the anterior, lateral, and superior portion of the occipital condyle. The internal and external foramina delineated the HC, while an accessory foramen on the superior wall of the left HC connected the HC and the left jugular fossa (Figure 1B).

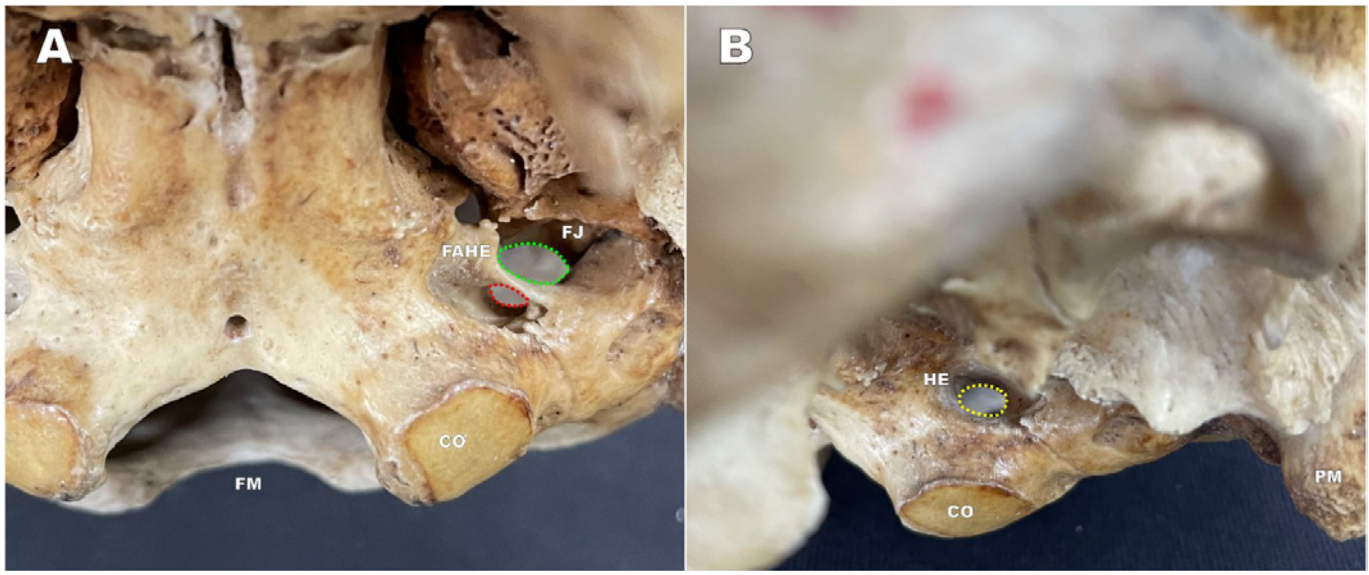

Figure 1. A: Antero-inferior view of the left extracranial hypoglossal canal, showing the accessory foramen communicating with the jugular foramen. **B:** Antero-lateral view of the left extracranial hypoglossal canal. Foramen magnum (FM); occipital condyle (CO); accessory foramen of the extracranial hypoglossal canal (AEHC); jugular foramen (FJ); and mastoid process (PM).

Regarding morphometry, the metric parameters for the intra- and extracranial HC were measured using a *Castroviejo* compass and a digital caliper.

The metric parameters for the intracranial hypoglossal canal (HI) were obtained as follows (Figure 2A): (1) vertical diameter of 0.35 mm on the right and 0.50 mm on the left; (2) transverse diameter of 0.75 mm on the right and 0.60 mm on the left; (3) distance between HI and occipital condyle of 11.00 mm on the right and 10.0 mm on the left; (4) distance from HI to the jugular foramen of 7.50 mm on the right and 6.00 mm on the left; (5) distance between HI and the jugular tubercle of 10.00 mm on the right and 10.50 mm on the left; (6) distance from HI to the basion of 15.50 mm on the right and 14.50 mm on the left; (7) distance from HI to the opistium of 3.50

mm on the right and 3.50 mm on the left; and (8) depth of the HC (i.e., from the intracranial to the extracranial HC) of 1.15 mm on the right and 1.20 mm on the left.

The metric parameters for the extracranial hypoglossal canal (HE) were also measured (Figure 2B): (1) vertical diameter of 0.45 mm on the right and 0.60 mm on the left; (2) transverse diameter of 1.05 mm on the right and 0.50 mm on the left; (3) distance between the HE and the occipital condyle of 0.5 mm on the right and 0.60 mm on the left; (4) distance from the HE to the jugular foramen of 0.30 mm on the right and 0.20 mm on the left; (5) distance from the HE to the basium of 1.90 mm on the right and 1.70 mm on the left; and (6) distance from the HE to the opistium of 4.50 mm on the right and 5.00 mm on the left.

Furthermore, the position of the HC in relation to the occipital condyle was measured. The maximal antero-posterior axis of this condyle can be divided into three equivalent parts: “a”, “b”, and “c” for the anterior, middle, and posterior third, respectively. In the present case, both HC were classified as type “a” because they were located in the anterior third (Figure 2C).

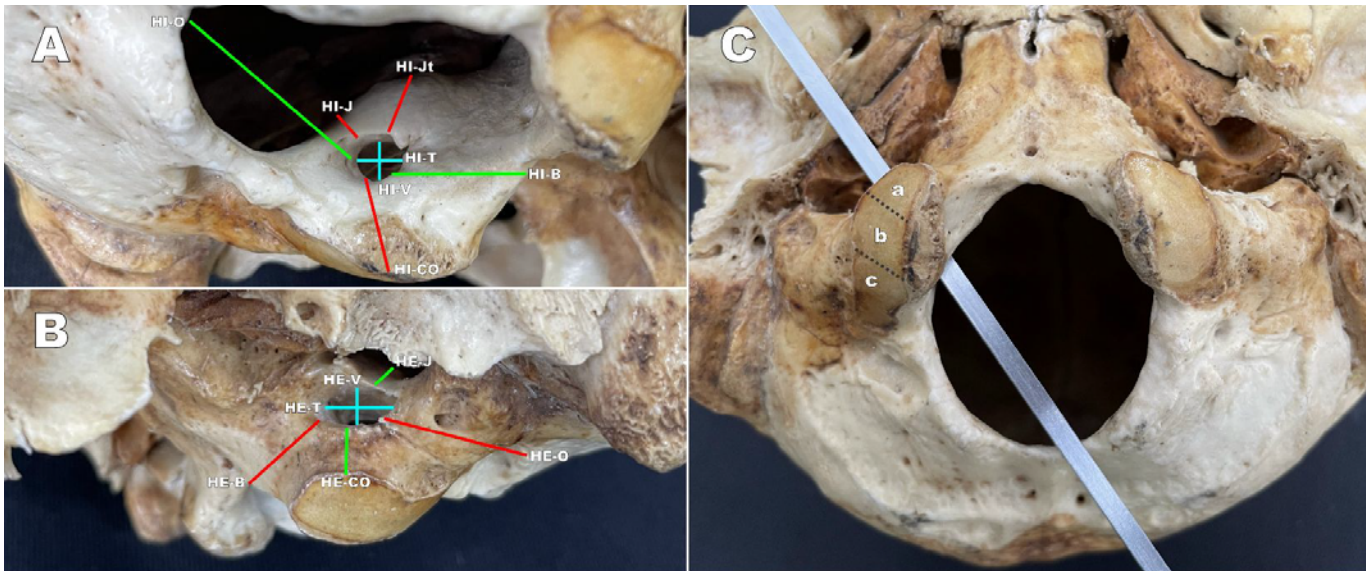

Figure 2. Postero-lateral view **(A)**, antero-lateral view **(B)**, and inferior view **(C)** of the skull base. **A:** Metric parameters obtained for the intracranial hypoglossal canal; **B:** Metric parameters obtained for the extracranial hypoglossal canal; and **C:** Location of the hypoglossal canal in relation to the occipital condyle. HI: intracranial hypoglossal canal; HI-V: vertical diameter of the HI; HI-T: transverse diameter of the HI; HI-OC: distance between HI and occipital condyle; HI-J: distance from HI to the jugular foramen; HI-Jt: distance between HI and the jugular tubercle; HI-B: distance from HI to the basion; HI-O: distance from HI to the basion; HE: extracranial hypoglossal canal; HE-V: vertical diameter of the HE; HE-T: transverse diameter of the HE; HE-OC: distance between HE and occipital condyle; HE-J: distance from HE to the jugular foramen; HE-B: distance from HE to the basion; HE-O: distance from HE to the basion; a, b, c represented the anterior, middle, and posterior third of the antero-posterior axis of the HC.

Another aspect evaluated was the non-morphometric parameter related to shape, which can be classified as round or oval. In this study, the HC exhibited a round shape. Conversely, this structure could not be categorized according to Hauser and De Stefano (type I to V)[3] since literature lacked studies about this specific variation.

Furthermore, the HC was photographed using a camera positioned 30 cm high and perpendicular to the anatomical specimen. The bone head was positioned on a flat surface, parallel to the ground, with the antero-inferior surface facing upwards. A ruler with a millimeter scale (ABFO ruler No 2, Crime Scene, Phoenix, Arizona, USA) was positioned next to the anatomical specimen to standardize the position of the lens (i.e., parallel to the anatomical accident). Consequently, the area of the foramen on the superior wall of the left HC was measured using the ImageJ software (National Institutes of Health, USA). For this, the software was calibrated by drawing a one-millimeter line on the ABFO ruler placed beside the HC. Subsequently, a cursor outlined the entire foramen to analyze the morphometry. The area of the accessory foramen was 0.55 mm².

DISCUSSION

Foramina are openings in the bone structure that allow the passage of nerves and blood vessels. Morphological alterations of the HC are relatively common and may vary in size, shape, and number of foramina or channels communicating with the main canal[5].

The anatomical variations of the HC are important for neurosurgeons and neuroradiologists due to the risks involved in surgical procedures at the skull base. This region is also associated with primary neoplasms, such as hypoglossal nerve schwannomas, vascular anomalies encompassing emissary vein dilation, and persistence of the primitive hypoglossal artery. Furthermore, although uncommon, deviations of the nerve trajectory may directly influence the likelihood of nerve injury during surgical procedures. Embryological modifications may generate bony crypts, resulting in variations in the trajectory of nerves or vascular elements or both associated with the HC and the condylar canal.

The presence of the blind foramen (i.e., partial or complete closure of the HC) is one of the most frequent variations. Bifurcations of the HC into two branches can also be found in this region[6].

Hauser and De Stefano were pioneers in classifying the anatomical variations of the HC by introducing a more detailed approach regarding the presence of bony crypts in the canal. The classification comprising five types has served as reference for other researchers in the field[3].

Limited information was found regarding the anatomical variations of the HC and its relationship with the occipital condyle. Additionally, no studies involving the Brazilian population or the presence of an accessory foramen communicating the jugular foramen to the HC were observed. Similar variations, such as triple canals, were only described in studies involving *Macaca mulata*

monkeys from the *Cercopithecidae* family[7].

From a clinical perspective, pathological conditions involving the HC include tumors (schwannomas and meningiomas), cysts (dermoid cysts), arteriovenous malformations, aneurysms, hematomas, and abscesses. These lesions may result in functional disturbances of the hypoglossal nerve, possibly due to their close associations and speech, swallowing, and chewing alterations[2]. Other conditions include extra- and intradural tumors, which are frequent at the skull base near the foramen magnum. These conditions are challenging for surgeons due to their deep location[1].

Several surgical approaches are employed according to the condition, demanding an in-depth understanding of the HC morphometry. These include the extreme lateral approach to vertebral artery aneurysms, meningiomas, and chondrosarcoma; the combined lateral approach to clivus tumors and the combined approach to jugular glomus tumors; the postero-lateral approach to the foramen magnum, transcondylar, supracondylar, and paracondylar for the lower clivus, craniovertebral junction, HC, and mastoid foramen, respectively; the lateral, dorsolateral, and suboccipital approaches to the lower clivus and craniovertebral junction; and the lateral approach to the petroclival region[3].

From a surgical perspective, the transcondylar approach is the most viable since it is a shorter and more direct route to the anterior part of the pontomedullary junction, with minimal retraction of the brainstem. The critical aspect of this surgery involves the drilling through the posterior part of the occipital condyle, threatening the HC[1]. Moreover, caution must be taken in cases of atlanto-occipital dislocation, in which occipital-cervical arthrodesis becomes necessary. In these surgical approaches, the hypoglossal nerve may be at risk; therefore, anatomical knowledge of the HC is crucial during drilling of the occipital condyle, jugular tubercle, and lateral mass of C1[3].

In this context, knowledge about the morphology and morphometry of the HC is needed to understand the lesions and choose and plan appropriate surgical approaches. HC variations must also be considered when interpreting imaging studies and during surgery to preserve the hypoglossal nerve function and prevent complications. Neurosurgeons should be aware of the morphological variations of the HC and its relationships with the occipital condyle.

In this study, an accessory foramen was observed connecting the HC to the left jugular fossa. Describing variations is essential since they may be associated with changes in the trajectory of nearby neurovascular structures. Therefore, we reinforce the importance of in-depth knowledge regarding the morphometry of the skull base, mainly the type and location of the extra- and intracranial foramina of the HC, to reduce morbidity and mortality in craniovertebral surgeries. This knowledge is also crucial for avoiding damaging the hypoglossal nerve and surrounding cranial nerves and preserving large vessels in various craniovertebral surgeries.

Our study had a limitation due to the lack of epidemiological data on the studied structures

of the skull. This lack of information may have also limited the analysis of some morphological and morphometric characteristics of the HC, especially regarding biological sex, age, and ethnicity.

Given the scarcity of literature regarding the morphology and morphometry of the HC, especially in the Brazilian population, and considering the relevance of this topic in surgery and imaging, we suggest future studies including the Brazilian population and considering variables such as age, biological sex, ethnicity, and height.

The morphological and morphometric characteristics of the HC may vary according to population, geography, and ethnicity. Consequently, further investigations are needed to improve understanding of the anatomical structure and its variations in the Brazilian population.

COMPETING INTERESTS

None.

AUTHOR CONTRIBUTIONS

FAP: Conceptualization, Data Curation, Investigation, Methodology, Project Administration, Resources, Supervision, and Writing – Original Draft Preparation, Writing – Review & Editing; **LFMSA:** Writing – Original Draft Preparation and Supervision & Writing – Review & Editing; **IFGG:** Writing – Original Draft Preparation and Supervision & Writing – Review & Editing; **PHLL:** Supervision & Writing – Review & Editing; **TJMBSV:** Writing – Original Draft Preparation and Supervision & Writing – Review & Editing; **AWPX:** Supervision & Writing – Review & Editing; and **RCFC:** Resources and Supervision & Writing – Review & Editing. All authors approved the final version submitted.

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Unusual anatomical variation of the sternal foramen: morphology morphometry

Variação anatômica incomum do forame esternal: morfologia e morfometria

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Abstract

The sternum bone may present anatomical variations acquired during its formation (i.e., from embryonic development to the beginning of adult life). These variations do not impair function but may leave the individual susceptible to injuries and complications. The present study aimed to report a foramen found in an unusual location in the sternum and discuss the main clinical implications when this anatomical variation is unknown.

Keywords: Anatomic variation; Anatomy; Sternum; Surgery; Measurement equipment.

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Resumo

O osso esterno pode apresentar variações anatômicas adquiridas durante o seu processo de formação, que vai desde o desenvolvimento embrionário até o início da vida adulta. Essas variações morfológicas não causam prejuízo da função, mas podem deixar o indivíduo susceptível a várias lesões e complicações. O presente estudo tem como objetivo relatar um forame encontrado numa localização não usual no osso esterno e discorrer, através de uma breve revisão da literatura, sobre as principais implicações clínicas quando essa variação anatômica é desconhecida.

Palavras-chaves: Anatomia; Esterno; Equipamentos de medição; Variação anatômica.

INTRODUCTION

Anatomical structures may present morphology variations during the embryonic development and formation process.[1] These variations differ from what is observed in most individuals, but they do not impair function; they are compatible with life.[1] The sternum is a bone located in the anterior wall of the chest, directly articulated with the clavicles and costal cartilages of the first seven ribs, overlapping the mediastinum region and protecting the viscera in this region.[2] The sternum presents several cartilages since intrauterine life. In the juvenile phase, the ossification centers divide the bone into the manubrium, sternal body, and xiphoid process.[2] Some failures may occur during the development, such as the appearance of a hole (i.e., foramen) in some region of the sternum bone, mainly in its distal portion.[3]

Clinically, the sternum is easily accessible and has a porous and compact composition, facilitating some practices, such as spinal puncture and acupuncture.[4-5] The sternal foramen is filled with connective tissue, hindering its palpation during a procedure. In addition, this foramen may be confused with pathological processes during radiological examination.[4] Therefore, ignoring the existence of the sternal foramen may lead to misdiagnosis and iatrogenesis, justifying the importance of recognizing this anatomical variation.[3,5]

The present study aimed to report a case of an unusual location of the sternal foramen and address the main clinical implications of this anatomical variation.

CASE REPORT

This research was conducted at the Forensic Anthropology and Osteology Laboratory of the Federal University of Pernambuco. During routine washing and drying of the skeletons for storage, a foramen was observed in the upper third of the sternum. The bone belonged to a male individual aged about 28 years old. Regarding morphology, the foramen was medially located and presented an elliptical shape with its largest diameter in the longitudinal direction. The sternal foramen was located between the second and third intercostal space, specifically at the level of

the sternocostal joint of the third costal cartilage. Regarding morphometry, the sternum was measured using a digital caliper (Figure 1A), while diameters (vertical and horizontal) were measured using a Castroviejo-type curved dry point compass (Figure 1B).

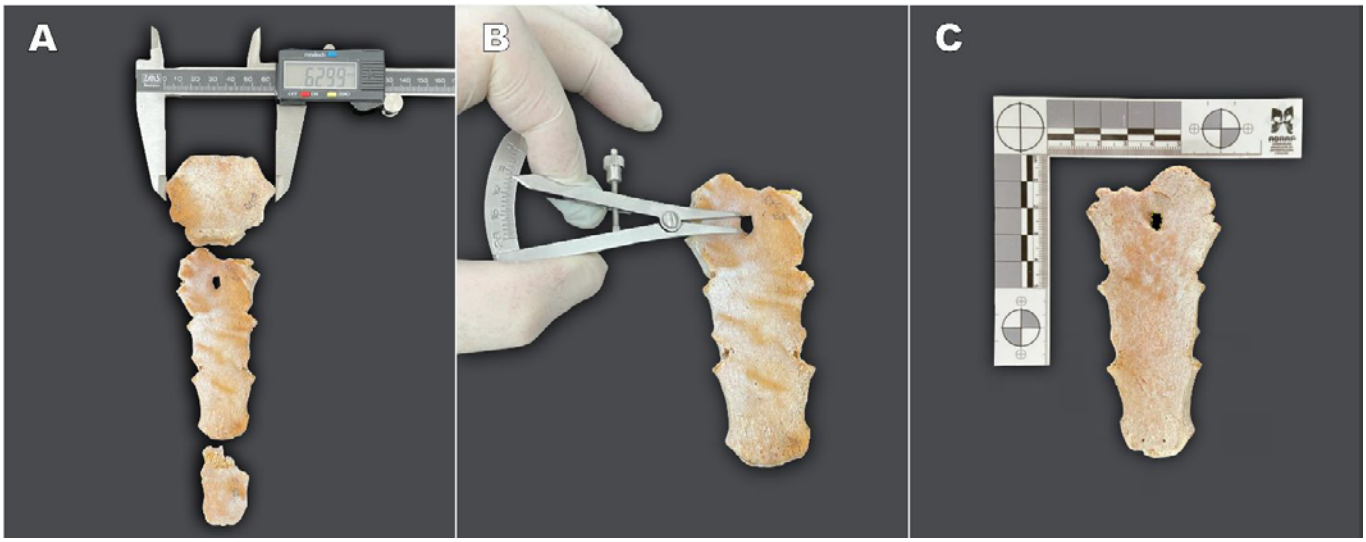

Figure 1. Measurement method and instruments for morphometry of the sternum bone. **A:** Measurement of the sternum bone and its parts using a digital caliper; **B:** Measurement of the diameters of the sternal foramen using a curved dry point compass; and **C:** Measurement of the sternal foramen area using the ImageJ and ABFO ruler nº 2.

The maximum length (height) of the sternum and the height and width of the manubrium, body, and xiphoid process were measured (Figure 2). The maximum length of the sternum bone was 201.19 mm. The width and height of the manubrium were 62.99 mm and 56.41 mm, respectively. The body height was 105.70 mm, and the width was 48.54 mm, 31.06 mm, and 25.92 mm in the upper, middle, and lower thirds, respectively. The width and height of the xiphoid process were 24.89 mm and 39.08 mm, respectively. The sternal foramen had a height and width of 0.65 mm and 0.4 mm, respectively, and was 17.95 mm distanced from the angle of Louis.

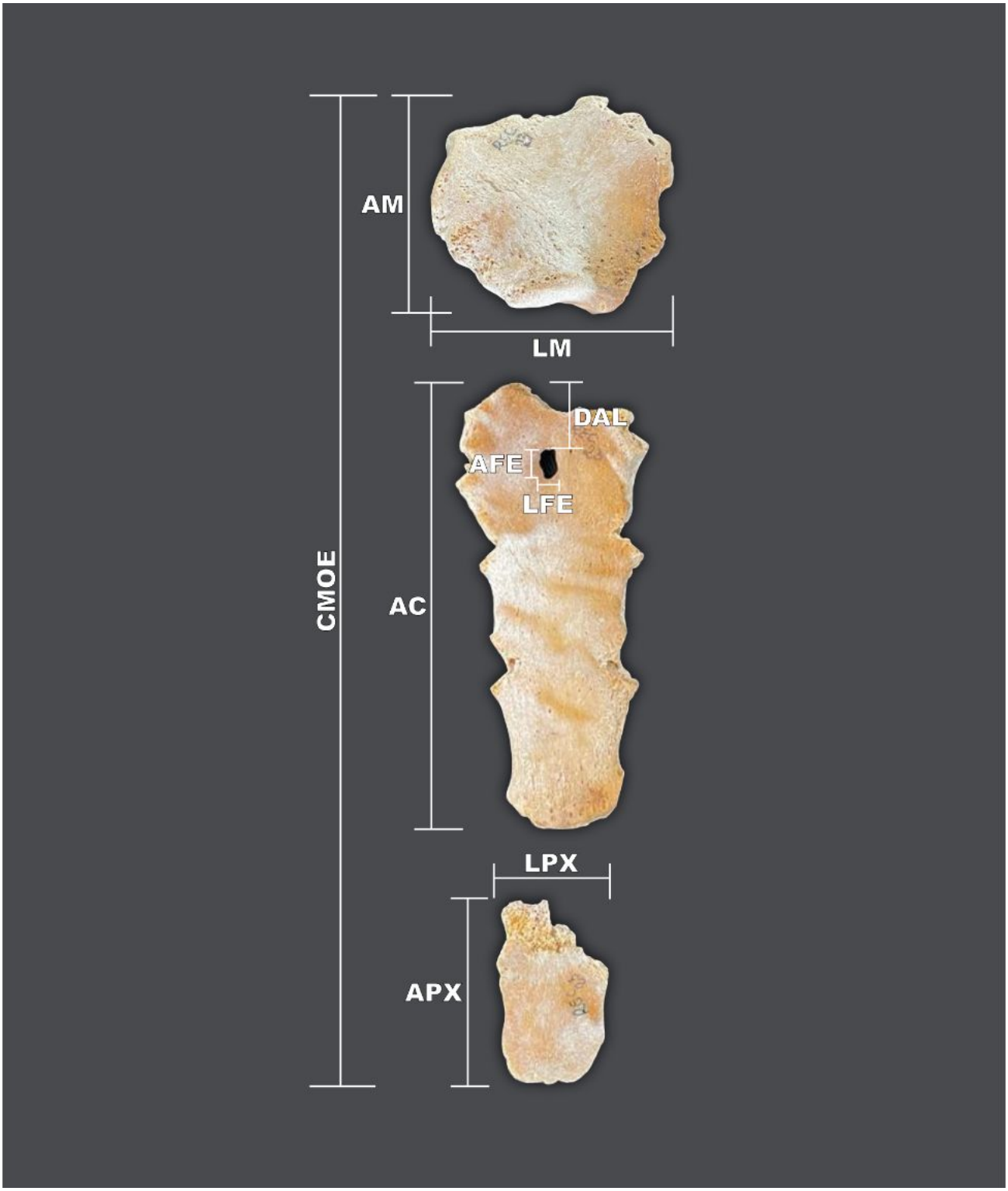

Figure 2. Measurements of the sternum bone and its parts. Maximum sternum bone length (CMOE); manubrium height (AM); manubrium width (LM); body height (AC); xiphoid process height (APX); xiphoid process width (LPX); sternal foramen height (SFA); sternal foramen width (LFE); and distance from the sternal foramen to the angle of Louis (DAL).

Then, the sternal foramen was photographed with a camera positioned at a 30-cm height of the specimen. The sternum bone was positioned on a flat surface, parallel to the ground, with the ventral surface facing upwards and downwards. The camera was positioned to form an imaginary line from the lens to the anatomical variation as perpendicular as possible. A ruler with a millimeter scale was positioned next to the anatomical piece (American Board of Forensic Odontology [ABFO] ruler nº 2, Crime Scene, Phoenix, Arizona, USA) to demonstrate the parallelism of the lens concerning the anatomical variation. In this way, the foramen area was measured using ImageJ (National Institutes of Health, USA). The software was calibrated by drawing a one-millimeter straight line on the ABFO nº 2 rulers next to the sternum bone. After calibration, morphometry was performed with a cursor, completely contouring the foramen, with the area expressed in square millimeters (mm2). The area of the sternal foramen was 0.264 mm2 (Figure 1C).

DISCUSSION

Anatomical variations of the sternum occur when the bone presents an incomplete closure during its formation. They are divided into clefts, sternal foramina, or supernumerary xiphoid process.[5,6]

The appearance of the sternal foramen is caused by a developmental defect in the midline of the sternum due to incomplete fusion of the ossification centers.[5] This defect happens during embryonic development when mesenchymal cells group to form the pre-cartilage; then, they fuse in the midline to form the cartilage of the sternum.[7,8] The ossification process begins from the fifth intrauterine month and completes its development, forming the manubrium and the xiphoid process after birth.[7,8]

Sternal foramina are generally found accidentally during imaging exams and, more commonly, post-mortem.[6,7] Furthermore, some studies are similar when analyzing the characteristics of the sternal foramen according to ancestry, biological sex, location, and age. In these studies, the foramen was more prevalent in individuals of African descent, and more in males than females. A higher incidence was also observed in individuals from South American individuals than in North American and European populations. Furthermore, this foramen is more common between puberty and the beginning of adulthood because the ossification process is completed in this phase.[5,8,9,10,11]

Furthermore, a study conducted at the Center for Studies in Forensic Anthropology of the Faculty of Dentistry of the University of Pernambuco (CEAF/FOP/UPE) with 126 skeletons found that 13 (10.3%) had the sternal foramen; 9 (7.1%) in the lower part of the sternal body and 4 (3.1%) in the xiphoid process.[5] Furthermore, a meta-analysis (n = 35 studies; 16,666 individuals) on the prevalence and morphometry of the sternal foramen found a higher prevalence in the lower region of the sternal (6.5%) than in the xiphoid process (2.9%).[9]In the first study, the prevalence of the sternal foramen was 10.3%.[5] However, the meta-analysis demonstrated an oscillation from

0.2% to 57.8%, suggesting that the prevalence changes according to the population studied.[9]

Previous studies did not report the presence of the foramen in the upper third of the body of the sternum, as described in the present study. This anatomical variation is typically observed only in the lower third or the xiphoid process (or both). Regarding morphometry, in a study conducted at the CEAF/FOP/UPE, a foramen presented a longitudinal dimension with a mean size of 0.6 cm and a vertical dimension of 0.5 cm. On the other hand, a meta-analysis revealed a prevalence of 4.7 mm in transverse diameter and 5.6 mm in vertical diameter.[9]

In this sense, the presence of anatomical variations deserves special attention because they may resemble gunshot wounds or osteolytic lesions. Furthermore, these variations may harm the pericardium and adjacent soft tissues in some procedures (e.g., acupuncture and bone marrow puncture), causing serious clinical implications for the patient.[4,5,10] For this reason, the sternal foramen has been associated with several risks, including injury to the pericardium, resulting in cardiac tamponade, decreased chest resistance, increased infections after heart surgery, and a greater likelihood of fracture associated with osteoporosis. Moreover, this foramen may harm vital organs due to perforation of the heart chambers, mainly in the right ventricle and the lungs.[6,9,10,11]

In this context, healthcare professionals must be aware of the existence of this anatomical variation. This awareness would make it possible to consider an early examination of the sternal region before any clinical procedures, preventing accidents and undesirable complications.[5,10,11]

Last, the literature regarding the epidemiology, morphology, and morphometry of the sternal foramen is scarce, especially about the Brazilian population.

Considering the importance of this topic in clinical procedures, further studies must encompass the Brazilian population and consider variables such as age, biological sex, ancestry, and height. Moreover, morphological and morphometric aspects often present variations between different populations and regions within the same country, according to the ethnic groups. Therefore, additional studies are needed to comprehensively understand this anatomical landmark and its variations in the Brazilian population.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest

AUTHOR CONTRIBUTIONS

Pacífico FA: conceptualization, data curation, investigation, methodology, project administration, resources, supervision, writing of the original draft writing, and writing (review and editing); **Gonçalves AAIS**: writing of the original draft; **Maia ER**: writing of the original draft; **Lages DB**: writing of the original draft; **Lima PHL**: resources and writing of the original draft; **Campina RCF**: resources, supervision, and writing (review and editing). All authors approved the final version.

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Anais da Faculdade de Medicina de Olinda
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afmo.emnuvens.com.br ISSN: 2674-8487 Case Report

Morphological and morphometric study of elongation of the styloid process with calcification of the stylohyoid ligament in a human skull: a case report

Estudo morfológico e morfométrico do alongamento do processo estiloide com calcificação do ligamento estilo-hioideo em crânio humano: um relato de caso

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Abstract

Elongation of the styloid process (i.e., Eagle syndrome) can compress nearby structures, causing varied symptoms. Studies on the morphological and morphometric aspects of the elongation of the styloid process are scarce, especially in the Brazilian population. Therefore, the present study reports a case of elongation of the styloid process with calcification of the stylohyoid ligament bilaterally. These structures on both sides were two-fold longer than needed to meet the anatomical criterion of the syndrome. Morphological and morphometric aspects and the clinical implications of the structures were also discussed.

Keywords: Anatomy; Temporal bone; Surgery; Measurement equipment; Anatomic variation.

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Resumo

O alongamento do processo estiloide pode comprimir estruturas próximas causando um conjunto de sintomas que caracterizam a Síndrome de Eagle. Nota-se uma escassez de estudos, em especial na população brasileira, sobre os aspectos morfológicos e morfométricos do alongamento do processo estiloide. Sendo assim, o presente estudo relata um caso de alongamento do processo estiloide com calcificação do ligamento estilo-hioideo bilateralmente. O comprimento dessas estruturas em ambos os lados excedeu o dobro do necessário para atender ao critério anatômico de existência da síndrome, bem como detalhou os aspectos morfológicos e morfométricos e as implicações clínicas das estruturas.

Palavras chaves: Anatomia; Osso temporal; Cirurgia; Equipamentos de medição; Variação anatômica.

INTRODUCTION

The temporal bone is characterized by bony projections, depressions, foramina, and bony processes. One of the main bony projections is the styloid process (SP). Derived from the Greek “stylosoide” it is named for its spearhead or stake-like shape[1].

The SP is positioned between the posterior edge of the neck of the mandibular condyle and the anterior edge of the mastoid, and projects caudally, anteriorly, and medially from the base of the skull[2]. The normal length usually ranges between 25 mm and 30 mm; however, this length can vary among individuals and even between the two sides of the same individual. Moreover, the SP is considered elongated when extensions exceed this mean length[3]. Due to its peculiar anatomical configuration, the SP supports three muscles and two ligaments that keep the airway passage in the pharynx[2]. Elongation of the SP can result from ossification of the stylohyoid ligament or excessive SP growth (or both); the former can be triggered by factors that stimulate osteogenesis, such as cervicopharyngeal trauma[3].

Computed tomography of the head and neck is considered the gold standard for identifying elongation in living individuals, which can differentiate the excessive growth of the SP from the calcification of the stylohyoid ligament[3]. However, the identification in post-mortem studies can be achieved by observing bony thickening at the insertion point of the calcified stylohyoid ligament.

Eagle syndrome (ES), or elongated SP syndrome, was described in the literature in 1937 by an otolaryngologist named Watt Weems Eagle[2]. The author described, in a case report, a female individual experiencing throat and neck pain caused by the elongation of the SP and calcification of the stylohyoid ligament[2].

Thus, ES comprises a set of rare symptoms triggered by the compression of structures near the growth of the SP or calcification of the stylohyoid ligament (or both). The impaired functioning of these structures causes pain in the pharyngeal and cervical regions[1]. Moreover, the internal carotid artery influences the SP anatomy, especially due to the proximity between these

structures. Thus, their association may cause a rare vascular variant of ES (i.e., stylocarotid syndrome)[2].

From this perspective, the present study aimed to report a case of elongated SP with bilateral calcification of the stylohyoid ligament, describing its morphological and morphometric aspects and reviewing the key characteristics of ES.

CASE REPORT

The present study was conducted at the Laboratory of Anthropology and Forensic Osteology of a Higher Education Institution. A bilateral elongation of the SP and calcification of the stylohyoid ligament were observed in a skull during the routine washing and drying process of the skeleton collection for storage (Figures 1A and 1B). The studied skeletal belongs to an 84-year-old male individual.

Figure 1. Elongated styloid process (SP) with bilateral calcification of the stylohyoid ligament. **A.** left lateral view; **B.** right lateral view; **C.** length of the SP with ligament calcification.

Regarding morphometry, the following measurements were taken (Figures 1 and 2): the length of the SF and calcified stylohyoid ligament (distance between the bases and tips of the elongated SP) using a digital caliper; distance between the bases of the SP using a digital caliper; distance between the tips of the SP using a digital caliper; measurement of the anterior angulation (between the Frankfurt line and the longitudinal axis of the SP, crossing the tip of the SP) using ImageJ; measurement of the medial angulation (line crossing the bases and the longitudinal axis that cross the tip of the SP) using ImageJ; measurement of the thickness (anteroposterior and horizontal dimensions) at the base, middle region, and tip of the SP using a digital caliper.

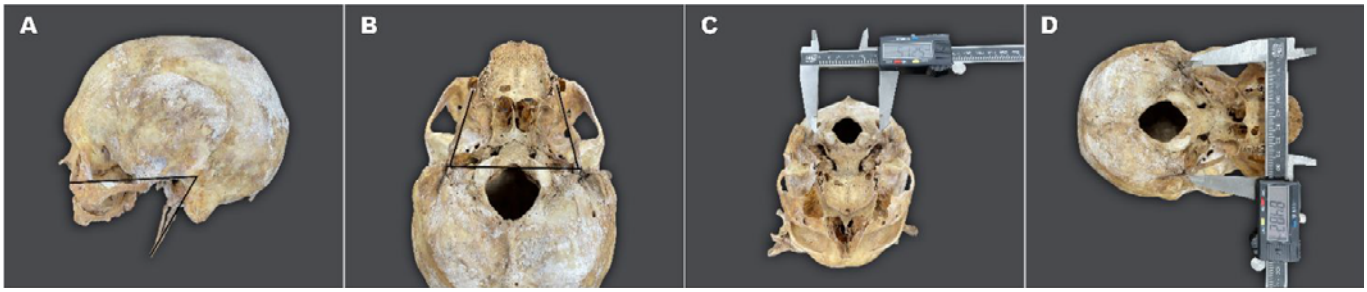

Figure 2. Elongated styloid process (SP) with bilateral calcification of the stylohyoid ligament **A:** measurement of the anterior angulation (between the Frankfurt line and the longitudinal axis crossing the tip of the SP); **B:** measurement of the medial angulation (line crossing the bases), and the longitudinal axis (crossing the tip of the SP); **C:** distance between the bases of the SP; **D:** distance between the tips of the SP.

The measurement of the elongated SP length was 61.91 mm (left) and 66.36 mm (right). The measurement from the base to the bony thickening was 30.11 mm (left) and 20.37 mm (right), while the measurement from the bony thickening to the tip was 41.54 mm (left) and 36.25 mm (right). The distance between the bases of the SP was 84.78 mm, and the distance between the tips of the SP was 46.55 mm. The measurement for the anterior angulation was 55.53°; the medial angulation was 73.56° (right) and 76.18° (left). The thickness of the SP at the base, middle, and tip were 3.68 mm, 5.25 mm, and 2.68 mm on the right (respectively), and 4.31 mm, 7.13 mm, and 2.88 mm on the left (respectively) (Figures 1 and 2).

Regarding the SP, the elongation on both sides was two-fold longer (over 60 mm) than the normal length (25 mm to 30 mm). Additionally, the elongation of SP originated from different processes: the calcification of the stylohyoid ligament (right side), and an elongation caused by abnormal growths and the calcification of the stylohyoid ligament (left side).

DISCUSSION

First described by surgeon Pietro Marchetti in 1652, the SP is a cylindrical and thin projection whose ossification starts at the end of gestation and continues until the first eight years of life[2]. Additionally, the SP is in the anteromedial region to the mastoid process of the temporal bone, from which three muscles (styloglossus, stylohyoid, and stylopharyngeus) and two ligaments (stylohyoid and stylomandibular) originate[4]. Furthermore, the SP relates caudally, medially, and anteriorly to the carotid arteries, internal jugular vein, and cranial nerves VII, IX, X, and XII, respectively. The elongation and compression of these structures cause ES[5].

Elongated SP has an incidence ranging from 4% to 28% of the population and is more predominant in female individuals (3:1 ratio), especially in those aged from 30 to 50 years[4,5]. However, symptoms are prevalent in only 0.16% of individuals with this anatomical variation[6].

In 1937, Eagle proposed two syndromes associated with elongated SP: the classic and stylocarotid syndrome[7]. The classic syndrome can be triggered by post-tonsillectomy scarring or trauma in the pharyngeal region. This process can lead to reactive hyperplasia and metaplasia, overgrowth of the elongated SP, or post-trauma ossification of the stylohyoid ligament (mainly in the mesenchymal tissue), compressing the cranial nerves (especially the glossopharyngeal nerve)[1]. Histological analysis of the SP may reveal deep staining reversal lines along its length. This alteration is associated with multiple recurrent microfractures due to trauma or traction, the differentiation process of mesenchymal tissue into bone, and dystrophic bone deposition[7,8]. On the other hand, stylocarotid syndrome is characterized by direct compression of the carotid arteries by the elongated SP, arterial dissection, or thromboembolism (secondary to injury to the arterial wall)[9]. Stenosis of these arteries, especially the internal carotid artery, is associated with transient ischemic attacks and pseudoaneurysms due to repetitive traumas[6].

The ES is commonly associated with compression of the cranial nerves, resulting in neuropathic pain in the pharyngeal region (ipsilateral tonsillar fossa and cervical area) or the ear[9]. This pain is reported unilaterally or bilateral (rare) and can be exacerbated by head movement, swallowing, and yawning and normally does not improve with medication[1,7]. Other symptoms may include a feeling of a foreign body in the hypopharyngeal region (in 55% of cases), odynophagia, dysphagia, headache, and tinnitus[1,7]. Conversely, the stylocarotid syndrome, leads to syncope, affects perivascular sympathetic fibers, and results in Horner syndrome[4,10].

Furthermore, ES may present as facial paralysis on rare occasions. Facial paralysis occurs due to the compression of the facial nerve (VII cranial nerve), potentially damaging different regions. Consequently, damage to the supranuclear region can cause central facial paralysis, while infranuclear damage is characteristic of peripheral paralysis[11]. However, due to the compression of the extratemporal part, taste and the functions of the sublingual, submandibular, and lacrimal glands remain preserved[11].

From the analysis of ES, differential diagnoses are essential to consider, especially during conditions that cause cervicofacial pain. Among these, differential diagnoses include temporomandibular joint dysfunction, trigeminal neuralgia, cervical masses, poorly fitted dental prostheses, esophageal diverticula, otitis media, and externa, mastoiditis, glossopharyngeal neuralgia, foreign bodies in the pharynx, and tumors in the pharynx or at the base of the tongue[1,8].

Besides the clinical picture, radiological findings and their potential causes can establish the ES diagnosis; they can classify ES as an etiology to be investigated among secondary headaches. The syndrome can also be associated with a clinical history of prior tonsillectomy; however, this association is not mandatory for diagnosis[12]. The gold standard examination for assessing ES is a three-dimensional non-contrast computed tomography of the head and neck, aiming to analyze the parameters of length and thickness of the SP[7].

Furthermore, a reliable diagnostic test can be requested by infusing 3 mL of 2% lidocaine. SE is characterized when the pain is reduced; therefore, this test predicts a good response to styloidectomy[13].

Conservative treatment for pain in SE is the first-line approach and typically precedes surgery, especially when the individual refuses it[13]. The initial preferred drugs are anticonvulsants (e.g., carbamazepine and gabapentin), which may be combined with selective serotonin reuptake inhibitors, nonsteroidal anti-inflammatory drugs, or opioids, depending on the pain intensity[14].

However, styloidectomy via transcervical or transoral is the most effective surgery in individuals with persistent symptoms, vascular involvement, and neurological sequelae[13,14]. The transoral is safer since the other has low surgical exposure, lack of control over the main vessels in the region, and possible bacteriological contamination of deep spaces[15]. In addition, a study of 103 individuals with ES found that this procedure was curative in 46% of cases, effective in 34%, and ineffective in 20%[15].

Last, despite the extensive literature on the clinical aspects of SE, the morphology and morphometry of the SP addressed in this study should be further studied, particularly in the Brazilian population. Considering the importance of this topic in surgeries and imaging, future studies must consider the Brazilian population and include variables, such as age, biological sex, ancestry, and height. Morphological and morphometric aspects of the SP are important because they may vary across different populations and regions within the country, depending on the ethnic group. Therefore, future studies are needed to comprehensively understand the anatomy and its variations in the Brazilian population.

CONFLICTS OF INTEREST

The authors declared no conflicts of interest.

AUTHOR CONTRIBUTIONS

Pacífico FA: conceptualization, data curation, investigation, methodology, project administration, resources, supervision, writing of the original draft, and review and of the original draft. **Saad BS**: writing of the original draft, and review and of the original draft. **Valente TJMBSV**: writing of the original draft, and review and of the original draft. **Galvão IFG**: writing of the original draft, and review and of the original draft. **Lages DB**: writing of the original draft, and review and of the original draft. **Albuquerque LCA**: writing of the original draft, and review and of the original draft. **Campina RCF**: resources, supervision, and writing (review).

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Anais da Faculdade de Medicina de Olinda
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afmo.emnuvens.com.br ISSN: 2674-8487 Case Report

Surgical treatment using Keystone flap for functional and aesthetic recovery of the hallux after chemical burn – case report

Tratamento cirúrgico com retalho keystone para recuperação funcional e estética do hálux após queimadura química - relato de caso

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Abstract

This study describes the case of a patient who suffered a chemical burn on the left hallux. The patient presented onychocryptosis, which was treated with phenol; the finger progressed to necrosis, a foul odor, and purulent discharge. After a medical assessment, the patient was diagnosed with an infected third-degree burn and was initially submitted to a non-surgical approach. Then, the Keystone flap was used to close the lesion, which presented complete recovery after two months. This study concluded that using acids may lead to severe chemical burns, impairing the function and viability of the finger. Furthermore, the Keystone flap is a good alternative for rapid recovery in deep wounds.

Keywords: Burns; Hallux; Onychocryptosis; Surgical wound.

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Resumo

O trabalho tem como objetivo descrever o caso de uma paciente que sofreu queimadura química no hálux esquerdo. Paciente com onicocriptose foi submetida a tratamento com ácido fênico, evoluindo com necrose, odor fétido e secreção purulenta. Após avaliação médica, diagnosticou-se queimadura de terceiro grau infectada, sendo submetida, a princípio a abordagem não cirúrgica, e posteriormente a realização de retalho Keystone para fechamento da lesão com recuperação completa após dois meses. Concluiu-se, com tal estudo, que o uso de ácidos pode evoluir com queimaduras químicas graves, comprometendo a função e viabilidade do dedo. Ademais, em feridas profundas, retalho Keystone mostra-se boa alternativa local com rápida recuperação.

Palavras-chave: Queimaduras; Hálux; Onicocriptose; Ferida cirúrgica.

INTRODUCTION

Burns are tissue injuries resulting from the action of agents that produce excessive heat, causing damage to body tissues and cell death. According to the causative agent, they can be classified as thermal, electrical, or chemical.[1]

Chemical burns, the level of tissue damage, and the degree of toxicity are determined by the chemical nature of the agent, its concentration, and exposure time on the skin.[2] Chemical products cause injury by destroying proteins via denaturation, oxidation, the formation of protein esters, or tissue dissection.[2]

Chemical products are frequently used for matricectomy in onychocryptosis (i.e, ingrown toenails).[3] Among the acids, phenol is the most commonly used. Due to its keratolytic properties, phenol can cause erythema and may progress to total skin necrosis.[4] Other options for this purpose are sodium hydroxide and 80% trichloroacetic acid. These acids must be handled cautiously due to the possible local or systemic complications.[3]

Onychocryptosis causes inflammation of the nail fold, leading to ingrowth into the lateral sulcus and pus formation. The pyogenic granuloma associated with the proliferation of blood vessels forms a tumorous lesion.[5] The onychocryptosis may be caused by wearing tight shoes and cutting the nails incorrectly. In addition, hyperhidrosis, circulatory insufficiency, obesity, anatomical abnormalities, and trauma may contribute to its appearance.[4]

Podiatrists are usually consulted for resolving onychocryptosis.[6] However, a trained physician is required in advanced stages because of the possible complications related to invasive methods. In this context, various surgical and non-surgical methods can be used for treatment.[7]

This study reports the case of a patient who suffered a chemical burn on the left hallux due to a substance used by a podiatrist to remove an onychocryptosis. An orthopedist with experience in wound reconstruction performed the surgical intervention.

CASE REPORT

L.R.L.S, female, 16 years old, without comorbidities, presenting recurrent onychocryptosis of the toenails for four years without significant damage. She presented a more severe episode affecting the left lateral paronychium with pain, heat, and redness in January 2022. Initially, she sought treatment with a podiatrist; however, the phenol application led to a chemical burn. After 12 days, the finger progressed to severe pain, extensive necrosis, foul odor, and purulent discharge.

Due to the clinical worsening, medical attention was sought, revealing a reduced range of movement of the dorsal flexion of the left hallux and an infected third-degree burn on the lateral side of the toe. X-rays showed erosion of the lateral cortex of the distal phalanx. Hospitalization and surgical treatment were indicated and conducted in two stages.

In the first stage, about a month after the onset of symptoms, the surgical debridement of the wound was performed; material for soft tissue and bone cultures was also collected. Intravenous antibiotic therapy (clindamycin and ciprofloxacin) was started in the immediate postoperative period. A de-escalation occurred because the lesion presented a pseudomonas culture sensitive to ciprofloxacin; therefore, the clindamycin was removed from treatment.. The wound was managed by changing dressings on alternate days using silver hydrofiber.

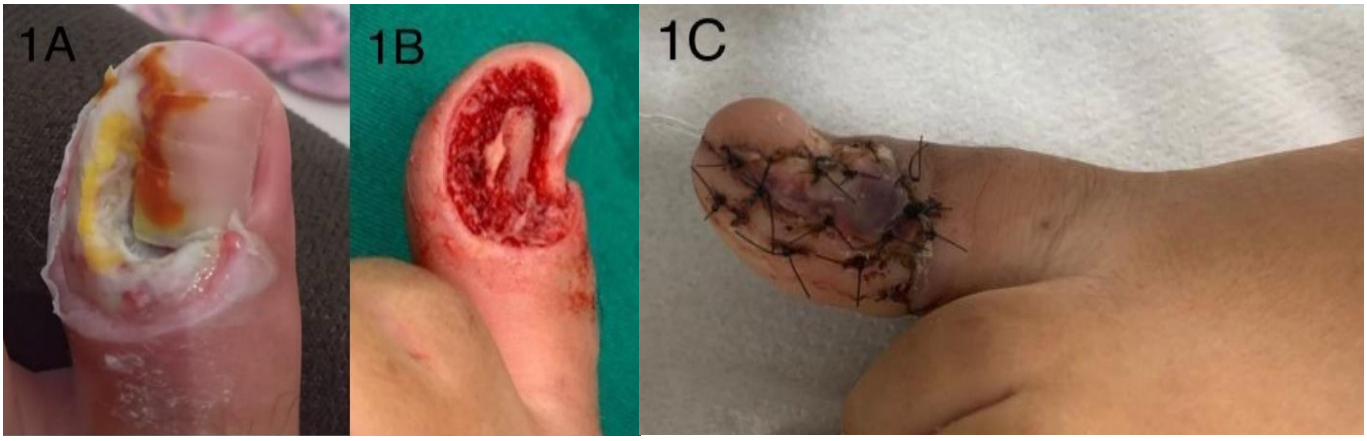

Figure 1: Evolution of onychocryptosis. **1A:** Third-degree chemical burn on the lateral aspect of the left hallux. **1B:** Immediate postoperative debridement with exposure of the distal phalanx. **1C:** Fifth postoperative day of Keystone flap reconstruction

The second stage occurred five days after the initial procedure, and a Keystone flap was chosen to close the lesion. The patient was discharged two days later, using the same oral antibiotic for 15 days. The condition resolved two months after surgery. The hallux was reconstructed and functional.

Figure 2: *two months after surgery.* **2A:** *Dorsal view,* **2B:** *Plantar view,* **2C:** *Lateral view*

As this case involved an adolescent, all the information was obtained after her legal guardian had signed an informed consent form. This case report was approved by the research ethics committee of the Olinda School of Medicine (OSM).

DISCUSSION

Burns are lesions resulting from agents that produce excessive heat, damaging body tissues and leading to cell death.[8] Acids induce thermal injuries by generating heat and damage to soft tissues. In addition, this substance induces the breakdown of proteins by hydrolysis and coagulative necrosis, resulting in a hard eschar that does not penetrate as deeply as alkalis.[2]

When treating patients with chemical burns, the initial step involves removing all chemical products by denuding the affected area and irrigating it abundantly.[2] The chemical agent cannot be neutralized due to the possible exothermic reaction that elevates the temperature and deepens the lesion.[9] In the present study, the inadequate phenol application caused product leakage beyond the desired area for matricectomy. This factor, combined with the lack of early identification, increased the extent of necrosis in the hallux.[9]

Additionally, the nature of the acid associated with other determining factors of severity (e.g., concentration, volume, and the time the substance remained in contact with the skin) directly influenced the deep tissue lesion, classified as a third-degree chemical burn.[9]

The literature supports that the infection found in this study presents a high risk of complications, including bacterial infection of the wound involving bones and joints.[2] Furthermore, the progression of this condition may lead to functional and aesthetic complications.[10]

The Keystone flap, initially described in 2003 by Behan[11], is elliptical, based on vascular, musculocutaneous, or fasciocutaneous perforators that require tissue laxity for advancement. Considering the halux, the flap was based on the subdermal plexus of the digital pulp and is considered a random skin flap for advancement. The defect is closed directly, with the midline

area presenting the greatest tension. Moreover, the isolated flap fills the defect using the V-Y advancement of each flap end, allowing the closure of the secondary defect on the opposite side.[11]

This surgical treatment is a versatile and reliable option for repairing large defects, especially in lower limbs. In addition, the flap has a high survival rate, low risk of complications, reduced pain and donor site morbidity, and a low risk of necrosis, and it is a way to avoid graft.[10]

The Keystone flap is rare in fingers and toes; however, the literature considers its use for lesions in which the usual flaps are impossible due to size or location.[10,12] Thus, the use of the Keystone flap in the present study was adequate because the lateral edge of the hallux and the extent of the lesion limited the coverage options.[11]

In this way, inappropriate use of acids for treating onychocryptosis may cause serious chemical burns, impairing function and the viability of the finger. Additionally, in deep wounds with the exposing of noble structures, the Keystone flap can be a good alternative due to low donor site morbidity and rapid recovery of the patient.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

MAR: conceptualization, data curation, visualization, research, writing of the original draft, and writing (revision and editing). **CBAM:** conceptualization, data curation, visualization, research, project management, supervision, writing of the original draf,t and writing (revision and editing)**. JPVSA:** research and writing of the original draft. **ABA**: research and writing of the original draft. **MBGT:** research and writing of the original draft. **MEFE:** research and writing of the original draft. **MJBM:** conceptualization, research, supervision, writing of the original draft, and writing (revision and editing). All the authors approved the final version.

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Necrotizing complication and intercurrences in rhinomodeling with hyaluronic acid: integrative literature review

Complicações necrosantes e intercorrências na rinomodelação com ácido hialurônico: revisão integrativa da literatura

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Abstract

Objective: To describe the adverse events, intercurrences, and complications of rhinomodeling with hyaluronic acid and indicate the possible causes for problems after the procedure. **Methods:** This integrative review was conducted in the Medline/PubMed, SciELO, and LILACS databases. The search included articles from 2013 to 2023 and used the following descriptors: hyaluronic acid, necrosis, dermal fillers, and nose. The integrative search combined the descriptors using the Boolean operator AND. Nine publications were analyzed. **Results:** The selected articles were identified, and data related to title, author, year of publication, type of study, methodology, main intercurrences, and conclusion were retrieved. Complications after the application of hyaluronic acid are not frequent. The first signs and symptoms must be analyzed to avoid complications, followed by applying the most appropriate protocol for prevention or reversal. **Conclusion:** The application of fillers following simple steps and knowledge about anatomy can be optimal options for safe and comprehensive rhinomodeling.

Keywords: Hyaluronic acid; Necrosis; Dermal fillers; Nose.

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Resumo

Objetivo: Descrever os efeitos adversos, intercorrências e complicações do preenchimento com ácido hialurônico na região de nariz, indicando possíveis causas para os problemas apresentados após o procedimento. **Metodologia:** Trata-se de uma revisão integrativa realizada nas seguintes bases de dados: Medline via PubMed, SciELO e Lilacs, com artigos incluídos no período 2013 a 2023, utilizando os descritores, Ácido hialurônico; Necrose; Preenchedores dérmicos; Nariz. A busca integrada foi realizada unindo os descritores com o operador booleano "AND". Foram analisadas 9 publicações. **Resultados:** Foi realizada a identificação dos trabalhos selecionados, elencando-se os dados relacionados à título, autor, ano de publicação, tipo de estudo, metodologia, principais intercorrências encontradas e a conclusão do estudo. Após análise dos estudos, observou-se que a ocorrência de complicações após a aplicação de ácido hialurônico não é frequente. Para que não ocorra o agravamento, é necessário que os primeiros sinais e sintomas sejam analisados para assim seguir com o protocolo mais adequado a fim de prevenir ou reverter**. Conclusão:** Seguindo passos simples de segurança e tendo um conhecimento anatômico refinado, os preenchedores podem ser uma boa ferramenta para um aprimoramento seguro e abrangente da rinomodelação.

Palavras-chave: Ácido hialurônico; Necrose; Preenchedores dérmicos; Nariz.

INTRODUCTION

Vanity is commonly associated with aesthetic procedures to improve appearance. Besides the nasal configuration having a fundamental role in balance, harmony, and facial proportion, each nasal structure has an exclusive aesthetic beauty. Also, the inclination of the nose in relation to the face contributes to an aesthetic aspect that refers to beauty.[1] In this context, non-surgical rhinoplasty (i.e., rhinomodeling) stands out among the main existing aesthetic procedures.

Rhinomodeling with hyaluronic acid (HA) is a simple and quick procedure that provides satisfactory results, similar to surgical rhinoplasty, and does not need absence from activities during recovery.[2] HA is considered the preferred product for rhinomodeling because it is moldable (e.g., enables skin remodeling in the nose region), has immediate and lasting results, and can be reversible after injecting hyaluronidase.[3] HA is a biodegradable filler (i.e., non-permanent) absorbed by the body within 6 to 18 months. Refinements in application techniques and technological advances in injectable products based on HA are some factors that helped this product reach the gold standard as a filler agent.[1,4] Complications after the application of HA in rhinomodeling are uncommon, and some adverse events are considered mild. However, severe adverse events, such as ischemia and necrosis, may also occur.[5]

The nasal region is located in the median plane of the face (middle third) and corresponds to a pyramidal protrusion called external nose. This structure is distinguished by its several small and fragile vessels, nerves, and a subcutaneous layer with limited adipose tissue.[6] The two semi-rectangular and oblique nasal bones cover approximately one-third of the nasal dorsum.

The upper lateral nasal cartilage connects to the upper margin of the septal cartilage and can be separated by a small gap in the anterior-inferior part. Also, the greater alar cartilage, a flexible and thin plate present below the lateral nasal cartilage, forms a sharp curve in the anterior region of the nostrils that divides into two branches: medial and lateral.[7]

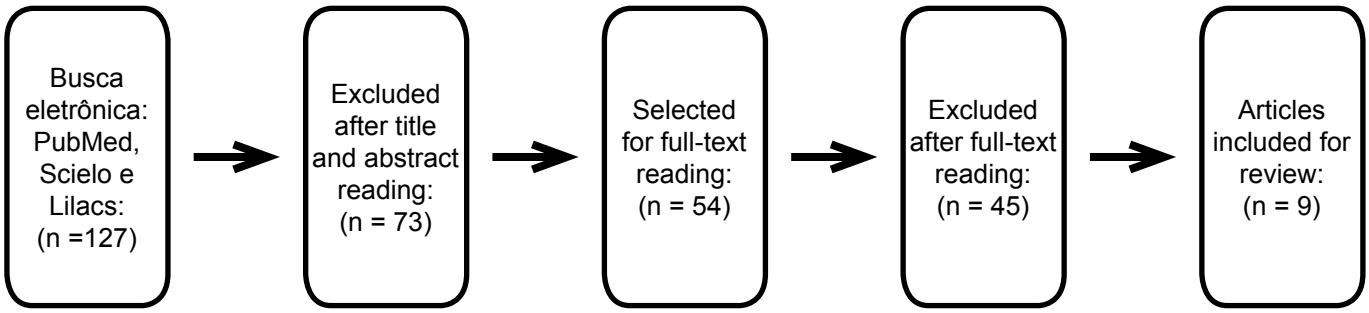
In this context, this study aimed to describe the necrotizing complications and intercurrences in rhinomodeling with HA by analyzing the effects of this procedure and the possible causes for problems after filling.

METHODS

This study is an integrative review of literature on the effects, complications, and intercurrences of rhinomodeling with HA in the nose region. This type of review allows a broad view of a topic that has the potential to gather diverse primary research methods to become a larger part of evidence-based practice initiatives.[8]

The search was conducted from December 2022 to May 2023 in the Medline/PubMed, SciELO, and LILACS databases using the following keywords: “hyaluronic acid”, “necrosis”, “dermal fillers”, and “nose”. The integrative search was performed by combining the descriptors using the Boolean operator AND.

Scientific articles covering the proposed topic in the title, abstract, or descriptors and published in English or Portuguese between 2013 and 2023 were included. Those articles not related to the topic and unavailable in full were excluded. Editorials, letters to the editor, opinion articles, duplicate articles, dissertations, and theses were also excluded. The articles found and published until May 2023 were selected for title and abstract reading. After this phase, the selected articles were read in full.



Source: Authors

Figure 1. Flowchart of study selection

RESULTS

Nine studies published between 2013 and 2020 in national and international journals were selected. Table 1 presents the characteristics of the articles according to author, year of publication, objectives, main complications and intercurrences, and conclusions of the study.

Two studies were retrospective reviews from 2015 and 2019, two were cross-sectional studies published in 2019, and five were case reports published between 2013 and 2020.

Complications after rhinomodeling are uncommon and may range from hematomas, edema, and delayed granulomatous reactions to more severe skin necrosis.

Table 1. Characterization of the included studies

Authors	Objectives	Intercorrences and complications	Conclusions of the studies
Lee J. e*t al.,* 2017.[9]	Describe a case of blepharoptosis and skin necrosis resulting from rhinoplasty.	Ecchymosis on the left nasal ridge, ptosis of the left eye, conjunctival hyperemia, and dilated pupil in the left eye were observed.	The skin lesion was treated twice daily with epidermal growth factor spray and antibacterial ointment. The skin lesion improved after six months, and the persistent diplopia was progressively resolved.
Kwon SG. *et al*., 2013.[10]	Report a case of ischemic oculomotor nerve palsy and skin necrosis after filler injection.	Blepharoptosis, exotropia, and diplopia developed suddenly after injection, followed by gradual skin necrosis.	The symptoms and signs of oculomotor nerve palsy improved with steroid therapy. Consultations and cooperation with ophthalmologists are needed.
Oh BL. *et al*., 2014.[11]	Report a case of intra-arterial infusion of hyaluronidase into the ophthalmic artery and other arteries supplying the facial skin.	The increased tissue pressure probably allowed filler particles to pass through the anastomosis and reach the artery.	Although intra-arterial infusion of hyaluronidase failed to recanalize the central retinal artery and improve vision, the authors achieved partial recanalization of the ophthalmic artery and its branches and restored ocular motility.
Rivkin A. 2019.[12]	Determine the overall adverse events rate for non-surgical rhinoplasty.	The overall adverse events rate was 7.6%; five cases (0.20%) were considered severe (ischemia and necrosis).	Rhinomodeling is a relatively safe procedure, and most reactions are present in common sites of adverse events. Patients with previous surgical rhinoplasty demonstrated a significantly higher chance of adverse events.

Harb A, Brewster CT. 2019.[13]	Review the demographics, indications, treatments, and results of treated patients.	Swelling and erythema were self-limited adverse event in approximately half of patients. Infection and localized skin necrosis were observed in two and three patients, respectively.	Non-surgical rhinoplasty is a safe procedure with positive aesthetic results when performed by an experienced clinician.
Furtado, GRD *et al*., 2020.[14]	Report a case of treatment of complications after aesthetic rhinomodeling.	The patient (no history of systemic diseases) underwent rhinomodeling. After 24 hours, the patient reported edema, purplish color, and paleness at the nose tip. Subsequently, an injection of hyaluronidase (1000U) was applied.	The areas affected after rhinomodeling (nose tip, columella, and upper lip) progressed to necrosis. After adequate treatment, a small scar remained compared to the initial lesions.
Sun, ZS *et al*., 2015.[15]	Report a study with 20 patients that developed necrosis after hyaluronic acid fillers.	Twenty patients developed impending nasal skin necrosis as a primary concern after nose or nasolabial fold augmentation with fillers or both.	Filling the nose and nasolabial folds with hyaluronic acid fillers may lead to nasal skin necrosis, possibly due to intravascular embolism or extravascular compression or both. Early combination treatment (<2 days) with hyaluronidase is associated with complete resolution of the complication.
Ramos, R *et al*., 2019.[16]	Describe a technique for applying fillers to the nose, paying attention to safety aspects.	Nasal tip edema, pain, and satisfaction with the result were evaluated. A total of 52% of patients had mild edema, 74% had mild pain, 15% were very satisfied, and 74% were satisfied with the results.	Rhinomodeling with resorbable fillers is a simple procedure with acceptable aesthetic results. However, in-depth anatomical knowledge is needed to reduce the risks of complications.
Chen, Q *et al*., 2016.[17]	To present a typical case of skin necrosis after non-surgical rhinoplasty with hyaluronic acid.	The patient felt intense pain, and the skin on the intermediate forehead turned pale. Persistent sensitivity was reported, and a progressive change in skin color was noted before returning to the hospital 48 hours later.	Surgeons and dermatologists must know the vascular anatomy before performing hyaluronic acid injections.

DISCUSSION

According to the analyzed studies, several complications related to HA have been described. However, each author presented methods and measures based on clinical experience,

indicating a lack of consensus regarding the appropriate technique and consideration about severe complications.

Harb and Brewster[13] emphasized that rhinomodeling was a safe procedure with positive aesthetic results when performed by an experienced clinician. However, swelling and erythema might occur due to allergic reactions in people sensitive to the filler. Comprehensive training and the use of appropriate materials are needed, considering that the first strategy against vascular complications is prevention. Ramos *et al*[16] reported that risk factors (e.g., bruising and swelling) are common in the short term; thus, in-depth knowledge of nasal anatomy is also needed to avoid applications in regions of higher risk.

Sun *et al*[15] reported a study of 20 consecutive patients who developed impending nasal skin necrosis as a primary concern after nose or nasolabial fold augmentation with HA fillers or both. Seven patients developed total skin necrosis, and thirteen patients fully recovered after a combination treatment with hyaluronidase. Also, 85% of those who developed total skin necrosis were late presenters and did not receive the combination treatment with hyaluronidase within two days after the vascular complication. Ischemia needs to be early identified and treated to prevent its progress to necrosis. The early combination treatment (before two days) with hyaluronidase was associated with complete resolution of the complication.

Hyaluronidase is an enzyme that accelerates the absorption of the filler by the body. In the study by Furtado et al[14], hyaluronidase was used in the reversal process. The patient was 34 years old, female, without history of systemic diseases, and underwent rhinomodeling with 0.8 mL of hyaluronic acid between the nasal dorsum, nasal spine, and columella. Edema, purplish color, and pallor on the nose tip were reported after 24 hours of the procedure; the patient used a cold compress in the region until the next day. The patient reported burning in the mouth on the third day and underwent an injection of 1000IU of hyaluronidase, warm compresses several times a day, and oral medication (acetylsalicylic acid 500 mg every 12 hours for 7 days). Subsequently, skin damage and persistence of redness were observed. The patient improved progressively after 30 sessions of hyperbaric oxygen therapy and medication. Despite the positive evolution, cold compresses are not recommended for treating necrosis because of the vasoconstriction and potential decrease in blood supply.

Chen *et al*[17] reported a case who experienced severe pain and pale skin on the mid-forehead during non-surgical rhinoplasty. The patient subsequently developed persistent sensitivity and progressive changes in skin color, resulting in hospitalization and surgical decompression of the nasal tip. Vasodilator, antimicrobial, and supportive treatment, including hyperbaric oxygen therapy, were used. Despite treatments, the affected area showed notable roughness and angulation in the bilateral soft triangles.

The intercurrences and complications of rhinomodeling are not limited to the nose region.

A case of a healthy female patient, 20 years old, who underwent filling of the nasal dorsum with HA developed partial visual impairment, pain on the right side of the eye, nausea, vomiting, and headache[10].

Oh et al[11] also reported a case of visual loss following the application of HA. A 33-year-old female patient arrived in the emergency room with sudden visual loss in the right eye. Ten hours earlier, the patient had undergone HA injection in the glabella and nasal ala. Retinal arterial perfusion was not restored despite direct infusion of hyaluronidase into the ophthalmic artery; however, branches of the ophthalmic and facial arteries were recanalized. Skin discoloration was normalized, while retinal perfusion and eye movement were partially and fully recovered, respectively.

All studies confirmed the importance of early diagnosis since, when treated correctly, it may guarantee the safety and success of results. Lee *et al*[9] reported a case of a 25-year-old female patient admitted to the plastic surgery service of the hospital due to severe pain, blepharoptosis, and decreased visual acuity immediately after filler injection. The patient received a hyaluronidase injection immediately after the intercurrence. Almeida and Saliba[18] suggested that, although hyaluronidase influenced the reduction of vascular complications caused by the filler, its isolated use might be ineffective if applied more than 24 hours after the filler injection.

Last, Rivkin[12] contributed to literature regarding rhinomodeling with injectable fillers by performing a retrospective chart review of 2,488 procedures. The overall rate of adverse events was 7.6%, and previous surgical rhinoplasty increased by 51% the chances of adverse events. Injecting fillers into the nasal tip or lateral wall significantly increased the chances of adverse events compared with other areas, regardless of prior surgery status. The author also reinforced the caution when injecting the nose, regardless of surgical history, and the need for experienced professionals with in-depth knowledge of nasal anatomy.

CONCLUSION

Rhinomodeling with HA presents significant risks, including infection, allergic reactions, aesthetic irregularities, necrosis, hematoma, material displacement, and abnormal healing. Comprehensive assessments by experienced professionals and an open discussion about the medical history are essential to minimize the risks and ensure safe and satisfactory results. The reaction of the body after the procedure must also be observed since immediate adverse events may occur. The management of complications includes hyaluronidase to remove HA and antibiotics to prevent infections. In conclusion, rhinomodeling is safe when performed by trained and experienced professionals with knowledge of nasal anatomy and appropriate techniques (e.g., cannulas, small boluses, and prior aspiration). Applying fillers and prophylactic measures are optimal options for a safe rhinomodeling procedure.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

MEBOM: conceptualization, data analysis, supervision, validation, visualization, writing of the original draft, and revision and editing. **ITHA:** data analysis, validation, visualization, and writing of the original draft. **MFC**: data analysis, validation, visualization, and writing of the first draft. **RFL**: conceptualization, data analysis, methodology, project administration, supervision, validation, visualization, writing of the original draft, and review and editing. All authors approved the final version.

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Exploring the gastrointestinal tract in SARS-CoV-2 infection: route of infection, manifestations, and impacts on the clinical course of patients with COVID-19

Explorando o Trato Gastrointestinal na Infecção por SARS-CoV-2: Via de Infecção, Manifestações e Impactos na Evolução do Pacientes com COVID-19

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Abstract

The Severe Acute Respiratory Syndrome Coronavirus-2 virus (SARS-CoV-2) infection may lead to respiratory symptoms and dysfunctions in the gastrointestinal tract (GIT), including abdominal pain, diarrhea, nausea, and vomiting episodes. Also, growing evidence suggests an oral-fecal route of transmission in SARS-CoV-2 infection. Thus, this integrative review discussed the influence of SARS-CoV-2 infection on the GIT function. An automatic search was performed in the PubMed and Scielo databases, and studies were screened according to eligibility criteria and by reading the title and abstract. Ten studies meeting the inclusion criteria described symptoms in the GIT related to SARS-CoV-2 infection. Also, other abdominal symptoms were described, such as involvement of the liver and viral RNA in the feces of infected patients. Thus, further studies are needed to elucidate the underlying mechanisms of SARS-CoV-2 infection, manifestations in the GIT, and disease progression.

Keywords: SARS-CoV-2; COVID-19; Coronavirus; Gastrointestinal diseases.

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Resumo

Evidências mostraram que a infecção pelo SARS-CoV-2, além de desencadear sintomas respiratórios, pode promover anormalidades e manifestações no trato gastrointestinal (TGI), como dor abdominal, diarreia, náuseas e episódios eméticos. Estudos sugerem uma possível rota de infecção oral-fecal através do TGI após a infecção pelo SARS-CoV-2. Este estudo realizou uma revisão integrativa sobre a influência da infecção pelo SARS-CoV-2 no TGI. Uma busca automática nas bases de dados PubMed e Scielo foi conduzida e 10 estudos atenderam aos critérios estabelecidos, compreendendo a amostra final. As manifestações do TGI relacionadas ao COVID-19 foram observadas em todos os estudos incluídos nesta revisão. Além disso, outras condições associadas ao TGI, como envolvimento hepático e presença de RNA viral nas fezes, foram relatadas. Estudos adicionais são necessários para elucidar os mecanismos subjacentes à infecção por SARS-CoV-2, manifestações do TGI e agravamento do quadro.

Palavras-chave: SARS-CoV-2; COVID-19; Coronavírus; Gastroenteropatias.

INTRODUCTION

The Coronavirus disease 2019 (COVID-19) is caused by the Severe Acute Respiratory Syndrome Coronavirus-2 virus (SARS-CoV-2). Considering its high rate of spread, the World Health Organization (WHO) declared the pandemic in March 2020. Since then, COVID-19 emerged as a global public health emergency, leading to numerous severe cases and a high mortality rate[1].

COVID-19 presents several clinical conditions, ranging from asymptomatic and mild to severe. The most common signs and symptoms of COVID-19 occur in the respiratory system (e.g., dry cough, dyspnea, hyposmia, and pulmonary infiltrates) but also include general symptoms, such as fever, headache, and myalgia[1]. Moreover, patients infected with SARS-CoV-2 may experience symptoms and dysfunctions in the gastrointestinal tract (GIT), such as abdominal pain, diarrhea, nausea, and vomiting[2]. The involvement of the GIT during SARS-CoV-2 infection suggests an oral-fecal route of transmission since the virus can infect epithelial cells of the esophagus, stomach, duodenum, and rectum glands. Also, studies have indicated that feces from patients with COVID-19 are potentially infectious[3-6].

Additional studies investigated the relationship between the SARS-CoV-2 infection and manifestations in the GIT. Some patients presented the symptoms previously mentioned, anorexia, and digestive bleeding. Also, those with severe COVID-19 were more likely to develop abdominal pain and changes in biomarkers of liver function, suggesting the involvement of the GIT and a worse prognosis[6].

In this sense, studies investigating the impact of SARS-CoV-2 infection on the GIT are

essential for understanding the clinical condition and decision-making for effective therapeutic approaches. Thus, this integrative review aimed to identify the GIT role as a route of SARS-CoV-2 infection, prevalence of gastrointestinal manifestations related to the infection, and its impact on the health of adults and older people.

METHODS

This integrative literature review (semi-systematic) was conducted between April 2022 and January 2023 with no meta-analysis.

RESEARCH QUESTION

What is the influence of SARS-CoV-2 infection on the GIT (including route of infection, manifestations, and impacts on the clinical course) of patients?

SEARCH STRATEGY

The following descriptors (DeCS and MeSH) were used as search strategy in the PubMed and Scielo databases: “SARS-CoV-2”, “COVID-19”, “coronavirus”, “gastroenterology”, “gastrointestinal symptoms”, and their equivalents in Portuguese and Spanish. Inclusion criteria comprised free access to the full text, specific focus on gastrointestinal manifestations in patients with COVID-19, published between January 2020 and December 2022, and availability in Portuguese, English, or Spanish. Opinion articles, studies exclusively addressing pediatric cases, narrative reviews, dissertations, theses, preprints, and duplicates were excluded.

Seventy studies were identified after the automatic search and application of the inclusion and exclusion criteria (44 in PubMed and 26 in Scielo). Titles and abstracts were read, and 60 studies were excluded. Thus, ten studies (eight from PubMed and two from Scielo) were selected for full reading and considered in this review. Figure 1 shows the flowchart of studies selection.

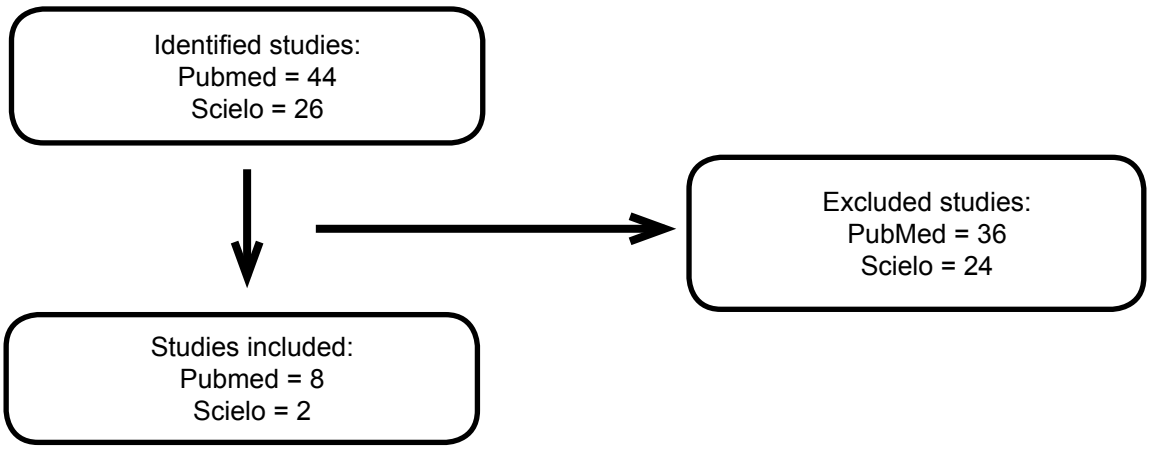

Figure 1. Flowchart of studies selection

RESULTS

The ten studies included were published in English, mostly (n = 7) in 2020; only one study was published in 2021, and two in 2022. Most studies were conducted in China, followed by the United States of America. The average age of patients in the studies was 40 years; one included patients over 18 years, and one included children and adolescents over 10 years. Five studies were meta-analyses, four were cohort studies, and one was a multicenter cross-sectional study. Chart 1 presents characteristics of the included studies (i.e., title, author and year of publication, objective, and main findings and conclusion). Also, Chart 2 describes the sample of each study, highlighting the prevalence of manifestations in the GIT of patients with COVID-19, especially diarrhea, nausea, vomiting, abdominal pain, and anorexia.

Chart 1. Characteristics of the included studies

Title	Author (Year)	Objective	Conclusion
Gastrointestinal symptoms of 95 cases with SARS-CoV-2 infection	Lin et al. (2020)	To study the gastrointestinal symptoms in patients infected with SARS-CoV-2.	The GIT may be a route of infection and a target organ for SARS-CoV-2.
Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study	Lei et al. (2020)	To identify the prevalence and outcomes of digestive symptoms in patients with COVID-19.	Digestive abnormalities (e.g., diarrhea) were common in patients with COVID-19, especially in hospitalization.
COVID-19 and the gastrointestinal tract: what do we already know?	Almeida et al. (2020)	To review the relationship of the SARS-CoV-2 infection with gastrointestinal tract and liver diseases and possible oral-fecal transmission.	COVID-19 affected the GIT, resulting in specific symptoms, changes in blood tests, and viral RNA in feces.
COVID-19 gastrointestinal manifestations: a systematic review	Silva et al. (2020)	To analyze the prevalence of gastrointestinal symptoms, increase in serum levels of biomarkers of liver function, and associated factors in patients infected with SARS-CoV-2.	Gastrointestinal symptoms were observed during SARS-CoV-2 infection (i.e., diarrhea, nausea, vomiting, and abdominal pain), and most patients were categorized as severely ill. Thus, gastrointestinal symptoms were common in patients with COVID-19, and a possible hepatic involvement was observed.
COVID-19 and its effects on the digestive system and endoscopy practice	Aguila et al. (2020)	To describe the effects of the SARS-CoV-2 virus on the GIT.	Gastrointestinal symptoms varied and usually preceded pulmonary symptoms. The most common GIT symptoms were anorexia, nausea, vomiting, diarrhea, and abdominal pain.

Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study	Chen et al. (2020)	To elucidate the epidemiological and clinical characteristics of COVID-19 associated with pneumonia, including systemic symptoms, such as myalgia, headache, confusion, chest pain, and gastrointestinal symptoms (e.g., diarrhea, nausea, and vomiting).	Older patients with other risk factors presented an increased risk for COVID-19 associated with pneumonia. Also, 11% of patients showed gastrointestinal symptoms.
Prevalence and characteristics of gastrointestinal symptoms in patients with severe acute respiratory syndrome coronavirus 2 infection in the United States: a multicenter cohort study	Redd et al. (2020)	To characterize the prevalence and features of gastrointestinal manifestations associated with SARS-CoV-2 infection and evaluate gastrointestinal-specific health outcomes in a cohort study	Two thirds of patients with COVID-19 reported at least 1 gastrointestinal symptom, with loss of appetite and diarrhea being the most common.
Gastrointestinal and hepatic abnormalities in patients with confirmed COVID-19: a systematic review and meta-analysis	Zarifian et al. (2021)	To identify the prevalence of gastrointestinal and hepatic manifestations in patients with COVID-19.	Gastrointestinal and hepatic manifestations were common in patients with COVID-19, and pre-existing conditions may affect their prevalence. Diarrhea and mild liver disorders were relatively common in individuals with COVID-19, regardless of comorbidities.
Gastrointestinal symptoms and fecal shedding of SARS-CoV-2 RNA suggest prolonged gastrointestinal infection	Natarajan et al. (2022)	To define the characteristics of SARS-CoV-2 infection in the GIT and its impact on human health in the short and long term.	Gastrointestinal symptoms were associated with fecal shedding of SARS-CoV-2 RNA. The persistence of viral RNA in feces for a long period compared with respiratory samples indicated a possible manifestation and relationship of viral infection with the GIT, leading to a potentially prolonged infection.
Are gastrointestinal symptoms associated with a higher risk of mortality in COVID-19 patients? A systematic review and meta-analysis	Wang et al. (2022)	To investigate the relationship between gastrointestinal symptoms and mortality from COVID-19.	Gastrointestinal symptoms were not associated with increased mortality from COVID-19. However, the prognostic value of these symptoms in COVID-19 still requires investigation.

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2 virus; GIT: gastrointestinal tract; COVID-19: coronavirus disease.

Chart 2. TSample size and prevalence of gastrointestinal abnormalities in patients during SARS-CoV-2 infection

Author (Year)	Total Patients	Patients with Gastrointestinal Symptoms	Patients with Diarrhea	Patients with Nausea And Vomiting	Patients with Abdominal Pain	Patients with Anorexia
Lin et al. (2020)	95	58 (61.0%)	14 (24.2%)	10 (17.9%)	Not reported	10 (17.9%)
Lei et al. (2020)	204	103 (50.5%)	35 (34.0%)	4 (3.9%)	2 (1.9%)	81 (78.6%)
Almeida et al. (2020)	2,352	815 (34.0%)	399 (48.0%)	352 (41.0%)	76 (9.0%)	264 (32.0%)
Silva et al. (2020)	18,246	1,841 (30.5%)	2,115 (11.5%)	1.158 (6.3%)	424 (2.3%)	Not reported
Aguila et al. (2020)	4,243	747 (17.6%)	90 (12.0%)	77 (10.2%)	69 (92.0%)	200 (26.8%)
Chen et al. (2020)	99	58 (58.6%)	2 (2.0%)	1 (1.0%)	Not reported	Not reported
Redd et al. (2020)	318	195 (61.3%)	107 (33.7%)	Nausea: 84 (26.4%) Vomiting 49 (15.4)	46 (14.5%)	110 (34.8%)
Zarifian et al. (2021)	13,251	Não relatado	10,652 (80.3%)	Nausea: 5,089 (38.4%) Vomiting: 4,567 (34.5%)	2342 (17.6%)	3871 (29.2%)
Natarajan et al. (2022)	113	54 (49.0%)	29 (26.0%)	36 (31.85%)	13 (12.0%)	Not reported
Wang et al. (2022)	55,245	8,535 (15.5%)	1,341 (12.2%) (considering 10,983 patients)	525 (7.3%) (considering 7,175 patients)	92 (1.8%) (considering 5,012 patients)	Not reported

DISCUSSION

This review had an integrative and comprehensive approach to analyze the relationship between SARS-CoV-2 infection and GIT, identifying the main signs and symptoms in the GIT related to the infection. Thus, this study contributed to the understanding of clinical manifestations of COVID-19, providing information for its early identification in patients, updating the scientific knowledge, and improving the healthcare related to COVID-19.

After fully reading the selected studies, they were categorized into three distinct dimen-

sions: GIT as a route of transmission for SARS-CoV-2 (i.e., presence and persistence of viral RNA in feces indicated the GIT as a potential route for viral transmission); main gastrointestinal manifestations and abnormalities related to the SARS-CoV-2 infection (i.e., diarrhea, nausea, vomiting, abdominal pain, and anorexia related to the viral infection); and impact of manifestations in the GIT on the evolution and outcomes of patients with COVID-19 (i.e., clinical impact of gastrointestinal abnormalities on disease evolution, including possible complications, worsening of the clinical condition, and adverse outcomes). These dimensions allowed a comprehensive and structured understanding of the available information, provided insights into the GIT role in SARS-CoV-2 infection, and its possible influence on the clinical outcomes of patients with COVID-19.

GIT as a route of transmission for SARS-CoV-2

Some studies have addressed the involvement of the GIT in patients with COVID-19 and suggested a fecal-oral route of infection since the SARS-CoV-2 may infect epithelial cells of the GIT, increasing its potential for dissemination and contamination within the body[3,4]. Also, the virus may damage these cells when infecting the GIT, resulting in gastrointestinal inflammation and dysfunction[3,4]. Thus, these findings suggested that SARS-CoV-2 transmission is not restricted to the respiratory tract but may also occur through infected feces.

Lin et al.[5], Almeida et al.[9], and Natarajan et al.[15] corroborated the hypothesis of a fecal-oral route of transmission of SARS-CoV-2. These studies identified the presence of viral RNA in the feces of patients with COVID-19, reinforcing the GIT as a potential route of transmission. Also, they described that the viral RNA in feces may persist longer than in samples from the respiratory tract. Thus, considering the prolonged manifestations and viral shedding in feces even after the resolution of respiratory symptoms, SARS-CoV-2 infection may impact the GIT. These findings reinforced the need to consider the GIT as a potential source and route of transmission for SARS-CoV-2 and appropriate hygiene measures to prevent viral spread, such as washing hands and correctly disposing of fecal waste[17].

Although the fecal-oral route was not considered the main route of infection for SARS-CoV-2, this possibility should be analyzed. However, detecting viral RNA in feces may not indicate effective virus transmission, and no robust epidemiological evidence was found to support this hypothesis. Also, possible biases in the studies should be considered[18]. Studies included in this review were conducted before the occurrence of new SARS-CoV-2 variants (e.g., Delta and Omicron), which are currently prevalent in many regions. Thus, these variants might present distinct characteristics, such as different tropisms and rates of viral elimination in the GIT[5,9,15], and further studies are needed to understand their impact on the GIT.

Main gastrointestinal manifestations and abnormalities related to the SARS-CoV-2 infection

The prevalence of gastrointestinal symptoms in patients infected with SARS-CoV-2 varied

considerably among the studies included in this review, ranging between 15.5% and 61.3% (Chart 2). This variation may be attributed to several factors, mainly due to the nature of COVID-19 evolution in each patient but also the study design, methodology, and population characteristics.

All studies in this review addressed the prevalence of symptoms in GIT (e.g., diarrhea, nausea, and vomiting) of patients infected with COVID-19. However, the approach of the studies varied on other symptoms; 30% and 40% did not report the prevalence of abdominal pain and anorexia related to COVID-19, respectively. The absence of these data may be attributed to several reasons, such as differences in study designs, emphasis on other predominant symptoms, and limitations in data availability. Although this absence may be a limitation in the studies, their findings showed a high prevalence of manifestations in the GIT related to the SARS-CoV-2 infection.

The presence of symptoms in the GIT of patients with COVID-19 affected their quality of life and recovery. For example, diarrhea and vomiting may lead to further complications, such as dehydration and nutritional dysfuntions[19], and abnormalities in the GIT may indicate a more serious clinical condition[20]. Thus, the findings highlighted the importance of a systemic and global evaluation of patients with COVID-19, considering its negative impact on the GIT.

Impact of manifestations in the GIT on the evolution and outcomes of patients with COVID-19

Silva et al.[10] and Zarifian et al.[14] identified that patients with manifestations in the GIT during SARS-CoV-2 infection also presented changes in biomarkers of liver injury and function. Although no causal relationship has been established between the manifestations in GIT and liver damage, studies suggested that these biomarkers indicate damage by viral infection[10,14]. Thus, the relationship of SARS-CoV-2 infection with manifestations in the GIT and changes in liver function still needs to be investigated.

Wang et al.[16] showed that gastrointestinal symptoms during COVID-19 were not associated with an increased mortality rate. However, they emphasized that the prognostic value of the manifestations in the GIT should be investigated in further studies. Although some limitations (e.g., selection bias) should be considered when elucidating the results, this was a preliminary study, highlighting the need for further prospective observational studies to understand the role of gastrointestinal symptoms during the COVID-19 evolution. Thus, this study contributed to the understanding of the topic, but future studies need to confirm and expand these findings[1].

Limitations and strengths

Despite the biases from an integrative review, strengths can be observed, such as the relevant databases for search to establish a solid foundation for the analysis. Also, this review followed a rigorous methodological process, defining and following inclusion and exclusion criteria to ensure the reliability of the findings. Moreover, it addressed an emerging and relevant topic,

adding valuable perspectives on the possible relationship between SARS-CoV-2 infection and manifestations in the GIT.

CONCLUSION

The results of this review emphasized the influence of SARS-CoV-2 infection on manifestations in the GIT, such as diarrhea, nausea, vomiting, abdominal pain, and anorexia. Also, the presence of viral RNA in the feces of infected patients indicated the potential for a fecal-oral route of infection. However, some gaps still need to be addressed, and further studies should expand the understanding of the GIT role in the transmission and pathogenesis of SARS-CoV-2. Thus, future studies will allow to identify the manifestations in the GIT related to the SARS-CoV-2 infection, adequate management of symptoms, and develop therapeutic interventions for general support of the patient. In addition, the possible oral-fecal route of infection highlighted the importance of adopting adequate hygiene and sanitation measures to prevent viral spread and the need for further prevention strategies.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

JIA: conceptualization, data curation, supervision, validation, review, writing of the original draft, and review. **LDPSP:** data curation, validation, review, and writing of the original draft. **PHLL:** data curation, validation, review, and writing of the original draft. **FMM:** conceptualization, data curation, validation, review, methodology, management, supervision, writing of the original draft, and review. All authors approved the final version.

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Pitavastatin as the preferred statin for control of dyslipidemia in patients with HIV infection using antiretrovirals

Pitavastatina como estatina de escolha para o controle da dislipidemia em pacientes infectados pelo HIV em uso de antirretrovirais

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Abstract

Objective: To elucidate the use of pitavastatin as the preferred lipid lowering agent for dyslipidemia and cardiovascular risk in patients with HIV infection. **Methods**: A comprehensive search was conducted on the PubMed and Virtual Health Library (VHL) using the following descriptors in English and Portuguese: “Pitavastatin”, “HIV”, “Statins”, “Infected by HIV”, “Dyslipidemia”, and “Antiretrovirals”. A total of 46 articles were identified, and nine (six from PubMed and three from VHL) were included. **Results**: Antiretroviral therapy significantly changes lipid parameters in patients with HIV infection, justifying its association with statins. However, some antiretrovirals can inhibit the cytochrome P450 3A4 enzyme, which metabolizes most statins. In this context, pitavastatin is preferred since it is mainly metabolized by glucuronidation and is more effective in reducing low-density lipoprotein cholesterol and inflammatory markers than pravastatin, which is also metabolized by glucuronidation. **Conclusion**: Pitavastatin is the preferred lipid lowering agent for dyslipidemia in patients with HIV infection due to its low drug interaction and high efficacy in reducing lipids and inflammatory markers.

Keywords: Antiretrovirals; HIV; Hyperlipidemia; Hypolipidemic; Statins.

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Resumo

Objetivo: Justificar o uso da pitavastatina para o controle lipídico e redução do risco cardiovascular em pacientes infectados pelo HIV. **Métodos**: Foram realizadas buscas na PubMed e na Biblioteca Virtual em Saúde (BVS), com uso dos seguintes descritores, em inglês e português: “Pitavastatina”, “HIV”, “Estatinas”, “Infectados pelo HIV”, “Dislipidemia” e “Antirretrovirais”. Foram encontrados 46 artigos, reduzidos, após o refinamento, a nove (seis da PubMed e três da BVS). **Resultados**: O uso de antirretrovirais (ARV) altera significativamente o perfil lipídicode pacientes infectados pelo HIV, sendo necessária a associação com uma estatina. No entanto, a maioria das estatinas são metabolizadas pelo sistema do citocromo P450 3A4, o qual é inibido por alguns ARV. Nesse contexto, destaca-se a pitavastatina, visto que ela é metabolizada, primariamente, por glucoronidação. Além disso, comprovou-se que esta estatina reduziu mais significativamente os marcadores inflamatórios e os níveis do LDL-c, do que a pravastatina, cuja metabolização é através do mesmo mecanismo. **Conclusão**: A pitavastatina é, preferencialmente, a estatina de escolha para corrigir a dislipidemia em pacientes infectados pelo HIV, devido às suas mínimas interações medicamentosas e maior redução lipídica e dos marcadores inflamatórios.

Palavras-chave: Antirretrovirais; HIV; Hiperlipidemia; Hipolipemiantes; Estatinas.

INTRODUCTION

The human immunodeficiency virus (HIV) infection causes dysfunction of TCD4+ lymphocytes, intense inflammatory and coagulative processes (especially within the vasculature), and increases the immune response (i.e., macrophage recruitment for viral destruction)[1]. Considering the chronic nature of this infection, antiretrovirals (ARV) should be used continuously to delay and alleviate this pathophysiological process[2].

Patients with HIV infection using ARV commonly have an increased risk of developing dyslipidemia and cardiovascular diseases (CVD), which are the main cause of mortality in this population[3]. In this sense, statins are recommended to reduce serum lipid levels and risk of CVD since they are inhibitors of the 3-hidroxi-3-methyl-glutaril-CoA (HMG-CoA) reductase and directly affect cholesterol synthesis[4].

Patients with HIV infection receiving ARV (especially protease inhibitors [PI]) need caution on using statins since most of them interact with PI due to similar metabolism pathways, which may change the glycemic parameter[5]. However, pitavastatin does not interfere with glycemic parameters, interacts less with ARV, and has greater potential to reduce lipid and inflammatory markers than other statins[6].

Considering the relevance of pitavastatin in treating dyslipidemia and reducing CVD in patients with HIV infection using ARV, this study aimed to elucidate its use as a preferred medication in this population.

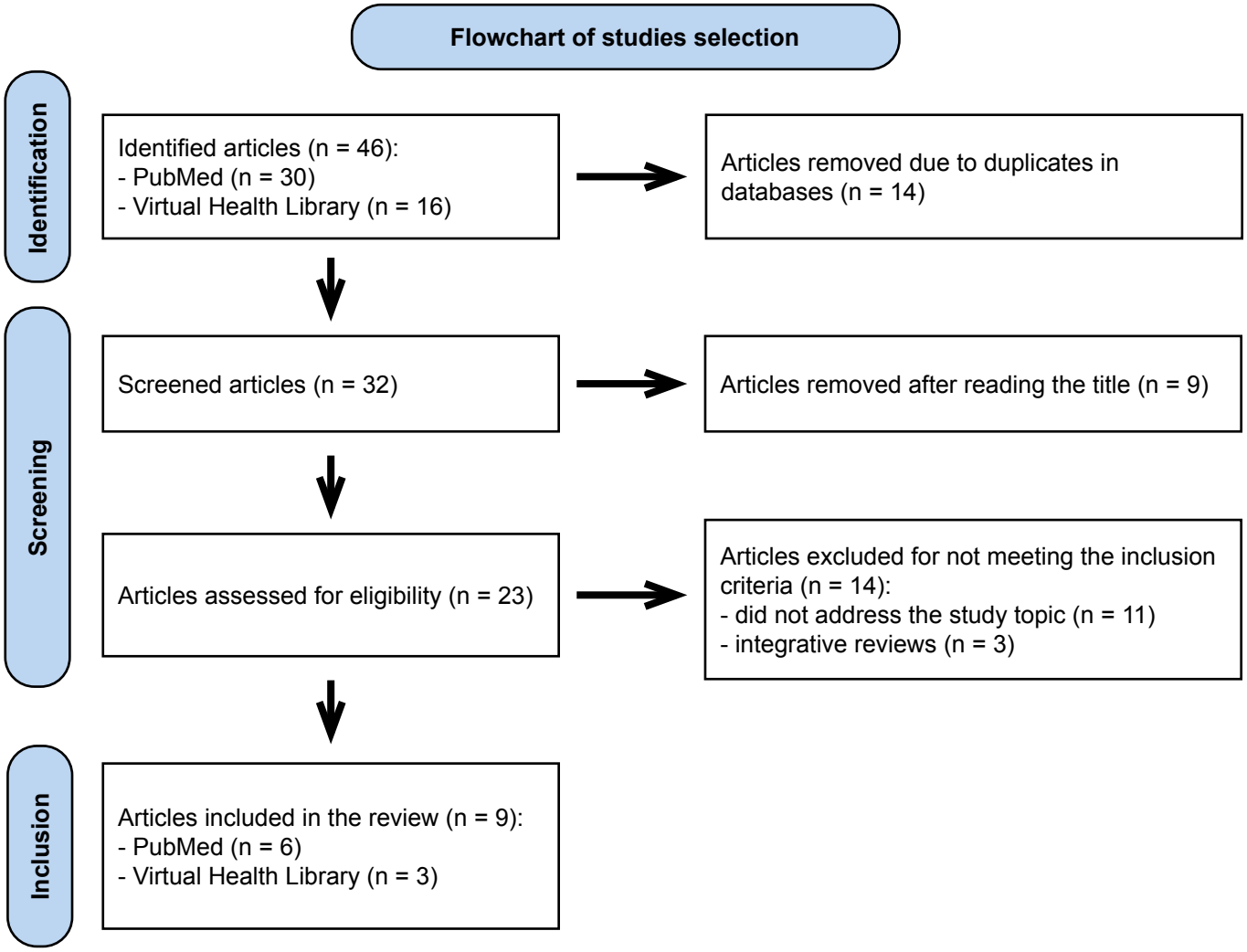
METHODS

This integrative literature review used the PubMed and Virtual Health Library databases.

The following free terms (FT) and Health Sciences Descriptors (DeCS) with Boolean operator (AND) were used as search strategy in Portuguese and English: “pitavastatin” (FT) AND “HIV” (DeCS); “statin” (DeCS) AND “HIV”; “statin” AND “HIV infected” (DeCS); “HIV” AND “dyslipidemia treatment” (FT); “HIV infected” AND “dyslipidemia” (FT); “statin” AND “antiretroviral” (DeCS).

Articles in English or Portuguese addressing the study topic (statins and HIV), studying pitavastatin in patients with HIV infection treated with ARV, dyslipidemia in patients with HIV infection, and interaction between ARV and statins were included. The following articles were excluded: unrelated to the inclusion criteria; not addressing statins or pitavastatin in patients with HIV infection treated with ARV; published more than eight years ago; or integrative reviews. A total of 46 articles were identified, and nine (six from PubMed and three from the Virtual Health Library) were included after screening (Figure 1).

Figure 1. Flowchart of studies selection



Source: The authors

RESULTS

Table 1. Integrative table with the included articles

PITAVASTATIN AS THE PREFERRED STATIN FOR CONTROL OF DYSLIPIDEMIA IN PATIENTS WITH HIV INFECTION USING ANTIRETROVIRALS				
No.	**Title**	**Authors and publication year**	**Study design**	**Objective**
01.	"Effects of Pitavastatin on Lipid Profiles in HIV-Infected Patients with Dyslipidemia and Receiving Atazanavir/ Ritonavir: A Randomized, Double-Bind, Crossover Study"	Wongprikorn A et al., 2016	RCS	To determine the efficacy and safety of pitavastatin in patients with HIV infection and dyslipidemia receiving atazanavir and ritonavir therapy.
02.	"Lipid-lowering therapy in HIV-infected patients: relationship with antiretroviral agents and impact of substance-related disorders"	Bednasz C et al., 2016	Cohort	To examine the relationship of substance-related disorders with ARV therapy and lipid lowering agents in patients with HIV infection.
03.	"Effects of pitavastatin and pravastatin on markers of immune activation and arterial inflammation in HIV"	Toribio M et al., 2017	RCT	To compare the effects of pitavastatin and pravastatin on markers of systemic immune activation and arterial inflammation in patients with HIV infection.
04.	"Pitavastatin versus pravastatin in adults with HIV infection and dyslipidaemia (INTREPID): 12 week and 52-week results of phase 4, multicentre, randomized, double-bind, superiority trial"	Aberg JA et al., 2017	ECIR.	To evaluate the safety and efficacy of pitavastatin compared with pravastatin in adults with HIV infection and dyslipidemia.
05.	"Assessing statin effects on cardiovascular pathways in HIV using a novel proteomics approach: Analysis of data from INTREPID, a randomized controlled trial"	Toribio M et al., 2018	RCT	To analyze the hypothesis that pitavastatin leads to greater changes in the cardiovascular system of patients with HIV infection.
06.	"Rationale and design of the Mechanistic Substudy of the Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE): Effects of pitavastatin on coronary artery disease and inflammatory biomarkers"	Hoffmann U et al., 2019	RCT	To evaluate the effects of statin on CVD in patients with HIV infection and improve the understanding of results from the REPRIEVE study.

07.	"Cardiovascular risk and response to lipid-lowering therapy in patients with HIV infection according to different recommendations"	Pawlos A et al., 2020	Case-control	To estimate the risk of CVD in patients with HIV infection using the Data Collection on Adverse Effects of Anti-HIV Drugs, Systematic Coronary Risk Evaluation, and Framingham scales. Also, to evaluate the achievement of the therapeutic goal and lipid lowering therapy according to the European AIDS Clinical Society 2019, Polish AIDS Society 2019, and European Society of Cardiology/European Atherosclerosis Society 2019 Dyslipidemia guidelines.
08.	"Real-life management of drug-drug interactions between antiretrovirals and statins"	Courlet P et al., 2020	Cohort	To evaluate the interactions between ARV and statins in patients with HIV infection, considering the serum level of statins, compliance with dosing recommendations, and achievement of lipid targets.
09.	"Effect of Statin Use on Inflammation and Immune Activation Biomarkers in HIV-Infected Persons on Effective Antiretroviral Therapy"	Hussain SK et al., 2020	MCT	To investigate the association of statins and serum levels of immune activation markers in patients with HIV infection receiving ARV therapy.

RCS, randomized control study; ARV, antiretroviral; RCT, randomized clinical trial; CVD, cardiovascular disease; MCT, multicenter clinical trial

Source: The authors

Table 2. Integrative table with results and conclusions of the included articles

PITAVASTATIN AS THE PREFERRED STATIN FOR CONTROL OF DYSLIPIDEMIA IN PATIENTS WITH HIV INFECTION USING ANTIRETROVIRALS			
No.	**Author and year**	**Results**	**Conclusion**
01.	Wongprikorn A et al., 2016	Patients (n = 12) of each group received pitavastatin for 12 weeks. The treatment reduced total cholesterol, LDL, and TG and increased HDL compared with the placebo. Liver enzymes and creatine phosphokinase levels had no significant changes.	Pitavastatin reduced lipid parameters without causing hepatotoxicity or increasing creatine phosphokinase levels compared with placebo.

02.	Bednasz C et al., 2016	Smoking was prevalent in patients with substance-related disorders. Statins were the most used lipid lowering agent (66%), followed by fibrates. The type of ARV might not affect the treatment with lipid lowering agents, and lopinavir was the most prescribed for substance-related disorders.	Statins were the main treatment for dyslipidemia in patients with HIV infection, followed by fibrates. Smokers with substance-related disorders had greater risk of metabolic changes, and lopinavir was the main ARV used. The management of dyslipidemia in this population needs to be optimized due to the low use of lipid lowering agents.
03.	Toribio M et al., 2017	Patients received pitavastatin (n = 126) or pravastatin (n = 126). Before treatment, the mean LDL levels was 153 mg/dL, HIV-1 viral load was 1.1 ± 0.2 copies/mL, and TCD4+ lymphocytes count was 580 cells/µL. After 52 weeks, pitavastatin reduced sCD14, oxidized LDL, and Lp-PLA2 more than pravastatin.	Pitavastatin (4 mg/day) reduced markers of immune activation and arterial inflammation more effectively than pravastatin (40 mg/day) in patients with HIV infection in 52 weeks. However, whether immune modulation by pitavastatin mitigates the risk of CVD in this population needs to be elucidated.
04.	Aberg JA et al., 2017	Pitavastatin (n = 126) significantly reduced LDL levels (31.1%) compared with pravastatin (n = 126; 20.9%). Patients receiving pitavastatin (n = 85) and pravastatin (n = 88) reported adverse effects, and six and five dropped out, respectively. Seven patients receiving pitavastatin had severe effects (e.g., atrial septal defect and heart failure), and three receiving pravastatin had stroke, coronary artery arteriosclerosis, acute myocardial infarction, and muscle hemorrhage.	The INTREPID study supported pitavastatin as the preferred treatment for dyslipidemia in patients with HIV infection.
05.	Toribio M et al., 2018	The mean age of the patients was 49.5 ± 8.0 years old, LDL levels were 155 ± 25 mg/dL, and TCD4+ lymphocyte count was 620 ± 243 cells/mm^3. TFPI, PON3, and LDLR levels reduced, and Gal-4 and IGFBP-2 increased in all patients. TFPI levels related to LDL and Lp-PLA2 differed between pitavastatin and pravastatin groups.	Statins significantly reduced TFPI, PON3, and LDLR and increased Gal-4 and IGFBP-2 levels, which participate in coagulation, redox signaling, oxidative stress, and glucose metabolism. Pitavastatin reduced TFPI more than pravastatin, highlighting the importance of these drugs for patients with HIV infection.
06.	Hoffmann U et al., 2019	The mechanistic substudy had enrolled 805 patients.	This was the first study using coronary computed tomography angiography to evaluate the primary prevention strategy for CVD in patients with HIV infection and elevated risk of coronary artery disease, immune activation, and inflammation. Pitavastatin reduced coronary plaques and interaction with immune activation and inflammation markers, preventing CVD and improving the outcomes.

07.	Pawlos A et al., 2020	Patients with HIV infection (n = 389) had mean total cholesterol of 177.2 ± 36 mg/dL, HDL of 48.9 ± 18 mg/dL, LDL of 103.8 ± 36 mg/dL, TG of 143.3 ± 81 mg/dL, plasma atherogenic index of 0.45 ± 0.3, and non-HDL of 129.2 ± 36 mg/dL. Of these, 360 had an elevated risk for CDV. According to ESC/EAS and PTN AIDS guidelines (respectively), 10.3% and 17.2% of those with very high and 12% and 45.9% of those with high cardiovascular risk achieved therapeutic LDL levels. According to EACS guidelines, they had a 2.5% success rate in secondary and 24.7% in primary prevention. Mean statin doses were 8.75 ± 6 mg for rosuvastatin and 22.35 ± 19 mg for atorvastatin.	Achievement of therapeutic LDL levels according to recommendations was unsatisfactory, especially in patients receiving lipid lowering agents. Treatment of patients with HIV infection was based on low-dose statins.
08.	Courlet P et al., 2020	Patients were treated with rosuvastatin (n = 99), atorvastatin (n = 92), pravastatin (n = 46), and pitavastatin (n = 21). Overdose of the first two led to suboptimal response. High doses of atorvastatin caused insufficient lipid control in patients using protease inhibitors due to low hepatic uptake of statins. Unboosted integrase inhibitors achieved better lipid values. Pitavastatin and pravastatin were also insufficient, regardless of the ARV used and their maximum doses, suggesting lower efficacy than the first two statins.	Suboptimal management of drug interactions and statin overdose was observed in 29% of prescriptions. In patients with refractory dyslipidemia, regimens with integrase inhibitors or treatment with rosuvastatin or atorvastatin were recommended.
09.	Hussain SK et al., 2020	Of 1031 patients with HIV infection, 31.5% were receiving statins and had lower levels of IP-10, IL-10, and IL-12p70 than those not using statins.	Statins reduced the levels of high-sensitivity C-reactive protein, IL-12p70, IL-6, and markers of immune activation and inflammation in patients receiving ARV therapy without aspirin, which may reduce the burden of disease.

LDL, low-density lipoprotein; TG, triglycerides; HDL, high-density lipoprotein; LpPLA2, lipoprotein-associated phospholipase A2; TFPI, tissue factor pathway inhibitor; PON3, paraoxonase 3; LDLR, LDL receptor; Gal-4, galectin-4; IGFBP-2, insulin-like growth factor; ARV, antiretroviral. EACS, European AIDS Clinical Society; PTN AIDS, Polish AIDS Society; ESC/EAS, European Society of Cardiology/European Atherosclerosis Society

Source: The authors

DISCUSSION

Patients with HIV infection have a 1.5 to 2-fold higher risk of developing CVD than those not infected, especially non-calcified atherosclerotic plaques and acute myocardial infarction favored by dyslipidemia and increased arterial inflammation[7,8]. In this context, a study with 389 patients with HIV infection showed that 360 had an elevated risk and 14 developed CVD, including ischemic stroke, acute coronary syndrome, and transient ischemic attacks[9].

Dyslipidemia in HIV infection has multifactorial etiology, such as increased proinflammatory and profibrotic cytokines, lipogenesis, and adverse effects of ARV therapy[10]. These factors are triggered by monocytes, macrophages, and TCD8+ lymphocyte activation, resulting in endothelial dysfunction, hypercoagulation, vascular thrombosis, excessive collagen production, fibrotic remodeling of the left ventricle, and hyperlipidemia[11]. Also, TCD4+ lymphocytes are mainly located in the intestinal mucosa, and their destruction increases the permeability to bacteria and lipopolysaccharides, contributing to inflammation.[12] Thus, chronic inflammation in HIV infection and its mechanisms involved in lipogenesis contribute to visceral obesity and lipohypertrophy, increasing the risk of CVD[11]. Despite the increased susceptibility to CVD, many patients are not properly monitored due to the lack of a multidisciplinary approach and stigmas on HIV infection.

ARV is associated with the pathophysiology of HIV infection and significantly increases serum lipid levels, particularly low-density (LDL), intermediate-density (IDL), and very low-density lipoproteins (VLDL); the latter two are triglyceride-dependent, which are also elevated in this context[13]. In addition, ARV has been associated with increased carotid intima-media thickness, carotid or coronary stenosis, and reduced vascular dilation, contributing to atherosclerotic mechanisms and CVD[11]. These changes are common in ARV therapy with non-nucleoside reverse transcriptase (TrR), proteases, and nucleoside TrR inhibitors[4,14]. Therefore, ARV should be prescribed carefully, individualizing their use and monitoring metabolic effects.

In this sense, lipid lowering strategies (e.g., using statins) are essential for patients with HIV infection, especially those receiving ARV therapy, to reduce its adverse effects on the risk of CVD[15]. In these patients, statins reduce LDL, immune activation, oxidative stress, and inflammatory markers (e.g., soluble CD14 [sCD14], lipoprotein-associated phospholipase A2 [LpPLA2], and oxidized LDL [ox-LDL][6,16].

Statins and ARV are mostly metabolized by the cytochrome P450 3A4 (CYP3A4) system, increasing the risk of drug interactions[17]. However, pitavastatin and pravastatin have distinct metabolisms from other statins, being glucuronidated before metabolized via CYP3A4, interacting less with ARV and safer to treat dyslipidemia than other statins[6]. Considering the immunosuppression and high prevalence of comorbidities in patients with HIV infection, potential drug interactions must be considered to avoid systemic effects.

A study with patients with HIV infection (INTREPID) showed that a 52-week treatment with 4 mg/day of pitavastatin was more effective than 40 mg/day of pravastatin in modulating inflammatory markers (e.g., sCD14, LpPLA2, oxLDL, and LDL-c), which are increased in HIV infection and favors the risk for atherosclerosis[18]. Also, pitavastatin and atorvastatin increased the levels of procollagen C-endopeptidase enhancer (PCOLCE) in patients with HIV infection, which is reduced in this population[16,19]. PCOLCE is an enzyme responsible for cleaving type I and III procollagen and activating C-proteinase, predominantly found in the extracellular matrix of blood

vessels and essential in atherosclerotic processes[19]. However, atorvastatin has a high magnitude of drug interactions and should be prescribed with caution, especially when associated with PI therapy[20,21].

Although PI inhibits CYP3A4 and statin transporters, pitavastatin is minimally metabolized by this enzyme and can be safely used with PI[22,23]. In contrast, simvastatin and lovastatin levels increase due to ARV inhibition of the metabolic system, leading to muscle and liver toxicity and resulting in myopathy and rhabdomyolysis[20,24,25]. Supporting its efficacy, a base-case analysis demonstrated that pitavastatin reduced LDL and total cholesterol (19.1%) and increased HDL (8.9%), preventing CVD and reducing morbidity and mortality in patients with HIV infection[26].

CONCLUSION

Results suggested that pitavastatin was the preferred statin to treat dyslipidemia in patients with HIV infection receiving ARV therapy due to its minimal interactions with ARV and efficacy in reducing markers of immune activation, inflammation, and lipid parameters. Also, these markers should be monitored in patients with HIV infection to choose the most suitable lipid lowering agent, especially considering the interactions with ARV.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

TJMBSV: conceptualization, data curation, research, methodology, management, resources, writing of the original draft, and review and editing. **FAP**: draft review and editing. **ADCF**: conceptualization, supervision, and draft review and editing. All authors approved the final version.

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afmo.emnuvens.com.br ISSN: 2674-8487 Experience Report

The importance of health education in the rescue of patients registered in HIPERDIA: an experience report

A importância da educação em saúde no resgate do paciente cadastrado no HIPERDIA: um relato de experiência

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Abstract

Systemic arterial hypertension and diabetes mellitus constitute serious public health problems throughout the world. After the creation of HiperDia, prevention and health promotion actions involving hypertensive and diabetic users were implemented in primary care. During academic experience in basic health units, a group of students realized the need to rescue users of this program with low adherence to medication treatment. After carrying out strategic actions with these users through conversation circles, glycemic screening and blood pressure measurement, users were more motivated to adhere to treatment.

Keywords: Diabetes mellitus; Primary health care; Systemic arterial hypertension.

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Resumo

A hipertensão arterial sistêmica e o diabetes mellitus constituem graves problemas de saúde pública em todo o mundo. Após a criação do HiperDia, ações de prevenção e promoção a saúde envolvendo usuários hipertensos e diabéticos foram implementadas na atenção primária. Durante vivência acadêmica em unidades básicas de saúde, um grupo de estudantes percebeu a necessidade de resgatar os usuários deste programa com baixa adesão ao tratamento medicamentoso. Após a realização de ações estratégicas junto à esses usuários por meio de roda de conversa, triagem glicêmica e aferição da pressão arterial, foi observado uma maior motivação dos usuários na adesão ao tratamento.

Palavras chaves: Diabetes mellitus; Atenção primária à saúde; Hipertensão arterial.

INTRODUCTION

Systemic arterial hypertension (SAH) is a non-communicable chronic disease defined by pressure levels, in which the benefits of treatment (non-pharmacological or pharmacological [or both]) overcome the risks. This disease is multifactorial and is characterized by persistent high blood pressure.[1] About 40 million people in Brazil suffer from this problem, consuming time and resources from the Unified Health System (SUS). Additionally, diabetes mellitus (DM) (i.e., increased glycemic levels) is a disease as serious as SAH. It causes sequela and leads to death when not properly treated.[1]

Despite being diseases with a significant genetic influence, other predisposing factors are relevant. Although incurable, they can be adequately controlled, providing quality of life to the affected individuals. In the primary health care of SUS, users can find autonomy, integrality, and longitudinally in care, which are fundamental for managing individuals with chronic diseases (SAH and DM).[2]

The SUS ensured closer care to users by creating the family health strategy and basic health units (BHU) nationwide. The care is centered on family and collectivity, aiming at to prevent and control diseases, especially non-communicable chronic diseases.[3] In this context, aiming to promote interventions for detecting, controlling, and reducing these diseases, the Brazilian Ministry of Health created HiperDia, a program for registering and monitoring individuals with SAH and DM, and the National Pharmaceutical Care Program for SAH and DM.[4,5]

Regarding control and treatment, implementing an individualized care plan by the BHU healthcare team is essential; users and healthcare professionals have goals to achieve, and results to be evaluated.[3,6] Therefore, interventions are crucial to strengthen the care of DM and adult SAH, such as rescuing HiperDia users with low adherence to pharmacological treatment. These data were presented by medical students and the healthcare team in the BHU of Olinda and Paulista (Pernambuco).

METHODS/EXPERIENCE REPORT

This study was an experience report on the applicability of an intervention based on the problem-solving methodology, which encompasses the observation of concrete reality, identification of key points, theorization of the theme, solution hypotheses, and the practical application of reality.[7]

A group of medical students visited the BHU of Olinda and Paulista as part of theoretical-practical activities of the Academia-Service-Community Integration. They observed a high number of individuals with SAH and DM needing continuous medication, besides the low treatment adherence and difficulties in planning treatment. The students discussed with the healthcare teams and planned a brief intervention using banners and leaflets containing information on the topic. Community health agents played a crucial role in this phase.

On the planned day, the students and the nurse welcomed individuals, conducted screening, and checked capillary blood glucose levels. Then, they discussed with users, addressed their queries, filled in individual medication cards (with recommended dosages), and provided support for organizing medications according to days of the week.

A total of 30 middle-aged individuals (80% women and 20% men) participated in the actions. Women are more present in the BHU because they often seek health services, providing greater opportunities for diagnosis and self-care.[8]

During the reception of each individual, they answered whether they presented any disease and the medications taken (and their frequency). The students recorded all this information on a card to facilitate adherence to medications, distributed medication holders for each day of the week, and recorded blood pressure and capillary glucose values to help the appointment with the physician (Figure 1 and 2). Low adherence to medication therapy is the main cause of failure in SAH control.[3]

Figure 1. Activities with patients during HiperDia intervention

Figure 2. Distributed material to patients during HiperDia intervention

Last, the final conversation with the individuals focused on promoting healthy habits and lifestyles and preventing and treating SAH and DM. Topics included healthy habits, proper food choices, and physical activity. Regarding medication treatment for SAH and DM, individuals were reminded that medications are provided by the SUS and distributed at the BHU. Currently, SUS offers at least one medication among the seven classes of most used antihypertensive drugs in clinical therapy.[9]

CONCLUSION

In summary, individuals with SAH and DM must be encouraged to have healthy habits and lifestyles, and raise their awareness of the proper prevention and treatment to improve quality of life. Treatment adherence (pharmacological and non-pharmacological treatment) is essential in this context. During the HiperDia, the students observed that non-adherence to treatments occurred due to lack of time. In addition, the individuals did not perform physical activity, and were not aware that they need to use drugs even in the absence of symptoms. Therefore, the intervention was crucial to turn these individuals into protagonists of their treatment, health, and quality of life.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

LCS: conceptualization, data curation, visualization, and writing of the original draft. **ACOA:** investigation, data curation, visualization, and writing of the original draft. **DTCN:** investigation, data curation, visualization, and writing of the original draft. **ECS:** investigation, data curation, visualization, and writing of the original draft. **GLASF:** investigation, data curation, visualization,

and writing of the original draft. **JLVS:** conceptualization, formal analysis, project administration, supervision, and writing (review and editing). All authors approved the final version.

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Anais da Faculdade de Medicina de Olinda
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afmo.emnuvens.com.br ISSN: 2674-8487 Experience Report

Strategies to engage the male population in actions promoting male health: an experience report

Estratégia de adesão do público masculino às ações voltadas para a saúde do homem: relato de experiência

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Abstract

The male population is more likely to develop diseases, particularly chronic and severe conditions, leading to elevated mortality rates. This susceptibility occurs due to a cultural tendency to neglect healthcare services, resulting in delayed diagnoses and irreversible complications. The National Policy for Integrated Attention to Men's Health (PNAISH) was created to overcome this challenge. This study focuses on an action implemented at a basic health unit in Pernambuco to engage the male population in healthcare services. This action may reduce the male morbidity and mortality related to their health in the long term.

Keywords: Men's health; Primary health care; Health policy.

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Resumo

A população masculina é mais propensa a doenças, principalmente crônicas e graves, com maiores taxas de mortalidade. Isso decorre de uma cultura marcada pela falta do hábito de procurar pelo atendimento médico, resultando em diagnósticos tardios e complicações irreparáveis. Assim, para superar esse quadro, foi estabelecida a Política Nacional de Atenção Integrada à Saúde do Homem (PNAISH). Nesse contexto, o presente trabalho relata uma experiência em uma Unidade Básica de Saúde, localizada em um município Pernambucano, que utilizou estratégias para aproximar a população masculina dos serviços de saúde. Ao passo que, em longo prazo, pode ter como resultado a redução da morbimortalidade masculina por causas previsíveis associadas à saúde do homem.

Palavras-Chave: Saúde do homem; Atenção primária à saúde; Política de saúde.

INTRODUCTION

In 2008, the Federal Government introduced the National Policy for Comprehensive Attention to Men's Health (PNAISH) to address and prevent health issues of the male population. This policy was created because men have low adherence to preventive and health-promoting actions, increasing costs within the Unified Health System (SUS). This scenario occurs due to delayed access to specialized tertiary care, increasing complications and morbidities[1,2].

The PNAISH has been structured around five themes: access and reception, sexual and reproductive health, paternity and care, prevalent diseases in the male population, and violence and accident prevention[1,3]. These themes aim to increase access to health services for the Brazilian male population (20 to 59 years old).

The significant challenge of the male population to access health services has been recognized in this policy. The challenge is often based on prejudice, sexism, a culture of misinformation, and reluctance to embrace healthcare practices[2]. Additionally, men predominantly undertake extensive and demanding work activities, resulting in a mismatch between free time and the operating hours of the basic health unit (BHU). This mismatch reduces access to health services[4]. The health of the male population must be understood as a common and multifaceted entity since it encompasses aspects that may change according to age, nationality, race, social class, and sexual orientation[5]. Other factors, such as place of residence (i.e., rural or urban), incarceration status, physical and mental disability, and non-hegemonic gender identity, also influence the male health.[5;6].

Given the substantial male population within the BHU area, measures are needed to mitigate the spread of diseases associated with male health, whether chronic or acute. These measures must focus on diagnosing and treating men already affected, and identifying those more susceptible to developing diseases. Comprehensive population-wide strategies are needed to prevent the emergence of these diseases. Moreover, male health issues are a significant public

health challenge in Brazil that contributes to a high rate of mortality compared with women.

OBJECTIVE

To describe a strategy implemented in a BHU of Pernambuco to engage the male population and enhance their adherence to initiatives aimed at their health.

METHODS

This cross-sectional descriptive study reported the experience of implementing the PNAISH using a strategy to engage the male population from April to November 2022. Participants were adolescents, young adults, and older adults who lived in the BHU area in a municipality from Pernambuco.

RESULTS

Primary care interventions, particularly health education strategies, were pivotal for reducing diseases related to male health in the community.

Professionals of the BHU in Paulista, Pernambuco, reported that men were not the most proactive attendees; however, they were inclined to seek consultations during advanced stages of diseases or when confronted with sexually transmitted infections.

Thus, medical students assigned to the BHU proposed a strategy focused on caring for and monitoring couples living in the area. They presented the potential benefits of incorporating this practice into primary care, and the multidisciplinary professional team welcomed the idea.

Adjustments to existing measures (i.e., popular health education initiatives) were recommended. The aim was to challenge the idea that men do not need to seek health services proactively and to optimize methods for engaging them. This strategy was crucial in Paulista, a city that significantly contributes to the population of the Metropolitan Region of Recife in Pernambuco.

CONCLUSION

The implemented strategy increased engagement and access, and improved the response of men to health services and programs. In addition, registrations of the male population in the BHU information system significantly increased in the covered area. The strategy also facilitated health promotion and disease prevention efforts, such as the widespread distribution of condoms to the male population, especially those whose spouses are accompanied in the service.

This experience enhanced the overall access to quality healthcare for the male population served by the BHU, operating within a gender-inclusive framework and aligning with the principles of comprehensive healthcare.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

JANN: investigation, data curation, visualization, and writing of the original draft. **LFMN:** investigation, data curation, visualization, and writing of the original draft. **MVFF:** investigation, data curation, visualization, and writing of the original draft**. MFO:** investigation, data curation, visualization, and writing of the original draft. **NGLT:** investigation, data curation, visualization, and writing of the original draft. **RRLGP:** conceptualization, formal analysis, project administration, supervision, writing (review and editing). All authors approved the final version.

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afmo.emnuvens.com.br ISSN: 2674-8487 Critical Review

Critical Review

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Cicurel R, Nicolelis M. The relativistic brain: how it works and why it cannot be simulated by a Turing machine. São Paulo: Kios Press, 2015.

Ronald Cicurel (June 3, 1945, Cairo) is a mathematician, philosopher, and writer known for being one of the founders of the Blue Brain project. This project aimed to create a synthetic brain using reverse engineering. Ronald has been a professor at the EPFL IT laboratory since 2006 and the coordinator of the International Institute of Neurosciences in Natal, Brazil, since 2010.

Miguel Angelo Laporta Nicolelis (March 7, 1961, São Paulo) is a Brazilian scientist and physician, noted as one of the top twenty scientists in his field of research by Scientific American. He is the first native Brazilian to have an article published on the cover of Science, one of the main journals in general science. Furthermore, the scientist is an emeritus professor at Duke University (Durham, USA) and studies organs, systems, and their interactions. His area of activity throughout his career, which initially was to understand a “brain code”, is connecting the functions of the human brain to electronic machinery. Nicolelis and his allied researchers were responsible for developing a system that allows the formatting of robotic artifacts controlled by the brain, including in several areas of the globe at the same time, through what the neuroscientist called “Brainet”, a cerebral translation that connects the actions of peers in decision making.

The monograph brings concepts from previous books by

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Cicurel and Nicolelis: “The Computer Will Not Digest The Brain” and “Much Beyond Our Self”, respectively. In this context, the authors highlighted that the language used will be understandable for laypeople of health academics because they need to understand the two theses presented in the monograph. Primarily, the reader is introduced to a new theory of the functioning of complex brains (i.e., those from Homo sapiens) called Relativistic Brain Theory (RCT) which is partially included in the title of the work. This theory is discussed in the first two chapters, being proposed as a modern neurophysiological model that focuses on explaining how the range of complex neural functions that integrate sensations, such as pain to the sense of conscious self, is generated by the immense networks of cells in the brain. While this impressive dynamic is discussed in the book, the monograph is interesting for professionals and other students in the health field because it exposes how these extensive neural networks can confer pathological mental states, creating a spectrum of neurological and psychiatric illnesses. The RCT requests extensive experimental investigations, which can be refuted or reaffirmed. According to the authors, the RCT offers a radical paradigm in understanding the brain of animals in general and human beings.

In addition to this theory, which brings a neuroscientific tool scope for understanding general neurological aspects, the work evidences its basic proposition: the series of postulates that refute the hypothesis, in English, of computationalism, which tries to relate complex brains to digital computers (i.e., Turing machines). Turing was a British mathematician considered the father of computational science and considered a Nazi code-breaking hero during the Second World War.

The propositions of computationalism became a source of inspiration for many science fiction and futurist works but were questioned by the concepts of Nicolelis. Both propose that complex nervous systems translate information using a dynamic one-component hybrid action (digital and analog). The analog part involves various neural electromagnetic fields, which cannot have their generation and repercussions considered computable (i.e., treated programmatically or mathematically), with any proposal to simulate the full complexity of the animal brain being limited in a Turing device or its derivative digital models.

In summary, the monograph is elegant, demonstrative, and accessible in language to the public, also bringing arguments that increase interest in the neurobiological field, which provided revolutionary experiments, such as Nicolelis’ brain-machine interface and character investigations of Cicurel mathematician. The authors explain that they do not intend to reduce the impact of Turing machines and artificial intelligence as promoters of human progress. However, they reinforce the appreciation of the brain at the level of a complex evolutionary block that will be far from reproduced by sophisticated and electronic machine versions.