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SUMMARY

Letter to the editor

CARTA AO EDITOR
Dr. Inácio de Barros Melo Neto

Editorial

A look at new epistemological possibilities and graduation in Medicine
UM OLHAR PARA NOVAS POSSIBILIDADES EPISTEMOLÓGICAS E GRADUAÇÃO EM MEDICINA
Paulo Sávio A. de Goes

Original Articles

Hospital Productivity and Impact of Quality Management in Two University Hospitals of the Brazilian National Health System
PRODUTIVIDADE HOSPITALAR E IMPACTO DA GESTÃO DA QUALIDADE EM DOIS HOSPITAIS DE ENSINO DO SISTEMA NACIONAL DE SAÚDE BRASILEIRO
Luiz Henrique de Souza Neto, Bruno Chaves Morone-Pinto, Leslie Clifford Noronha Araújo, Flávia Cristina Morone Pinto

Toxicological screening of *Pimenta pseudocaryophyllum* (Gomes) L.R. Landrum extracts using *Artemia salina* Bioassay
TOXICOLOGICAL SCREENING OF EXTRACTS FROM PIMENTA PSEUDOCARYOPHYLLUM *(GOMES) L.R. LANDRUM ON* ARTEMIA SALINA *LEACH*.
Daniela de A. Menezes, Artur D. N. da Silva, Gabriela S. Dantas, Helder Carvalho S. L. Silva, Ricardo P. Lyra, Bruno L. de Lima, Fabiana L. Silva, Paulo R. Hrihorowitsch Moreno, Thárcia K. B. de Oliveira, Joelmir L. V. Silva

Incidence and morphometry of the oval forame patent in corpse
INCIDÊNCIA E MORFOMETRIA DO FORAME OVAL PATENTE EM CADÁVERES HUMANOS
Fernando A. Pacífico, Esmaella N. L. Sabino, Gabriela R. Silva, Laís dos S. Ximenes, Gilberto C. Sousa Filho, Eduardo L. Paixão

Sperm Characteristics Of Men At Different Ages
Andy Petroianu, Marco Antônio Barreto de Melo, Luciana Magalhães de Almeida

Case Reports

Multiple anatomical variations in the branches of the aortic arch and middle cerebral artery: an angiographic study
MÚLTIPLAS VARIAÇÕES ANATÔMICAS NOS RAMOS DO ARCO AÓRTICO E ARTÉRIA CEREBRAL MÉDIA: UM ESTUDO ANGIOGRÁFICO
Paula M. Barbosa Lima, Fernando A. Pacífico, Clarissa A. Passos, Felipe D. S. Fonsêca, Marcos A. B. Silva

Spontaneous dissection of the right coronary artery in a patient with acute coronary syndrome
DISSECÇÃO ESPONTÂNEA DA ARTÉRIA CORONÁRIA DIREITA EM PACIENTE COM SÍNDROME CORONARIANA AGUDA
Arnórbio Mariz, José Breno Souza Filho, Érika T. Lopes, Maria Rafaela R. Mello, Carolline A. Mariz

The effect of lifestyle modification in a patient with severe hypertriglyceridemia
EFEITO DA MUDANÇA DO ESTILO DE VIDA EM PACIENTES COM HIPERTRIGLICERIDEMIA GRAVE
Carolline A. Mariz, Arnórbio Mariz, Adson Y. Holanda, Elisabeth U. Melo, Érika T. Lopes

Absorption of a twin pregnancy: a case report
ABSORÇÃO DE GEMELAR NA GRAVIDEZ: UM RELATO DE CASO
Ana Paula P. F. Alves, Maria Eduarda C. Salgueira, Suzane M. S. Sá, Wiary S. M. Mendes, Kassandra F. P. Oliveira

Secondary hypertension to pheochromocytoma: a case report
HIPERTENSÃO SECUNDÁRIA AO FEOCROMOCITOMA: RELATO DE CASO
Matheus T. Paffer, Natalia C. F. Albuquerque, Pedro T. Paffer, Silvio H. Paffer Filho

Disagreement between the relationship of the BI-RADS® US 4B finding with benign outcome in a patient with suspected breast cancer: a case report
DESACORDO ENTRE A RELAÇÃO DO ACHADO BI-RADS® US 4B COM DESFECHO BENIGNO EM PACIENTE COM SUSPEITA DE CÂNCER DE MAMA: RELATO DE CASO
Esmaella Nahama Lacerda Sabino, Petrus Augusto Dornelas Câmara, Adriana Caroso Torrisi, Carolina Carlsson Delambert Berenstein

Laparoscopic partial nephrectomy for T2b tumor in a patient with a solitary kidney: a case report
NEFRECTOMIA PARCIAL LAPAROSCÓPICA PARA TUMOR T2B EM PACIENTE COM RIM ÚNICO: RELATO DE CASO
Antonio Cesar Cruz, Guilherme Lima, Isabella Pinheiro Litvin, Paulo Eugênio M. A. Costa

Review Articles

Exogenous melatonin and its metabolic effects: a literature review
MELATONINA EXÓGENA E SEUS EFEITOS METABÓLICOS: REVISÃO DA LITERATURA
Paula M. Barbosa Lima, Fernando A. Pacífico, Clarissa A. Passos, Felipe D. S. Fonsêca, Marcos A. B. Silva

Perception of users from the Unified Health System regarding the presence of medical students in school clinics: a review article
PERCEPÇÃO DOS USUÁRIOS DO SISTEMA ÚNICO DE SAÚDE QUANTO À PRESENÇA DE ACADÊMICOS DE MEDICINA NAS CLÍNICAS-ESCOLA: REVISÃO BIBLIOGRÁFICA
Petrus A. D. Câmara, Paulo E. M. A. Costa, Iago H. P. Bezerra, Luanna G. V. Leite, Andreza M. Silva

Instructions for authors

LETTER TO THE EDITOR

CARTA AO EDITOR

Dr. Inácio de Barros Melo Neto

General director at the Faculdade de Medicina de Olinda

Dear Editor,

I would like to congratulate the editorial board and collaborators of this edition of the journal Anais da Faculdade de Medicina de Olinda for their availability and effort in producing knowledge of high quality, as expressed through various types of academic production.

The Faculdade de Medicina de Olinda continues its trajectory as an institution with a clear purpose of becoming a reference for its values and commitment to excellent medical education, with strong investment in its structure, the training of its students, and the qualification of its teaching staff.

With this thought, the Faculdade de Medicina de Olinda recently launched a new stage of its institutional development plan, with extension notices, launching the Scientific Initiation Institutional Development Program (PRODIIC), and with accessibility and internationalization strategies, which will enable gains for our students in exercising a more humanized profession and an even more diverse and inclusive institution.

Like the Olinda lighthouse that guides helmspersons to their navigation destinations, the Faculdade de Medicina de Olinda is a beacon of knowledge for young people who have chosen Medicine as their career. For them, it is essential to share our values, among which ethics and social responsibility must be paramount in ensuring the future of society.

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EDITORIAL

EDITORIAL

Prof. Paulo Sávio Angeiras de Goes

Editor-in-Chief, PhD

A look at new epistemological possibilities and graduation in Medicine

In another edition of the Anais da Faculdade de Medicina de Olinda, we have the opportunity to show the production of more enthusiastic students and teachers every day; not just with an anchored training on scientific bases, but also committed to the ethical and human values of physicians; that is, the training of a new professional for a new time.

In fact, training based on the National Curricular Guidelines proposed for the medical course must be highlighted, which goes beyond a debate that seems disconnected from reality or the whim of a few, ending up looking like a dispute between a reductionist perspective on the traditional and the new. On the contrary, the contextualization between what is taught or researched and the linking of this way of seeing the world to available technologies addresses the most important debate since the 3rd Industrial Revolution, with important repercussions on the way people live, love, and, naturally, how they prepare for entry into the world of work.

The realization that the traditional way of doing science and training for a profession has been exhausted is not a new one. Signs of this exhaustion were evident at least two decades before the beginning of this century, when renowned universities worldwide and governments of developed countries commissioned prominent thinkers to propose alternatives for training in the new century. Even in Brazil, avant-garde thinkers drew attention to the need for a new training model, especially in higher education, such as Darcy Ribeiro and Anísio Teixeira.

However, the development of higher education is strongly influenced by scientific knowledge, which seeks to improve technologies or make their use more accessible to humanity. Therefore, the crisis deepens at this point, as science would reach the beginning of this century without providing answers to serious societal issues, such as the eradication of hunger (despite large parts of the globe dedicated to cultivation), the climate and environmental issue, and in medicine, without an effective response to so-called neglected diseases.

The result of an immense, decontextualized, and compartmentalized scientific production, leading scientists to reflect on the purpose of their experiments, making a broad discussion of integrated and interdisciplinary research agendas imperative, both internationally and nationally, by non-governmental and governmental organizations.

However, while contemporary science did not rethink the profound paradigmatic crisis in which it was inserted, higher education training was in agony. It is Morin who diagnoses "the student is taught everything at school, except how to think", and by formalizing his theory of complex thinking, he highlights the competence-based training and the great challenges of contemporary teaching, including the civic challenge (of social responsibility) and the challenge of reforming thinking; the author considers the latter as the biggest challenge.

In Medicine, it could not be different, the paradigmatic crisis represented by the ways of doing science and training, caused important and traditional institutions to sink; generate a large concentration of doctors in large urban centers, especially in developing countries, such as Brazil, that the training would focus on the major problems that make our population sick and die, with serious and negative consequences for humanity.

Thus, the Faculdade de Medicina de Olinda will seek not only to be a new faculty with yet another new Medicine course, but also to offer an innovative one. Our physicians will be able to address the disease and its consequences from both a scientific and a patient-centered perspective by seeking to incorporate therapeutic conduct into the patient's daily life, including how they live and interact with society. Therefore, nothing is removed from the scientific training necessary for physicians, but the qualities are added to become a human physician: one who feels like people and lives like people. Society will know how to recognize him and, even more, reward him for the great benefits he will bring to society.

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HOSPITAL PRODUCTIVITY AND IMPACT OF QUALITY MANAGEMENT IN TWO UNIVERSITY HOSPITALS OF THE BRAZILIAN NATIONAL HEALTH SYSTEM

PRODUTIVIDADE HOSPITALAR E IMPACTO DA GESTÃO DA QUALIDADE EM DOIS HOSPITAIS DE ENSINO DO SISTEMA NACIONAL DE SAÚDE BRASILEIRO

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ABSTRACT

Objectives: This study aimed to evaluate the performance of two large university hospitals in the Northeast of Brazil before and after administration by the Brazilian Hospital Services Company (EBSERH), and to analyze the impact of a quality certification program implanted in one of the institutions. **Methods:** A quantitative, cross-sectional, and analytical study evaluated the performance of the institutions from January to July 2013 and 2016. **Results:** The number of hospital beds increased by 3.23% at the University Hospital of the Federal University of Pernambuco (HU/UFPE), while no change was observed at the University Hospital of the Federal University of Bahia (HU/UFBA). Regarding the human resources indicator, a significant increase in staff was observed after EBSERH administration: 60.86% at HU/UFPE and 28.22% at HU/UFBA. For mortality rates, HU/UFPE showed an increase of 60.71%, while HU/UFBA a decreased of 33.33%. **Conclusion:** Both hospitals demonstrated improved performance following implementation of EBSERH. Additionally, the implementation of a quality certification program at HU/UFBA may have contributed to its more favorable outcomes.

Keywords: Hospital administration; Efficiency; Management

RESUMO

Objetivo: O objetivo deste estudo foi avaliar o desempenho de dois grandes hospitais de ensino do Nordeste brasileiro, antes e após a gestão administrativa da Empresa Brasileira de Serviços Hospitalares (EBSERH), e analisar comparativamente o impacto de um programa de certificação de qualidade implantado em um dos hospitais. **Metódos:** Foi realizado uma pesquisa quantitativa, transversal e estudo analítico para mensurar o desempenho dessas instituições, constituído em uma avaliação de desempenho. Foi realizada de janeiro a julho, dos anos de 2013 e 2016. **Resultados:** Em relação ao Hospital das Clínicas de Pernambuco (HC/UFPE), houve um aumento de 3,23% do número de leitos de internação. No entanto, no Hospital Universitário da Bahia (HU/UFBA), não houve alterações no mesmo período. Em relação ao indicativo de recursos humanos, observou-se um aumento significativo no número de funcionários após a gestão da EBSERH: 60,86% no HC/UFPE e 28,22% no HU/UFBA. Em termos de mortalidade, o HC/UFPE apresentou um aumento de 60,71% no número de óbitos, enquanto o HU/UFBA registrou uma redução de 33,33%. **Conclusão:** O estudo mostra que o desempenho em ambos os hospitais de ensino, HC/UFPE e HU/UFBA, foi satisfatório, o que pode ser justificado pela inserção do EBSERH e também pelo programa de acreditação de gestão da qualidade, especificamente implementado no HU/UFBA.

Palavras-chave: Administração hospitalar; Eficiência; Gestão

INTRODUCTION

Hierarchization organizes the health system into levels of care, starting with primary care and referring unresolved cases to higher complexity services when appropriate[1].

One of the main challenges faced by hospitals is the length of hospital stay, which is a key quality indicator used to evaluate bed turnover and productivity by specialty. It also reflects the amount of care provided, shorter hospitalizations, and reduced healthcare costs[2]. In Brazil, the average cost of inpatient care is 100 times higher than outpatient care[3].

Due to their complexity and relevance, especially hospitals requires an evaluation of services using performance and quality indicators to monitor operational processes and support decision-making[4].

In this context, the Brazilian Hospital Services Company (EBSERH) was created in 2011 by Law No. 12,550/11 to address administration and investment needs in university hospitals and overcome challenges related to performance indicators. As a public company linked to the Ministry of Education (MEC)[5], EBSERH manages the National Program for the Restructuring of Federal University Hospitals (REHUF), established by Decree no. 7.082 of 2010[6].

The impact of this administrative shift on healthcare productivity and quality have not yet been evaluated. This study aimed to evaluate the performance of two large university hospitals in Northeastern Brazil before and after implementation of EBSERH administration.

METHODS

This study evaluated the performance of two university hospitals over two periods: January to July 2013 (212 days) and January to July 2016 (213 days).

The 2013 period was selected as it marked the contractual agreement between EBSERH and the university hospital of the Federal University of Pernambuco (HU/UFPE) and Bahia (HU/UFBA). The 2016 period was selected to enable a comparative analysis of institutional performance following the implementation of administrative management by EBSERH.

In 2009, HU/UFBA implemented the international hospital accreditation program, a quality certification model ensuring care quality and patient safety.

Data were obtained from the hospital information system (SIH) and the National Registry of Health Establishments (CNES) for both periods. The aim was to evaluate hospital bed utilization, human resource indicators, mortality rates, and the impact of EBSERH management[7].

Indicators related to bed utilization were categorized as follows: total number of active beds, hospital admission authorizations (HAA), total hospitalizations, total cost of hospitalizations, mean HAA costs, mean cost per hospitalization, total length of stay (days), and mean length of stay[7]. Box 1 details the indicators and their corresponding variables.

Box 1. Hospital performance indicators: bed utilization, human resources, and mortality and corresponding variables.

Measured dimensions	Corresponding variables
Bed utilization	- Total number of active beds Paid HAA Total hospitalizations Total cost of hospitalizations Cost of hospital services Mean HAA costs Mean cost per hospitalization Length of stay (in days)
Human resources	- Total number of staff Nurses/bed Physicians/bed Nursing technicians/bed Other professionals (number)/bed Cost of professional services
Mortality	Number of deaths

Source: Developed by the author based on Brazil (2016)[7].

Mean length of stay, hospital productivity, and hospital mortality rate were used to evaluate hospital performance. Box 2 presents the calculation basis for these indicators.

Box 2. Indicators for the evaluation of hospital performance and calculation methods.

Indicators	Acronyms	Calculation methods
Mean length of stay	ALS	Numerator: total number of patients per day during a given period Denominator: total number of discharges during the same period
Hospital productivity rate	HPR	Numerator (output): number of discharges per period Denominator (input): number of admissions per period Multiplication factor: 100
Hospital mortality rate	HMR	Numerator: Number of deaths during the period Denominator: Number of discharges during the period Multiplication factor: 100

Source: Developed by the author based on ordinance no. 1101/GM by June 12, 20028 and the work of RAMOS & MIYAKE (2010)9. Legend: ALS: mean length of stay; HPR: hospital productivity rate; HMR: hospital mortality rate.

Descriptive statistics were used to present the results. As this study used publicly available secondary data sources, submission to the research ethics committee of UFPE (CEP/CCS/UFPE) was not required.

RESULTS AND DISCUSSION

a) Bed utilization

According to MEC, 13 university hospitals operate in the Northeast region of Brazil, apart from three maternity hospitals and one pediatric hospital. EBSERH manages all of these institutions. Box 3 presents the university hospitals and their respective contract dates. The institutions selected for this study were HU/UFPE and HU/UFBA, chosen due to their location in the same geographic region and similar institutional characteristics, which made them suitable for comparative analysis.

Box 3. List of university hospitals in the Northeast region of Brazil.

No.	Universities / University hospitals (HU) (*)	FU	Contract date with EBSERH
1	Federal University of Sergipe / HU	SE	October 2013
2	Federal University of Alagoas / HU PROF. ALBERTO ANTUNES	AL	January 2014
3	Federal University of Bahia (**) / HU PROFº EDGARD SANTOS	BA	December 2013
4	Federal University of Pernambuco (**) / HOSPITAL DAS CLÍNICAS	PE	December 2013
5	Federal University of Vale do São Francisco (***) / HU DR. WASHINGTON ANTÔNIO DE BARROS	PE	January 2014
6	Federal University of Campina Grande / HU ALCIDES CARNEIRO	PB	December 2015
7	Federal University of Campina Grande (***) / HU JÚLIO MARIA BANDEIRA DE MELLO	PB	December 2015
8	Federal University of Paraíba / HU LAURO WANDERLEY	PB	December 2013
9	Federal University of Rio Grande do Norte / HU ANA BEZERRA	RN	August 2013
10	Federal University of Rio Grande do Norte / HU ONOFRE LOPES	RN	October 2013
11	Federal University of Ceará / HU WALTER CANTÍDIO	CE	November 2013
12	Federal University of Piauí / HU	PI	April 2013
13	Federal University of Maranhão / HU	MA	January 2013

Legend: FU: federative unit. (*) University maternity hospitals (03) and the Prof. Heriberto Ferreira Bezerra Pediatric Hospital were excluded from the list. (**) University hospitals included in the analysis of this study. (***) Not listed by the Ministry of Education, but included in the list of the EBSERH[10].

Data from the SIH on hospital bed utilization at HU/UFPE in 2013 included an analysis of 371 beds across clinical, surgical, day hospital, pediatric, obstetric, and complementary categories.

For HAA, total cost was BRL 7,728,150.45, corresponding to 6,841 approved HAA and effective hospitalizations. Mean length of stay was 6.8 days.

In 2016, HU/UFPE had 383 beds for all specialties. Total cost of approved HAA for this period was estimated at BRL 8,476,580.39, referring to 8,254 approved HAA and effective hospitalizations. Mean length of stay was 6.2 days.

In 2013, at HU/UFBA, a total of 272 hospital beds was recorded. An increase in the number of surgical beds was observed, from 61 in May to 72 in July. Regarding clinical specialty beds, the number increased from 92 to 100. Beds categorized under other specialties increased from 12 to 14, and day hospital beds increased from 13 to 23. No records of obstetric beds were found.

In the HAA and hospital admissions records for 2013, a total cost of BRL 7,844,147.80 was verified, corresponding to 4,561 approved HAA and effective hospitalizations. Mean cost per case was BRL 1,719.83, and length of stay was 10.1 days.

In 2016, HU/UFBA had 256 beds. Total cost of approved HAA was BRL 7,212,817.26, with 4,591 hospitalizations and mean length of stay of 7.8 days.

In the comparison from 2013 to 2016, HU/UFPE increased 3.23 beds. However, HU/UFBA did not change bed availability. Regarding approved HAA in HU/UFPE, an increase of 20.66% was registered, while HU/UFBA increased HAA and effective hospitalizations by 0.66%.

The mean costs of approved HAA and hospitalizations decreased by 9.09% at HU/UFPE and 8.65% at HU/UFBA. Notably, an increase in the provision of care was observed, reflected by the number of approved HAA and hospital admissions. However, this increase was not accompanied by a rise in

the mean expenditure, indicating a reduction in the financial resources allocated per authorization and length of stay.

For total costs of approved HAA, HU/UFPE showed an increase of 9.68%, whereas HU/UFBA decreased by 8.05%.

The mean length of stay at both HU/UFPE (-8.82%) and HU/UFBA (-22.77%) decreased between 2013 and 2016. Table 1 summarizes the data mentioned above.

Table 1. Number of hospital beds and hospital admissions, including the mean and total costs of hospital services for approved admissions, hospital discharges, and mean length of stay from January to July of 2013 and 2016.

Variables	Beds	HAA/approved hospitalizations	Mean costs of HAA (BRL)	Total costs of approved HAA (BRL)	Hospital discharges	Mean length of stay (days)
2013						
HU/UFPE	371	6,841	1,129.68	7,728,150.45	1,006	6.8
HU/UFBA	272	4,561	1,719.83	7,844,147.80	452	10.1
2016						
HU/UFPE	383	8,254	1,026.97	8,476,580.39	1,331	6.2
HU/UFBA	256	4,591	1,571.08	7,212,817.26	589	7.8
Comparison 2013 – 2016 (%)						
HU/UFPE	+3.23	+20.66	-9.09	+9.68	+32.30	-8.82
HU/UFBA	-5.88	+0.66%	-8.65	-8.05	+30.30	-22.77

Source: Brazil. Ministry of Health - CINES/SIH (National Registry of Health Facilities / Hospital Information System), 20167.
Legend: HU/UFPE: university hospital of the Federal University of Pernambuco. HU/UFBA: university hospital of the Federal University of Bahia. SH: Hospital service. HAA: hospital admission authorizations. BRL: monetary unit of Brazil.

b) Human resources management

In the human resources indicator for 2013 at HU/UFPE, the number of employees was 1,505 in January and 1,377 in July, including 817 physicians, 102 nurses, 255 nursing technicians and assistants, and 203 other professionals. Total cost of professional services was BRL 1,939,546.05.

In 2016, the number of employees at the HU/UFPE was 2,215, comprising 1,165 physicians, 219 nurses, 481 nursing technicians and assistants, and 350 other professionals (healthcare and administrative staff). Total cost of professional services was BRL 1,985,029.77, with the highest monthly expense in March (BRL 342,082.61) and the lowest in February (BRL 206,417.14.) In 2013, the total number of employees at the HU/UFPE was 1,846, including 679 physicians, 180 nurses, 563 nursing technicians and assistants, and 424 other professionals. Total cost of human resource services was BRL 1,121,439.38. In 2016, the 2,367 professionals included 800 physicians, 239 nurses, 701 nursing technicians and assistants, and 627 other professionals. Total cost of professional services over the period was BRL 1,082,201.80. In March, the expenses of BRL 194,874.55 corresponded to the highest amount recorded among the analyzed months, while the lowest was observed in January, at BRL 106,027.39. The workforce at both university hospitals included medical residents, statutory public servants, federal employees, and contracted professionals.

In human resources indicator analysis before and after the implementation of EBSERH, a significant increase in staff was observed at HC/UFPE (60.86%) and HU/UFBA (28.22%). Regarding physicians, HU/UFPE increased by 42.59%, and HU/UFBA increased by 17.82%. For nursing staff, an increase of 114.71% at HU/UFPE and 32.78% at HU/UFBA was observed.

For nursing technicians and assistants, HU/UFPE increased by 88.63% and HU/UFBA increased

by 24.51%. For other professionals, HU/UFPE increased by 72.41%, and HU/UFBA increased by 47.88%. Total costs of professional services slightly increased for HU/UFPE (+2.35%), whereas HU/UFBA experienced a negative variation (-3.50%) in salary expenses. Table 2 summarizes the information above.

Table 2. Total number of employees, physicians, nurses, nursing technicians, and other professionals relative to available beds and the cost of professional services, from January to July of 2013 and 2016.

Variables	Total employees	Physicians	Nurses	Nursing technicians and assistants	Other professionals	Available beds	Cost of professional services
2013							
HU/UFPE	1377	817	102	255	203	371	1,939,546.05
HU/UFBA	1846	679	180	563	424	272	1,121,439.38
2016							
HU/UFPE	2215	1.165	219	481	350	383	1,985,029.77
HU/UFBA	2367	800	239	701	627	256	1,082,201.80
Comparison 2013-2016 (%)							
HU/UFPE	+60.86	+42.59	+114.71	+88.63	+72.41	+3.23	+2.35
HU/UFBA	+28.22	+17.82	+32.78	+24.51	+47.88	-5.88	-3.50

Source: Brazil. Ministry of Health - CINES/SIH (national registry of health facilities/hospital information system), 20167.
Legend: HU/UFPE: university hospital of the Federal University of Pernambuco. HU/UFBA: university hospital of the Federal University of Bahia.

c) Productivity of university hospitals

In 2013, 157 deaths were recorded at HU/UFPE, with the highest incidence in March and May (28 deaths each) and the lowest in April (17 deaths), resulting in a hospital mortality rate of 2.29. In 2016, 202 deaths were recorded during the study period at the same hospital. An increase was observed for number of deaths (+30.32%) and mortality rate (+43.67%).

At HU/UFBA, 150 deaths were recorded in 2013, corresponding to a mortality rate of 3.29. In 2016, 90 deaths were observed, with the highest number in April (20 deaths) and the lowest in January (8 deaths), resulting in a mortality rate of 1.96. Overall, the total number of deaths decreased by 40.00% and the mortality rate decreased by 40.43%. Table 3 summarizes these results.

Table 3. Total number of deaths, highest and lowest monthly values, hospital mortality rate, and hospital productivity rate from January to July of 2013 and 2016.

Variables	Month ≥ number of deaths	Month ≤ number of deaths	Total deaths	Hospital mortality rate	Hospital productivity rate	Mean length of stay
2013						
HU/UFPE	28	17	157	2.29	14.71	6.8
HU/UFBA	30	8	150	3.29	9.90	10.1
2016						
HU/UFPE	45	20	202	3.29	16.13	6.2
HU/UFBA	20	8	90	1.96	12.82	7.8
Comparison 2013 – 2016 (%)						
HU/UFPE	+60.71	+17.65	+30.32	+43.67	+9.65	-8.82
HU/UFBA	-33.33	0.00	-40.00	-40.43	+29.49	-22.77

Source: Brazil. Ministry of Health - CINES/SIH (National Registry of Health Facilities/Hospital Information System), 20167.
Legend: HU/UFPE: university hospital of the Federal University of Pernambuco. HU/UFBA: university hospital of the Federal University of Bahia.

The mean length of stay decreased at HU/UFPE (-8.82%), with a more significant reduction at HU/UFBA (-22.77%). The productivity rate increased at both HU/UFPE (9.65%) and HU/UFBA (29.49%).

Many factors may influence death and mortality rate, including aspects related to therapeutic care for patients, such as health equipment, qualified human resources, and the clinical complexity of the patients11.

By comparing hospitals, before and after administration by EBSERH and the implementation of a quality certification program at HU/UFBA, the perspective is to examine progress, performance, and potential weaknesses. Notably, in 2008, 1,124 hospital beds were deactivated nationwide in teaching institutions due to personnel shortages[12].

The implementation of hospital accreditation programs is of great importance, leading to reduced costs and morbidity and mortality rates. Quality certification ensures planning and efficiency of care services and identify potential weaknesses in work processes that affect treatments provided to patients13.

Regarding human resources, the HU/UFPE showed significant performance, with all health professional categories presenting positive growth, alongside increases in bed capacity and service costs, likely due to administration by EBSERH.

The literature supports this finding, noting that two government measures were proposed to mitigate the human resource shortage in university hospitals; the first was implementing of the compensation for additional hospital shifts, and the second conducting public examinations for staff hiring via EBSERH[14].

However, to mitigate issues in shift coverage due to insufficient staffing, the additional compensation failed to effectively resolve the human resource deficit in university hospitals. This measure did not adequately address the workforce shortages in these facilities.

Although both universities share similar management structures, each institution has unique characteristics that influence outcomes. These include differences in hospital infrastructure, which affect beds capacity and admissions, and organizational management and work processes tailored to epidemiological demands, such as prevalent morbidities and causes of mortality, which can lead to different final and productivity results.

Through REHUF, several measures were implemented, including physical and technological restructuring of facilities with modernization of technological equipment; revision of network financing with progressive budget increases for institutions; improvement of management processes; recovery of hospital human resources; and enhancement of hospital activities linked to teaching, research, extension, and healthcare services, all based on Brazilian population projections[15].

CONCLUSION

As positive aspects, the indicators related to

bed utilization show that HU/UFPE increased in the overall number of beds, differing from HU/UFBA that maintained a stable bed count. As for human resources, both hospitals reported an increase in their workforce.

Regarding deaths and mortality rate, HU/UFBA showed favorable results, with reductions in both indicators, unlike HU/UFPE, where increases were observed along with funding issues related to HAA payments. These differences are likely due to the implementation of accreditation programs exclusively at HU/UFBA.

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ORIGINAL ARTICLE

TOXICOLOGICAL SCREENING OF *PIMENTA PSEUDOCARYOPHYLLUM* (GOMES) L.R. LANDRUM EXTRACTS USING *ARTEMIA SALINA* BIOASSAY

TRIAGEM TOXICOLÓGICA DE EXTRATOS DE PIMENTA PSEUDOCARYOPHYLLUM *(GOMES) L.R. LANDRUM FRENTE À* ARTEMIA SALINA *LEACH*

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ABSTRACT

Objectives: To evaluate and compare the acute toxicity of leaf (Ppf) and stem (Ppc) extracts of *Pimenta pseudocaryophyllum* in *Artemia salina*. **Methods:** The Ppf and Ppc extracts were tested at concentrations of 1, 10, 100, and 1000 µg/mL in acute toxicity assays using the microcrustacean Artemia salina. Nauplii were incubated for 24 and 48 hours, and all experiments were performed in triplicate. Nauplii mortality was recorded, and LC_{50} values were calculated using nonlinear regression analysis. **Results:** The Ppc extract exhibited moderate toxicity only after 48h (LC_{50} = 140.2 ± 76.7 µg/mL). In contrast, the Ppf extract showed moderate toxicity at 24 hour (LC_{50} = 372.0 ± 58.1 µg/mL) and high toxicity at 48 hours (LC_{50} = 0.8 ± 0.1 µg/mL). **Conclusion:** Both stem and leaves of P. pseudocaryophyllus contain bioactive metabolites that induce toxicity in A. salina, which are likely different compounds or present at higher concentrations in the leaves.

Keywords: Medicinal plant; Vegetal extract; Toxicity

RESUMO

Objetivo: verificar e comparar a toxicidade aguda de extratos das folhas (Ppf) e do caule (Ppc) de *Pimenta pseudocaryophyllum* em *Artemia salina*. **Métodos:** Os extratos Ppf e Ppc, nas concentrações de 1, 10, 100 e 1000 µg/ mL, foram utilizados nos ensaios de toxicidade aguda utilizando o microcrustáceo Artemia salina, incubados por um período de 24 e 48 horas, realizados em triplicata. O número de náuplios mortos foram quantificados e a CL_{50} foram calculadas por regressão não linear. **Resultados:** o extrato Ppc apresentou toxicidade apenas em 48hs (CL_{50} = 140,2 ± 76,7 µg/mL), considerada moderada. Já o extrato Ppf foi tóxico tanto na exposição por 24hs (CL_{50} = 372,0 ± 58,1 µg/mL), quanto por 48hs (CL_{50} = 0,8 ± 0,1 µg/mL), apresentando toxicidade moderada e alta, respectivamente. **Conclusão:** caule e folhas de P. pseudocaryophyllum possuem metabólitos ativos que levam toxicidade a Artemia salina, que provavelmente são substâncias diferentes ou estão mais concentrados nas folhas.

Palavras-chave: Planta medicinal; Extrato vegetal; Toxicidade

INTRODUCTION

In developing countries,traditional medicine and medicinal plants are commonly used for health maintenance[1].

According to the toxic-pharmacological information system, poisoning from medicinal plants ranks as the second leading cause of intoxication-related deaths in humans. Several contributing factors include lack of knowledge about cultivation, misidentification of plant species, adverse reactions, drug interactions, and inappropriate dosage or frequency of herbal medicine use[2].

In Brazil, the most recent regulatory frame-

work to guide and strengthen health initiatives is the National Policy on Integrative and Complementary Practices of the Unified Health System (SUS)[3], which initially encompassed medicinal plants and herbal medicine, homeopathy, traditional Chinese medicine/acupuncture, and anthroposophical medicine. Additionally, the National Policy on Medicinal Plants and Regulation of Herbal Medicines was established[4].

The Myrtaceae family includes 121 genera and between 3,800 and 5,800 species of woody shrubs and trees, predominantly found in tropical and subtropical regions worldwide[5]. In Brazil, this family comprises around 23 genera and 1,000 species[6]. Among them is *Pimenta pseudocaryophyllum* (Gomes) L.R. Landrum, commonly known as "*pau-cravo*," "*craveiro-do-mato*," "*louro-cravo*," or "*chá-de-bugre*." Traditionally, leaf infusions of this species are used as tranquilizers, digestive regulators, and to relieve flu symptoms[7]. Studies identified that leaves of *P. pseudocaryophyllum* contain polyphenolic compounds, such as tannins and flavonoids[8, 9], and an oil rich in phenylpropanoids[10, 11]. Many biological activities have been reported for this species, including antioxidant[12, 13], anxiolytic[14] antifungal[15, 16], antidepressant[9], anti-inflammatory and anti-hyperuricemic[17], insecticidal[18], and antimicrobial effects[19, 20]. Despite these properties, no reports of toxicity have been found.

The lack of studies on the toxicity of *P. pseudocaryophyllum* prompted the present investigation, which aimed to evaluate and compare the acute toxicity of leaf (Ppf) and stem (Ppc) extracts of P. pseudocaryophyllum in *Artemia salina*.

MATERIALS AND METHODS

Leaves and stems of *P. pseudocaryophyllum* were macerated in 95% ethanol, and the extracts were obtained after solvent removal using a rotary evaporator. The extracts were provided by the Institute of Chemistry at the University of São Paulo (USP). The extracts used in the assays were solubilized in 0.1% Cremophor and diluted in distilled water to a concentration of 2.5 mg/mL. During the experiments, serial dilutions were performed to achieve the desired concentrations.

Acute toxicity was determined using the A. salina bioassay[21]. A total of 0.3 g of A. salina cysts was maintained in artificial seawater and incubated for 24 – 36 hours under artificial light at 22 °C. After hatching, ten nauplii were transferred to test tubes containing extract solutions (1, 10, 100, and 1000 µg/mL) and a saline control. After 24 and 48 hours of incubation, the number of surviving and dead nauplii was recorded. Nauplii were considered dead if they exhibited no active movement within approximately 20 seconds of observation. The median lethal concentration (LC50) for each extract was determined by nonlinear regression analysis of the number of viable nauplii at each concentration. All assays were performed in triplicate.

All analyses were performed using GraphPad Prism. Results were expressed as mean ± standard error of the mean (M ± SEM) and statistically analyzed with Student's t-test, with $p < 0.05$ considered as significant.

RESULTS AND DISCUSSION

To evaluate potential toxic activities of plant-derived products, bioassays using the microcrustacean A. salina are widely used for screening and therapeutic safety. Its ease of maintenance under laboratory conditions and broad geographic distribution make it a common organism in toxicity assays[22,23]. The lack of cytotoxicity in this model suggests that the plant extract is well tolerated by biological systems.

The Ppc extract did not reduce A. salina viability at any tested concentration after 24 hours of incubation, indicating no acute toxicity at this timepoint (Figure 1A). However, after 48 hours of incubation (Figure 1B), the Ppc extract was able to reduce viability, presenting an LC50 of 140.2 ± 76.7 µg/mL, which corresponds to moderate toxicity (100 < LC50 ≤ 500 µg/mL)[21]. These findings suggest that stem-derived metabolites may not be efficiently metabolized by A. salina, leading to toxicity upon prolonged exposure.

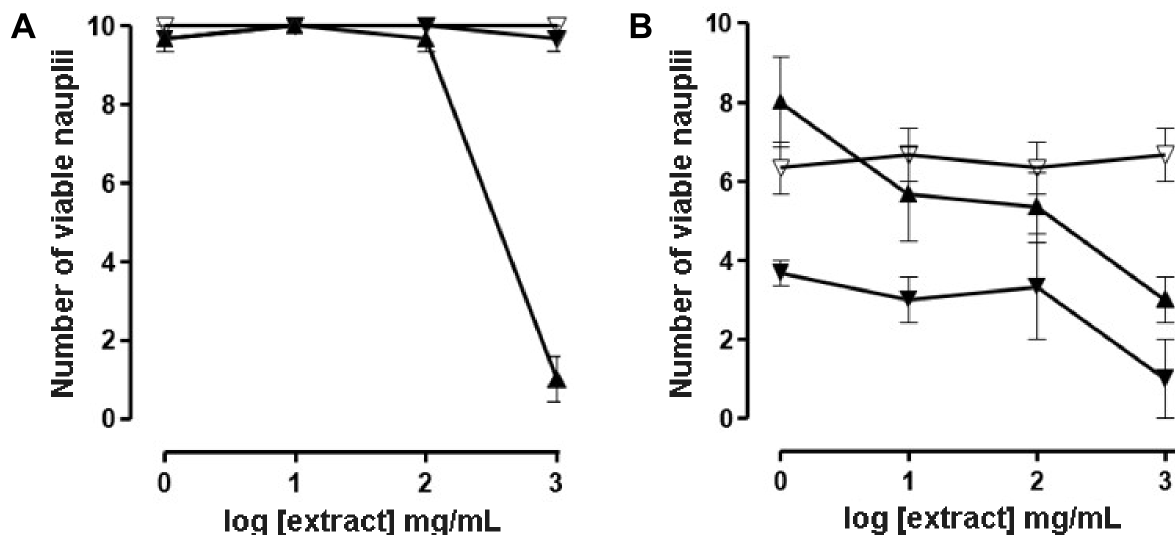

Figure 1. *A. salina* viability in the absence (▽) or presence of Ppc (▲) and Ppf (▲) extracts after 24 h (A) or 48 h (B) of incubation.

In contrast, the Ppf extract exhibited toxicity at both 24 and 48 hours (Figures 1A and 1B), with significantly greater lethality observed at 48h. This was confirmed by a significantly lower LC50 value ($p < 0.01$) at 48 hours compared to 24 hours (Table 1), indicating high toxicity (LC50 < 100 μg/mL). The observed cytotoxicity of the Ppf extract supports its potential for further investigation in cytotoxic studies[24]. These findings suggest that the leaves of *P. pseudocaryophyllus* also contain bioactive metabolites that are toxic to *A. salina*, which may differ from those found in the stem or may be present at higher concentrations in the leaves. This is consistent with previously reported insecticidal[18] and antimicrobial activities[19-20], reinforcing the biological relevance of its secondary metabolites.

Table 1. LC_{50} values of Ppc and Ppf extracts using *A. salina*.

Incubation period	LC_{50} (μg/mL)	
	Ppc	Ppf
24h	n.d.	372.0 ± 58.1
48h	140.2 ± 76.7*	0.8 ± 0.1**

n.d. (not determined). Student's t-test, *p < 0.05 (Ppc vs. Ppf); **p < 0.01 (Ppf 24 h vs. 48 h).

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ORIGINAL ARTICLE

INCIDENCE AND MORPHOMETRIC ANALYSIS OF PATENT FORAMEN OVALE IN HUMAN CADAVERS

INCIDÊNCIA E MORFOMETRIA DO FORAME OVAL PATENTE EM CADÁVERES HUMANOS

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ABSTRACT

Objective: Considering the influence of the diagnostic method and their accuracy in estimating the patent foramen ovale (PFO) incidence, this study aimed to investigate the incidence and morphometry of PFO in human cadaveric hearts. **Methods:** Ninety human hearts were randomly selected from the cadaveric specimen collection of the Department of Anatomy of the Federal University of Pernambuco. Inclusion criteria comprised human hearts with dissected right and left atria that allowed visualization of the internal structures and an intact interatrial septum (without dissection). Hearts with removed atria exposing the valvular plane or those without dissection were excluded. The study was carried out in three phases: (1) screening and selection of suitable human hearts; (2) investigation of the presence of PFO; and (3) morphometric analysis of PFO. A total of 40 cadaveric human hearts were analyzed for PFO incidence. Morphometric parameters analyzed comprised the interatrial septum, oval fossa, and limb, and the presence or absence of PFO was determined from right and left atrial perspectives. Morphometric parameters of PFO (vertical and horizontal diameters) were obtained using a digital caliper. **Results:** PFO was registered in six out of 40 human cadaveric hearts (incidence of 15%). The maximum potential diameter of the PFO ranged from 1 to 5 mm, with a mean of 3.5 mm. In addition, one heart presented two PFO. **Conclusion:** This study showed a 15% PFO incidence, with a mean of 3.5 mm of maximum potential diameter.

Keywords: Anatomy; Cadaver; Cardiology; Surgery; Foramen Ovale

RESUMO

Objetivo: Investigar a incidência e morfometria do forame oval patente (FOP) em corações humanos cadavéricos, sabendo que o método e a acuidade do exame diagnóstico interferem na estimativa da incidência do FOP. **Métodos:** Noventa corações humanos foram selecionados da coleção de partes de cadáveres do Departamento de Anatomia da Universidade Federal de Pernambuco. Incluídos no estudo estavam corações humanos que apresentavam os átrios direito e esquerdo dissecados para visualização das estruturas internas, bem como o septo interatrial intacto (sem dissecção). Corações cujos átrios foram removidos para visualização do plano valvar ou os átrios, não foram dissecados, foram excluídos. O estudo foi dividido em três etapas, a saber: (1) triagem e seleção de corações humanos; (2) investigação da presença de FOP em corações humanos selecionados; e (3) morfometria do FOP. Após a triagem, 40 corações humanos cadavéricos foram selecionados para estudar a incidência e a morfometria do FOP. Em cada coração humano cadavérico, o septo interatrial, a fossa oval e seu limbo foram analisados, e a presença ou ausência do FOP pelo átrio direito e pelo átrio esquerdo. Para realizar a morfometria, foi utilizado um paquímetro digital e medidos os diâmetros vertical e horizontal do FOP. **Resultados:** Dos 40 corações humanos selecionados, apenas seis apresentavam o FOP, indicando uma incidência de 15%. O FOP variou de 1 a 5 mm no diâmetro potencial máximo (média = 3,5 mm). Além disso, em um dos corações foi observada a existência de dois forames ovais. **Conclusão:** Com base nos resultados, foi observada uma incidência de 15% do FOP, com uma média de 3,5 mm de diâmetro potencial máximo.

Palavras-chave: Anatomia; Cadáver; Cardiologia; Cirurgia; Forame Oval

INTRODUCTION

The foramen ovale is a critical embryological structure for fetal survival. It is formed by the overlapping free edges of the primum and secundum septa, creating a virtual opening that allows blood to pass from the right to the left atrium[1-3]. The foramen closes after birth because it is no longer required.

With the expansion of lungs, pulmonary venous return to the left atrium increases, leading the primum and secundum septa to adhere, and to the closure of the foramen ovale[1]. When closure fails, a patent foramen ovale (PFO) persists, allowing right-to-left interatrial blood flow.

In some cases, primum and secundum septa may fail to adhere, forming a tunnel that allows continuous interatrial shunting (including at rest), which may be classified as high-risk PFO[2].

In 1877, the German pathologist Cohnheim described the presence of a foramen ovale during the autopsy of a young woman who died from a cerebrovascular accident (CVA). He hypothesized that the cause was embolic passage through the foramen, representing the first documentation of paradoxical embolism[3]. Subsequent studies established the association between paradoxical embolism and atrial septal defects[4,5].

PFO occurs in 25% to 30% of the general population and is benign in most cases. However, it has also been linked with cerebral thromboembolic events and migraine with aura, some of which are classified as cryptogenic due to the difficulty in identifying an embolic source[5]. One proposed mechanism of embolism in PFO is thrombus formation within the foramen itself, resulting from blood stasis under low-pressure gradients between atria during certain phases of the cardiac cycle[3,5].

The diagnostic method of choice for confirming PFO is transesophageal echocardiography, which provides high sensitivity and enables visualization of cardiac regions inaccessible via the transthoracic approach. Color Doppler with saline contrast also allows direct visualization and documentation of right-to-left shunting[6]. Another confirmatory method is transcranial doppler[3,7], which detects microbubbles in the cerebral circulation after intravenous injection of saline contrast[3,7]. The optimal therapeutic approach for patients with PFO and cerebrovascular events remains under discussion.

Several case-series studies suggest that percutaneous closure may be more effective than medical therapy for the secondary prevention of recurrent cerebrovascular events in patients with ischemic CVA or transient ischemic attack related to PFO[2].

Several devices have been developed to solve PFO, and high-risk PFO should be identified and assessed on a case-by-case basis. Percutaneous closure of PFO is currently performed in most hemodynamic laboratories worldwide, and has been demonstrated to be safe, effective, and reproducible, with excellent outcomes largely attributable to improved prosthetic devices technology[1,3].

Considering the influence of the diagnostic method and their accuracy in estimating PFO incidence, this study aimed to investigate the incidence and morphometry of PFO in human cadaveric hearts.

METHODS

Ninety human hearts were randomly selected from the cadaveric specimen collection of the Department of Anatomy of the Federal University of Pernambuco. Hearts with dissected right and left atria that allowed visualization of the internal structures, and preserved interatrial septum (without dissection) were included. Specimens with removed atria exposing the valvular plane, or those without dissection, were excluded. The study was carried out in three phases: (1) screening and selection of suitable human hearts; (2) investigation of the presence of PFO; and (3) morphometric analysis of the PFO. Forty hearts from human cadavers were analyzed for PFO incidence and subjected to morphometric evaluation. The interatrial septum, fossa ovalis (and its limbus), and the presence of PFO from the right and left atrial perspectives were examined. Morphometric measurements were obtained using a digital caliper, with vertical and horizontal diameters of the PFO recorded.

RESULTS

PFO was identified in six out of 40 human cadaveric hearts, corresponding to an incidence of 15%. The maximum potential diameter ranged from 1 to 5 mm, with a mean of 3.5 mm. Additionally, one heart presented two PFO.

Table 1. Morphometry of the patent foramen ovale.

Hearts					
1	2	3	4	5	6
0.3	0.5	0.3	0.5	0.1	0.3 and 0.4

Morphometric measurements in mm

Figure 1. Hearts with patent foramen ovale.

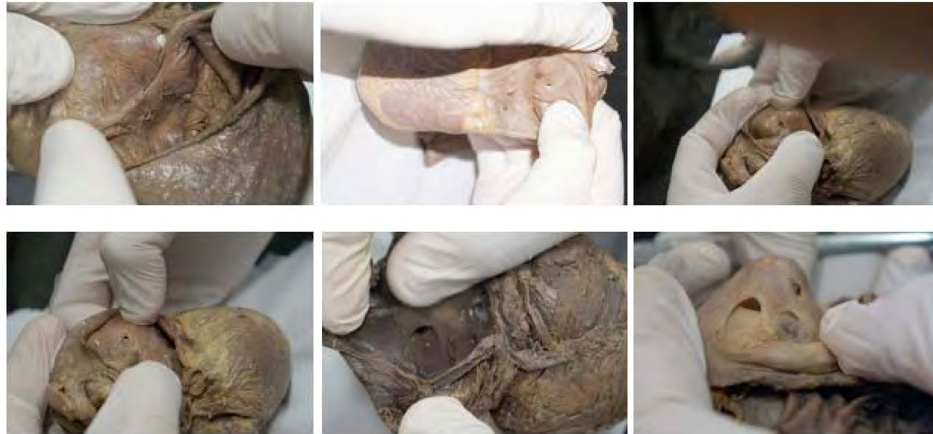

Figure 2. Patents foramen ovale.

DISCUSSION

The PFO consists of a functional, but not anatomical, closure. In this case, the interatrial septum is sustained by pressure-dependent apposition rather than fibrous adhesion between the primum and secundum septa[1]. Morphological variations of PFO include differences in septum primum thickness and shape, atrial septal flexibility, tunnel length, a multiperforated membranes with spontaneous left-to-right shunting, atrial septal aneurysms, and the presence of various anatomical structures within both atria, such as the Chiari network, Eustachian valve, and incompletely subdivided left atrium. A prominent Eustachian valve, when present, is thought to contribute to paradoxical embolism in PFO by facilitating right-to-left atrial flow and allowing thrombi to pass from venous to arterial circulation[3]. The presence of an atrial septal aneurysm is strongly associated with an increased incidence of CVA in patients with PFO. Paradoxical embolism refers to the passage of thrombi or other embolic particles from venous to arterial circulation through a right-to-left shunt. Our findings indicated a mean diameter of PFO of 3.5 mm, a dimension sufficient to allow emboli to occlude cerebral arterial branches, such as the middle cerebral artery and large cortical branches. Randomized studies have demonstrated a stronger causal association between CVA, increased PFO diameter, and atrial septal hypermobility[8].

The incidence of PFO in the general population is 25%, with a mean diameter of 4.9 mm[2]. However, the exact incidence varies depending on the diagnostic method and its respective accuracy[8], and the reference standard for PFO diagnosis remains controversial. PFO may account for up to 50% of cryptogenic CVA. Patients younger than 55 years show an increased relative association between PFO and cryptogenic stroke compared with older patients[8]. Nonetheless, this association has also been observed in older patients, whose PFO diameter tends to decrease with age. No consistent data currently correlate PFO prevalence with race or sex. The absence of epidemiological data on the individuals is a limitation of this study, as specimens were selected from the cadaveric collection of the Federal University of Pernambuco. Cryptogenic CVA is an exclusion diagnosis; however, topographic findings, such as cerebral infarcts in multiple vascular territories in young patients, reinforce the likelihood of an embolic cause. Therefore, documentation of a pos-

sible PFO should be considered in the differential diagnosis, given its high prevalence in the general adult population.

CONCLUSION

The incidence of PFO was 15% with an average of 3.5 mm of maximum potential diameter.

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ORIGINAL ARTICLE

SPERM CHARACTERISTICS OF MEN AT DIFFERENT AGES

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ABSTRACT

Background: Knowledge regarding aging, seminal fluid, and spermatozoids is controversial in the literature. This study analyzed the relationship between male age and sperm characteristics.

Methods: Semen samples were collected from 80 healthy adult men aged between 21 and 60 years, following three to five days of sexual abstinence. Participants were divided into four age groups (n = 20 per group): 21 to 30, 31 to 40, 41 to 50, and 51 to 60 years.

Results: No significant differences were observed in sperm physical and chemical properties (smell, color, volume, viscosity, and pH), as well as motility across age groups. Sperm concentration was higher in men over 41 years. The 41 to 50 age group presented a higher proportion of normal (oval-shaped) sperm ($p = 0.03$) and a lower proportion of abnormal (tapered-shaped) sperm ($p = 0.02$) than other groups.

Conclusion: Men aged 41 to 50 years demonstrated a higher proportion of normal sperm shapes.

Keywords: Spermatozoid, Sperm, Semen, Man, Age.

INTRODUCTION

Research into the impact of male age on fertility has gained increasing attention due to the general perception that older men experience reduced sex life, including a lower ejaculate volume and diminished sperm morphology and motility than younger men. However, studies comparing the seminal characteristics of fertile men over 60 years of age with those under 35 have reported that older men may exhibit higher sperm density despite reduced motility. These studies found no significant difference in seminal volume or the concentration of morphologically normal sperm[1,2,3,4,5]. Additionally, sperm deficiencies occur in 30% of infertile men[3,6,7,8].

Several studies have reported a decline in daily spermatogenesis among aging men. This reduction is associated with elevated serum gonadotropin and decreased testosterone levels[1,8,9,10,11]. Testicular biopsies and radioimmuno assays of gonadotrophic hormones indicate diminished Sertoli cell function, reduced cytoplasm volume in Leydig cells, and diminished, thickened lamina propria in the seminiferous tubules[5,8,10,11,12,13,14].

Although semen quality appears to decline with age, sperm characteristics in older men remain within normal ranges, according to World Health Organization (WHO) standards[1,2,4,16,17]. However, in cases of infertility, aging can affect semen quantity and sperm function[3]. A reduced semen quality combined with reduced sexual activity may negatively affect the fertility potential of a couple[3,5].

Given the scarce and conflicting data on age-related changes in semen quality, this study evaluated the sperm characteristics across different age groups and the relationship between age and sperm forms.

METHODS

This study was conducted in accordance with the Helsinki Declaration and was approved by the research ethics committee of the Federal University of Minas Gerais, Brazil (no. 0429/15). All participants provided written informed consent before enrollment.

Semen samples were obtained from 80 healthy men aged between 21 and 60 years, following a period of three to five days of sexual abstinence. This abstinence period was established based on the recommendations of the New 2010 WHO Standards (5th edition) for the Evaluation of Human Semen [2,15,16,17,18]. Participants were divided into four age groups (n = 20 per group): 21 to 30 (mean 23 ± 5 years), 31 to 40 (33 ± 4 years), 41 to 50 (45 ± 2 years), and 51 to 60 (58 ± 3 years).

Participants were selected based on an anamnesis focused on sexual history, including frequency of sexual activity, erectile or ejaculation dysfunction, and previous paternity. Those with a history of urological or endocrine disorders, such as diabetes mellitus, use of any drug, known infertility or family history of infertility, leukocytospermia, and any other sexual dysfunction were excluded.

Each participant provided a single specimen

of sperm, collected in a sterile container that was immediately hermetically sealed. Seminal volume, aspect, odor, viscosity, and pH were assessed immediately after collection. Microscopic characteristics of the sperm were reported about one hour later, including total motility at room temperature of 26°C and morphological features.

Semen samples were diluted at a ratio of 1:20 (0.1 mL sperm in 1.9 mL of a 0.9% saline solution), and sperm cells were counted in a Neubauer chamber using a binocular optical microscope. Morphological evaluation was conducted blindly and included counts from five chamber quadrants: the four lateral quadrants (used for leukocyte counts) and the central area (used for erythrocyte counts). Total sperm counts were multiplied by one million to determine the exact number of spermatozoa per mL. Sperm morphology was classified as normal (oval) or abnormal (tapered, round, amorphous, immature, double-headed, double-tailed, macrocephalic, or microcephalic)[3,14,16].

Descriptive statistics were expressed as mean and the standard error of the mean (SEM). Comparisons among groups were performed using analysis of variance (ANOVA), followed by the Tukey-Kramer multiple comparison test. Bonferroni correction was applied to the ANOVA. Statistical significance was set at $p < 0.05$.

RESULTS

Semen volume, sperm concentration, or sperm morphology were not significantly different among the age groups. Similarly, no significant differences were found in sui generis smell, light gray color, viscosity within normal limits, or pH of 7. The ejaculated volume ranged from 2.0 to 3.2 (mean 2.5 ± 0.2) mL. Sperm concentration was higher in the two older age groups (41 to 50 and 51 to 60 years) than in the younger groups (21 to 30 and 31 to 40 years) (Table 1). No cases of leukocytospermia were identified.

Microscopic analysis revealed similar percentages of mobile sperm across all four age groups (Table 1). However, the 41 to 50 age group presented the highest percentage of normal oval sperms ($p = 0.03$), and the lowest percentage of abnormal sperms than the other age groups ($p = 0.02$) (Table 2). Plasma membrane integrity was preserved in all sperm across all samples.

Table 1. Sperm concentration (mean ± standard deviation) in the seminal fluid and percentage with normal mobility.

AGE GROUP (years)	CONCENTRATION (X 10^6 /mL)	NORMAL MOBILITY (%)
21 to 30	83 ± 49	70.0
31 to 40	76 ± 46	69.1
41 to 50	105 ± 49	76.7
51 to 60	173 ± 25	75.4

Table 2. Sperm morphologic characteristics (percentage) across age groups.

MORPHOLOGY	AGE GROUP (years)			
	21 - 30	31 - 40	41 - 50	51 - 60
Oval	**27.8 ± 4.4**	**28.2 ± 6.3**	**38.0 ± 8.1 ***	**30.4 ± 7.7**
Tapered	**24.4 ± 3.1**	**23.7 ± 5.0**	**16.1 ± 4.1 ****	**21.3 ± 6.5**
Round	**22.4 ± 4.1**	**23.3 ± 5.9**	**25.7 ± 4.1**	**24.6 ± 8.9**
Immature	**7.2 ± 1.0**	**8.4 ± 2.0**	**7.4 ± 1.9**	**7.7 ± 2.5**
Amorphous	**9.2 ± 0.9**	**8.6 ± 2.9**	**7.8 ± 2.3**	**9.1 ± 3.0**
Double-headed	**1.2 ± 0.0**	**0.3 ± 0.0**	**0.5 ± 0.0**	**-**
Double-tailed	**0.7 ± 0.0**	**0.4 ± 0.0**	**-**	**4.6 ± 1.0**
Macrocephalic	**4.7 ± 0.4**	**3.6 ± 0.6**	**2.0 ± 0.1**	**2.3 ± 0.2**
Microcephalic	**2.4 ± 0.2**	**3.5 ± 0.6**	**2.5 ± 0.2**	**-**

* Higher percentage than in the other age groups ($p = 0.03$) ** Lower percentage than in the other age groups

(p = 0.02) (ANOVA followed by Tukey-Kramer test for multiple comparisons).

DISCUSSION

Previous inconclusive and conflicting studies have reported that increasing age is significantly associated with decreased semen volume, sperm concentrations, progressive motility, and the proportion of morphologically normal sperm[1,2,4,15,16]. Although the semen quality serves as an indirect measure of fertility, it cannot be used to predict the fertility of a given sample. Comparative studies with healthy individuals showed that spermatogenic capacity is higher after three to five days of sexual abstinence[2,3,15,16,18]. In contrast, shorter abstinence intervals have been associated with a higher proportion of immature sperm and reduced motility. In the present study, all sperm samples were collected after a standardized abstinence period of three to five days.

The atherosclerotic vascular disorder is associated with impaired testicular blood flow, leading to parenchymal loss and sclerosis of the seminiferous tubules. This process is often attributed to autoimmune inflammatory testicular atrophy and has been implicated in the cause of reduced spermatogenesis and libido with advancing age[2,10,13,19,20]. Additionally, prostatic disorders commonly observed in older men may contribute to a reduced seminal fluid[13,20]. Biochemical changes in human semen associated with aging have been reported, including decreased fructose concentrations, kallikrein, and prostate-specific antigen (PSA), as well as prolonged liquefaction times. Recent studies suggest that sperm DNA damage is significantly more prevalent in older men[21,22], contributing to reduced motility and fertilization capacity[2,4,8].

In this study, none of the participants reported any sexual dysfunction, and all seminal fluid presented normal physical and chemical characteristics. Furthermore, the concentration of normal (oval) sperm shape, considered ideal for fertilization, was higher in men aged over 41 years. No participants aged 60 years or older were included due to the difficulty in recruiting healthy men in this age group who agreed to participate. Sperm motility was assessed at a room temperature of 26ºC, which was lower than the physiological temperature of 36ºC to 37ºC. Although this suboptimal temperature may have inhibited motility, the uniform temperature testing conditions across all samples ensured that any potential measurement bias was consistent among the groups.

The findings of this study conflict with much of the existing literature regarding sperm characteristics. Our results suggest that, up to the age of 60, aging may be associated with improved sperm morphology and motility without a negative influence on seminal fluid characteristics. Additionally, the lower prevalence of abnormal sperm shapes observed in men over 41 years of age may indicate a relatively higher fertility potential in this age group.

CONCLUSION

Men aged between 41 and 50 years presented a higher proportion of morphologically normal sperms.

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CONFLICT OF INTERESTS

The authors declare no conflict of interests.

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MULTIPLE ANATOMICAL VARIATIONS IN THE BRANCHES OF THE AORTIC ARCH AND MIDDLE CEREBRAL ARTERY: AN ANGIOGRAPHIC STUDY

MÚLTIPLAS VARIAÇÕES ANATÔMICAS NOS RAMOS DO ARCO AÓRTICO E ARTÉRIA CEREBRAL MÉDIA: UM ESTUDO ANGIOGRÁFICO

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ABSTRACT

The understanding of anatomical variations of blood vessels requires prior knowledge of embryonic vasculogenesis and angiogenesis. This study reports the case of a 32-year-old female with a 24-hour history of holocranial headache and nausea, unresponsive to analgesics. Imaging revealed occlusion of the right vertebral artery and dissection of the left vertebral artery. The aortic arch presented non-pathological anatomical variations, including an anomalous origin of the right subclavian artery and a common carotid trunk. Additionally, a trifurcation of the middle cerebral artery, not considered a non-pathological variant, was also observed. In this way, anatomical variations are clinically essential for safe and effective decision-making.

Keywords: Aorta; Subclavian Artery; Brachiocephalic Trunk; Middle Cerebral Artery; Anatomic Variation

RESUMO

A compreensão das variações anatômicas de vasos sanguíneos requer o conhecimento prévio da vasculogênese e angiogênese do embrião. Esse estudo reportou um caso de um paciente do gênero feminino, 32 anos, com historia de cefaleia holocraniana e náusea por 24 h, e não foi responsiva a analgésicos. Foi submetida a exames de imagem que evidenciaram oclusão da artéria vertebral direita e dissecção da artéria vertebral esquerda, arco aórtico apresentando variações anatômicas não patológicas com a origem anômala da artéria subclávia direita e um tronco comum das artérias carótidas, além de variação anatômica não patológica da trifurcação de artéria cerebral média. As repercussões clínicas das variações anatômicas são clinicamente importantes para uma análise individual mais adequada e segura na tomada de decisão.

Palavras-chave: Aorta, Artéria Subclávia; Artéria Cerebral Média; Tronco Braquiocefálico; Variação Anatômica.

INTRODUCTION

The left common carotid artery (LCCA), left subclavian artery (LSA), and brachiocephalic trunk (BT) originate from the convexity of the aortic arch, which is formed from the fourth left primitive arch.[1]

The arteries of the internal carotid and vertebrobasilar systems provide cerebral perfusion and arise directly or indirectly from the aortic arch. Together, these arteries form the circle of Willis at the base of the skull, from which the major cerebral arteries emerge.[2]

Although less frequent than in other major cerebral arteries, the middle cerebral artery (MCA) may present several anomalies. The MCA typically arises as a single trunk from the internal carotid artery. However, in some cases, two MCAs may originate from the internal carotid artery, presenting as either an accessory MCA or a duplicated MCA.[3–5] In other instances, the MCA may arise as a single trunk but shows fenestration.[6] A duplicated MCA may also occur when two separate MCA arise from the terminal internal carotid artery and merge to form an arterial ring [7]. In a branch-like MCA anomaly, the MCA forms an arterial network resembling tree branch.[8–12]

Understanding the anatomical variations of blood vessels directly or indirectly related to cerebral perfusion is essential for surgeons, as it allows accurate and safe preoperative planning while reducing the risk of intraoperative complications. There-

fore, the present study reported a rare case of multiple anatomical variations involving branches of the aortic arch and the MCA.

CASE REPORT

A 32-year-old female patient with no history of diabetes mellitus, systemic arterial hypertension, or family history of stroke presented to the emergency department with a 24-hour holo-cranial headache and nausea, unresponsive to analgesics. Brain magnetic resonance imaging and cervical arterial angiography revealed occlusion of the right vertebral artery and dissection of the left vertebral artery. To clarify the diagnosis and guide treatment, angiographic studies of the aortic arch, carotid arteries, and vertebral arteries were performed.

Intracranial nuclear magnetic resonance imaging and cerebral magnetic resonance angiography (arterial and venous phases) showed no evidence of intracranial expansive process, extra-axial fluid collections, intraparenchymal hemorrhage, or midline shift. The ventricular system presented normal topography, morphology, and dimensions. The brain parenchyma, brainstem, and cerebellum presented usual signal intensity and preserved morphology. The cerebellar tonsils were located above the foramen magnum. A common origin of the right and left common carotid arteries from the aortic arch was observed. Post-gadolinium imaging revealed signal defects in segments V2 and V3 of the right vertebral artery, with reduced caliber in segment V4 compared with the contralateral side. Additional angiographic investigation evaluation was recommended. No arteriovenous malformations, aneurysms, or dural sinus thrombosis were identified.

Arteriography was performed via percutaneous puncture of the right common femoral artery, with selective catheterization of the aortic arch, common carotid arteries, and vertebral arteries. Images were acquired using digital radiography. Anatomical variations included an aberrant right subclavian artery and a common trunk of the carotid arteries (bovine trunk) arising from the aortic arch (Figure 1). The right common carotid artery presented normal bifurcation, and the internal carotid artery showed smooth, regular walls without evidence of dissection or arteritis; intracranial segments demonstrated normal venous drainage and patent dural sinuses. The left common carotid artery also demonstrated bifurcation, and the internal carotid artery had smooth, regular walls with no evidence of dissection or arteritis. Additionally, a trifurcation of the MCA was identified (Figure 2), with preserved venous drainage and patent dural sinuses. Within the vertebrobasilar system, the left vertebral artery was patent with normal caliber, whereas the right vertebral artery was patent but narrowed. The basilar artery and its branches were occluded, though their calibers and contours were otherwise normal. Either supra- and infratentorial venous drainage were preserved and visualized in real time.

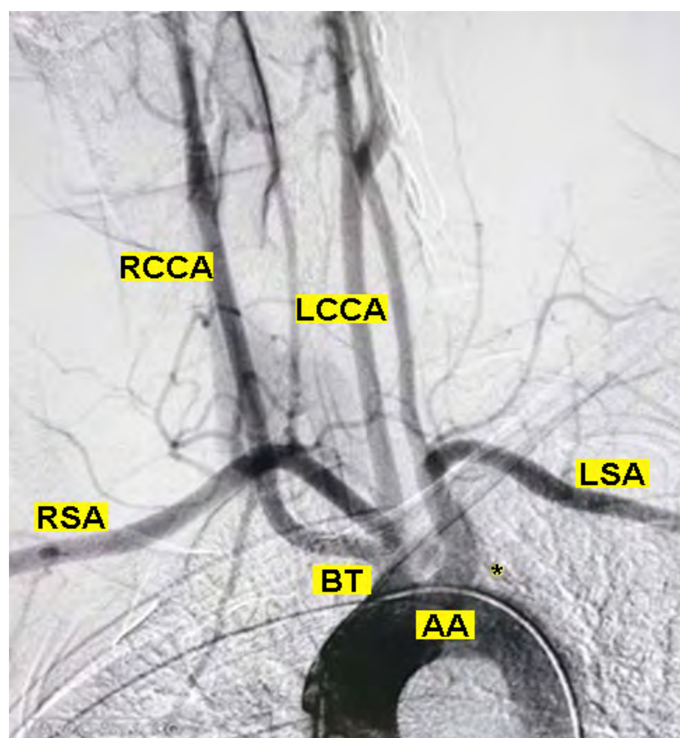

Figure 1. Arteriography of the aortic arch showing a common origin of the common carotid arteries (bovine trunk) and anomalous origin of the right subclavian artery (aberrant). Aortic arch (AA), brachiocephalic trunk (BT), right common carotid artery (RCCA), left common carotid artery (LCCA), left subclavian artery (LSA), right subclavian artery (RSA), *Origin of the right subclavian artery in the aortic arch.

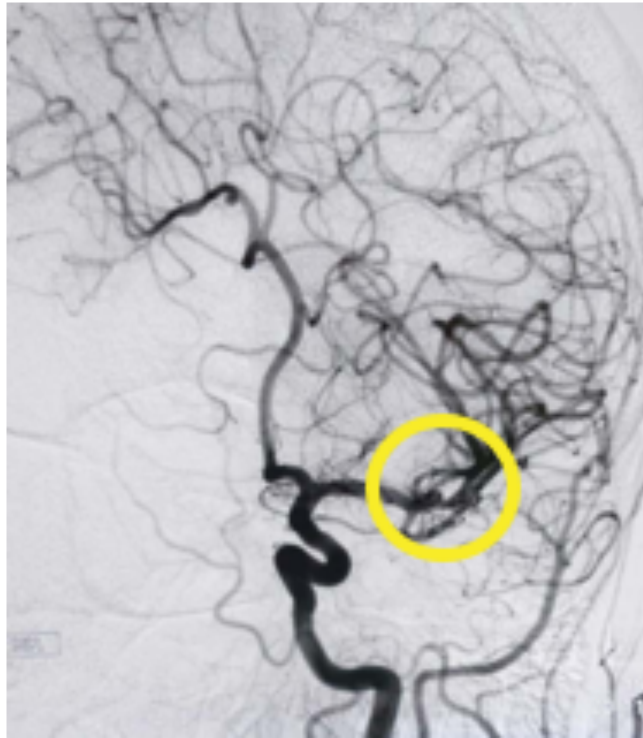

Figure 2. Oblique angiographic image showing trifurcated middle cerebral artery (MCA).

COMMENTS

Numerous anatomical variations may occur in blood vessels originating from the aortic arch. The most common branching pattern consists of three branches: (1) the BT, which divides into the right subclavian artery (RSA) and the right common carotid artery (RCCA), (2) the LCCA, and (3) the LSA.13

The literature describes between 8 and 15 types of aortic arch branching patterns13-14 In the eight-type classification, type I is the most common, whereas type VIII is the rarest. In this system, branches are described from right (first branch) to left (last branch). Type I is the most frequent or "normal" type of aortic arch with three branches: (1) BT (innominate artery), which splits into RSA and RCCA, (2) LCCA, and (3) LSA. Type II is the second most common pattern, with only two branches: (1) a common trunk giving rise to RSA, RCCA, and LCCA and (2) LSA. In type III, the left vertebral (LV) arises directly from the arch and not from the LSA, setting a pattern of four branches in the aortic arch: (1) BT, (2) LCCA, (3) LV, and (4) LSA. The type VI is characterized by common origin of the common carotid arteries and common origin of the subclavian arteries: (1) common trunk for the RCCA and LCCA and (2) common trunk for the RSA and LSA. Type VII is characterized by the absence of BT, with four separate branches: (1) RSA, (2) RCCA, (3) LCCA, and (4) LSA, while type VIII presents an additional branch of the aortic arch, the thyroid ima artery, (arch with four branches): (1) BT, (2) thyroid ima artery, (3) LCCA, and (4) LSA.14

In the 15-type classification, the pattern observed in the present case had a prevalence of 0.7%.13 In this variant, the aortic arch presented three branches (from right to left): (1) a common trunk for the RCCA and LCCA, (2) LSA, and (3) RSA (aberrant).

The MCA is the largest and most complex cerebral artery due to the highly developed cerebral neocortex in humans. It represents a relatively recent phylogenetic development and may be considered as a collateral branch of the anterior cerebral artery. Although MCA anomalies are less frequent than those of other major intracranial arteries, several variants have been reported, including accessory MCA, duplicated MCA, early bifurcation, and fenestration.15

Additional branching patterns of the MCA have also been described, such as lateral bifurcation (48% of cases), trifurcation (25% of cases), lateral pseudo-bifurcation (18.5% of cases), pseudobifurcation in the middle of the sphenoidal segment (origin of the orbitofrontal or temporopolar artery; 6% of cases)1, and medial bifurcation (2.5% of cases). The present study identified a trifurcation of the left MCA associated with the aforementioned aortic arch variations.

Anatomical variations and vascular anomalies may markedly affect cerebral perfusion and are frequently detected incidentally during neurosurgical or endovascular procedures for tumors, aneurysms, or arteriovenous malformations. Their recognition is essential for surgical planning to minimize iatrogenic injury by accounting for vessel origin and course, and to accurately assess the vascular territories at risk during occlusion.

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CASE REPORT

SPONTANEOUS DISSECTION OF THE RIGHT CORONARY ARTERY IN A PATIENT WITH ACUTE CORONARY SYNDROME

DISSECÇÃO ESPONTÂNEA DA ARTÉRIA CORONÁRIA DIREITA EM PACIENTE COM SÍNDROME CORONARIANA AGUDA

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ABSTRACT

This study describes a case of acute coronary syndrome with ST-segment elevation and spontaneous dissection of the right coronary artery, diagnosed by coronary angiography in a male patient who underwent angioplasty and stent implantation three years ago.

Keywords: Coronary Artery Disease; Percutaneous Coronary Intervention; Myocardial Infarction; Spontaneous Coronary Artery Dissection; Stents.

RESUMO

Apresentamos um caso de síndrome coronariana aguda com supra desnivelamento do segmento ST (SCACSST) e dissecção espontânea da artéria coronária direita, evidenciada através da cineangiocoronariografia, em paciente do sexo masculino, previamente submetido à angioplastia primária com implante de stent há 03 anos.

Palavras-chave: Doença da Artéria Coronária; Intervenção Coronária Percutânea; Infarto do Miocárdio; Dissecção espontânea da artéria coronária; stents.

INTRODUCTION

Spontaneous coronary artery dissection (SCAD) is a rare type of acute myocardial ischemia, usually reported as isolated cases in the literature[1],[2]. This underdiagnosed ischemia presents a varied clinical presentation that may lead to acute coronary syndromes (ACS) and sudden death3,4.

The etiology of SCAD is unknown; however, it is usually observed in arteries free of atheromatous obstruction2 and after the invasive approach of ACS5. The presence of atheromatosis in the arteries does not exclude SCAD since endothelial dysfunction may be the pathophysiological basis for the onset of dissection2.

This study aimed to report the following case due to its peculiarity, specifically the occurrence of SCAD in a patient previously affected by ACS with ST-segment elevation who underwent stent implantation three years ago.

CASE REPORT

A 50-year-old male patient, hypertensive, diabetic, ex-smoker (two packs/day for 20 years) with a previous history of ACS and implantation of a non-pharmacological stent in the proximal and mid one-third of the right coronary artery (three years ago). He sought medical attention due to tightness and precordial pain. After 24 hours of admission, the patient presented a clinical worsening with strong intensity pain with irradiation to the back associated with vomiting, sweating, and palpitations in the last three hours. He had reported progressive angina during physical efforts and regular use of bisoprolol, simvastatin, and acetylsalicylic acid a few months ago.

The electrocardiogram on admission revealed sinus rhythm with isolated ventricular extrasystoles, a QS pattern in the lower leads, and no signs of acute ischemia. He was admitted to the emergency room and medicated with acetylsalicylic acid, morphine,

and isosorbide dinitrate. The first dosage of biochemical markers of myocardial necrosis was normal (troponin 0.007 ng/mL, normal < 0.014 ng/mL).

After ten hours, the patient reported another episode of chest pain associated with dynamic alteration of the ECG and ST-segment elevation in lower leads. Continuous infusion of intravenous nitroglycerin was started, and the patient was taken to the Hemodynamics laboratory for urgent coronary angiography. The examination conducted through the right femoral artery revealed diffuse proliferative restenosis in the proximal and mid-third of the right coronary artery and a spontaneous spiral dissection in the transition from the mid-third to the distal, immediately after the distal edge of the stent (Figure 1). The other coronary arteries and their respective branches did not present significant obstructive lesions. First, we chose percutaneous coronary intervention with pre-dilation of all segments affected by restenosis, followed by the implantation of two zotarolimus-eluting stents (3.5 x 38 mm and 3.0 x 24 mm) with a small overlap between them. Control laminography revealed a good final result, with no residual lesion, no dissection image, and maintenance of the distal thrombolysis in myocardial infarction III flow (Figure 2).

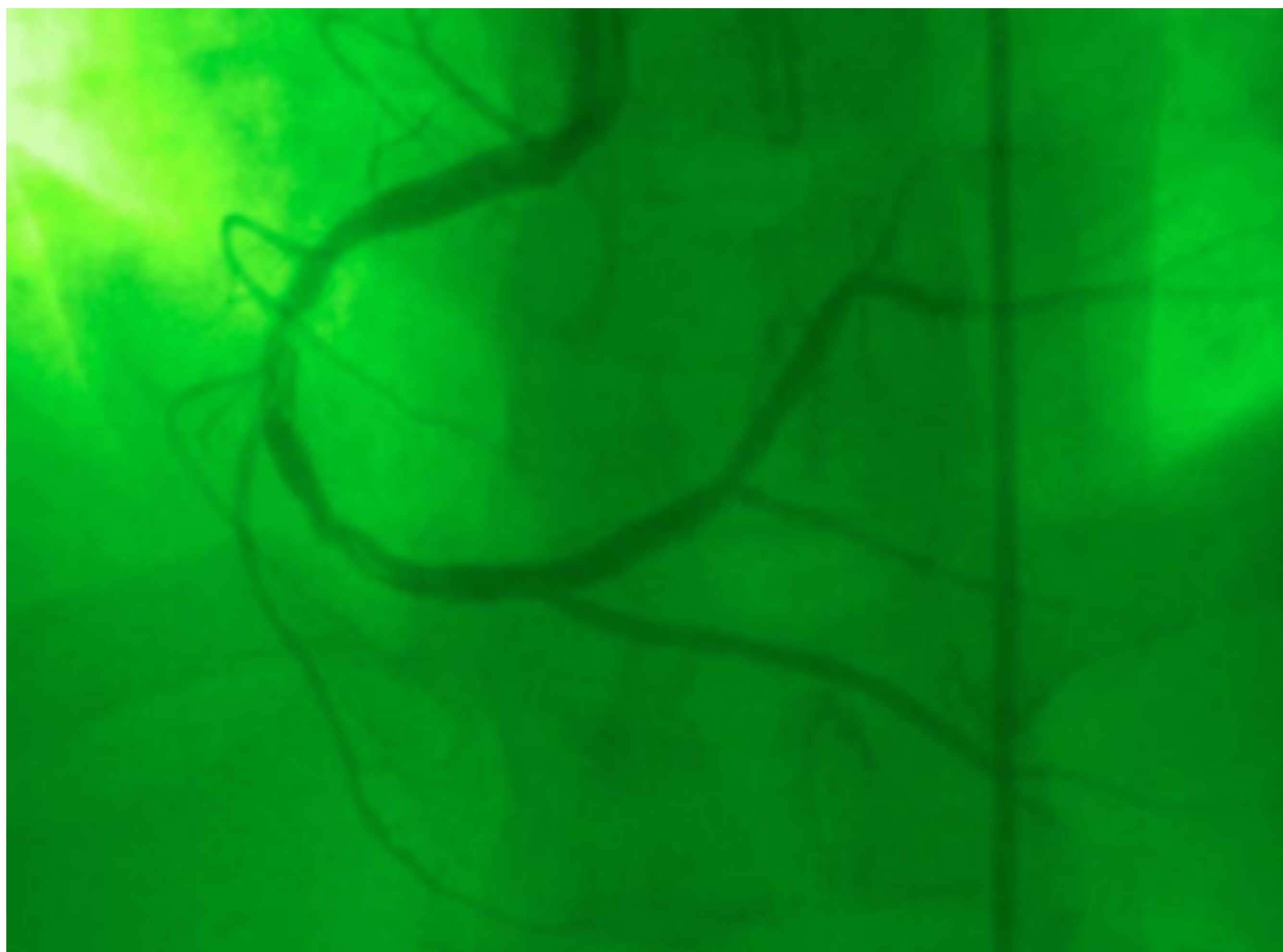

Figure 1. Right coronary artery in posteroanterior cranial showing the line of dissection starting at the level of the stent previously implanted in the one-third proximal artery.

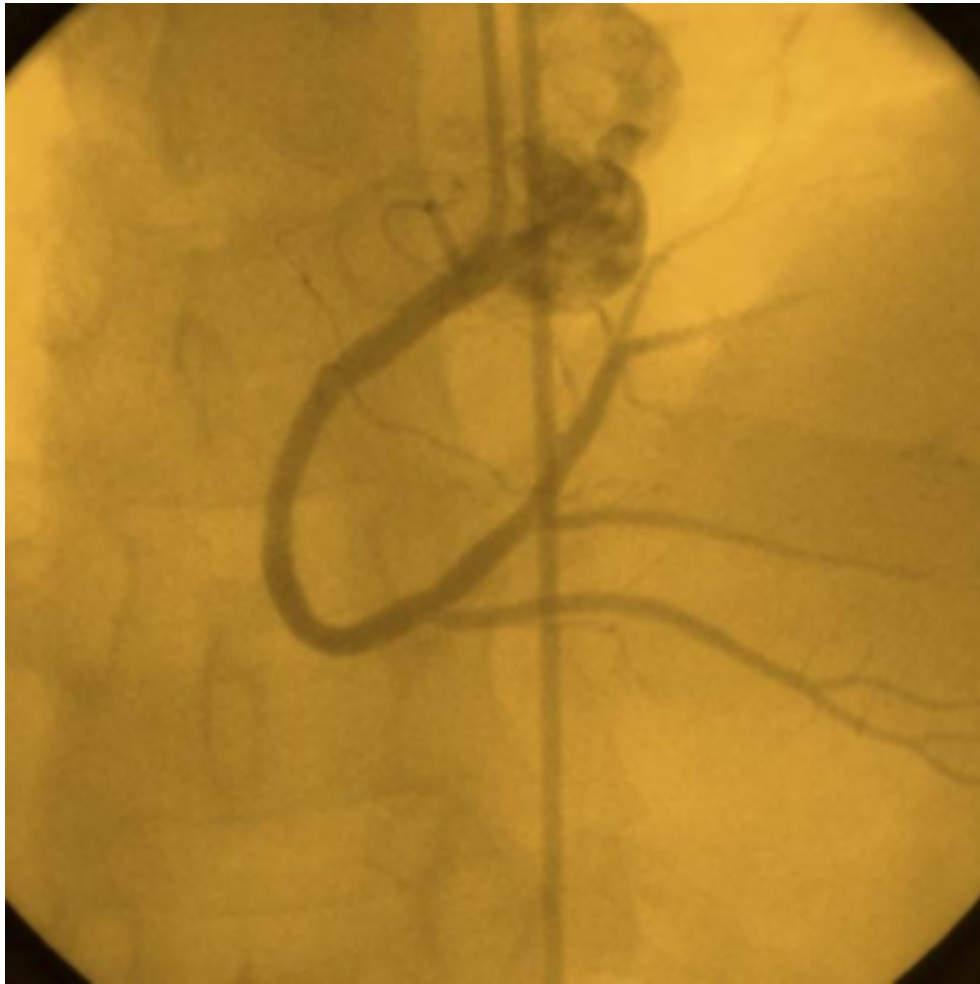

Figure 2. Right coronary artery in posteroanterior cranial after the implant of Zotalimus-eluting stents in one-third of proximal, mid, and distal arteries.

After angioplasty, the patient progressed satisfactorily without complications and was discharged on the fifth postoperative day with prescriptions for enalapril, bisoprolol, acetylsalicylic acid, clopidogrel, and atorvastatin for use at home. Two months later, the patient returned for outpatient follow-up, and he was asymptomatic and clinically stable. Maintenance of dual antiplatelet therapy was indicated for at least one year (from the date of the infarction), and periodic clinical reevaluations were recommended.

COMMENTS

The first report of SCAD was made by Pretty in 1931 after performing a necropsy on a 42-year-old woman who evolved to sudden death after presenting chest pain6. Since then, sporadic case reports have been published.

SCAD predominantly affects young female patients under 50 years old, using contraceptive drugs or around the time of delivery, and without a history of cardiovascular risk factors7. However, this disease may be associated with underlying coronary atherosclerosis, connective tissue diseases, vasculitis, cocaine abuse, and thoracic trauma[1]. SCAD rarely affects males, and about half of the cases among them are preceded by intense physical exertion, similar to the case described in this study. Although the cause is unknown, the literature indicates that its incidence is low, ranging from 0.1% among patients with stable anginal symptoms to 4.0% of all cases of ACS[8].

Two pathophysiological mechanisms may be related to SCAD. The first is attributed to increased shear stress in the endothelial wall, and the second is related to hemorrhage in the middle layer, which may arise from tissue weakening of the arterial wall associated with inflammation, abnormal collagen synthesis, or rupture of the vasa vasorum[9]. In both cases, the coronary artery lumen reduces, resulting in myocardial ischemia[1].

The ACS spectra can be described as a clinical presentation of SCAD, including sudden death. Autopsy is usually the diagnosis of SCAD since angio-

graphic documentation is limited. However, in sporadic cases, such as the present study, SCAD may be diagnosed by coronary angiography. The few reports of SCAD diagnosed by this type of intervention show that the anterior descending coronary artery is the most affected vessel (75%), followed by the right coronary artery (20%), the circumflex artery and its branches (4%), and the left main coronary artery in rare cases (< 1%)[8].

Interventions for SCAD range from clinical treatment to myocardial revascularization surgery or stent implantation. Some criteria, such as the degree of clinical severity, hemodynamic status, and topography of the dissection, should be considered when establishing a treatment[10].

Although percutaneous coronary intervention for SCAD is associated with a high rate of technical failures, in this particular case, the medical team chose this procedure due to an ACS with ST-segment elevation, restenosis of the stent, and alteration of the distal flow through the coronary artery. The percutaneous coronary intervention was promptly performed with the implantation of Zotarolimus-eluting stents, achieving immediate success without intercurrences.

We report a rare and successful case of SCAD diagnosed by coronary angiography in a male patient. Other imaging techniques, such as intracoronary ultrasonography and optical coherence tomography, when available, coupled with early coronary angiography in ACS, may help the therapeutic and prognostic decisions on SCAD[11].

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CASE REPORT

THE EFFECT OF LIFESTYLE MODIFICATION IN A PATIENT WITH SEVERE HYPERTRIGLYCERIDEMIA

EFEITO DAS MUDANÇAS DO ESTILO DE VIDA EM PACIENTE COM HIPERTRIGLICERIDEMIA GRAVE

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ABSTRACT

This study reports a case of severe hypertriglyceridemia in a 61-year-old woman, identified during a cardiologic routine consultation. Despite pharmacological prescription, lipid levels remained uncontrolled. The patient is retired and sedentary, lacks healthy lifestyle habits, and lives alone. She was referred to nutritional counseling, and a structured lifestyle intervention program was proposed, including dietary modification, initiation of regular physical activity, and encouragement of social engagement. Nutritional recommendations followed the latest Brazilian guidelines for dyslipidemia, combined with strategies to promote social reintegration. In this case, the combination of lifestyle intervention, body image improvements, and return to social interaction reduced the serum triglyceride levels. Thus, we believe that these additional actions were crucial to accomplish the proposed dietary plan and avoid the risk of pancreatitis.

Keywords: Hypertriglyceridemia; Lifestyle; Healthy diet; Diet therapy.

RESUMO

Relatamos um caso de hipertrigliceridemia grave em uma mulher de 61 anos, durante uma consulta de rotina no ambulatório de cardiologia, que foi diagnosticada com hipertrigliceridemia grave e resistente ao tratamento medicamentoso prescrito. Ela é aposentada, sedentária, nãoapresentava hábitos de vida saudáveis e mora sozinha em seu domicílio. Foi encaminhada ao ambulatório de nutrição, e sugerimos um plano terapêutico para mudanças no estilo de vida. A combinação de terapias de estilo de vida foram: atividade física, modificação dietética e inserção na vida social. As recomendações dietéticas seguiram as propostas pela atualização da diretriz brasileira de dislipidemia, com adição do convívio social. Neste caso, foi demonstrado a redução drástica dos níveis séricos de triglicerídeos, com a combinação de terapia de estilo de vida, aliado à melhora de imagem corporal e retorno ao convívio social. Assim, acreditamos que estes adicionais foram cruciais para motivar o seguimento do plano dietético proposto e evitar risco de pancreatite.

Palavras-chave: Hipertrigliceridemia; Estilo de vida; Dieta saudável; Dietoterapia.

INTRODUCTION

Body weight and dietary composition are risk factors for dyslipidemia, including isolated hypertriglyceridemia[1,2]. This condition is characterized by increased serum triglyceride levels, resulting in alterations in lipid metabolism, particularly affecting chylomicron lipoproteins and very low-density lipoprotein[1,3].

Triglyceride levels above 500mg/dL are classified as severe hypertriglyceridemia and potentially increase the risk of acute pancreatitis, requiring drug treatment alongside lifestyle changes[1,2,4]. Management should include a thorough evaluation of causative factors to guide individualized interventions[3]. This case report encompassed lifestyle changes associated with multidisciplinary care at the school clinic as a potential aggregator in choosing evidence-based non-drug treatment for hypertriglyceridemia.

CASE REPORT

A 61-year-old woman, retired, former smoker, and sedentary, was referred for nutritional follow-up at a school clinic in Olinda after being diagnosed with severe isolated hypertriglyceridemia during a routine cardiology consultation. The anamnesis re-

vealed dietary errors with a preference for carbohydrate-rich foods (i.e., sweets), and a weight gain of 12 kg over the last three years.

She denied food intolerances and allergies and was resistant to the use of lipid-lowering drugs. Anthropometric assessment revealed a weight of 64 kg; height of 1.55 m; body mass index of 26.6 Kg/m^2; waist circumference of 90 cm; waist-to-hip ratio of 0.85; and neck circumference of 34.5 cm. These values indicated an eutrophic status and strong predictors for cardiovascular disease. The serum triglyceride levels were at 548 mg/dL.

An intervention focusing on lifestyle changes was initiated, including the daily practice of physical activities, a normoglycemic (48% of the total caloric intake), normolipidic (35% of the total caloric intake), and hyperproteic (16% of the total caloric intake) diet, adjusted to the socioeconomic status of the patient. Emphasis was placed on adequate intake of both soluble and insoluble fiber, increased consumption of polyunsaturated and monounsaturated fatty acids (e.g., fish containing high levels of eicosapentaenoic and docosahexaenoic), complex carbohydrates, grains, fruits, and vegetables, all while maintaining affordability.

Physical activity was introduced via participation in the “City Academy Project”, a public health program of the city of Recife, which promotes community-based exercise. Additionally, the patient was encouraged to engage in home-based dance activities for at least one hour daily.

The patient demonstrated excellent adherence, joining a local gym and consistently participating in physical activities. Over four months, she achieved an intentional weight loss of 8 kg, reported improved body image satisfaction, adopted healthier eating habits, and experienced a substantial reduction in serum triglyceride levels from 548 mg/dL to 133 mg/dL. Importantly, she also re-established social interactions and described enhanced self-esteem and psychosocial well-being, attributing these improvements to the support received from the multidisciplinary care team.

DISCUSSION

The improvement in the triglyceride levels of the patient resulted from adherence to the proposed diet and nutritional counseling. This positive outcome was made possible by the motivation fostered through the supportive approach of the multidisciplinary team, which provided confidence in facing the proposed challenges and also demonstrated sensitivity to the environment in which the patient was inserted.

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ABSORPTION OF A TWIN PREGNANCY: A CASE REPORT

ABSORÇÃO DE GEMELAR NA GRAVIDEZ: UM RELATO DE CASO

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ABSTRACT

Single fetal demise by the end of the first trimester occurs in about 50% of twin pregnancies and is often associated with complete resorption of the gestational sac, leaving no evidence of a prior twin gestation at birth[1]. A 42-year-old patient (A.C.S.) underwent a transvaginal ultrasound in May 2018, which identified a thickened endometrium with two anechoic images compatible with gestational sacs. Serum beta-human chorionic gonadotropin (β-hCG) levels confirmed pregnancy. Subsequent ultrasound in July 2018 revealed the intrauterine demise of one twin, and by September, only one pregnancy was identified. The patient continued routine prenatal care and experienced an uncomplicated pregnancy, resulting in a healthy newborn. About 14% of twin pregnancies undergo spontaneous reduction to a single gestation by the end of the first trimester. Monochorionic pregnancies are associated with increased risk for complications, such as the twin-to-twin transfusion syndrome, selective intrauterine growth restriction, intrauterine fetal demise, and acardiac twin. Management depends on gestational age, the severity of fetal involvement, and cervical length. In most cases, twin pregnancies with single fetal demise do not result in significant complications, allowing the pregnancy to progress safely to term[2].

RESUMO

A morte unifetal até o fim do primeiro trimestre, cuja incidência orça em 50%, está associada à completa reabsorção do ovo, não havendo, no parto, qualquer evidência de gravidez gemelar1. A. C. S., 42 anos, realizou ultrassonografia (USG) transvaginal em maio de 2018, com os seguintes achados: endométrio espessado, apresentando duas imagens aneicóicas compatíveis com sacos gestacionais. Realizou logo a seguir, dosagem da fração beta do hormônio gonadotrófico coriônico humano (BHCG), confirmando a gravidez. Em novo USG em julho de 2018 evidenciou-se óbito em um gemelares e no exame seguinte em setembro do mesmo ano, o relato é de gestação única. A gestante, com gestação única, continuou a fazer suas consultas pré-natais, e evoluiu para parto normal sem intercorrências com recém-nascido saudável. Aproximadamente 14% das gestações gemelares são reduzidas espontaneamente a gestação única, até o final do primeiro trimestre. A monocorionicidade está relacionada a muitas complicações tais como: síndrome de transfusão gêmeo-gemelar (STGG), restrição seletiva do crescimento fetal (CIUR), óbito fetal intrauterino e gêmeo acárdico. O manejo das situações irá depender da idade gestacional, da gravidade do acometimento dos fetos e do comprimento do colo uterino. A gestação gemelar com perda fetal por absorção no primeiro trimestre, em sua maioria, não resulta em maiores complicações, podendo a gestação resultante seguir até o termo sem maiores intercorrências[2]

INTRODUCTION

Single-fetal demise by the end of the first trimester occurs in about 50% of early twin pregnancies, and it is associated with complete resorption of the gestational sac, leaving no ultrasound (US) evidence of a prior twin gestation at birth. The presence of a blighted ovum (i.e., evanescent twin) alongside a viable pregnancy is typically benign. Although early vaginal bleeding may occur more frequently in these pregnancies, perinatal outcomes are generally favorable. While the clinical incidence of twin pregnancy delivery is about 1 in 90 births, the US in the first trimester detects twin pregnancy in nearly 1 in 60 pregnancies. Spontaneous reduction from twin to singleton pregnancy is estimated to occur in about 14% of cases before the end of the first trimester. Ultimately, only half of twin pregnancies identified in early gestation result in twin deliveries[1].

CASE REPORT

A 42-year-old patient (A.C.D.S), G1P0A0, underwent a transvaginal US on May 28, 2018, which showed a thickened endometrium and two anechoic images suggestive of gestational sacs. Serum β-hCG testing confirmed pregnancy.

Prenatal care was initiated at a basic health unit, with the completion of a prenatal record, routine laboratory exams, a new US, and calculation of gestational age (GA) based on the last menstrual period (LMP: April 29, 2018), corresponding to nine weeks and three days at the time of initiation.

A US conducted on July 7, 2018, revealed a monochorionic diamniotic twin pregnancy, with one embryo measuring 11 weeks with positive cardiac activity and a second embryo measuring eight weeks and three days without cardiac activity, showing signs of mummification.

The patient was subsequently referred to high-risk prenatal care, and a serial US was performed:

1. July 31, 2018: One embryo measuring 14 weeks and 5 days with spontaneous movements and cardiac activity. The second embryo had no vital signs (GA: 7 weeks and 5 days).
2. September 22, 2018: Singleton pregnancy, GA of 22 weeks, estimated fetal weight of 450g, fetal heart rate of 143 bpm, with normal biophysical profile and fetal morphology.

Routine laboratory investigations showed negative serologies for HIV/Anti-HIV syphilis (VDRL test), hepatitis B surface antigen (HBsAg), and indirect Coombs (second trimester). Toxoplasmosis IgG was positive, and IgM was underreported. The ABO/Rh of the patient was O negative.

The patient maintained prenatal routine care, and the pregnancy progressed uneventfully, resulting in a term vaginal delivery of a healthy newborn without complications.

DISCUSSION

The natural history of twin pregnancies is poorly described in the literature[3].

Monochorionic pregnancies carry higher risks of adverse perinatal outcomes due to complications, such as the twin-to-twin transfusion syndrome, selective intrauterine growth restriction, intrauterine fetal demise, and acardiac twin[3-6].

Fetal loss in twin pregnancies occurs with notable frequency, especially in monochorionic gestations[4]. The demise of one twin increases the risk of complications for the surviving co-twin, including thromboembolic phenomena[5]

This report describes a relatively common yet underreported event. In this case, the patient had a monochorionic twin pregnancy; most fetal losses occur in the first trimester and are more often attributed to anembryonic gestations. Although chromosomal abnormalities or other causes could not be excluded in this case, the monochorionic pregnancy was considered the cause of the early fetal demise. Further studies are needed to better elucidate the diagnosis, enabling evidence-based interventions and prevention.

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SECONDARY HYPERTENSION TO PHEOCHROMOCYTOMA: A CASE REPORT

HIPERTENSÃO SECUNDÁRIA AO FEOCROMOCITOMA: RELATO DE CASO

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ABSTRACT

Pheochromocytomas (PCC) are tumors that originate from chromaffin cells, which produce catecholamines, and are typically located in the adrenal glands. This rare condition has an incidence of 0.8 per 100,000 person-years, with a higher prevalence in women aged between 40 and 59 years. One of the main clinical manifestations is hypertension, classified as secondary hypertension due to PCC. We reported the case of a 53-year-old woman who sought medical care at a private cardiology clinic for a routine consultation and preoperative assessment for tumor excision in the right adrenal gland. She had previously been diagnosed with secondary arterial hypertension due to PCC. This type of tumor causes high blood pressure that requires pharmacological adrenal blockade until tumor excision. Normalization of blood pressure is expected after the procedure (i.e., adrenergic stimulus), with the patient returning to a normotensive state.

Keywords: Hypertension; Pheochromocytoma; Adrenal Glands.

RESUMO

Os feocromocitomas são tumores de células cromafins produtoras de catecolaminas, que podem ocorrer nas glândulas adrenais. É considerado raro, atingindo 0,8 por 100.000 pessoas/ano, com maior prevalência em mulheres entre 40 a 59 anos. Um dos problemas acarretados *é a hipertensão, sendo classificada como hipertensão secundária ao feocromocitoma. Relatamos o caso de* uma mulher de 53 anos, que procurou auxílio médico em uma clínica particular especializada em cardiologia, para consulta de rotina e avaliação pré-operatória para fins de exérese de tumoração em glândula adrenal direita. A mesma relata ter sido diagnosticada com hipertensão arterial secundáriaaofeocromocitoma. Ofeocromocitoma é uma causa de hipertensão secundária que resulta no aumento dos níveis tensionais, sendo necessário o bloqueio adrenérgico, até que seja feita a excisão do tumor, quando se espera que haja a normalização dos níveis pressóricos, à medida que o estímulo adrenérgico é superado com a retirada da neoplasia, voltando o paciente ao seu estado de normotensão.

Palavras-chave: Hipertensão; Feocromocitoma; Glândulas Suprarrenais.

INTRODUCTION

Systemic arterial hypertension (SAH) is a multifactorial clinical condition with high prevalence, defined by sustained blood pressure (BP) levels of ≥ 140/90 mmHg[1]. This condition is a major risk factor for other comorbidities, including acute myocardial infarction and stroke.

The prevalence of SAH in Brazil is variable, ranging from 2.5% to 30.9%; the prevalence increases with advancing age[2,3].

SAH can be primary or secondary. Primary SAH accounts for about 95.0% of cases and is associated with risk factors, such as genetic predisposition, smoking, obesity, and black skin color[4]. In these cases, the condition is considered chronic and incurable, with management focused on BP control.

Secondary SAH is less common, accounting for about 5.0% of cases. It occurs when patients with previously normal BP levels develop SAH following an underlying disease, including chronic kidney disease, obstructive sleep apnea or hypopnea syndrome, primary hyperparathyroidism, and pheochromocytoma (PCC). In contrast to primary SAH, secondary SAH can often be resolved with appropriate treatment of the disease, in addition to SAH treatment. However, prolonged exposure to elevated BP during secondary SAH promotes arterial stiffening, a risk factor for primary SAH.

PCC is a neuroendocrine tumor originating from chromaffin cells of the adrenal medulla. These tumors produce, store, metabolize, and secrete catecholamines[5]. They are rare, with an estimated prevalence of 0.1% to 0.2% among patients with SAH[6] across all ages; however, they are most prevalent between the ages of 40 and 59, and rarely after 60 years of age.

CASE REPORT

A 53-year-old woman (C.L.), white, married, teacher, attended a cardiologist for a routine consultation and preoperative evaluation for tumor excision in the right adrenal gland. She reported a diagnosis of SAH following clinical suspicion of PCC. The diagnosis was based on an abdominal and pelvic computed tomography scan with non-ionic contrast, which revealed an expansive lesion in the left adrenal gland measuring 3.2 x 2.8 cm, with subtle contrast enhancement during the imaging phases. During a consultation with her general surgeon, she exhibited a BP of 150/105 mmHg, and atenolol (100 mg orally) was prescribed once daily. Laboratory investigations revealed elevations of vanillylmandelic acid and urinary metanephrines. Physical examination at cardiology consultation showed a BP of 140/100 mmHg and a heart rate of 73 bpm. Then, she underwent home blood pressure monitoring (HBPM), which demonstrated normal values, and she was cleared for the proposed surgery. Histopathological findings of the surgical specimen revealed macroscopic alterations described as "irregular, elastic, yellowish tissue formation, weighing 38.18 g and measuring 5.5 x 3.5 x 3.0 cm. Sections disclosed a yellowish nodular lesion measuring 4.0 x 3.5 x 3.0 cm, centered by a cystic cavity of 3.0 x 2.8 cm filled with brownish fluid." Microscopy analysis reported "adrenal medullary hyperplasia origin composed of cells with abundant, basophilic, granular cytoplasm and small, clear nuclei, occasionally with visible nucleoli, arranged in nests surrounded by sustentacular cells and delicate fibrous septa. The foci of a fusiform cell pattern were observed. Two mitotic figures were identified in 10 high-growth fields, with tumor-free surgical margins". The final diagnosis was PCC with a pheochromocytoma of the adrenal gland scaled score (PASS) of 2, suggesting benign behavior (i.e., scores below 4)[7]. After the results, the patient returned to her cardiologist, who confirmed the diagnosis. Following the surgery, the patient returned to a cardiologic consultation, still using antihypertensive medication and presenting a BP of 110/70 mmHg and a heart rate of 70 bpm; she was instructed to discontinue medication gradually. After 30 days of medication discontinuity, a repeat HBPM revealed normal BP values. Another evaluation was conducted nine months later, confirming sustained normotension without the need for antihypertensive medication.

COMMENT

PCCs are neuroendocrine tumors arising from chromaffin cells of the adrenal medulla. They manifest a wide range of signs and symptoms, resulting in a heterogeneous and complex clinical presentation, with a high risk of cardiovascular morbidity and mortality[8]. Among these manifestations, SAH stands out as a highly prevalent and multifactorial condition.

PCC-related SAH is classified as secondary SAH. Initial control of secondary SAH may be achieved with pharmacotherapy, as demonstrated in this case with atenolol. Nevertheless, BP levels normalize with the removal of the PCC, resolving secondary AH.

In this report, the patient presents a case of secondary SAH, with BP normalized after tumor excision and histopathological confirmation of PCC. Additionally, the tumor was benign based on the PASS. Following surgery, her BP stabilized at 110/70 mmHg, and antihypertensive therapy was discontinued. The resolution of hypertension was confirmed in the 90-day follow-up assessment (including HBPM), supporting the effectiveness of the surgery.

Although the patient no longer has SAH, prolonged exposure to elevated BP levels may have induced arterial stiffness, increasing the long-term risk of developing primary SAH.

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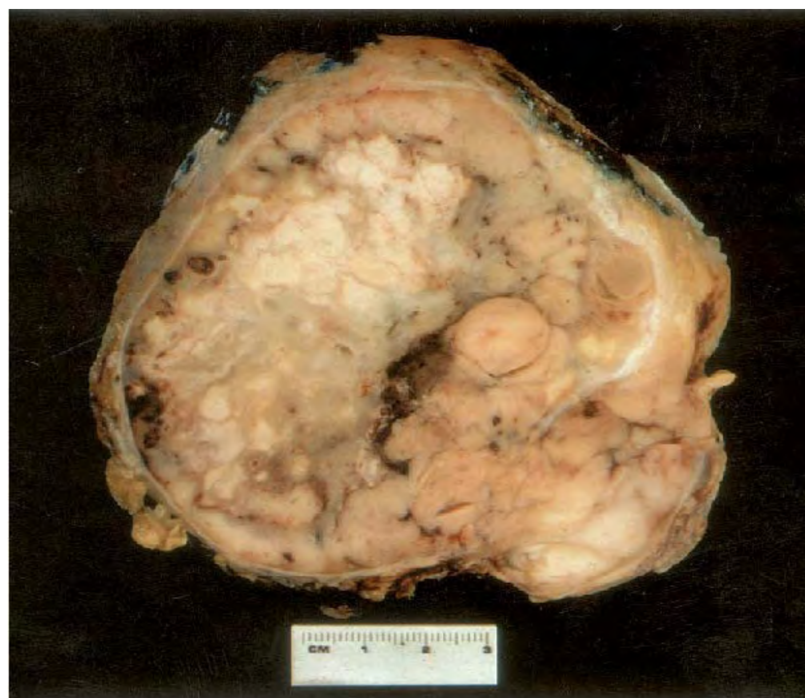

Figure 1. Macroscopic appearance of a pheochromocytoma tumor[7].

Pheochromocytoma of the Adrenal Gland Scale	
Microscopic Feature	Score
Vascular invasion	1
Capsular invasion	1
Periadrenal adipose tissue invasion	2
Cell nests of large proportions or Diffuse growth	2
Focal necrosis or confluent	2
High cellularity	2
Cellular Monotony	2
Mitotic figures > than 3 in 10 fields of great increase	2
Atypical mitotic figures	2
Marked Nuclear Pleomorphism	1
Hyperchromasia	1

Table 2. Pheochromocytoma of the adrenal gland scale score (PASS) according to Thompson's (2002)[7].

DISAGREEMENT BETWEEN THE RELATIONSHIP OF THE BI-RADS® US 4B FINDING WITH BENIGN OUTCOME IN A PATIENT WITH SUSPECTED BREAST CANCER: A CASE REPORT

DESACORDO ENTRE A RELAÇÃO DO ACHADO BI-RADS® US 4B COM DESFECHO BENIGNO EM PACIENTE COM SUSPEITA DE CÂNCER DE MAMA: RELATO DE CASO

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ABSTRACT

Cancer is the leading cause of death worldwide. Breast cancer is the most prevalent among women, and in Brazil, it is the primary cause of cancer-related mortality in this population. During a gynecological consultation, a 29-year-old nulliparous woman reported right breast pain on palpation for the last seven days; the patient presented a palpable nodule in the inferomedial quadrant of the right breast during physical examination. Breast ultrasound (US) revealed a complex cystic-solid lesion, parallel to the skin, with indistinct margins, located at the 6 o'clock position in the right breast, measuring 2.4 x 1.1 x 0.9 cm (volume = 1.3 cm^3), with Doppler-detected vascularization, and categorized as BI-RADS® 4B. A US-guided core biopsy was performed, yielding five tissue samples using a 14-gauge needle. The lesion was reclassified as BI-RADS® 4A after the biopsy. Histopathology analysis demonstrated an inflammatory process with abscess formation, usual ductal hyperplasia, and clustered cysts exhibiting apocrine metaplasia. A follow-up US was performed 30 days after the first examination to localize the lesion before excision, revealing no detectable nodule. A six-month follow-up US confirmed the absence of the lesion, with only residual cystic images. Disagreement in radiological reports may cause psychological stress for patients; thus, it is important to minimize the potential psychological harm due to breast cancer misdiagnosis.

Keywords: Breast cancer; Breast ultrasonography; Psychological stress.

RESUMO

Introdução: O câncer lidera as causas de morte no mundo e, entre mulheres, o tumor de mama *é* o mais prevalente. No Brasil, a neoplasia mamária é a maior causa de morte por câncer nas mulheres. Relato de caso: Paciente de 29 anos, nulípara, que em consulta ginecológica relatou dor à palpação em mama direita que durava sete dias. Foi percebido nódulo palpável em quadrante *ínfero-medial* da mama direita durante exame físico. A ultrassonografia (USG) descreveu imagem compatível com complexo sólido cístico, paralelo a pele, de margens não circunscritas localizada *às* 6h da mama direita medindo 2,4x1,1x0,9 (vol=1,3cm^3), vascularizado ao Doppler, categorizado como BI-RADS 4B. Foi indicada investigação com CORE BYOPSY guiada por USG, onde foram retirados 5 fragmentos com agulha calibre 14 e com mudança de classificação para BI-RADS 4A. A histopatologia mostrou um processo inflamatório com abscedação, hiperplasia ductal usual, típica, focal, com cistos com metaplasia apócrina agrupados. Trinta dias após a primeira ultrassonografia ser realizada outra USG foi feita para marcação da lesão e exérese e não foi visualizado nódulo. O controle com USG seis meses após confirmou ausência de lesão, apenas com achado de imagem cística. Comentários: Persiste a preocupação de laudos radiológicos discrepantes causando estresse psicológico *às* pacientes. O intuito *é* evitar possíveis prejuízos psicológicos provocados pelo diagnóstico equivocado de câncer de mama.

Palavras-chave: Neoplasia de mama; Ultrassonografia mamária; Estresse psicológico.

INTRODUCTION

Cancer is the leading cause of mortality worldwide. Breast cancer is the most prevalent among women, and in Brazil, it represents the primary cause of cancer-related death in this population[1].

The development of breast cancer is multifactorial, including biological and environmental factors, such as age, endocrine, and genetic components. Genetic predisposition accounts for about 5% to 10% of total cases[2]. Most breast cancers are diagnosed at a subclinical stage via routine mammography or population-based screening programs.

Breast cancer can also be detected by breast self-examination, mammography, or ultrasound (US) and confirmed using biopsy[3]. Delay in the diagnosis often leads to worse prognoses.

In the United States, early detection has led to a mortality reduction of 30% and 19% in women aged over 50 and 40 to 49 years, respectively. The Breast Imaging Reporting and Data System Ultrasonographic (BI-RADS® US™) was implemented to standardize breast imaging reports, terminology, and management recommendations, as endorsed by the American College of Radiology[2].

Once imaging findings suggest malignancy and the diagnosis is confirmed by biopsy, treatment options include chemotherapy, radiotherapy, hormone therapy, or surgery (mastectomy, quadrantectomy) 5.

The BI-RADS® US™ system classifies US findings on a scale of 0 to 6, with stage 4 subdivided to refine the probability of malignancy and guide clinical management.

Figure 1. Breast Imaging Reporting and Data System Ultrasonographic (BI-RADS® US™) rating scale.

Category		Management	Probability of cancer
0	Need additional imaging or prior examinations	Recall for additional imaging and/or await prior examinations	N/A
1	Negative	Routine screening	0%
2	Benign	Routine screening	0%
3	Probably benign	Short-interval follow-up or continued surveillance mammography	≤ 2%
4	Suspicious of malignancy	Tissue diagnosis	4A: 2% to 10% - low suspicion 4B: 10% to 50% - moderate suspicion 4C: 50% to 95% - high suspicion
5	Highly suggestive of malignancy	Tissue diagnosis	> 95%
6	Known biopsy-proven malignancy	Surgical excision when clinically appropriate	100%

CASE REPORT

This case report aimed to discuss the relationship between the BI-RADS®US 4B findings and a benign histopathological outcome in a patient with suspected breast cancer after US with the BI-RADS®US criteria.

During a gynecological consultation, a 29-year-old nulliparous woman reported pain on palpation in the right breast for the last seven days. Physical examination identified a palpable nodule in the inferomedial quadrant of the right breast.

The patient reported no family history of breast or ovarian cancer. Breast US, performed on the same day of gynecological consultation, identified a complex cystic solid lesion, parallel to the skin, with indistinct margins located at the 6 *o´clock position* of the right breast, measuring 2.4 x 1.1 x 0.9 cm (volume = 1.3 cm^3), exhibiting vascularization on Doppler assessment, and categorized as BI-RADS®4B. Two days later, a US-guided core needle biopsy was performed at a different facility by another specialist, obtaining five fragments using a 14-gauge needle, and the lesion was reclassified to BI-RADS®4A.

Histopathology revealed an inflammatory process with abscess formation, usual focal ductal hyperplasia, and clustered cysts exhibiting apocrine metaplasia. Thirty days after the first US, a subsequent US was performed for preoperative lesion localization, which showed no detectable nodule. A

follow-up US conducted six months later confirmed the absence of a lesion, revealing only cystic changes.

DISCUSSION

Disagreement in radiological reports is a concern due to the psychological stress caused to patients. Thus, it is important to minimize the potential psychological harm caused by breast cancer misdiagnosis.

Breast cancer diagnosis and mastectomy may cause most repercussions due to the impact on intimate and emotional feminine aspects, which can be intensified by a lack of knowledge about the disease, sounding like a death sentence. Feminine emotions are rarely considered by healthcare professionals, who focus more on the physical and biological aspects because they are more visible. However, the intrinsic link between body and mind warrants equal attention, as the diagnosis often induces lifestyle changes[6].

Besides the physical effects, cancer diagnoses and the adverse effects of treatments cause a psychological burden on these women. Social stigma, fear of death, bodily mutilation, and perceived social devaluation lead to psychosocial difficulties for patients and their families[5].

A cancer diagnosis confronts the patient with the question of the imponderable, finitude, and death[4]. The disease lethality and the physical losses imposed by treatment may cause a feeling of vulnerability and loss of control over life.

This case report highlights the importance of managing radiological reports that may cause disagreement to minimize psychological harm in patients undergoing cancer diagnosis, affecting the physical integrity (a primary patient concern) and the psychological self-image of the women and of their femininity, sexuality, and finitude of life.

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CASE REPORT

LAPAROSCOPIC PARTIAL NEPHRECTOMY FOR T2B TUMOR IN A PATIENT WITH A SOLITARY KIDNEY: A CASE REPORT

NEFRECTOMIA PARCIAL LAPAROSCÓPICA PARA TUMOR T2B EM PACIENTE COM RIM ÚNICO: RELATO DE CASO

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ABSTRACT

For T2 renal tumors, most authors recommend radical nephrectomy. However, reports of partial nephrectomy for these tumors in patients with solitary kidneys are scarce. This study describes a case of a 32-year-old male (R.J.A.L) with a 12-cm tumor in the left kidney and with agenesis of the right kidney. Preoperative renal function was normal. In June 2016, he underwent a laparoscopic partial nephrectomy. Postoperatively, the patient developed anuria and elevated serum creatinine, requiring renal replacement therapy with hemodialysis. After 20 days, the renal function recovered, and hemodialysis was discontinued. Histopathology confirmed renal cell carcinoma. At present, the patient remains hemodialysis-free, with preserved renal function and no evidence of tumor recurrence on follow-up imaging with computed tomography. Laparoscopic partial nephrectomy of T2b renal tumors may be feasible and oncologically effective in selected cases, including those involving a solitary kidney, while preserving adequate renal function.

Keywords: Renal cell carcinoma; Solitary kidney; Nephrectomy.

RESUMO

Para tumores T2, a maioria dos autores sugere a nefrectomia radical, porém, a literatura carece de relatos de nefrectomia para tumores T2b em pacientes com rim *único. RJAL, sexo masculino, 32 anos com* tumor em rim esquerdo medindo 12 cm e agenesia renal direita. No pré-operatório apresentava função renal normal. Foi submetido *à* nefrectomia parcial laparoscópica em junho de 2016. Evoluiu com elevação da creatinina sérica e anúria, sendo então iniciada terapia renal substitutiva com hemodiálise. Após 20 dias, por apresentar normalização da função renal, optou-se por suspender a mesma. O anatomopatológico revelou tratar-se de carcinoma de células renais. No momento, o paciente encontra-se fora de hemodiálise e com TC mostrando rim sem evidências de recidiva tumoral. A nefrectomia parcial laparoscópica para tumores renais estádio T2b, *é* factível e pode ser indicada em casos selecionados como agenesia renal, com resultado oncológico eficaz e manutenção da função renal.

Palavras-chaves: Carcinoma de células renais; Rim único; Nefrectomia.

INTRODUCTION

Renal cell carcinoma (RCC) accounts for about 2% to 3% of malignant tumors in adults, with a higher incidence in Western countries. The peak incidence of RCC occurs between 60 and 70 years, and mostly in males[1-2]. Advances in diagnostic imaging have improved the detection and staging of renal tumors, with about half of the cases discovered incidentally[2].

Surgery remains the standard treatment for most renal tumors, including benign lesions, with the choice between radical or partial nephrectomy depending on tumor location and clinical staging[3].

Partial nephrectomy can be performed using open, laparoscopic, or robotic techniques, and is the recommended intervention for T1 tumors to preserve renal function; the latter two techniques offer similar oncologic outcomes and superior post-surgery recovery. This procedure is safe and effective for patients with solitary kidneys. For T2 tumors, radical nephrectomy is typically advised[4]-5; however, reports of partial nephrectomy for these tumors in patients with solitary kidneys are scarce.

CASE REPORT

A 32-year-old male patient with a history of hypertension and smoking sought an emergency service reporting gross hematuria for at least two weeks. Laboratory investigations revealed normal renal function, and an abdominal ultrasound identified a renal mass. Contrast-enhanced magnetic resonance imaging of the abdomen (Figure 1) confirmed a 12-cm tumor on the left kidney involving the middle

and lower poles. An agenesis of the right kidney was also identified.

The preoperative evaluation revealed a serum creatinine level of 0.9 mg/dL. Given the solitary kidney and preserved renal function, nephron-sparing surgery was elected. In June 2016, the patient underwent a laparoscopic partial nephrectomy. The procedure was uneventful, with a pedicle clamping time of 50 minutes and an estimated blood loss of 400 mL. The total surgical time was 130 minutes. Postoperatively, the patient developed anuria and elevated serum creatinine in the first 24 hours, requiring hemodialysis. After 20 days, renal function normalized, and the hemodialysis was discontinued.

Histopathological examination revealed a clear RCC (Fuhrman's grade 3) with negative surgical margins and no invasion of perirenal adipose tissue. The final pathological stage was pT2b Nx Mx.

Follow-up imaging with computed tomography (Figure 2) revealed no evidence of recurrence, with preserved renal function (serum creatinine level of 1.3 mg/dL).

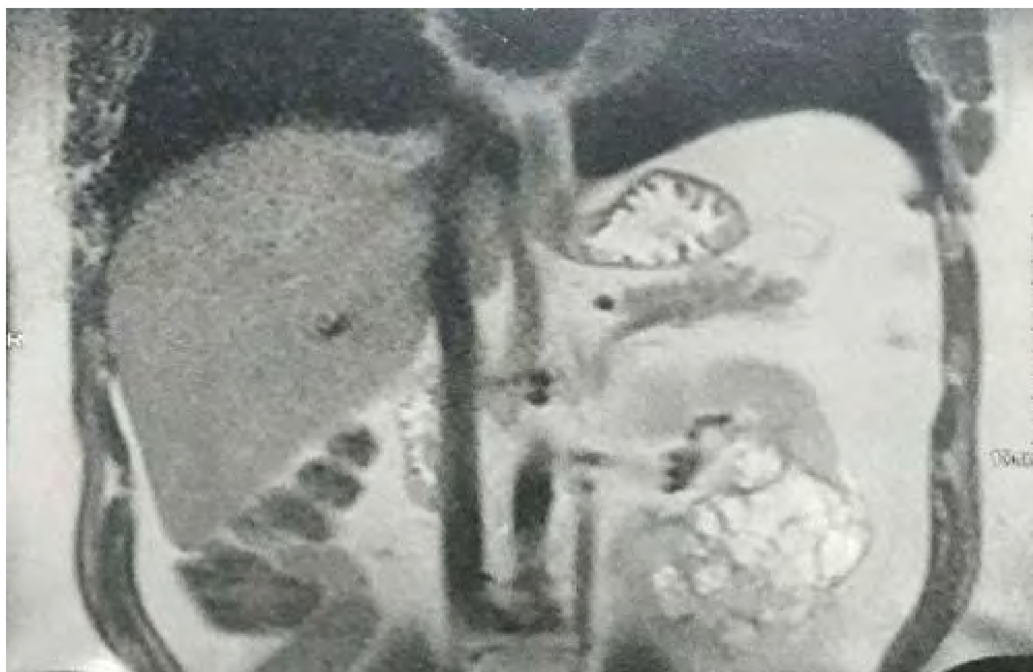

Figure 1. Preoperative magnetic resonance imaging showed a 12-cm left renal mass.

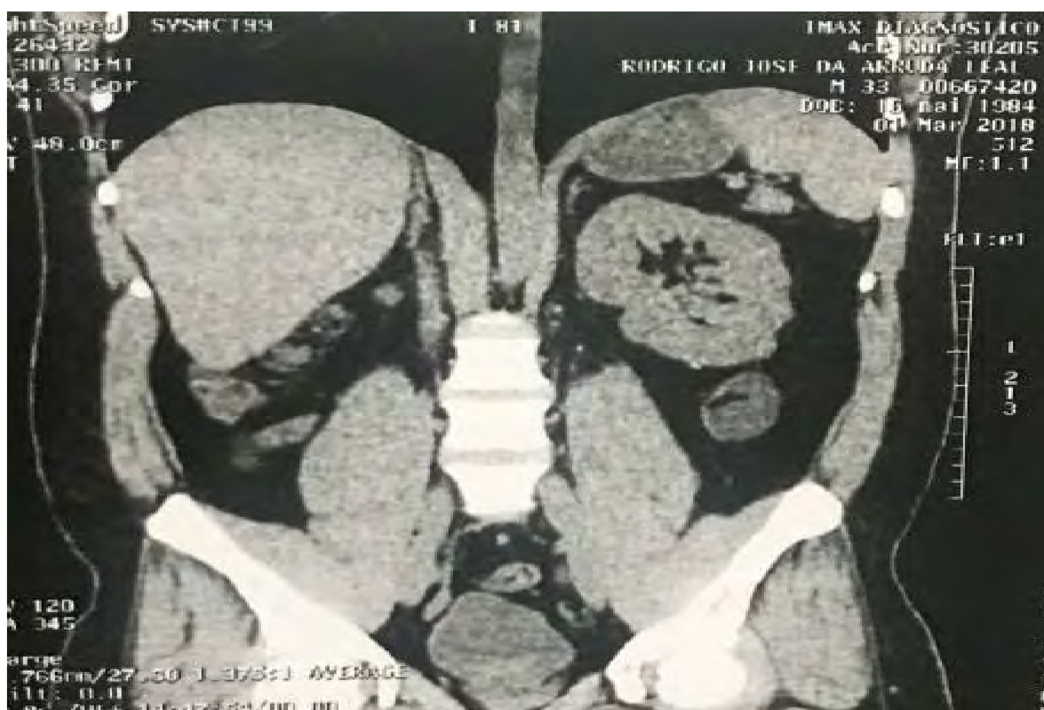

Figure 2. A postoperative computed tomography scan showed no evidence of recurrence.

DISCUSSION

RCC ranks among the ten most common malignancies in Western countries. Worldwide, about 270,000 new cases and 116,000 deaths occur annually6.

Nephrectomy is the indicated intervention for removing malignant tumors of the kidney. Partial nephrectomy can be performed via open, laparoscopic, or robotic-assisted (using little incisions and a videocamera) interventions to preserve as much renal mass as possible without disregarding the safety of removing tissue affected by the tumor.

The main indications for partial nephrectomy include solitary kidney, bilateral tumors, and small, peripherally located renal lesions (< 4 cm) or complex cysts (Bosniak III and IV)8.

In this case, laparoscopic partial nephrectomy for a T2b renal tumor (> 10 cm limited to the kidney) proved technically feasible and oncologically effective in a patient with a solitary kidney.

This case report contributes to the limited evidence regarding nephron-sparing surgery in T2b, particularly in solitary kidneys, highlighting the possibility of preserving renal function without hindering oncologic outcomes.

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EXOGENOUS MELATONIN AND ITS METABOLIC EFFECTS: A LITERATURE REVIEW

MELATONINA EXÓGENA E SEUS EFEITOS METABÓLICOS: REVISÃO DA LITERATURA

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ABSTRACT

Introduction: Melatonin is a hormone produced mainly by the pineal gland, playing a key role in the regulation of physiological processes, particularly the circadian rhythm. **Objectives:** To discuss the diverse effects of exogenous melatonin administration. **Methods:** This descriptive and exploratory study summarized recent publications in English or Portuguese. Twenty-four studies indexed in Scielo, PubMed, Science Direct, and Cochrane databases were included and analyzed. **Results:** Melatonin regulates the circadian rhythm, modulates the immune and cardiovascular systems, and promotes protection to oxidant stimuli while inducing antioxidant activities. It also exerts gastroprotective, neuroprotective and neuromodulatory effects. **Conclusion:** Melatonin induces beneficial effects across different physiological processes in humans. It is considered a safe and well-tolerated pharmacological agent, associated with minimal side effects and no withdrawal symptoms.

Keywords: Effects; Melatonin; Physiological regulation

RESUMO

Introdução: A melatonina é um hormônio produzido majoritariamente pela glândula pineal e que tem ação direta sobre a regulação de processos fisiológicos, especialmente o ritmo circadiano. ***Objetivo:*** Demonstrar através da literatura, os diferentes efeitos fisiológicos relacionados à administração da melatonina exógena. ***Métodos:*** Trata-se de um estudo descritivo e exploratório, baseado na sumarização de trabalhos recentes publicados em inglês ou português. Foram analisados e incluídos 25 artigos indexados nas bases de dados Scielo, Pubmed, ScienceDirect e Cochrane. **Resultados:** Este hormônio está diretamente envolvido na regulação de processos fisiológicos, como o ciclo circadiano, regulação imune e cardiovascular, atividade pró-oxidante e antioxidante e gastroproteção, além de possuir efeito neuroprotetor e neuromodulador. ***Conclusão:*** A melatonina está diretamente ligada a efeitos positivos em processos dos mais diversos sistemas corporais. Trata-se de uma molécula de uso terapêutico seguro e de boa tolerância, estando relacionada a poucos efeitos colaterais e não ocasionando sintomas de retirada.

Palavras-chave: Efeitos; Melatonina; Regulação fisiológica

INTRODUCTION

Insomnia is the most common sleep disorder, with a prevalence ranging from 10% to 25%. Individuals with insomnia experience reduced work productivity and increased healthcare utilization. Despite the availability of numerous medications, no pharmacological strategy has yet been firmly established for its management[1].

Melatonin (N-acetyl-5-methoxytryptamine) is a hormone primarily produced by the pineal gland that affects the secretion of several endogenous substances (e.g., cortisol, adrenaline, etc.). Consequently, melatonin also plays a key role in regulating activity-rest and sleep-wake rhythms[2].

The synthesis of melatonin begins with the conversion of the amino acid tryptophan into 5-hydroxytryptophan (5-HTP) by tryptophan hydroxylase 1 enzyme. Next, 5-HTP is decarboxylated by 5-HTP decarboxylase into serotonin, which is subsequently acetylated to N-acetylserotonin. Last, melatonin is formed from N-acetylserotonin and released into the bloodstream[3].

Owing to its high lipophilicity and ability to easily cross the blood-brain barrier, melatonin has been extensively investigated in clinical and experimental studies. Beneficial effects on the central nervous system have been reported, with high safety

and tolerability even at elevated doses[4].

Moreover, melatonin exerts diverse physiological effects, including regulation of the circadian rhythm, modulation of the immune and cardiovascular systems, reduction of pro-oxidant activity with concomitant enhancement of antioxidant activities, gastroprotection, and neuroprotective and neuromodulatory actions[5].

Based on the extensive evidence supporting its effects, the present study aimed to discuss the clinical use of exogenous melatonin.

METHODS

This descriptive and exploratory study summarized recent publications in English or Portuguese. A total of 24 articles indexed in Scielo, PubMed, ScienceDirect, and Cochrane databases were included and analyzed. The search strategy employed the following DeCS/MeSH descriptors: “melatonin”, “physiology”, and “drug effects”. Grey literature was excluded.

DISCUSSION

Light stimuli regulate melatonin synthesis: darkness increases production, whereas light exposure inhibits it. Sleep propensity is associated with the daily rise in melatonin secretion, with serum levels starting to increase approximately two hours before usual bedtime[6].

Clinical studies with middle-aged and older adults showed improvements in primary insomnia symptoms following daily administration of 2 mg of slow-release melatonin. The largest trial, involving more than 500 patients, demonstrated particularly favorable outcomes in individuals aged 55 years or older, with efficacy sustained for over six months[7].

Exogenous melatonin combined with antidepressants has been shown to improve depressive symptoms; however, no significant effect was observed when administered as monotherapy[8].

In addition to its role in regulating the circadian rhythm, melatonin also modulates immunobiological processes by influencing key cellular components of the innate immune response. In rats, multiple daily injections of melatonin into the pineal gland and adjacent brain regions significantly increased phagocytic microglia cellularity[9].

Moreover, melatonin administration significantly increased the chemotaxis index[10], enhanced the concentration of natural killer cells and monocytes in the bone marrow of healthy young mice, and attenuated the excessive production of pro-inflammatory mediators, particularly cytokines, in several in vitro inflammation models[11].

Recent evidence also suggests that melatonin exerts relevant antiviral, antibacterial, and antiparasitic effects[12, 13]. In immunocompetent mice, melatonin reduced viral levels in the brain, whereas such effects were absent in immunosuppressed mice, indicating that its antiviral action requires an intact immune system.

Several studies using experimental models of endotoxin-induced and polymicrobial sepsis have demonstrated the protective role of melatonin[15, 16]. This protective effect has been attributed to its pleiotropic action, including the inhibition of pro-inflammatory cytokine production, especially tumor necrosis factor alpha (TNF-α), and increased levels of the anti-inflammatory interleukin-10 (IL-10)[15, 17].

Exogenous melatonin also has also shown benefits in gastrointestinal diseases. In experimental colitis models, melatonin has been shown to reduce visceral hyperalgesia and attenuate disease severity[18, 19]. Clinical studies have further reported improvements in irritable bowel syndrome, suggesting a close relationship between this condition and circadian rhythm regulation[20].

In the cardiovascular system, melatonin administration combined with conventional treatment for acute myocardial infarction induced significant protective effects against ischemia-reperfusion injury in clinical trials[21]. Additional studies have described improvements in macrovascular and microvascular diseases. In mice exposed to a hyperlipidemic diet and an experimental model of streptozotocin-induced diabetes mellitus, melatonin restored endothelial function and improved microvascular responses.

The expression of melatonin membrane receptors (MT1 and MT2) in pancreatic islets of Langerhans and diffusely in the human pancreas was confirmed immunohistochemically. In pancreatic β-cells, these receptors play in three parallel signaling pathways that distinctly modulate insulin secretion[23].

Chronic oral administration of melatonin in mice for three months significantly reduced total cholesterol and low-density lipoprotein levels, while increasing serum high-density lipoprotein levels. Serum triglyceride levels were decreased by 39%, and

insulinemia was reduced by 33%[24].

Furthermore, oral administration of melatonin reduced hepatic steatosis and liver inflammation, as evidenced by decreased serum aspartate aminotransferase (AST) levels. In hepatocytes, melatonin also downregulated pro-inflammatory cytokines levels and inhibited apoptosis[25].

Table 1. Main physiological effects related to exogenous melatonin administration.

Effects of Exogenous Melatonin		
Author	**Objective**	**Results**
Wade et al., 2011	To analyze the effect of melatonin on sleep regulation in individuals with insomnia.	Insomnia was significantly improved, especially in patients over 55 years of age.
Srinivasan et al., 2006	To evaluate the use of melatonin in the treatment of mood disorders.	Patients with depression presented improved symptoms when treated with antidepressants combined with exogenous melatonin compared with antidepressants alone.
Tang et al., 2009	To analyze the effect of sleep on colitis and irritable bowel syndrome.	Melatonin induced antinociceptive effects in colitis. Improved sleep was associated with reduced severity of irritable bowel syndrome symptoms.
Hussein et al., 2007	To evaluate the effects of melatonin on lipid metabolism.	Reduced serum total cholesterol, LDL, and triglycerides levels, and increased HDL levels after treatment with melatonin.
Tahan et al., 2009	To analyze the use of melatonin in the treatment of hepatic steatosis.	Reduced hepatic steatosis, liver tissue inflammatory status, and decreased hepatocyte apoptosis.

CONCLUSION

Melatonin is widely regarded as a safe and well-tolerated compound, characterized by minimal side effects and the absence of withdrawal symptoms. Beyond its regulatory function in circadian rhythm, melatonin exerts anti-inflammatory effects and modulates the immune, cardiovascular, and gastrointestinal systems. Additionally, it enhances the efficacy of other pharmacological agents by synergistically attenuating infectious processes.

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PERCEPTION OF USERS FROM THE UNIFIED HEALTH SYSTEM REGARDING THE PRESENCE OF MEDICAL STUDENTS IN SCHOOL CLINICS: A REVIEW ARTICLE

PERCEPÇÃO DOS USUÁRIOS DO SISTEMA ÚNICO DE SAÚDE QUANTO À PRESENÇA DE ACADÊMICOS DE MEDICINA NAS CLÍNICAS-ESCOLA: REVISÃO BIBLIOGRÁFICA

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ABSTRACT

Introduction: The assessment of patient satisfaction with healthcare services has become an increasingly used indicator of the quality of care provided, as it evidences the perceptions of patients regarding medical students in patient care. **Objectives:** To evaluate the perception of patients in school clinics regarding the participation of medical students during consultations. **Methods:** This narrative review was conducted using the LILACS, MEDLINE, and SciELO databases. A total of 14 full-text studies published in Portuguese, English, and Spanish over the past decade were included. **Results:** Most patients reported satisfaction with consultation involving medical students, perceiving an enhancement in the quality of care. However, a few patients reported discomfort during physical examinations, preferring consultations without the presence of students. **Conclusion:** Most patients expressed satisfaction in contributing to the education of medical students, believing that this collaboration improves the healthcare quality.

Keywords: Patient Satisfaction; Health Evaluation; Quality Control; Medical Education; Unified Health System.

RESUMO

Introdução: A avaliação da satisfação dos pacientes quanto aos serviços na *área* da saúde, tem sido cada vez mais utilizada como variável da qualidade da assistência prestada. Enfatizando assim a importância de conhecer a percepção dos usuários frente à assistência realizada por estudantes de medicina. **Objetivos:** Avaliar a percepção dos usuários em serviços de clínica escola, quanto *à* participação de estudantes de medicina durante os atendimentos médicos. **Métodos:** Foram utilizadas as bases de Literatura: LILACS, MEDLINE e SciELO. Foram selecionados 14 artigos completos redigidos em língua portuguesa, inglesa e espanhola, publicados nos últimos 10 anos. C**omentários:** Os estudos mostraram que a grande maioria dos usuários relatam estarem satisfeitos com o atendimento quando os estudantes estão presentes, trazendo mais qualidade ao atendimento. Entretanto, uma pequena parcela, demonstram-se intimidados no exame físico, optando pelo atendimento sem a presença dos estudantes. **Conclusão:** Evidenciou-se a satisfação da maioria dos usuários em poder colaborar para a construção do aprendizado dos estudantes e assim, contribuir para a melhoria da qualidade da atenção à saúde.

Palavras-chave: Satisfação do paciente; Avaliação em saúde; Controle de qualidade; Educação médica; Sistema único de saúde.

INTRODUCTION

The assessment of patient satisfaction with the healthcare services has been increasingly used as an important variable for defining service quality[1-4]. Patients have contributed to medical education since ancient times. Great masters transmitted their knowledge at the bedside of the sick or in outpatient clinics[5-7].

Undergraduate students gain diversified learning experiences that extend beyond theoretical knowledge of clinical protocols and procedures. Direct interaction with patients, embedded within their social contexts and unique health needs, is essential for developing professional maturity and clinical competence within teaching environments[5-6].

Most patients naturally accept the presence of medical students during their care; however, their perception may differ regarding consultations conducted solely by the physician compared with those involving the physician and medical students. Additionally, patients may question whether the behavior of the students is adequate[4].

Patient-centered care assessment tools provide valuable insights into the perception of patients about healthcare services, enabling the implementation of strategies to improve the quality of care[7].

Although Brazilian studies on patient satisfaction with healthcare services began in the 1990s, research in this area remains limited[5-6]. Moreover, research on instruments for measuring patient satisfaction with healthcare services is scarce[5-7].

Given the importance of delivering humane, high-quality care within teaching clinics, this study aimed to explore the perceptions of patients regarding the involvement of medical students in clinical care, identifying positive and negative aspects of healthcare to enhance its quality.

METHODS

A narrative review was conducted using the LILACS, MEDLINE, and SCIELO databases. The Health Sciences Descriptors terms encompassed patient satisfaction, healthcare evaluation, quality control, medical education, and Unified Health System. A total of 14 full-text studies published in Portuguese, English, and Spanish over the past decade were included. They addressed patient perceptions regarding the presence of medical students during clinical consultations.

RESULTS

Patients are fundamental to the teaching process, as direct observation and clinical practice foster scientific and humanistic development among medical students [9].

Most studies indicated that patients generally report satisfaction with the care they received when students are present. The participation of medical students was associated with the delivery of detailed information, as the students present increased proactive behavior and engagement, contributing to the understanding of patient*s* about their condition and the treatment process[9].

Nevertheless, a few patients reported discomfort and embarrassment related to their privacy during consultations and physical examinations involving students, particularly in the gynecology and urology. This discomfort may occur during physical examination and sometimes leads patients to withhold essential health information[9].

Understanding the opinions of patients regarding healthcare services is a valuable strategy for reflecting on patient reception and improving team-based care. Thus, patient profiles must be evaluated to identify factors that influence satisfaction and dissatisfaction[11].

Evaluating patient experience is the most relevant component in assessing healthcare quality and is commonly investigated using patient satisfaction surveys[1-3].

These surveys serve as final evaluative tools conducted after interaction of the patient with healthcare services, directly reflecting the perceived quality of the service received[14,15].

CONCLUSION

Most patients expressed satisfaction with participating in the educational process of medical students, perceiving their involvement as a contribution to improving the quality of healthcare. The patient perspective represents a reliable indicator of healthcare quality and may refine the teaching-learning process and healthcare management practices.

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Peer review is performed by at least two review- ers with extensive competence to evaluate the manuscript. The entire process is double-blind- ed; that is, reviewers and authors do not know each other's identities.

The editorial decision is made based on the comments from the reviewers. It may follow one of the following outcomes: (1) rejection, (2) new submission chance by addressing the com- ments received, or (3) approval with or without changes.

Manuscripts falling under outcome (1), rejec- tion, will be returned to the authors. In the case of outcomes (2) and (3), more than one round of review may be necessary. Conflicting opinions will have a third opinion requested or will un- dergo editorial arbitration. Failure by authors to comply with the review deadlines stipulated by the journal may result in the submission being archived. Approved manuscripts may receive layout changes as long as they do not alter the merit of the work.

The final editorial decision is recorded and is the responsibility of the editorial board. The manuscript content is the sole responsibility of the authors.

TYPES OF MANUSCRIPTS ACCEPTED FOR PUBLICATION

Original article: a full paper of a clinical or ex- perimental investigation with unpublished re- search results (limit of 3,400 words, seven au- thors, and 30 references).

Integrative, systematic review, and me- ta-analysis: they should address topics of in- terest in health. Narrative reviews will not be accepted. Authors must include the study mo- tivation in the Introduction. Summary and ab- stract must be formatted as a single paragraph in a block format with up to 250 words (limit of 3,400 words, seven authors, and 45 referenc- es).

Short Communication: short communication of original research results. In general, short communications are leaner analyses with a brief discussion of the results (summary and abstract must be formatted as a single para- graph in a block format with up to 120 words; the manuscript must be up to 1,000 words with Introduction, Methods, Results, and Discussion sections; up to two tables/figures can be includ- ed in up to three pages combined; references are limited to six).

Case reports: description of clinical cases of interest due to their rarity, presentation, innova- tive diagnosis, or treatment (summary and ab- stract must be formatted as a single paragraph in a block format with up to 120 words; the man- uscript must be up to 2,000 words with Introduc- tion, Case Report, and Discussion sections; up to two tables/ figures can be included in up to three pages combined; references are limited to fifteen; limit of seven authors).

Experience reports: detailed description of a successful or unsucessful experience of an author or a team, which contributes to the dis- cussion, exchange, and proposition of ideas for improving health care. It must include an in- troduction with a theoretical framework for the experience, objectives of the experience, meth- odologies used (including a description of the context and procedures), results, and final con- siderations. Summary and abstract must be for- matted as a single paragraph in a block format with up to 120 words; the manuscript must have up to 2,000 words and up to two tables/figures; limit of 15 references and seven authors).

Methodological paper and theoretical/tech- nical essays: manuscripts that deal with tech- niques or theories used in epidemiological stud- ies or that portray an original clinical observation or description of technical innovations. Manu- script should be concise, limited to 1,500 words, five references, two illustrations, four authors, summary and abstract in must be formatted as a single paragraph in a block format with up to 120 words.

Critical review: restricted to a book or film in the medical field and related sciences. Argu- mentative manuscript in which the author de- scribes and analyzes a social production aiming to influence his readers by recommending the work for its qualities

or rejecting it for its flaws. It must be presented as follows: (1) presentation - summary of the work analyzed with both techni- cal information and information about the book or film content; (2) analysis – interpretation and analysis of the work highlighting its main points, whether positive or negative, and the critical analysis from the author; (3) conclusion - opin- ion on the work, resuming the main points ana- lyzed (up to 1000 words and two authors);

Letters to the Editor: comments from read- ers on works published in the Annals of Olinda Medical School (500 to 700 words).

Editorial: It is the initial article of a volume and is generally requested by the Chief and Deputy Editors to guests with recognized technical and scientific skills.

The word count includes Introduction, Methods, Results, and Discussion (title page, summary, abstract, references, tables, and figures are not included in the word count).

Manuscripts submitted must be intended exclu- sively for the Annals of Olinda Medical School, and simultaneous submission to another jour nal is prohibited. The information and concepts presented in the manuscript, as well as the ve- racity of the research content, are the sole re- sponsibilities of the author(s).

FORMATTING

Manuscripts are accepted in Portuguese or En- glish and must have an abstract in the original language of the manuscript and English. Manu- scripts in English must have an abstract in En- glish and Portuguese.

Manuscripts must be sent in Word, dou- ble-spaced, and Arial font size 12. Do not use line breaks. Do not use force manual hyphen- ations. The full term must follow abbreviations cited for the first time in the document. Title and abstract must not contain abbreviations.

TITLE PAGE

Title of the manuscript in Portuguese and

English (up to 25 words for each title);

Author information (full name, email, ORCID, affiliation, city, state, and country — do not in- clude title and position);

Indication of the corresponding author, with their full address and email;

Conflicts of interest, in accordance with the Resolution of the Federal Council of Medicine (CFM) no. 1595/2000, which prohibits the pub- lication of works for advertisement purposes of medical products and equipment, available at https://sistemas.cfm.org.br/normas/visualizar/ resolucoes/BR/2000/1595. Conflicts of interest must be presented as follows: "The author(s) (name them) received financial support from the private company (mention its name) to conduct this study". If there are no conflicts of interest, the authors must declare: "The authors have no conflicts of interest to declare".

Source of financing, stating whether public or private; if there is none, mention that the study was not funded;

Number of the Certificate of Presentation for Ethical Assessment (CAAE) or number of Research Ethics Committee approval;

Authors contribution to the manuscript.

On the following pages, always starting on a new page, the following sections must be pre- sented:

SUMMARY AND ABSTRACT

Summaries must comply with the recommendations for each category of manuscript. In gen- eral, it must contain up to 250 words and be in structured format, covering the sections Ob- jective, Methods, Results, and Conclusion. The same rule applies to the abstract.

Authors must include a minimum of four and a maximum of six keywords in both English and Portuguese regardless of the language in which the manuscript was submitted.The key- words must be standardized according to the Health Sciences Descriptors (DeCS), available at http://decs.bvs.br/.

REFERENCES

References must be numbered consecutively according to the first mention in the manuscript and using superscript Arabic numerals in accor- dance with Vancouver style (www.icmje.org). The reference list must follow the numerical or- der of the manuscript, ignoring the alphabetical order of authors. Journal titles must follow the Index Medicus/ Medline. The name of the first six authors must appear, followed by the ex- pression et al. when this number is exceeded. Whenever available, the Digital Object Identifier (DOI) must be provided (see examples below). Personal communications, unpu-

work, citations from books, thesis, and dissertations should be avoided. The accuracy of references is the responsibility of the authors.

EXAMPLES

Reference to a journal publication:

Ng OT, Marimuthu K, Koh V, Pang J, Linn KZ, Sun J, et al. SARS-CoV-2 seroprevalence and transmission risk factors among high-risk close contacts: a retrospective cohort study. Lan- cet Infect Dis. 2021 Mar; 21(3):333-343. doi: 10.1016/S1473-3099(20)30833-1

Jardim BC, Migowski A, Corrêa FM, Azevedo e Silva G. Covid-19 no Brasil em 2020: impacto nas mortes por câncer e doenças cardiovascu- lares. Rev Saude Publica. 2022; 56:22. https:// doi.org/10.11606/s1518-8787.2022056004040.

Reference to a World Health Organization Report

World Health Organization. Clinical Care for Severe Acute Respiratory Infection—Toolkit— Update 2022. Genebra: World Health Organi- zation; 2022.

Reference to electronic documents

Brasil. Casos de aids notificados no SINAN, declarados no SIM e registrados no SISCEL/SI- CLOM, segundo capital de residência por ano de diagnóstico. Brasil, 1980-2021 [Internet]. 2021 [acessado em 12 abr. 2022]. Available at: http://www2.aids.gov.br/cgi/deftohtm.exe?tab- net/br.def

FIGURES AND TABLES

Figures and tables must be inserted at the end of the manuscript, followed by their respective captions. Submission in separate files is not permitted. There must be page breaks between each one, respecting the maximum number of three pages for tables and figures combined. Do not format tables using the TAB key.

Figures must be up to 15 cm wide in Portrait orientation and 24 cm wide in landscape orien- tation and be presented within the requested margin (Normal Word setting). Colored figures are accepted. Figures must be provided in high resolution, plots in editable format, and tables, equations, charts, and flowcharts must be sent in an editable file (Word or Excel), never as an image.

blished or on- going

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