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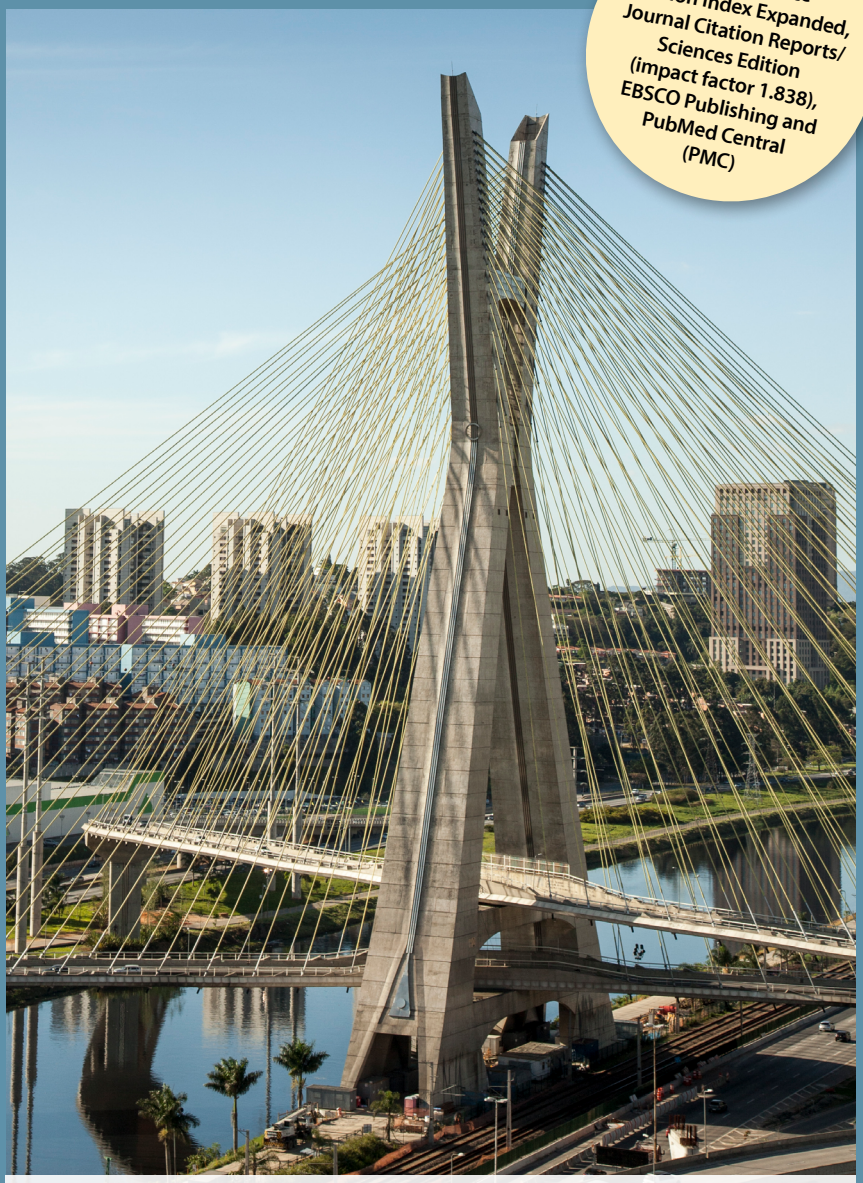

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Artificial Intelligence in Cardiac Surgery: From Assistance to Assurance

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Artificial intelligence (AI) has evolved from a futuristic concept into an essential clinical partner. In cardiac surgery—where decisions are made in millimeters and milliseconds—AI does not threaten surgical craftsmanship but strengthens it. Algorithms capable of learning from thousands of procedures now assist surgeons with preoperative risk assessment, intraoperative precision, and postoperative surveillance.[1-3] The number of AI-enabled medical devices cleared by the U.S. Food and Drug Administration has risen from 27 in 2017 to more than 1,200 in 2024, illustrating the unprecedented velocity with which digital intelligence is entering the operating room.[4]

The preoperative applications of AI are perhaps the most mature. Machine-learning models trained on multimodal datasets, from imaging to genomics, offer superior predictions of mortality, bleeding, and arrhythmic events compared with conventional risk scores. They help tailor patient selection, anticipate complications, and personalize procedural planning. Intraoperatively, AI-augmented robotics, automated perfusion control, and computer vision systems assist surgeons in maintaining accuracy and situational awareness even in complex and prolonged interventions.[5,6] In the postoperative phase, wearable sensors and predictive analytics enable real-time surveillance and early intervention, improving recovery trajectories and reducing readmissions.[7]

At the Instituto do Coração (InCor) in São Paulo, the TRAdA Project (Telemonitoramento Remoto Assistido de Arritmia) demonstrates this transition from episodic to continuous care. By integrating AI-driven wearable devices with clinical dashboards, clinicians can detect arrhythmic events earlier, such as supraventricular tachycardia or postoperative atrial fibrillation, prompting a timely anticoagulation or ablation. These examples demonstrate that AI is not confined to the operating table; it extends the surgeon's reach into the patient's home, creating a loop of connected care that redefines patient follow-up and safety.[8]

However, the potency of AI depends on how institutions and professionals adapt. The challenge is not technological scarcity but responsible integration. Data quality, interoperability, and algorithmic transparency are the essential prerequisites. Bias in datasets can propagate inequity while a lack of validation can erode trust. The safe implementation of AI requires governance frameworks, multidisciplinary ethics boards, and collaboration among engineers, clinicians, and regulators. Training surgeons in data literacy and the critical interpretation of AI outputs is now as vital as learning new surgical techniques.[7]

Ethical and societal dimensions also require attention. Medical institutions and professionals must inform their patients when and how AI contributes to their care, obtain their informed consent, and maintain the accountability. Surgeon's judgment, grounded in empathy, contextual reasoning, and experience, remains irreplaceable. AI should enhance this judgment rather than automate it. As the World Health Organization emphasizes, digital health must be human-centered and designed to strengthen, not substitute, professional expertise and compassion.

The convergence of surgery and AI marks a transformative era.[4] When aligned with ethical standards, continuous validation, and institutional vision, AI can deliver safer operations, optimize resources, and democratize access to specialized care. It can turn cardiac surgery into a living laboratory of augmented intelligence, where innovation serves humanity.[1] The future operating room will not be defined by who holds the scalpel, but by how intelligently the team—human and machine—thinks together.

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Impact of surgical volume and specialist availability on thyroidectomy outcomes in Brazil: an ecological study with a nationwide retrospective analysis of 230,345 cases (2008–2023)

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ABSTRACT

INTRODUCTION: Thyroid disorders affect a significant proportion of the population and often necessitate surgical intervention, particularly in cases of malignancy. In this study, we analyzed thyroidectomy procedures performed within the public health system (SUS) of Brazil from 2008 to 2023, with a focus on factors influencing in-hospital mortality.

METHODS: In the retrospective analysis, data on 230,345 thyroidectomies were extracted from SUS records and stratified by hospital volume and state-level distribution of head and neck specialists. Mortality rates were evaluated using non-parametric statistical analyses, including the Kruskal–Wallis and Spearman's correlation tests.

RESULTS: The overall in-hospital mortality rate was 0.15%. States with fewer than 0.5 head and neck specialists per 100,000 inhabitants exhibited significantly higher mortality rates (0.2 versus 0.15, $p = 0.02$). Hospitals performing fewer than 25 procedures annually (very low-volume) had a fivefold increase in mortality compared with high-volume hospitals (0.51 versus 0.10, $p < 0.001$). When hospitals performing fewer than 10 procedures per year were excluded, significant differences in mortality among volume groups were no longer observed.

CONCLUSION: Mortality increased significantly in very low-volume hospitals performing fewer than 25 thyroidectomies per year; however, this difference was no longer observed after excluding hospitals that performed fewer than 10 interventions per year. These results support restricting thyroidectomies to hospitals performing at least 10 procedures annually and promoting centralization to improve outcomes. Structured regionalization policies are needed to ensure equitable access to specialized surgical care across Brazil.

INTRODUCTION

Thyroid disorders are prevalent in Brazil, affecting as much as 12% of the population.[1] These conditions encompass a broad spectrum of thyroid disorders, including hypothyroidism, hyperthyroidism, goiter, nodules, thyroiditis, and malignancies. Although while many thyroid disorders can be effectively managed with medical treatment, thyroidectomy remains the cornerstone of surgical intervention for several benign and most malignant thyroid conditions.[2]

In recent decades, the global incidence of thyroid cancer has significantly increased. This increase is attributed to the widespread use of advanced medical imaging techniques, allowing the detection of incidental thyroid cancers that otherwise would have remained unnoticed.[3,4] Consequently, the number of thyroidectomies performed has risen, as surgical intervention is often essential in malignant cases. Despite existing literature advocating less invasive diagnostic and treatment approaches for thyroid diseases, this shift has not been significantly adopted.[5]

In Brazil, Braga et al.[6] reported 160,219 thyroidectomies performed in the public health system between 2010 and 2020. Comparatively, 871,644 patients underwent thyroidectomy in the United States between 1993 and 2008.[7] Thyroidectomy is associated with low in-hospital mortality rates, ranging from 0.03% to 0.61%.[8–10] Thus, most studies have focused on complications such as recurrent laryngeal nerve injury, hypoparathyroidism, and reoperations, rather than mortality. Although the mortality risk is minimal, given the high frequency of this procedure,

analyzing mortality outcomes remains crucial. Notably, comprehensive studies providing normative data on thyroidectomy outcomes at the national level are lacking.

The relationship between hospital volume and complication rates in thyroidectomies has received considerable attention. Several studies have demonstrated that higher hospital and surgeon volumes are correlated with better surgical outcomes.[9,11] However, these findings have not been thoroughly explored in Brazil. In this study, we analyzed the profile of thyroidectomies performed in the Brazilian public health system from 2008 to 2023 to identify factors associated with in-hospital mortality.

METHODS

A retrospective, quantitative, and descriptive approach was applied using aggregated population data. All information related to the surgical procedures was extracted from the public page of the Department of Information Technology of the Unified Health System (DATASUS),[12] a government digital platform that provides open-access data on procedures performed in the public health sector. Data were collected from 2008 to 2023.

The procedures were described in codes, and the following codes related to thyroidectomies were included in the analysis:

- Partial thyroidectomy (04.02.01.003-5)
- Total thyroidectomy (04.02.01.004-3)
- Total thyroidectomy with neck dissection in oncology (04.16.03.012-2)
- Total thyroidectomy with neck dissection (04.02.01.005-1)
- Total thyroidectomy in oncology (04.16.03.013-0 and 04.16.03.027-0)

The analyses included a quantitative evaluation of the total number of procedures, average hospital stay, number of deaths, amount reimbursed to healthcare facilities for the procedure, and the nature of hospitalizations. Demographic data were analyzed to evaluate the geographical distribution of surgeries across Brazilian states, patient flow between federative entities, and concentration of procedures in destination states. The main indications for surgical procedures were identified using the International Classification of Diseases codes associated with each Hospital Admission Authorization.

The number of head and neck surgical specialists was obtained from data provided by the Brazilian Medical Association.[13] Hospitals were stratified into quartiles based on the total number of procedures performed. This approach was adopted to classify facilities as high-, intermediate-, low-, or very low- volume institutions within our dataset, rather than relying on fixed thresholds established in the literature. This stratification allowed for a more context-specific assessment of surgical volume. In this stratification, hospitals in the high-, intermediate-, low-, and very low-volume groups performed > 98, 57–97, 25–56, and < 25 procedures each year, respectively.

Statistical analyses were conducted using Jamovi software (The Jamovi Project, Australia, 2022). The Kruskal–Wallis test was used to compare multiple groups, followed by the Dwass–Steel–Critchlow–Fligner test for post hoc comparisons. The Spearman's correlation test was used to evaluate relationships between quantitative variables, and the Mann–Whitney U test was used for two-group comparisons. Non-parametric methods were selected because of their robustness in analyzing aggregated and non-normally distributed data.

The Institutional Review Board of the Hospital Israelita Albert Einstein. approved this study (approval number: 6010). All data were anonymized and publicly accessible, ensuring compliance with ethical and privacy standards. Data extraction and cleaning procedures followed the Reporting of studies Conducted using Observational Routinely-collected Data statement.

RESULTS

Between 2008 and 2023, a total of 230,345 thyroidectomy procedures performed across 1,383 healthcare facilities were registered under the selected Brazilian public Unified Health System (SUS) codes. Of these, 205,316 (89.1%) were performed on in female patients. The mean age of patients at the time of surgery was 46.5 ± 9.9 years. The amount paid by the SUS per hospitalization was BRL 1,209.85, ranging from BRL 528.43 in Acre to BRL 1,707.37 in Rio Grande do Norte.

With regard to surgical diagnosis, the most common ICD code was C73 (malignant neoplasm of the thyroid), accounting for 84,474 procedures (36.7%), followed by D44 (neoplasm of uncertain behavior of the thyroid) in 54,190 procedures (23.5%) and D34 (benign neoplasm of the thyroid) in 51,332 procedures (22.2%).

When analyzing Brazilian federative units (FUs), Rio Grande do Norte recorded the highest number of procedures (160 procedures/100,000 inhabitants) during the study period, followed by Ceará (152 procedures/100,000 inhabitants). In contrast, the lowest rates were observed in Goiás (66 procedures/100,000 inhabitants) and Pará (51 procedures/100,000 inhabitants). Overall, 49.7% of the procedures were performed outside the patients' municipality of residence and 14.9% were conducted outside their state of origin. The Brazilian FUs with the highest percentages of procedures performed within their states of origin were São Paulo (99.9%) and Ceará (99.8%). Conversely, FUs with the highest patient referral rates to other states were Goiás (90.8% of procedures performed within the state) and Mato Grosso do Sul (88.8%). Descriptive data of FUs are detailed in **Table 1**, and patient flow between states of origin and procedure-performing states is illustrated in **Figure 1**.

In total, 352 in-hospital deaths were recorded during the study period, corresponding to an overall in-hospital mortality rate

of 0.15%. FUs with the highest in-hospital mortality rates were Tocantins (0.6%) and Amapá (0.35%), whereas the lowest rates were observed in Espírito Santo, which reported no in-hospital deaths, and in Pernambuco (0.06%).

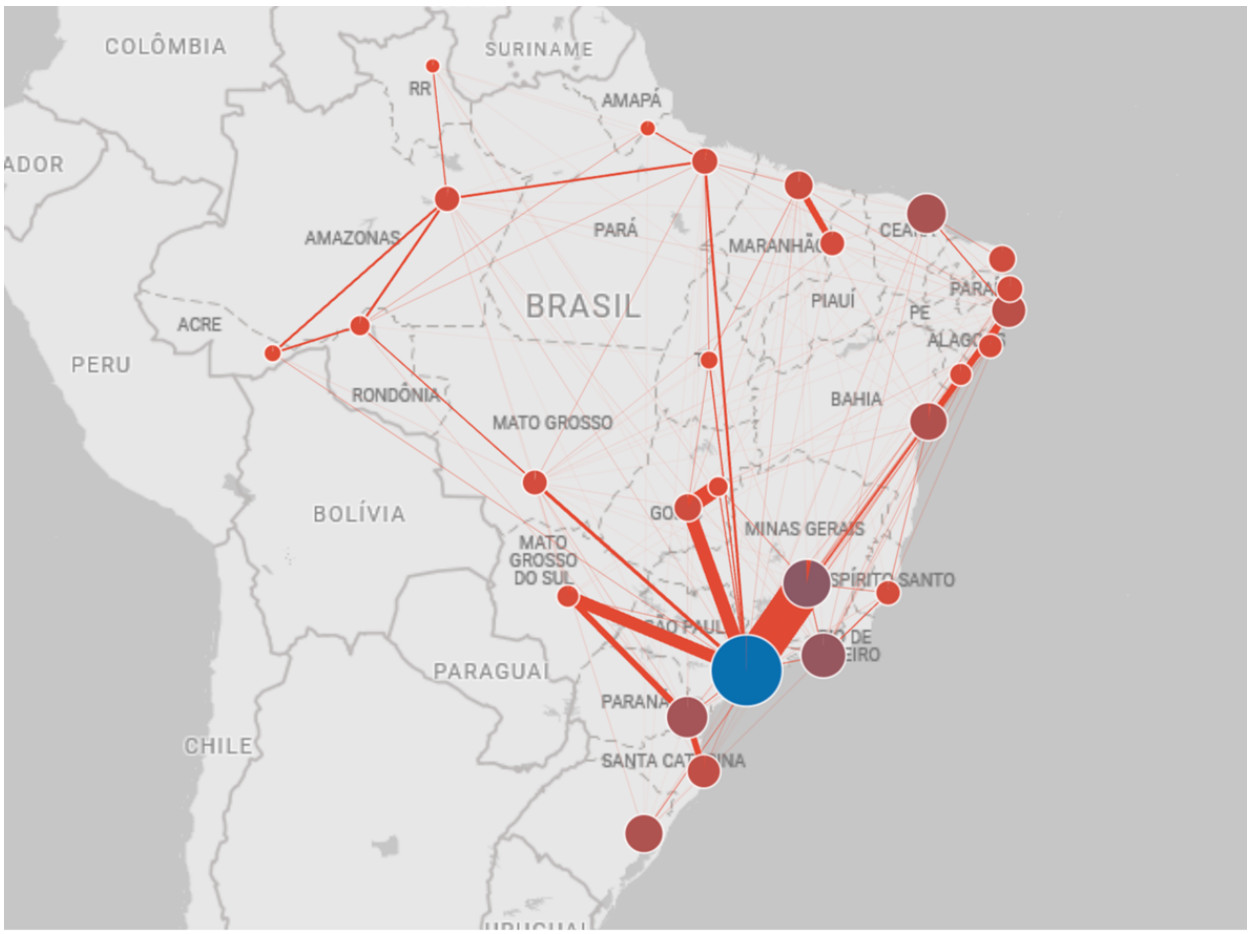
Head and neck surgery is the primary specialty performing thyroidectomies in Brazil, with 0.69 specialists per 100,000 inhabitants. Geographically, São Paulo (1.2 specialists per 100,000 inhabitants) and the Federal District (1.3 specialists per 100,000 inhabitants) had exhibit the highest proportions, whereas Amapá (0.25 specialists per 100,000 inhabitants) and Pará (0.13 specialists per 100,000 inhabitants) had have the lowest number. This represents a nearly fivefold difference between the highest- and lowest-density regions (1.3 versus 0.13 specialists per 100,000 inhabitants) and a fourfold difference between São Paulo and Amapá (1.2 versus 0.25). These variations reflect substantial disparities in specialist availability across countries.

Spearman's correlation test was conducted to identify the variables associated with higher mortality rates. We observed a significant negative correlation between the mortality rate and both the number of procedures per 100,000 inhabitants ($p = 0.046$; Rho coefficient −0.4) and number of specialists per 100,000 inhabitants ($p = 0.004$; Rho coefficient −0.55). However, no significant correlation was noted for the number of procedures per facility, facilities per 100,000 inhabitants, or the percentage of procedures performed within the state ($p = 0.5$; $p = 0.8$; $p = 0.2$, respectively). The correlation between mortality and the number of head and neck surgeons per 100,000 inhabitants is presented in **Figure 2**.

An exploratory analysis was conducted by testing thresholds in increments of 0.1 specialists per 100,000 inhabitants to determine the cutoff value at which the differences in mortality ceased to be significant. A threshold of 0.3 specialists per 100,000 inhabitants was not associated with significant differences in mortality (Mann–Whitney U test, $p = 0.18$). However, a cutoff of 0.5 specialists per 100,000 inhabitants marked the point at which a significant difference in mortality was observed (Mann–Whitney U test, $p = 0.02$). At this threshold, the mean mortality rate was

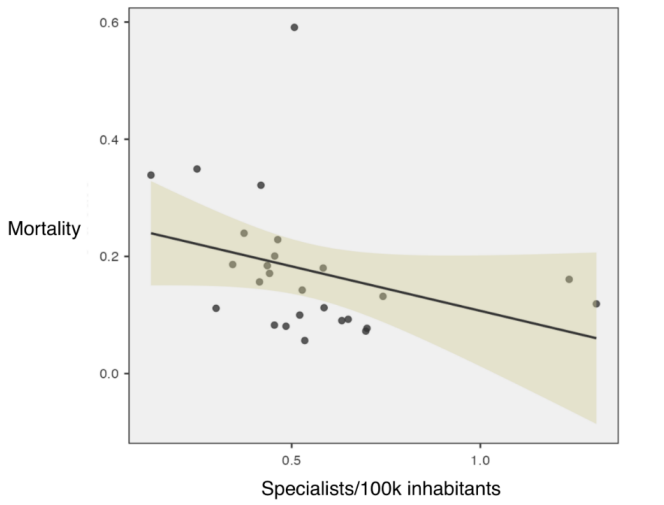
Table 1. General description of thyroidectomy procedures performed in the Brazilian public Unified Health System (SUS) by federal unit from 2008 to 2023

State of origin	Procedures performed(n)	Establishments (n)	Procedures/ establishment (n)	Establishments/ 100.000 people (n)	% Procedures Performed Within the State	Procedure Specialists per 100,000 people	Number of Specialists	Specialists per 100,000 people	Mortality
Acre	1,200	4	300	0,45	95.96	136.27	4	0.45	0.08
Alagoas	3,509	19	184.68	0,59	98.35	108.97	17	0.53	0.14
Amapá	859	4	214.75	0,5	98.2	107	2	0.25	0.35
Amazonas	4,173	16	260.81	0,37	98	97.47	16	0.37	0.24
Bahia	12,394	107	115.83	0,72	98.25	83.46	72	0.48	0.08
Ceará	14,032	55	255.13	0,6	99.86	151.97	60	0.65	0,09
Distrito Federal	2,522	15	168.13	0,5	98.75	84.55	39	1.31	0.12
Espírito Santo	3,887	32	121.47	0,78	99.25	94.76	30	0.73	0
Goiás	4,887	57	85.74	0,78	90.86	66.49	32	0.44	0.18
Maranhão	5,385	51	105.59	0,73	97.63	76.81	21	0.3	0.11
Mato Grosso	4,006	29	138.14	0,76	98.21	104.42	20	0.52	0.1
Mato Grosso do Sul	2,670	14	190.71	0,48	88.8	92.01	17	0.59	0.11
Minas Gerais	21,941	179	122.58	0,84	96.8	102.9	97	0.45	0.2
Pará	4,427	35	126.49	0,4	97.01	51.09	11	0.13	0.34
Paraíba	5,178	30	172.6	0,72	99.24	124.92	29	0.7	0.08
Paraná	15,549	91	170.87	0,77	99.67	131.5	69	0.58	0.18
Pernambuco	10,642	31	343.29	0,32	98.98	111.56	51	0.53	0.06
Piauí	4,473	22	203.32	0,65	99.58	132.51	14	0.41	0.16
Rio de Janeiro	18,715	128	146.21	0,74	99.8	108.68	76	0.44	0.17
Rio Grande do Norte	5,517	16	344.81	0,46	99.65	160.1	24	0.7	0.07
Rio Grande do Sul	12,245	107	114.44	0,95	99.79	109.04	52	0.46	0.23
Rondônia	2,149	8	268.63	0,46	98.26	123.07	6	0.34	0.19
Roraima	622	2	311	0,28	95.74	86.78	3	0.42	0.32
Santa Catarina	8,849	78	113.45	0,97	98.68	109.81	51	0.63	0.09
São Paulo	55,956	238	235.11	0,52	99.91	121.71	568	1.24	0.16
Sergipe	3,035	6	505.83	0,26	99.61	132.47	17	0.74	0.13
Tocantins	1,523	9	169.22	0,57	97.64	96.55	8	0.51	0.59



The thickness of the interstate lines represents the volume of patients and the size of the circles indicates the number of procedures. The blue circle represents the state of São Paulo, which admits and treats the highest number of patients.

Figure 1. Illustrative map of patient referral flows for thyroidectomy procedures within the SUS across Brazil's Federal Units from 2008 to 2023.



Legend: p = 0.004; Rho coefficient −0.55

Figure 2. Scatter plot illustrating the correlation between in-hospital mortality for thyroidectomy admissions and the rate of head and neck surgeons per 100.000 inhabitants in Brazil.

0.20 in the group with up to 0.5 specialists per 100,000 inhabitants compared to 0.15 in the group with more than 0.5 specialists per 100,000 inhabitants, representing a 25% reduction.

A total of 1,383 healthcare facilities performed thyroidectomies during the study period. Of these, 1,109 facilities (80.2%) performed fewer than 12 procedures annually, accounting for 32,070 procedures (13.9% of the national total). Facilities performing only 1 procedure annually accounted for 1.3% of the procedures; 25.7% (59,587 procedures) were conducted in facilities performing up to 25 procedures per year, and 34.8% (80,183 procedures) in facilities performing more than 76 procedures per year.

Table 2 provides comparative data for groups of facilities stratified by procedure volume regarding in-hospital mortality, the average amount paid for SUS hospitalization, length of stay, and percentage of hospitalizations involving intensive care unit (ICU) use. Significant differences were observed among the groups for all analyzed variables (Kruskal–Wallis test). Multiple comparisons using the Dwass–Steel–Critchlow–Fligner test revealed significant differences between the very low-volume and high-, intermediate-,

Table 2. Comparison of in-hospital mortality, amount paid by the Brazilian public Unified Health System (SUS), length of stay, and ICU utilization across facility volume groups

Group	High Volume (HV)	Intermediate volume (IV)	Low volume (LV)	Very low volume (VLV)	p (Kruskal–Wallis)	DSCF Multiple Comparisons
Hospitalizations/year, (n)	150.8 ± 52,3	72.8 ± 11.7	35 ± 8,3	3 ± 5.1		
Average amount paid by SUS per hospitalization (n)	1564.08 ± 694.8	1143.5 ± 577.7	1107,6 ± 555,9	744.5 ± 745	< 0.001	HV × IV p = 0.082 HV × LV p = 0.22 *HV × VLV* p = *<0.001* IV × LV p = 0.98 *IV × VLV* p = *<0.001* *LV × VLV* p = *<0.001*
Mortality rate (%)	0.1 ± 0.12	0.14 ± 0.16	0,13 ± 0,16	0.51 ± 4.36	< 0.001	HV × IV p = 0.954 HV × LV p = 1 *HV × VLV* p = *<0.001* IV × LV p = 0.95 *IV × VLV* p = *<0.001* *LV × VLV* p = *<0.001*
Average length of stay (n)	2.3 ± 0.76	2.77 ± 1.49	2,58 ± 1,47	2.60 ± 2.63	0.018	HV × IV p = 0.526 HV × LV p = 1 HV × VLV p = 0.91 IV × LV p = 0.304 *IV × VLV* p = *0.022* LV × VLV p = 0.53
Percentage of Hospitalizations with use of ICU (n)	2.08 ± 1.15	2.29 ± 2	2,74 ± 2,38	4.7 ± 15	< 0.001	HV × IV p = 0.997 HV × LV p = 0.907 *HV × VLV* p = *<0.001* IV × LV p = 0.732 *IV × VLV* p = *<0.001* *LV × VLV* p = *<0.001*

ICU, intensive care unit; DSCF, Dwass–Steel–Critchlow–Fligner.

and low-volume groups. The very low-volume group had lower hospitalization costs, higher percentage of ICU hospitalizations, and higher mortality rates. The mortality rates were 0.51%, 0.13 %, 0.14 %, and 0.1% in the very low-, low-, intermediate-, and high-volume groups, respectively. This difference was significant only when comparing the very low-volume group with the other groups, whereas no significant differences were observed among the low-, intermediate-, and high-volume groups.

After determining that higher mortality rates were associated with facilities performing very few procedures, we conducted a subgroup analysis that excluded facilities performing fewer than 10 procedures annually. The remaining facilities were re-stratified into quartiles based on the procedure volume. This exclusion accounted for 12% of procedures and 78.4% of facilities. Comparative analysis of the quartiles in this subgroup showed no significant differences in mortality rates (Kruskal–Wallis test, p = 0.3).

DISCUSSION

The Brazilian healthcare system operates within a dual structure, encompassing both the public and private sectors, each with distinct roles and contributions to the overall healthcare landscape. Only 28.5% of the population has access to private healthcare, whereas the remaining individuals rely exclusively on the public healthcare system.[14,15] In this study, we analyzed only thyroidectomies performed within the public healthcare system.

Although the volume of thyroid surgeries is widely recognized as an important factor in the literature, it remains poorly studied in Brazil. This has led to discussions based on the limited availability of supporting data.[16,17] The present study provides valuable new evidence regarding thyroidectomies performed in Brazil, specifically addressing hospital surgical volumes, distribution of specialists, and in-hospital mortality rates.

Recently, the number of thyroidectomies performed by the Brazilian public health system has remained relatively stable. Braga et al.[6] described the profile of thyroidectomies performed by the SUS between 2010 and 2020. Their findings indicated a significant decrease in procedures during the coronavirus disease 2019 pandemic in 2020; however, the volume stabilized at approximately 15,000 procedures annually for the remainder of the study period. They also discussed mortality rates and regional disparities within Brazil, noting that the highest mortality rate was reported in the northern region. However, they did not analyze other variables that may have influenced mortality, which were addressed in the present study. The overall mortality rate of 0.15% reported in our series aligns with those of Braga et al.[6] and with international literature, which reported in-hospital mortality rates ranging from 0.03% to 0.61%.[8,9]

In Brazil, the medical specialty responsible for performing thyroidectomies is head and neck surgery; however, this varies across countries. This specialty is among the 10 least common among the 55 recognized specialties in the country, with only 1,406 specialists registered in 2022. This number has significantly increased over the past 10 years, more than doubling from 631 specialists since 2012.[13] However, this growth has been insufficient and is further compounded by poor distribution across Brazil. For example, São Paulo had 568 specialists, whereas the entire state of Amapá had only 2. Access to specialists is often further hindered by the vast size of some states and the highly dispersed population in large areas, such as Amazonas and Pará. Specialists are primarily concentrated in the state capitals, exacerbating the challenges of accessing specialized care. Therefore, thyroidectomies are frequently performed by nonspecialists.

This study identified a negative correlation between the number of head and neck surgery specialists in Brazil and perioperative mortality rates. To the best of our knowledge, this association has not been established. The cut-off for this analysis was set at 0.5 specialists per 100,000 inhabitants, and approximately half of Brazil's states[13] did not meet this threshold.

However, this relationship reflects an ecological rather than causal association. Because DATASUS lacks surgeon-level identifiers and specialty information, the link between lower specialist density and higher mortality should be interpreted as an inference drawn from aggregated data and not as a directly measured finding. Moreover, as with any ecological association, the correlations observed at the state level may not accurately represent the individual-level risk. Nevertheless, the unequal geographical distribution of the specialists provides a coherent contextual rationale for the identified mortality patterns. Similarly, Stopenski et al.[18] analyzed the discrepancies in thyroidectomy outcomes between general surgeons and otolaryngologists specializing in thyroid surgery. Their findings indicated that specialized training led to better surgical outcomes, reinforcing the importance of the specialists involved in these procedures.

Data on thyroidectomy procedures analyzed in this study were extracted from DATASUS, the official and mandatory nationwide platform for hospital reimbursements in the SUS. Although regional inequalities in healthcare infrastructure are well recognized, the coding and reporting processes are standardized, minimizing systematic discrepancies across states. Nevertheless, the absence of surgeon-level information is a critical limitation. In regions with a very low specialist density, some thyroidectomies might have been performed by non-specialists; however, this factor could not be directly assessed in our dataset. Therefore, while specialist availability may contribute to regional disparities, the most consistent determinant of higher mortality was hospital surgical volume, particularly in very low-volume centers.

Moreover, recent studies have emphasized a global trend toward deintensified screening and treatment of thyroid diseases,[19] which may further reduce thyroidectomy rates over time. If this decline extends to Brazil, both individual and institutional surgical experience may decrease, potentially amplifying the risks associated with low-volume practices. Therefore, continuous surgical training and careful centralization of thyroid surgery are essential to maintain safety standards.

Surgical volume is a well-established factor associated with surgical quality and safety, both in general[20,21] and specifically in thyroid surgery.[11] Theodor Kocher was the first to demonstrate a significant reduction in operative mortality with increased surgical experience.[22] Although reports vary on the specific number of surgeries defining high and low volume, the consensus is that high-volume surgeons tend to have fewer complications.[7,11] Additionally, thyroidectomies performed by high-volume hospitals and surgeons also result in shorter hospital stays and lower costs compared to those performed by low-volume hospitals and surgeons.[9,23] However, most studies have focused on long-term complications rather than in-hospital mortality, given the latter's low frequency, and studies that have described mortality rates do not always show differences according to volume.[24]

In complex procedures such as pancreatectomy and liver transplantation, the literature strongly supports public policies that discourage surgeries at very low-volume hospitals. High-volume centers are consistently associated with better patient outcomes, including lower complication and mortality rates.[25] Policymakers are encouraged to incorporate these findings into strategies to optimize surgical care and ensure patient safety.[26,27] However, this relationship is less well established for mortality rates following thyroidectomies, particularly in Brazil, where limited data exist on the subject.

In this study, we focused on in-hospital mortality and found that very low-volume hospitals (those performing fewer than 25 thyroidectomies annually) were associated with significantly higher mortality rates than all other groups. This finding underscores the role of very low-volume hospitals as a key factor associated with increased mortality, with mortality rates five times higher than those of high-volume hospitals. Notably, when hospitals performing fewer than 10 thyroidectomies annually were excluded from the analysis, the mortality differences among the volume categories declined, representing 12% of procedures and 78.4% of establishments. These findings are highly relevant from a public health perspective, demonstrating that although thyroidectomy is not a highly complex procedure with elevated mortality, health systems could benefit from policies that restrict such procedures in very low-volume centers. Establishing a threshold of at least 10 thyroidectomies per year seems to offer meaningful benefits, particularly for outcomes as critical as in-hospital mortality.

Although the data analyzed in this study did not allow the evaluation of individual surgeon volume or nonfatal complications such as laryngeal nerve injury or hypoparathyroidism, we can reasonably infer that hospital volume largely reflects surgeon volume for thyroidectomies. Some authors argue that the favorable impact of hospital volume on surgical outcomes is explained by surgeon volume, especially for procedures requiring shorter stays and less dependence on hospital-based resources.[22] Thyroid surgery exemplifies such a procedure, where surgeon experience significantly impacts outcomes, and has been recognized for nearly a century.

This study has some limitations, mainly inherent to the use of secondary data. Information on the identity and specialty of the surgeon and postoperative complications beyond in-hospital mortality was not available, and data from the private healthcare system were not included. Moreover, the observed correlations should be interpreted as ecological associations rather than causal relationships, given the absence of individual-level data. Despite these limitations, this analysis provides nationwide evidence on the relationship between hospital volume and perioperative mortality in thyroidectomies, an aspect rarely explored in Brazil. These findings reflect the information currently available in national health databases and offer a valid contribution to understanding regional disparities and guiding future policy development.

Our results can help guide practical action to improve the care and quality of service provided in public health services. Creating regional flows in each state to direct potential surgical cases to hospital services with a capacity and volume exceeding 10 procedures per year could improve care. Creating a proposal with regulatory bodies for surgical procedures in Brazil, such as the High-Complexity Care Regulation System, with well-established flows, could be a viable alternative to optimize resources and offer high-quality health services for diseases within the specialty of Head and Neck Surgery.

CONCLUSION

Thyroidectomy has a low overall perioperative mortality rate; however, our data showed a significant increase in mortality in very low-volume hospitals. This difference disappeared when hospitals with fewer than 10 surgeries were excluded from the analysis.

Therefore, the centralization of thyroid surgery in hospitals that perform at least 10 cases annually may represent a cost-effective strategy to reduce preventable deaths and optimize resource allocation within Brazil's public health system.

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Reference intervals for complete blood count parameters in the Longitudinal Study of Adult Health (ELSA-Brasil): a cross-sectional analysis

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ABSTRACT

BACKGROUND: Complete blood count (CBC) is the most frequently requested laboratory test worldwide, providing essential clinical information. In Brazil, many laboratories still use reference intervals (RIs) that are inadequately defined or not representative of the local population. Establishing population-specific RIs is crucial for accurate interpretation, diagnosis, and clinical decision making.

OBJECTIVE: To establish RIs for CBC parameters in a sample of Brazilian adults.

METHODS: This cross-sectional study included 2,417 healthy individuals who participated in the baseline (2008–2010) of the Longitudinal Study of Adult Health (ELSA-Brasil). Venous blood collection and storage were performed according to the procedures established by the Clinical and Laboratory Standards Institute (CLSI) in 2018. CBC was performed in laboratories with laboratory proficiency. The RIs were calculated using the nonparametric method proposed by the CLSI.

RESULTS: The RIs were stratified by sex only for the following parameters: Red blood cells (RBC; $\times 10^6$/mm^3): Male (4.4–5.6), Female (3.9–5.1); Hemoglobin (g/dL): Male (13.2–16.7), Female (11.8–14.9); Hematocrit (%): Male (39–49), Female (35.3–44.2); Mean corpuscular hemoglobin concentration (MCHC; g/dL): Male (32.3–35.7), Female (32–35.1); Platelets ($\times 10^3$/mm^3): Male (146–319), Female: (170–352). The other parameters were as follows: mean corpuscular volume (MCV) (fL): (79.9–96); mean corpuscular hemoglobin (MCH) (pg): (26.4–32.5); White blood cells (WBC; /mm^3): (3,700–8,610); Neutrophils (/mm^3): (1,666–5,705); Eosinophils (/mm^3): (23.8–530); Basophils (/mm^3): (0–112); Lymphocytes (/mm^3): (1,121–2,824); Monocytes (/mm^3): (240–751.7).

CONCLUSION: Our results agree with those of other studies that have proposed RIs for CBC parameters. The differences found in MCV, neutrophil and WBC parameters (total population), and MCHC (both sexes) may be due to differences in the study populations, sample sizes, and pre-analytical and analytical study variables.

INTRODUCTION

Important diagnostic information can be found during a patient's anamnesis and physical examination;[1] however, the definitive diagnosis of many diseases depends on laboratory tests.[2] The complete blood count (CBC) is the most requested laboratory test worldwide. Important information can be obtained from a small amount of blood in about a minute and with a low probability of error through automation.[1,2] The CBC can be used to extract important quantitative and qualitative data on red blood cells (RBC), hematocrit, hemoglobin, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), RBC distribution width (RDW), white blood cells (WBC) and their subtypes (lymphocytes, neutrophils, monocytes, eosinophils, and basophils), platelet count, and mean platelet volume (MPV).[3,4]

In 1935, Villela and Rodrigues[5] were the first researchers to discuss the need to establish reference intervals (RIs) for CBC parameters to assess the health of the Brazilian population. In Brazil, most laboratories use RIs established by the manufacturers of reagents or hematological analyzers used to determine hematological parameters. Some studies have been performed in the Brazilian population, with limited sample sizes.[6–9]

The National Health Survey (Pesquisa Nacional de Saúde, PNS) established the first RIs for CBC parameters for the adult Brazilian population.[10] The RI is of paramount importance in

laboratory tests, since it supports health professionals in interpreting the results, caring for patients, supporting diagnoses, establishing prognoses, and guiding appropriate treatments.[11] The Brazilian population is characterized by considerable miscegenation, and RIs can be influenced by several factors: individual (age, sex, race, socioeconomic status, and physiological state) and ecological (exposure to chemical, physical, and biological agents). Therefore, RIs should preferably be defined for each specific population so that possible differences can be estimated more accurately. In Brazil, laboratories commonly define RIs using a methodology that is not suitable and/or not applicable to the local population.[12]

The Longitudinal Study of Adult Health (ELSA-Brasil) is a large Brazilian cohort study whose main objective is to investigate the incidence and progression of chronic noncommunicable diseases. Throughout the follow-up period, the participants are subjected to a wide variety of interviews and physical, imaging, and laboratory tests, including CBC. Thus, ELSA-Brasil offers a unique opportunity not only to obtain the RIs for blood counts but also to evaluate, over time, the predictive capacity of these RIs for the development of diseases and the determinants of their changes over time. Therefore, the aim of this study was to establish RIs for CBC parameters in a sample of Brazilian adults.

MATERIALS AND METHODS

Design and study population

The study population consists of participants from ELSA-Brasil. This cohort included 15,105 participants aged between 35 and 74 years. The main objectives of the study are to investigate the incidence and progression of chronic non-communicable diseases, particularly diabetes and cardiovascular diseases, and identify their determinants in Brazilian adults.[13,14]

All participants were active or retired civil servants from higher education or research institutions in six Brazilian state capitals. The first baseline examination took place between 2008 and 2010, and the study was completed in four waves (wave 1: 2008–2010; wave 2: 2012–2014; wave 3: 2016–2018; wave 4: 2022–2024). Ethical approval for the study was granted by the Comissão Nacional de Ética em Pesquisa (CONEP), linked to the Ministério da Saúde (approval date: August 4, 2006; CAAE 0016.1.198.000-06), in addition to approval from the institutional ethics committees of each participating center. The design and conduct of ELSA-Brasil followed international ethical standards for human research, including the principles of the Declaration of Helsinki. All participants provided written informed consent prior to study procedures.[13,14]

Of the 15,105 participants in the ELSA-Brasil study, 95 were excluded because they lacked CBC data. In addition, participants with factors that could alter their inflammatory status were excluded from the study (**Table S1, supplementary material**). According to the exclusion criteria, of the 15,105 participants, 12,688 were excluded (**Figure 1**), resulting in a sample of 2,417 individuals.

Biological samples

Venous blood was collected in the morning after a 12 h fast and stored at room temperature (18–25°C) until the CBC was measured (up to 2 h after collection), according to the procedure established by the Clinical and Laboratory Standards Institute (CLSI) and their guidelines for the collection of diagnostic blood samples by venipuncture and the use of an approved standard.[15] For the venipuncture technique, a vacuum blood collection system was used, with sample tubes containing the tripotassium salt of ethylenediaminetetraacetic acid (EDTA) identified with a specific barcode for each participant. The tourniquet time did not exceed 1 min. The CBC analysis was conducted locally for technical reasons using automated hematology analyzers in laboratories with internal and external quality controls. The equipments used to conduct the CBC at the local centers were: Bahia and Espirito Santo: MAXM® – Beckman Coulter; Minas Gerais and Rio Grande do Sul: XE 2100 D (Sysmex, Kobe); and São Paulo: CellDyn 3700® Abbott, with hemogram® brand reagents. All laboratories participated in laboratory proficiency programs (the National Quality Control Program, Laboratory Testing Proficiency Program, and College of American Pathologists Accreditation Program).[16]

Statistical analysis

The Kolmogorov–Smirnov test was used to evaluate the distribution of the CBC parameters. The RIs were calculated

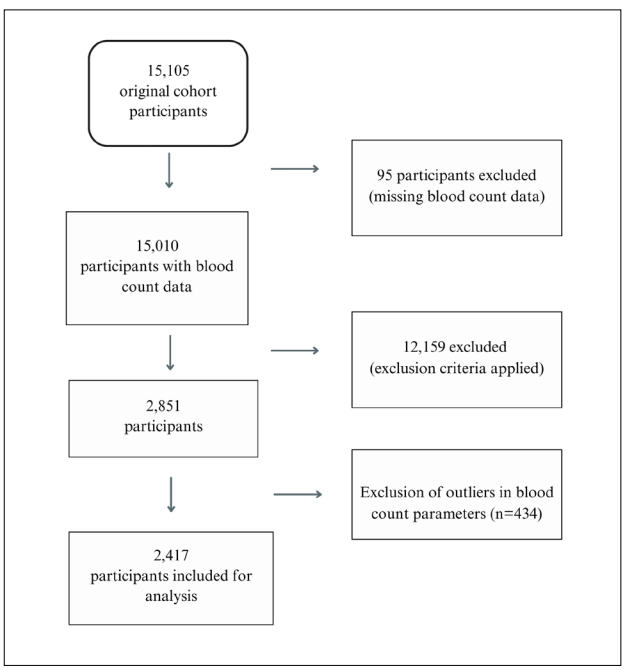

Figure 1. Flowchart of the study population.

step-by-step, following the CLSI[17] guidelines. A nonparametric method was used to determine the RIs, which were calculated as the intervals between the 2.5th and 97.5th percentiles of the parameter distribution. The Mann–Whitney U-test and Student's t-test were used, where appropriate, to evaluate differences between subgroups defined by sex and age. We assessed the need to recommend age- and sex-specific RIs for CBC parameters using the Harris–Boyd statistical approach. Following this approach, we calculated the z-scores of the means and standard deviations (SDs) of the parameters and compared them with the critical value (z*). RIs separated by age group and sex were recommended if at least one of the following conditions was met:

1. calculated z exceeds the critical value z*;
2. statistical differences exist between the SDs of the hematological parameters of each subgroup and the highest SD exceeds the lowest SD 1.5 times, or if the ratio [highest SD ÷ (highest SD – lowest SD)] is less than 3.

A p value of less than 0.05 was considered statistically significant, and the analyses were performed using the statistical package STATA 9.0 (Stata; College Station, Texas).

RESULTS

Most participants were enrolled at the São Paulo Study Center (34.4%), female (54.4%), aged 35–59 years (92%), self-declared white (52.6%), and most had completed higher education (57.8%) (**Table 1**). Histograms showing the distribution of hematological parameters are shown in **Figure 2**.

According to the Kolmogorov–Smirnov test, only the MCV showed a symmetrical data distribution, while the other parameters showed an asymmetrical distribution. With respect to sex, most parameters showed a statistically significant difference ($p < 0.05$), except for MCV, WBC, and lymphocytes. The median values of the RBC count, hemoglobin levels, hematocrit, MCHC, eosinophil and monocyte counts were higher among men, and those of the neutrophil, basophil, and platelet counts were higher among women. In relation to age, a statistically significant difference ($p < 0.05$) was observed for the MCV; MCH; basophil, lymphocyte, and platelet counts. The results showed higher median values for lymphocytes and platelets in the age group of 35–59 years and for MCV, MCH, and basophils in those aged 60 years and over (**Table 2**).

With respect to sex and age, we found statistically significant differences in the z-scores for the RBC, hemoglobin, hematocrit, MCHC, and platelet parameters. In the analysis by age, no parameter met any of the three conditions of the Harris–Boyd statistical approach for categorizing RIs. Therefore, we chose to present categorized RIs only for parameters that met at least one criterion of the Harris–Boyd statistical approach and CLSI[17] recommendations. **Table 3** shows the RIs for the stratified hematological parameters.

Table 1. Sociodemographic characteristics of the 2,417 reference individuals (ELSA-Brasil, 2008–2010)

Characteristics	Frequency n (%)
Study Center	
São Paulo	831 (34.4)
Minas Gerais	518 (21.4)
Bahia	357 (14.8)
Rio de Janeiro	301 (12.4)
Rio Grande do Sul	224 (9.3)
Espírito Santo	186 (7.7)
Sex	
Female	1,314 (54.4)
Male	1,103 (45.6)
Age (years)	
35–59	2,223 (92)
≥ 60	194 (8)
Self-reported skin color/race	
White	1,257 (52.6)
Brown	735 (30.7)
Black	310 (13)
Other[a]	89 (3.7)
Schooling (years)	
< 11	187 (7.7)
11–14	832 (34.4)
≥ 15	1,398 (57.8)

[a] Includes indigenous natives n = 23 (1%), Asian descendants n = 66 (2.8), and missing data n = 26 (1.1%).

DISCUSSION

This study established the RIs for CBC parameters, some of which were stratified according to sex. Men exhibited higher RBC, hemoglobin, hematocrit, and MCHC values than women, corroborating the data from the literature. These differences can be explained by the action of androgen hormones on erythropoiesis and blood loss during the menstrual period in women.[18,19] However, women had higher platelet counts than men, confirming what the literature indicates, because during menstruation, blood vessels responsible for irrigating the uterine region rupture, causing menstrual bleeding and increasing the number of platelets for stopping the bleeding.[20]

Our results are similar to those of other studies that have proposed RIs for CBC parameters (**Table S2, supplementary material**). Compared with the RIs reported for other populations, the RIs identified in this study showed a lower upper limit for MCV; slightly higher lower and upper limits in both sexes for MCHC; and lower upper and lower limits in the overall population for WBC and neutrophil counts, both of which exhibited narrower ranges. Pronounced sex-related differences were observed for platelets, with

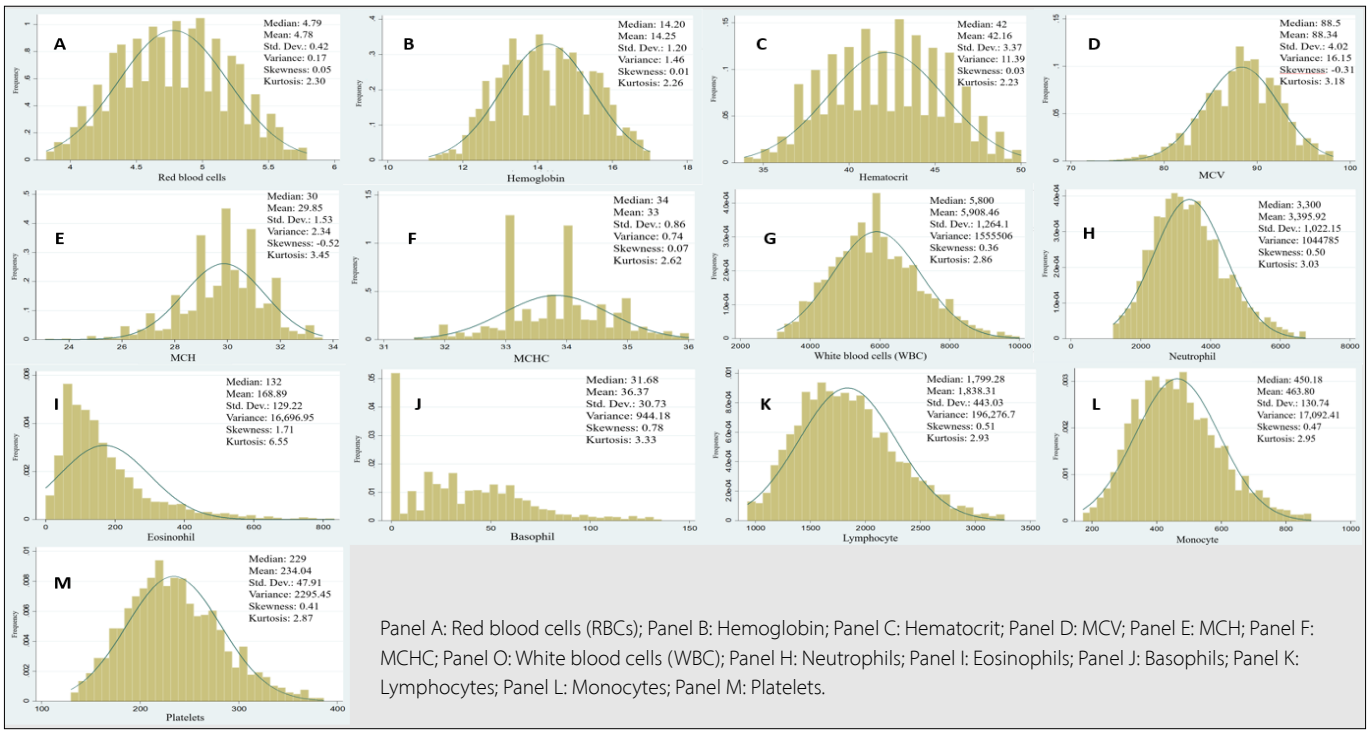

Figure 2. Distribution of hematological parameters in the sample.

Table 2. Hematological parameters in relation to sex and age group (n = 2,417) (ELSA-Brasil, 2008–2010)

	N total (n = 2,417)	Sex			Age groups		
		Male (n = 1,314)	Female (n = 1,103)	*p* value	Adults (35–59 years) (n = 2,223)	Elderly (≥ 60 years) (n = 194)	*p* value
RBC (× 10^6/mm^3)*	4.8 (4.5–5.1)	5 (4.8–5.3)	4.5 (4.3–4.7)	< 0.001	4.8 (4.5–5.1)	4.7 (4.5–5)	0.56
Hemoglobin (g/dL)*	14.2 (13.3–15.2)	15.1 (14.5–15.7)	13.3 (12.7–13.8)	< 0.001	14.2 (13.3–15.2)	14.4 (13.5–15.2)	0.186
Hematocrit (%)*	42 (39.5–45)	44.3 (42.8–46)	39.6 (38–41)	< 0.001	42 (39.5–45)	42 (40–45)	0.286
MCV (fL)$^{\Delta}$	88.3 (± 4)	88.3 (± 4)	88.4 (± 4.1)	0.367[a]	88.3 (± 4)	89.2 (± 3.8)	0.001[a]
MCH (pg)*$^{\Delta}$	30 (29–31)	30 (29–31)	30 (29–31)	< 0.001	30 (29–31)	30.4 (29.3–31)	< 0.001
MCHC (g/dL)*	34 (33–34.4)	34 (33.3–34.7)	33.7 (33–34)	< 0.001	33.9 (33–34.4)	34 (33.3–34.5)	0.149
WBC (/mm^3)	5,800 (5,000–6,700)	5,800 (5,000–6,650)	5,900 (5,000–6,830)	0.318	5,810 (5,000–6,710)	5,700 (4,880–6,480)	0.052
Neutrophils (/mm^3)	3,300 (2,655–4,026)	3,247 (2,650–3,931)	3,360 (2,673–4,102)	0.013	3,304 (2,668–4,050)	3,202 (2,576–3,843)	0.051
Eosinophils (/mm^3)*	132 (79–218.4)	141.5 (87.3–237.8)	122 (71–195)	< 0.001	132 (78.7–216.8)	138 (89.1–248)	0.163
Basophils (/mm^3)*$^{\Delta}$	31.7 (10.4–56)	30.7 (7–54)	32.6 (13.2–58.8)	0.001	31.3 (9.7–55)	36.6 (18.1–61)	0.016
Lymphocytes (/mm^3)$^{\Delta}$	1,799 (1,509–2,112)	1,792 (1,502–2,108)	1,800 (1,518–2,115)	0.636	1,800 (1,515–2,122)	1,704 (1,451–2,042)	0.026
Monocytes (/mm^3)*	450.2 (368.5–547.3)	469.6 (384–561.1)	432 (354–522)	< 0.001	451.5 (368–548)	441.8 (371.4–546)	0.776
Platelets (× 10^3/mm^3)*$^{\Delta}$	229 (199–265)	217.5 (190–249)	244 (216–279)	< 0.001	231 (200–267)	221.5 (188–253)	0.003

RBC, red blood cells; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; WBC, white blood cells. ***P*** value obtained using the Mann–Whitney U-test and [a]t-test; n, sample number. Data are presented as the median (25th–75th percentile) or mean ± standard deviation (SD). * There was a difference between sex; $^{\Delta}$ There was a difference between age groups.

both limits being higher than those commonly reported for international RIs. These discrepancies may reflect variations in population characteristics; sample size; and pre-analytical and analytical factors such as sample collection and processing procedures, analytical techniques, and the use of different hematology analyzers. Collectively, these findings highlight the importance of establishing RIs tailored to the Brazilian adult population. In terms of sample size, the PNS collected data from 8,952 individuals, whereas this study analyzed data from 2,417 participants. The PNS reported that there was no strict schedule for blood collection; the blood was collected at home and processed in local laboratories. The exclusion criteria used by the PNS were pregnant women and individuals diagnosed with serious or chronic illnesses such as cardiovascular disease myocardial infarction, angina, stroke, cancer, arthritis,

Table 3. Reference intervals and their respective confidence intervals (95% CI) for hematological parameters (n = 2,417) (ELSA-Brasil, 2008–2010)

Parameters		Median	Reference interval	
			Percentile 2.5 (95% CI)	Percentile 97.5 (95% CI)
RBC ($\times 10^6$/mm^3)	All	4.8	4 (4–4.05)	5.6 (5.5–5.6)
	Male	5	4.4 (4.3–4.4)	5.6 (5.6–5.7)
	Female	4.5	3.9 (3.9–4)	5.1 (5.1–5.2)
Hemoglobin (g/dL)	All	14.2	12.1 (12–12.2)	16.5 (16.4–16.6)
	Male	15.1	13.2 (13–13.4)	16.7 (16.6–16.8)
	Female	13.3	11.8 (11.6–11.9)	14.9 (14.7–15.1)
Hematocrit (%)	All	42.1	36 (36–36.4)	48.5 (48–49)
	Male	44.3	39 (38.4–39.2)	49 (49–49)
	Female	39.6	35.3 (35–35.8)	44.2 (44–45)
MCV (fL)	All	88.3	79.9 (79–80.2)	96 (95.3–96)
MCH (pg)	All	30	26.4 (26–26.6)	32.5 (32.4–32.9)
MCHC (g/dL)	All	34	32 (32–32.1)	35.5 (35.5–35.6)
	Male	34	32.3 (32–32.6)	35.7 (35.6–35.8)
	Female	33.7	32 (31.9–32)	35.1(35–35.3)
WBC (/mm^3)	All	5,800	3,700 (3,600–3,790)	8,610 (8,480–8,800)
Neutrophils (/mm^3)	All	3,300	1,666 (1,570.4–1,716.4)	5,705 (5,609.4–5,822.4)
Eosinophils (/mm^3)	All	132	23.4 (2.3–32.2)	530 (507.2–566.2)
Basophils (/mm^3)	All	31.7	0 (0–0)	112 (108–120)
Lymphocytes (/mm^3)	All	1,799	1,120 (1,092–1,149.7)	2,824 (2,760.3–2,886)
Monocytes (/mm^3)	All	450.2	240 (234.8–251.3)	751.7 (738.1–776.9)
Platelets ($\times 10^3$/mm^3)	All	229	151 (149–154.4)	339 (332–343.7)
	Male	217.5	146 (140–149)	319 (312–329.3)
	Female	244	170 (164–173.7)	352 (342.3–363.6)

RBC, red blood cells; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; WBC, white blood cells.

and chronic kidney disease. However, the exclusion criteria of the present study were more comprehensive than the PNS criteria,[10] as detailed in the Supplementary Material, resulting in the selection of a healthier population. Additionally, for the calculation of RBC parameters, individuals with hemoglobinopathy were excluded.[10]

Another difference in relation to the methodology adopted by Rosenfeld et al.[10] is that our study stratified the RI values only when the parameter presented any of the three conditions recommended by the Harris–Boyd statistic. In contrast, the PNS stratified its entire sample according to sex (male and female), age group (18 to 59 years and 60 years and over), and race/skin color (black, brown, and white). No specific RI by age group was established in our study, as we found no statistical differences with regard to age, possibly because our study included participants aged 35 years or older, whereas the PNS included individuals aged 18 or older.[10]

The establishment of RIs for laboratory tests is a rigorous and complex process that requires appropriate methodology, adequate sample sizes, and strict standardization and control throughout collection, processing, transport, and analysis. Owing to these challenges, many developing countries adopt parameters from studies conducted in developed nations, which may not accurately represent their populations.[10] In Brazil, defining population-specific RIs is crucial to improve the clinical interpretation of laboratory results, as these parameters reflect the country's genetic, environmental, and sociodemographic characteristics. Brazil has a high degree of miscegenation between European, African, and Indigenous ancestry, which influences hematological parameters such as hemoglobin levels, MCV, and leukocyte count. Furthermore, environmental differences (greater exposure to parasites, varying levels of pollution, and dietary habits) can modulate hematopoiesis and immune responses. Therefore, these results reflect the biological characteristics of the Brazilian adult population and reinforce the need to avoid the exclusive use of international reference values.[17–21]

The adoption of the RIs proposed in this study does not imply immediate changes in clinical practice because therapeutic decision points for conditions such as anemia, leukopenia, or thrombocytopenia are based on consolidated clinical guidelines. However, establishing specific RIs for the Brazilian population is fundamental for improving analytical quality and laboratory standardization and reducing inconsistencies between laboratories that currently use values from foreign situations or outdated methodologies. Although it does not alter the already defined clinical protocols, the use of national RIs improves the accuracy of result interpretation, favoring alignment with the biological characteristics of the

Brazilian adult population and strengthening quality control and laboratory accreditation processes. Thus, the main practical implication is the advancement of analytical reliability rather than the immediate redefinition of clinical diagnoses.[21]

The use of national RIs enhances diagnostic precision, strengthens standardization and quality control across laboratories, reduces interlaboratory variability, and ensures that acceptance limits align with local biological realities. Furthermore, such parameters support the creation of technical standards and public health policies, fostering uniformity in accreditation processes and promoting safer and more effective clinical practices nationwide.[22]

The limitation of the present study is that it only analyzed data from healthy adults (35–74 years old); no data was collected for adolescents, children, or other special groups such as pregnant women. Some of the exclusion criteria were self-reported, so that participants with diseases unknown to them could have been included in the study. Outliers were excluded to minimize this problem. The strengths of this study include the fact that the sample comprised healthy individuals, enabling a more appropriate analysis to establish RIs. Furthermore, although ELSA-Brasil is not representative of Brazilian adults, it consists of adults from three regions of Brazil, which adds diversity to the sample.

CONCLUSION

Our results are similar to those of previous studies. We believe that by defining specific RIs for our study population, we can obtain more reliable information on the real-world health status of the Brazilian population and contribute to better clinical care and disease control.

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Synovitis detection in rheumatology: a systematic review and meta-analysis of contrast-enhanced ultrasound and magnetic resonance imaging

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Microbubble contrast.
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Arthritis.

ABSTRACT

BACKGROUND: Synovial tissue proliferation in the bare area of the joint is an early indicator of synovitis. Vascularization of the pannus helps differentiate between inactive and inflammatory processes, directly impacting therapeutic management. Synovitis can be diagnosed through clinical assessment, ultrasound, and magnetic resonance imaging (MRI); however, uncertainty remains regarding the optimal imaging modality.

OBJECTIVE: This study aimed to determine the accuracy of ultrasonography with microbubble contrast and contrast-enhanced MRI in diagnosing synovitis, irrespective of its etiology. In addition, the study aimed to determine the joints that were most accurately assessed for synovitis using microbubble ultrasound.

METHODS: Electronic searches were conducted in the Cochrane Library, MEDLINE, EMBASE, LILACS, SCOPUS, CINAHL, and Web of Science up to February 8, 2025, with additional screening of reference lists. Studies assessing diagnostic accuracy or detection rates of contrast-enhanced ultrasound (CEUS) and contrast-enhanced MRI for synovitis were included without restrictions on language or publication status. Two studies were selected after quality assessment using QUADAS-2, and eight studies were assessed using the RTI item bank methodology.

RESULTS: Diagnostic accuracies of contrast-enhanced ultrasonography (87%) and contrast-enhanced MRI (87.7%) were comparable. For knee evaluation, CEUS showed a higher detection rate (93.8%) than MRI (82.9%). Across different joints and underlying diseases, the detection rates were 81.9% and 88.3% for contrast-enhanced MRI. In patients with rheumatoid arthritis, MRI demonstrated a higher detection rate (96.2%) compared with ultrasound (67.2%). These findings indicate a similar overall diagnostic performance, although the limited number of included studies restricted generalizability.

CONCLUSION: CEUS demonstrated diagnostic accuracy comparable to contrast-enhanced MRI, except in patients with rheumatoid arthritis. Given its low cost, portability, and favorable safety profile, CEUS may serve as a useful screening or follow-up tool for synovitis, pending validation in larger multicenter studies.

INTRODUCTION

In the synovial joint, the surface of the articulating bones is covered by cartilage, except for a small region between the insertion of the fibrous capsule and the cartilage. In this area, known as the "bare area" of the joint, the bone is covered only by the synovium. The bone surface in this region, which is in direct contact with the synovial tissue without a protective cartilage layer, is highly susceptible to bone destruction induced by synovitis.[1,2]

The proliferation of synovial tissue in this area is an early finding. Angiogenesis and hypervascularization, which result in pannus formation, are critical mechanisms that drive joint, cartilage, and bone destruction in the progression of rheumatoid arthritis. The presence of vascularization in the pannus can distinguish inactive from inflammatory processes and has significant implications for therapeutic management.[2] Differentiating between inactive fibrotic synovial tissue and active pannus, as well as quantifying synovitis, is currently an important area of investigation.[3]

Synovitis can be diagnosed through clinical evaluation, ultrasonography, and magnetic resonance imaging (MRI).[4] Among these diagnostic tools, both ultrasound and MRI have advantages and disadvantages. However, no consensus is available on which imaging method offers superior accuracy in detecting and grading synovial inflammation across different joints and rheumatological

diseases. This lack of comparative evidence warrants a systematic review of studies that directly assess both techniques.

The real-time capability of ultrasonography allows for the dynamic evaluation of joint movements, which can often help detect structural abnormalities. The advantages of ultrasound include its non-invasiveness, portability, cost-effectiveness, lack of ionizing radiation, and capability to be repeated as frequently as necessary, making it particularly useful for treatment monitoring. In contrast, ultrasound is operator-dependent, requiring highly experienced professionals with expertise in musculoskeletal anatomy and pathology as well as the ability to recognize artifacts that can often mimic lesions.[5]

On a global scale, MRI evaluates all structures, including bones, and is more easily interpretable, does not utilize radiation, and is less operator-dependent. It is currently considered the gold standard for the diagnosis of synovitis.[6] However, MRI is an expensive diagnostic technique not accessible to all patients, and has limitations in individuals with metallic implants, certain pacemakers, or claustrophobia.[7]

Previous studies have compared these modalities in isolated contexts or in small series. However, a unified synthesis of available evidence comparing contrast-enhanced ultrasound (CEUS) and contrast-enhanced MRI across multiple joints remains limited. Thus, this systematic review and meta-analysis aimed to evaluate and compare the diagnostic accuracy of CEUS and MRI for synovitis, and to identify the optimal technique for specific joints and clinical scenarios.

METHODOLOGY

Objectives

This study aimed to determine the accuracy of CEUS using microbubbles to diagnose synovitis, regardless of etiology. In addition, the study compared the accuracy of CEUS with microbubbles and contrast-enhanced MRI and determined which method was superior for diagnosing synovitis. Finally, the study aimed to identify which joints showed better accuracy for the detection of synovitis than using CEUS

Study design

A systematic review of diagnostic accuracy studies was conducted using the *Cochrane Diagnostic Reviewer's Handbook* version 5.1.

Inclusion criteria

Studies evaluating the diagnostic accuracy and detection rates of CEUS and MRI for synovitis were included, and specifically all studies regardless of publication status; no language restrictions were included in the analysis. The review was registered in the OPENSCIENCE database with the registration number DOI: 10.17605/OSF.IO/96HDC.

Participants

Patients of all ages and sexes with clinically confirmed synovitis, irrespective of disease severity or duration.

Tests evaluated

CEUS assessing synovial enhancement with microbubble contrast agents and contrast-enhanced MRI evaluating synovial enhancement with gadolinium contrast agents were compared.

Reference standard

The included studies described clinical and laboratory diagnoses of arthritis or osteoarthritis based on the established Rheumatology Society criteria.

Study selection and data extraction

Eligible publications were selected based on relevant articles or abstracts from indexed peer-reviewed journals. Independent selection by two authors. In cases of disagreement, a third reviewer was consulted. Data were extracted using a standardized form that included methods, participant characteristics, outcomes, and results.

Methodological quality assessment

Eligible studies with control groups were assessed using the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) tool.[8] The tool comprises four domains: patient selection, index test, reference standard, flow, and timing. Each domain was evaluated as having a high, low, or unclear risk of bias. The applicability of the first three domains was evaluated using the following classifications: high, low, or unclear. The Signaling questions supported the domain evaluations.

Eligible studies were assessed using the RTI Item Bank, a tool focused on evaluating bias and precision.[9,10] This tool comprises 29 multiple-choice questions covering 11 domains: sample definition and selection, interventions/exposure; outcomes; blinding; data robustness, follow-up; comparative analysis, interpretation; and reporting.

Responses included "Yes," "No," "Partially," "Cannot Determine," and "Not Applicable."

Search methods for study identification

Electronic Searches were conducted in Cochrane Library, MEDLINE, EMBASE, LILACS, SCOPUS, CINAHL, and WEB OF SCIENCE up to February 8, 2025; Reference lists of the included studies and key reviews on the topic were also checked. Manual Searches were performed in reference lists of identified articles.

The search strategy included MeSH terms: "synovitis," "ultrasonography," "microbubbles," "contrast media," and "magnetic resonance imaging," as detailed in **Table 1**.

Table 1. Search strategy

Database	Search strategy
Cochrane Library	#1: MeSH descriptor: [Synovitis] explode all trees #2: MeSH descriptor: [Ultrasonography] explode all trees #3: MeSH descriptor: [Microbubbles] explode all trees #4: MeSH descriptor: [Contrast media] explode all trees #5: MeSH descriptor: [Magnetic Resonance Imaging] explode all trees #6: #1 AND #2 AND #3 OR #4 AND #5
Medline	#1: "Synovitis"[MeSH] OR (Synovitides) OR (Synovial Plica Syndrome) OR (Plica Syndrome, Synovial) OR (Plica Syndrome) OR (Synovial Hypertrophy) OR (Hypertrophies, Synovial) OR (Hypertrophy, Synovial) OR (Synovial Hypertrophies) OR (Synovial Thickening) OR (Synovial Thickenings) OR (Thickening, Synovial) OR (Thickenings, Synovial) #2: "Ultrasonography"[MeSH] OR (Echotomography) OR (Diagnostic Ultrasound) OR (Diagnostic Ultrasounds) OR (Ultrasound, Diagnostic) OR (Ultrasounds, Diagnostic) OR (Sonography, Medical) OR (Medical Sonography) OR (Ultrasound Imaging) OR (Imaging, Ultrasound) OR (Imagings, Ultrasound) OR (Ultrasound Imagings) OR (Echography) OR (Ultrasonic Imaging) OR (Imaging, Ultrasonic) OR (Echotomography, Computer) OR (Computer Echotomography) OR (Tomography, Ultrasonic) OR (Ultrasonic Tomography) OR (Diagnosis, Ultrasonic) OR (Diagnoses, Ultrasonic) OR (Ultrasonic Diagnoses) OR (Ultrasonic Diagnosis) #3: "Microbubbles"[Mesh] OR (Microbubble) OR (Colloidal Gas Aphrons) OR (Aphron, Colloidal Gas) OR (Aphrons, Colloidal Gas) OR (Colloidal Gas Aphron) OR (Gas Aphron, Colloidal) OR (Gas Aphrons, Colloidal) #4: "Contrast media"[MeSH] OR (Media, Contrast) OR (Contrast Agent) OR (Agent, Contrast) OR (Contrast Materials) OR (Materials, Contrast) OR (Contrast Agents) OR (Agents, Contrast) OR (Contrast Material) OR (Material, Contrast) OR (Radiocontrast Media) OR (Media, Radiocontrast) OR (Radiocontrast Agent) OR (Agent, Radiocontrast) OR (Radiocontrast Agents) OR (Agents, Radiocontrast) OR (Radiopaque Media) OR (Media, Radiopaque) #5: "Magnetic Resonance Imaging"[MeSH] OR (Imaging, Magnetic Resonance) OR (NMR Imaging) OR (Imaging, NMR) OR (Zeugmatography) OR (Tomography, MR) OR (Tomography, NMR) OR (MR Tomography) OR (NMR Tomography) OR (Tomography, Proton Spin) OR (Proton Spin Tomography) OR (Magnetization Transfer Contrast Imaging) OR (MRI Scans) OR (MRI Scan) OR (Scan, MRI) OR (Scans, MRI) OR (fMRI) OR (MRI, Functional) OR (Functional MRI) OR (Functional MRIs) OR (MRIs, Functional) OR (Functional Magnetic Resonance Imaging) OR (Magnetic Resonance Imaging, Functional) OR (Imaging, Chemical Shift) OR (Chemical Shift Imagings) OR (Imagings, Chemical Shift) OR (Shift Imaging, Chemical) OR (Shift Imagings, Chemical) OR (Chemical Shift Imaging) #6: #1 AND #2 AND #3 OR #4 AND #5
EMBASE	#1: 'synovitis'/exp OR 'immune synovitis' OR 'inflammation, synovia' OR 'synovia inflammation' OR 'synovial disease' OR 'synovial inflammation' OR 'synovitis' OR 'synovium inflammation' OR 'toxic synovitis' OR 'villous synovitis' #2: 'echography'/exp OR 'diagnostic ultrasonic examination' OR 'diagnostic ultrasonic imaging' OR 'diagnostic ultrasonic method' OR 'diagnostic ultrasound' OR 'doptone' OR 'duplex echography' OR 'echogram' OR 'echographic evaluation' OR 'echography' OR 'echoscopy' OR 'echosound' OR 'high resolution echography' OR 'scanning, ultrasonic' OR 'sonogram' OR 'sonographic examination' OR 'sonographic screening' OR 'sonography' OR 'ultrasonic detection' OR 'ultrasonic diagnosis' OR 'ultrasonic echo' OR 'ultrasonic examination' OR 'ultrasonic scanning' OR 'ultrasonic scintillation' OR 'ultrasonogram' OR 'ultrasonographic examination' OR 'ultrasonographic screening' OR 'ultrasonography' OR 'ultrasound diagnosis' OR 'ultrasound scanning' #3: 'microbubbles' #4: 'contrast medium'/exp OR 'contrast agent' OR 'contrast dye' OR 'contrast material' OR 'contrast media' OR 'contrast medium' OR 'radiocontrast medium' OR 'radiography contrast medium' OR 'roentgen contrast medium' #5: 'nuclear magnetic resonance imaging'/exp OR 'mri' OR 'nmr imaging' OR 'imaging, magnetization transfer' OR 'magnetic resonance imaging' OR 'magnetic resonance tomography' OR 'magnetization transfer imaging' OR 'mr imaging' OR 'nuclear magnetic resonance imaging' #6: #1 AND #2 AND #3 OR #4 AND #5

Continue...

Table 1. Continuation.

Database	Search strategy
LILACS	#1: mh:" Sinovite" OR (Synovitis) OR (Sinovitis) OR (Synovite) OR (Espessamento Sinovial) OR (Hipertrofia Sinovial) OR (Síndrome da Prega) OR (Síndrome da Prega Sinovial) OR (mh: C05.550.870$) #2: mh: "Ultrassonografia" OR (Ultrasonografía) OR (Ultrasonography) OR (Ecografia) OR (Ecotomografia Computador) OR (Sonografia Médica) OR (Ecografia Médica) OR (Tomografia Ultrassônica) OR (Diagnóstico Ultrassom) OR (Imagem Ultrassônica) OR (Imagem Ultrassonográfica) OR (Imagem Ultrassom) OR (Imagem Ultrassom) OR (Ecotomografia) OR (mh:E01.370.350.850$) #3: mh:"Microbolhas" OR (Microbubbles) OR (Microburbujas) OR (Microbulles) OR (Microbolhas de Gás) OR (mh:E07.553$) #4: mh:"Meios de Contraste" OR (Contrast Media) OR (Medios de Contraste) OR (Produits de contraste) OR (Agente de Contraste) OR (Material de Contraste) OR (Meio Radiopaco) OR (Meio de Contraste) OR (Meios Radiopacos) OR (mh:D27.505.259.500$) OR (mh:D27.720.259$) #5: mh:"Imageamento por Ressonância Magnética" OR (Magnetic Resonance Imaging) OR (Imagen por Resonancia Magnética) OR (Imagerie par résonance magnétique) OR (IRM Funcional) OR (IRMf) OR (Imageamento Contrastado por Transferência de Magnetização) OR (Imageamento de Ressonância Magnética) OR (Imageamento de Spin-Eco) OR (Imageamento por Chemical Shift) OR (Imageamento por Ressonância Magnética Funcional) OR (Imagem Contrastada por Transferência de Magnetização) OR (Imagem de Ressonância Magnética) OR (Imagem de Spin-Eco) OR (Imagem por Chemical Shift) OR (Imagem por RMN) OR (Imagem por Ressonância Magnética) OR (Imagem por Ressonância Magnética Funcional) OR (Ressonância Magnética com Seqüências em Equilíbrio Estável) OR (Tomografia do Spin do Próton) OR (Tomografia por RM) OR (Tomografia por RMN) OR (Varreduras por IRM) OR (mh:E01.370.350.825.500$) #6: #1 AND #2 AND #3 OR #4 AND #5
SCOPUS	#1: Ultrasonography #2: Microbubble #3: Contrast media #4: Magnetic resonance imaging #5: Synovitis #6: #1 AND #2 OR #3 AND #4 AND #5
CINAHL	#1: Ultrasonography or ultrasound or sonography or echography #2: Microbubble #3: Contrast media or contrast medium or contrast agent #4: Magnetic resonance imaging or mri or mri scan #5: Synovitis
Web of Science	#1: Ultrasonography #2: Microbubble #3: Contrast media #4: Magnetic resonance imaging #5: Synovitis #6: #1 AND #2 OR #3 AND #4 AND #5

Statistical analysis and data synthesis

The study data were synthesized into 2 × 2 contingency tables, categorizing true positives, false positives, true negatives, and false negatives as absolute values. For the detection rate, the synovitis region was evaluated. All analyses were performed using RevMan 5.3. Diagnostic methods (CEUS and MRI) were compared based on the available patient data to minimize bias. No formal heterogeneity analysis (I^2 statistics) or publication bias tests (e.g., funnel plot)

were conducted because of the small number of included studies. This limitation was considered when interpreting our findings.

RESULTS

A total of 613 studies related to the topic were found in the literature searches, and eight studies that met the inclusion criteria were selected (**Figure 1**). One study[6] did not specify whether synovitis was detected in the examinations, nor did it distinguish it from joint effusion and bone erosion. Two studies[4,11] did not specify the exact number of patients who underwent examinations that showed synovitis on diagnostic tests. These studies were excluded from this systematic review. Additional data were requested by email; however, we did not receive any responses. In total, five studies were included in the final analysis (n = 235 patients), representing a small but methodologically consistent sample (**Table 2**).[12–16]

Two studies were conducted with control groups, Song et al.[12] and Szkudlarek et al.[13], thus allowing the evaluation of accuracy (**Figure 2**). Studies that did not have a control group (Magarelli et al.,[14] Stramare et al.,[15] and Wamser et al.[16]) were used to evaluate the detection rate of each method in conjunction with studies with a control group. This heterogeneity in the study design limited the statistical combination of the results but provided complementary evidence for comparative analysis.

Joints evaluated

Three studies evaluated the knees,[12,14,15] three evaluated the shoulders,[14–16] two evaluated the elbows,[14,15] two evaluated the wrists,[14,15] two evaluated the metacarpophalangeal joints,[13,15] one evaluated the carpal joints,[14] one evaluated the interphalangeal joints,[15] and one evaluated the ankles.[14] However, the study by Stramare[15] did not report the findings of synovitis in each joint, either by ultrasound or MRI, and the study by Magarelli[14] did not report the synovitis findings in all joints separately by MRI, except for the knees, wrists, ankles, and elbows.

The knees had complete data from two studies, Magarelli et al.[14] and Song et al.,[12] totaling 106 knees evaluated.

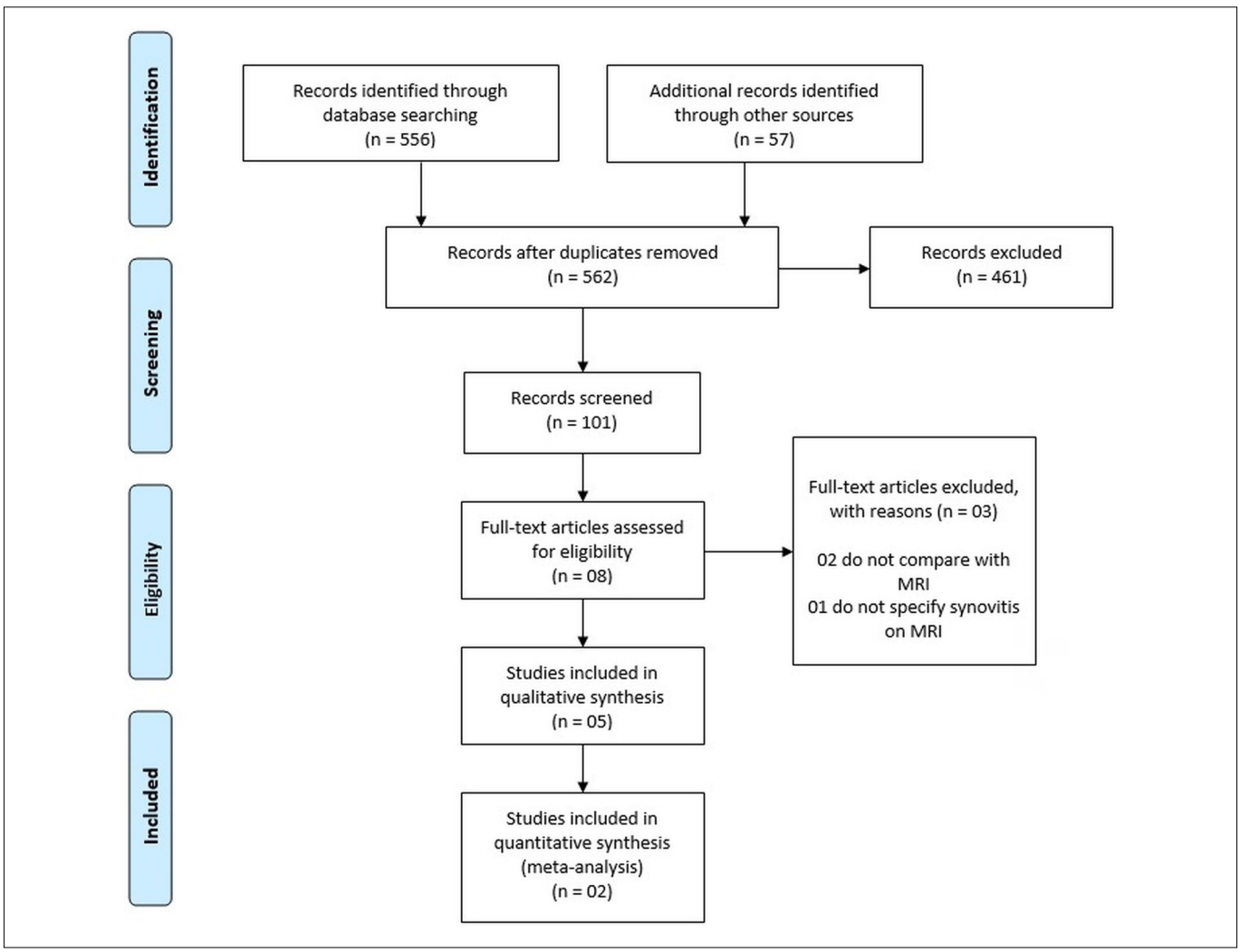

Figure 1. PRISMA diagram showing study selection.

Of the 65 knees assessed by CEUS, 61 showed synovitis, with a detection rate of 93.8%. Of the 41 knees evaluated using contrast-enhanced MRI, 34 showed synovitis, with a detection rate of 82.9% (**Figure 3**).

Underlying diseases evaluated

Three studies evaluated synovitis in rheumatoid arthritis,[13,15,16] and one in osteoarthritis.[12] Magarelli et al.[14] evaluated rheumatoid arthritis, psoriatic arthritis, chronic juvenile rheumatoid arthritis, gout, septic arthritis, and Behçet's disease, reporting synovitis findings on CEUS, but not on MRI.

Rheumatoid arthritis had complete data in three studies: Stramare et al.,[15] Szkudlarek et al.,[13] and Wamser et al.,[16] with a total of 108 patients. Of the 55 patients evaluated by CEUS, 37 showed synovitis, with a detection rate of 67.2%. Of the 53 patients evaluated using contrast-enhanced MRI, 51 showed synovitis, with a detection rate of 96.2% (**Figure 4**).

Evaluation of synovitis independently of the joint and underlying disease

The total number of patients evaluated was cited in five studies: Magarelli et al.,[14] Song et al.,[12] Stramare et al.,[15] Szkudlarek et al.,[13] and Wamser et al.,[16] with 235 evaluated patients. Of the 133 patients evaluated by CEUS, 109 had synovitis (detection rate, 81.9%). Of the 103 patients evaluated using CE-MRI, 91 (88.3%) had synovitis (**Figure 5**).

Despite similar rates, the limited number of studies and heterogeneous populations precluded definitive statistical comparisons.

Accuracy evaluation

Two studies were conducted with contrast enhancement, with a control group of patients affected by synovitis (Song et al.[12] and Szkudlarek et al.[13]), thus allowing for the evaluation of accuracy.

The evaluation of CEUS in patients with synovitis showed 84.9% sensitivity and 100% specificity, with a 95% confidence interval (95% CI), $p < 0.05$, and 87% accuracy (**Figure 6**).

Table 2. Summary of the main characteristics of the included studies

Study	Year	Sample (n patients)	Control group	Joints evaluated	Underlying diseases	Imaging methods compared	Main outcomes
Magarelli et al.[14]	2001	40	No	Knee, wrist, ankle, elbow	RA, psoriatic arthritis, JRA, gout, Behçet's	CEUS vs MRI	CEUS detected 93% of knees with synovitis
Szkudlarek et al.[13]	2003	42	Yes	Metacarpophalangeal	RA	CEUS vs MRI	MRI detected 96%, CEUS 67%
Wamser et al.[16]	2003	33	No	Shoulder	RA	CEUS vs MRI	Marked discrepancy in shoulder detection rates
Song et al.[12]	2008	41	Yes	Knee	Osteoarthritis	CEUS vs MRI	CEUS 93.8%, MRI 82.9%
Stramare et al.[15]	2013	79	No	Multiple joints	RA	CEUS vs MRI	Comparable accuracy

CEUS, contrast-enhanced ultrasound; RA, rheumatoid arthritis; JRA, juvenile rheumatoid arthritis; MRI, magnetic resonance imaging.

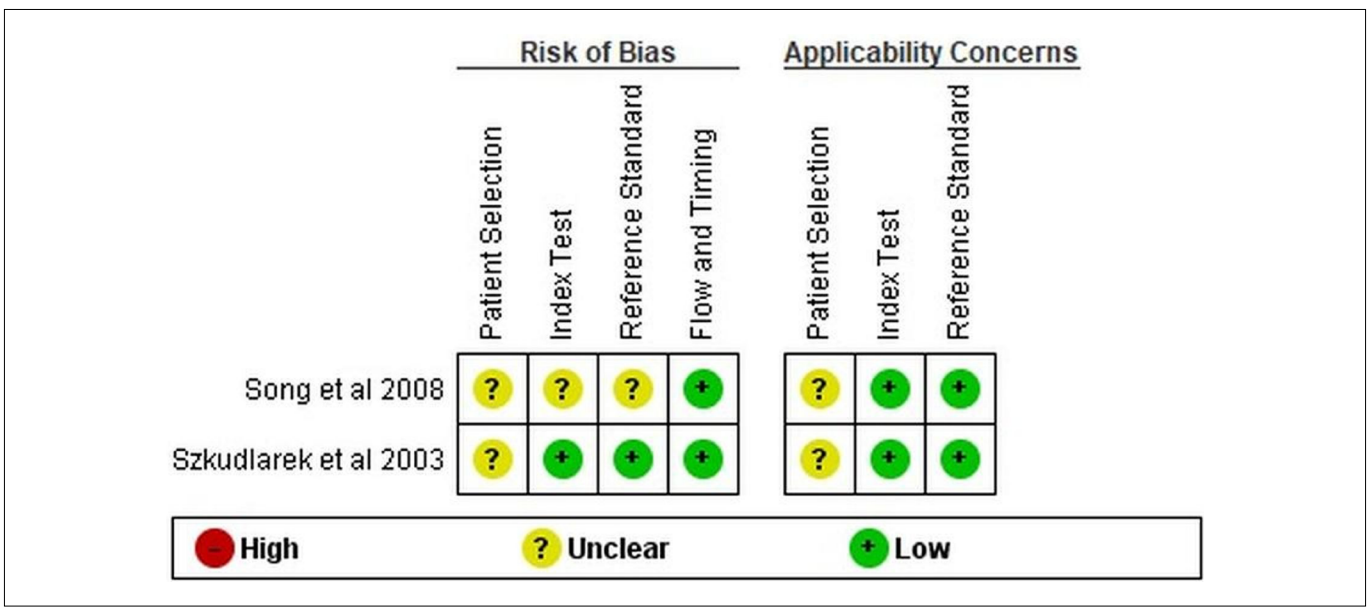

Figure 2. Tables assessing the risk of bias and the applicability of the quality of studies with a control group using the QUADAS-2 tool.

Two studies, Song et al.[12] and Szkudlarek et al.,[13] were conducted using contrast-enhanced MRI, with a control group of patients affected by synovitis, and thus, allowed for the evaluation of accuracy.

The evaluation of contrast-enhanced MRI in patients with synovitis showed 85.4% sensitivity and 100% specificity, with a 95% CI and $p < 0.05$, and 87.7% accuracy (**Figure 7**).

These results indicate a comparable diagnostic performance between the two modalities. However, the small sample size and variations in joint types should be considered when interpreting these values.

DISCUSSION

The diagnostic accuracy of the evaluated methods for synovitis showed no significant differences (87% for CEUS versus 87.7% for MRI. Regarding synovitis detection in patients with rheumatoid arthritis, contrast-enhanced MRI was superior (96.2%) to contrast-enhanced ultrasonography (67.2%).

Only one joint, the knee, presented data from different studies, which allowed for its evaluation. The synovitis detection rate in the knees was higher with CEUS (93.8%) than with CEMRI (82.9%). However, owing to the small number of joints evaluated, the forest plot did not show any differences between the diagnostic tests.

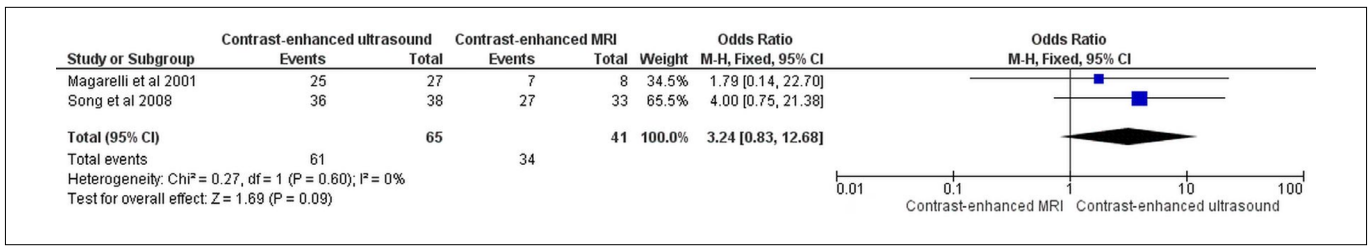

Figure 3. Comparison for knees: contrast-enhanced ultrasound versus contrast-enhanced MRI.

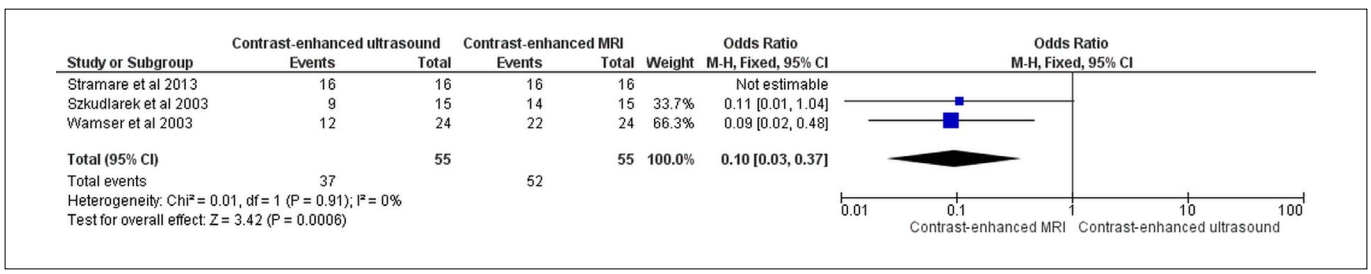

Figure 4. Comparison for rheumatoid arthritis: contrast-enhanced ultrasound versus contrast-enhanced MRI.

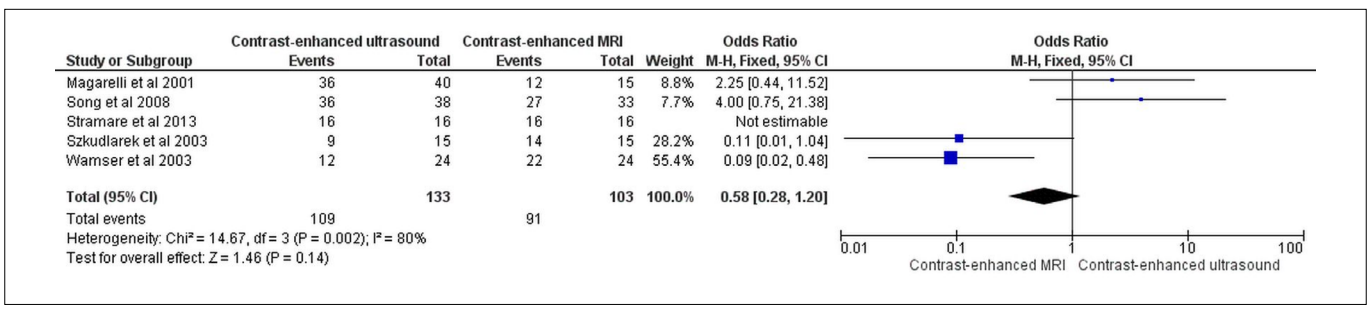

Figure 5. Comparison for synovitis regardless of the joint and underlying disease: contrast-enhanced ultrasound versus contrast-enhanced MRI.

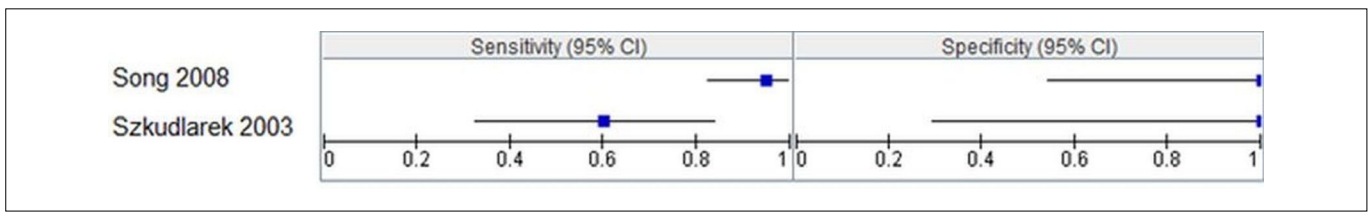

Figure 6. Accuracy Graph for synovitis: contrast-enhanced ultrasonography.

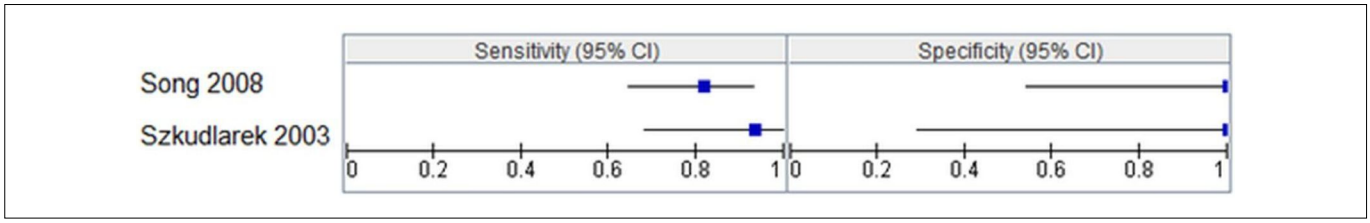

Figure 7. Accuracy Graph for synovitis: contrast-enhanced magnetic resonance imaging.

Evaluation of synovitis, independent of the joint and underlying disease, also showed a difference in detection rates between contrast-enhanced ultrasonography (81.9%) and contrast-enhanced MRI (88.3%). Both methods showed good sensitivity, with no significant difference between them (CEUS, 84.9%; contrast-enhanced MRI, 85.4%). Both methods showed 100% specificity. However, these findings should be interpreted with caution as they are based on a limited number of heterogeneous studies, including variations in disease type, joint distribution, and imaging protocols.

In terms of detecting inflammation, both ultrasound and MRI can detect more cases of synovitis than physical examination.[17] The benefit of ultrasound as a complement to physical examination is influenced by the ability of subclinical synovitis to predict disease progression. Owing to their three-dimensional acquisition, both ultrasound and MRI are more sensitive than conventional radiography in detecting damage from erosion and early signs of erosion.[17]

Osteoarthritis is a leading cause of labor disability worldwide, with synovitis being the earliest inflammatory sign.[18] Several arthroscopy studies have also shown that synovitis is a common finding in osteoarthritis and is associated with disease progression.[19–21] In 2007, rheumatoid arthritis was the fourth disease with the greatest budgetary impact on the Unified Health System in Brazil, consuming 10.4% of the resources.[22] With these data, using CEUS instead of contrast-enhanced MRI for synovitis diagnosis could lead to significant savings, as ultrasound is less expensive than MRI (US$ 86.1, or R$ 438.3 for ultrasound; US$ 181.95, or R$ 926.3 for MRI), and microbubble contrast is also slightly less expensive than gadolinium (US$ 42.6, or R$ 216.7 for microbubble contrast; US$ 42.9, or R$ 218.5 for gadolinium).[23] Although these values of rheumatoid arthritis reflect primarily Brazilian cost estimates, international comparisons show a similar cost gap favoring ultrasound. Thus, CEUS, being more accessible and performing faster, could reduce the waiting time for diagnosis and treatment, leading to lower hospitalization costs and reduced economic impact of patient disability.

After an intravenous bolus injection of microbubble contrast, the distribution can be monitored in real time, allowing for the delineation of structures and temporal evaluation. It is important to note that the adverse event rate is close to zero (1:10,000 compared with iodinated contrast agents, 1–12:100, and gadolinium contrast agents occurring in 0.04–0.3% of administrations, of which 0.4–9% are severe).[24–26] These adverse reactions include anaphylactic shock, skin allergic reactions, injection site reactions, dizziness or headaches, nausea or vomiting, chest discomfort, numbness, and low back pain, with more than 87% of adverse reactions being mild.[27]

A major disadvantage of ultrasound compared with MRI is that bone lesions, which are very common in rheumatologic diseases that are major causes of synovitis, such as bone marrow edema and small erosions, are only detected by MRI.[28] Such assessments are necessary for disease staging, such as in rheumatoid arthritis, influencing treatment. However, it should be considered that MRI is not the gold standard for detecting synovitis (histological analysis is the gold standard); the use of gadolinium contrast and evaluation of multiple joints is time-consuming and expensive for routine use.[29] In addition, the presence of metals in the body (such as prostheses or pacemakers) can interfere with MRI results, rendering the examination unfeasible for certain patients.

Given the similarity in accuracy and sensitivity between CEUS and contrast-enhanced MRI, and because both have 100% specificity for synovitis, combined with the greater accessibility and lower cost of ultrasound, one could envision a new direction for synovitis evaluation. However, further studies are needed to evaluate synovitis in rheumatoid arthritis to make CEUS compatible with contrast-enhanced MRI. This result aligns with a systematic review by Takase-Minegishi et al.,[30] which evaluated the accuracy of ultrasound and MRI for synovitis diagnosis in 17 studies, only one of which used CEUS[13] involving the metacarpophalangeal, interphalangeal, and knee joints, and concluded that ultrasound is a valid and reproducible technique. However, given the methodological variability and limited sample size, our findings reinforce the need for larger multicenter diagnostic accuracy studies using standardized protocols. Such studies should stratify the results by joint type and underlying disease to clarify the true diagnostic equivalence between modalities.

It should be noted that a significant discrepancy in the evaluation between CEUS and contrast-enhanced MRI was evidenced in the study by Wamser,[16] which evaluated only the shoulder joint in rheumatoid arthritis. This discrepancy may be due to the ability of MRI to visualize the entire joint and deep part of the synovium regardless of the amount of body fat, whereas ultrasound can only visualize superficial articular recesses, which are not necessarily

involved in cases of mild synovial joint synovitis. Another possible explanation is the difficulty in distinguishing synovitis from fluid, especially in old and long-lasting effusions when the fluid becomes hypoechoic. In this regard, MRI without contrast is also unable to differentiate between synovitis and synovial fluid, as both present the same signal intensity even in fluid-sensitive sequences, necessitating the use of gadolinium contrast.

Some studies did not specify which joints showed synovitis detected by CEUS and contrast-enhanced MRI; MRI evaluation did not specify whether the detected change was specifically synovitis, nor did it differentiate it from joint effusion and bone erosion, nor did it specify how many patients underwent MRI. CEUS features all the properties of a synovitis screening method, including low cost, availability, accessibility, high sensitivity, high specificity, and painlessness. Therefore, based on the results of this review, CEUS should be viewed as a potential screening tool rather than a replacement for MRI, especially until further evidence is available.

Future research should prioritize comparative trials including larger populations, diverse rheumatological conditions, and multicenter participation to ensure generalizability beyond the single-institution experience. These studies should specify the joints evaluated, the diseases of each patient, and the clinical stage of the underlying condition. Furthermore, diseases causing synovitis, such as ankylosing spondylitis, were not evaluated in these studies.[31] Only one study[12] evaluated osteoarthritis, the most common joint disease in people over 65 years of age, and a cause of synovitis,[32] indicating a need for additional studies regarding this disease. Evaluation of synovitis during the treatment of the underlying disease, especially rheumatoid arthritis, should also be considered, given its significant prevalence in the population and high treatment costs. Our systematic review identified the need for new clinical trials to evaluate joints with limited research or for which research still lacks definitive results, as seen with the hand and wrist joints, which were evaluated by only two studies without specifying their data individually.[14,15] The knee was the only joint with individualized data that showed good detection rates with both CEUS and contrast-enhanced MRI. Nonetheless, the hand and wrist joints are the most affected joints in many rheumatological diseases, such as rheumatoid arthritis.[33]

CONCLUSION

CEUS has significant potential as an essential tool for the early diagnosis of synovitis in clinical practice. Both contrast-enhanced microbubble ultrasonography and contrast-enhanced MRI demonstrated comparable diagnostic accuracies for synovitis, with values of 87% and 87.7%, respectively. Although these methods showed similar overall diagnostic performances, specific data for joint evaluation were only available for the knee, where CEUS outperformed MRI with a detection rate of 93.8% versus 82.9%. When assessing synovitis across different joints and underlying diseases, contrast-enhanced MRI achieved a slightly higher detection rate (88.3%) than ultrasonography (81.9%). However, these differences were not statistically significant and should be interpreted with caution, considering the small number of heterogeneous studies included. Given its portability, low cost, and safety profile, CEUS may be a feasible adjunct to MRI for routine evaluation and longitudinal follow-up of synovitis, particularly in outpatient or resource-limited settings. However, the current evidence remains limited. Larger multicenter diagnostic accuracy studies with standardized protocols are warranted to confirm the reproducibility and generalizability of these findings, particularly across different joints and rheumatological diseases.

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Non-surgical facial harmonization for gender affirmation and psychosocial well-being in transmasculine persons: an exploratory mixed-methods study

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ABSTRACT

BACKGROUND: Facial appearance plays a central role in gender recognition and identity congruence, particularly among transmasculine individuals. Although the demand for gender-affirming care has increased, evidence regarding the psychosocial implications of nonsurgical facial masculinization using hyaluronic acid remains limited, especially within public health systems.

OBJECTIVES: To describe the subjective and psychosocial experiences related to nonsurgical facial harmonization with hyaluronic acid among transmasculine individuals receiving care in public health settings.

DESIGN AND SETTING: A mixed-methods exploratory study with a qualitative core component was conducted in a public, gender-affirming outpatient clinic in Salvador.

METHODS: Six transmasculine patients participated in semi-structured interviews. The FACE-Q Satisfaction with Facial Appearance Overall Scale (SFAOS) and Beck Anxiety Inventory (BAI) were administered before and 30 days after the procedure as complementary quantitative measures. Qualitative data were analyzed using thematic content analysis based on Bardin's framework, with sampling guided by theoretical saturation.

RESULTS: Participants reported perceived reductions in facial dysphoria, improvements in self-perception, and greater social confidence after the procedure. Complementary quantitative measures indicated consistent short-term increases in facial satisfaction scores and a trend toward reduced anxiety.

CONCLUSIONS: In this exploratory study, nonsurgical facial harmonization with hyaluronic acid was associated with short-term improvements in self-perceived facial satisfaction and psychosocial comfort among transmasculine participants. Given the small sample size and short follow-up period, these findings should be interpreted as preliminary. Larger studies with longer follow-up periods and comparative designs are warranted to evaluate the durability and generalizability of our findings.

INTRODUCTION

Facial harmonization, traditionally associated with aesthetic enhancement in cisgender populations, has become an increasingly relevant strategy in transgender healthcare, especially for individuals seeking gender-affirming care. For transmasculine persons, the face constitutes a critical site in the gender affirmation process because of its prominent role in social gender perception. Masculine-coded features such as a broad jawline, projected chin, and balanced facial proportions are strongly tied to cisnormative ideals and often become sources of dysphoria for individuals whose appearance diverges from these standards.[1,2] Recent findings underscore the centrality of facial appearance for transgender and non-binary individuals who report specific preferences and expectations tied to aesthetic procedures as part of their identity expression.[3]

Although testosterone therapy significantly influences body composition, muscle mass, and voice pitch, its effects on craniofacial bone structure remain limited, leaving many transmasculine persons with facial features that do not align with their gender identity.[2,4] In this context, non-surgical interventions, such as injectable hyaluronic acid fillers, have gained attention as viable alternatives to orthognathic or implant-based procedures. These treatments offer not only aesthetic enhancement but also meaningful subjective impacts on self-image, self-esteem, and social integration.[5,6]

The growing use of hyaluronic acid fillers for facial masculinization demonstrates their relevance in gender-affirming care. Fillers enable structural modifications to the jaw, chin, and

midface with minimal risk, reduced downtime, and reversibility, factors that are especially valued by individuals seeking gradual and customizable transitions.[5] Rheological advancements have allowed clinicians to tailor product selection to skin thickness and target anatomical depth, further enhancing safety and precision.[7]

Despite these advances, transmasculine persons continue to face invisibility in terms of public policy and academic research. Much of the literature focuses on transfeminine persons, perpetuating a knowledge gap regarding specific needs, mental health outcomes, and healthcare barriers experienced by transmasculine individuals.[1,2] Recent integrative reviews emphasize the need to broaden the scope of gender-affirming care to include nonsurgical approaches as essential elements in the promotion of psychosocial well-being and identity affirmation.[4,5]

In this context, the present study aimed to describe subjective and psychosocial experiences related to nonsurgical facial harmonization with hyaluronic acid as a gender-affirming procedure in transmasculine persons.

METHODS

Study design and setting

This was a mixed-method exploratory study with a qualitative core component and complementary quantitative pre- and post-assessments. The qualitative component followed a descriptive and interpretative approach aimed at understanding the experiences of transmasculine individuals undergoing nonsurgical facial masculinization. The quantitative component assessed short-term changes in anxiety symptoms and satisfaction with the facial appearance.

This study was conducted at the Gender Facial Affirmation Outpatient Clinic of Hospital Universitário Professor Edgard Santos (HUPES), Faculdade de Medicina da Bahia of the Universidade Federal da Bahia (FMB-UFBA), Salvador, between March and June 2025.

Participants and sampling

Six transmasculine adults were recruited from among outpatient service users through purposive sampling. Eligible participants were individuals who self-identified as transmasculine, aged 18 years or older, had undergone continuous masculinizing hormone therapy for at least 2 years, and had not previously undergone facial harmonization procedures. All of the participants who met these criteria and agreed to participate were included in the study.

The sampling process followed the criteria of theoretical and thematic saturation, a methodological principle in qualitative research, whereby data collection is concluded when no new themes or relevant insights emerge from subsequent interviews. This approach ensured that the gathered material was sufficient to deeply explore the research questions and support a consistent and meaningful thematic analysis. Saturation was monitored continuously during the interview process. Once the narratives began to repeat key patterns without adding new dimensions, the research team determined that the saturation point had been reached, validating the adequacy of the sample size for the exploratory goals.[8]

Procedure

Facial masculinization was performed using a standardized hyaluronic acid injection protocol. A total of 3 mL was administered bilaterally, with 0.5 mL supraperiosteal bolus injections placed at each mandibular angle and the chin. The injections, consisting of hyaluronic acid with lidocaine (Restylane Lyft®, Galderma), were delivered using a needle directly on the periosteum to enhance projection and angular definition.

Along the mandibular body, at the level of the second lower premolar, a 22G × 50 mm cannula was introduced through a single entry point. A retrograde linear threading technique was performed in a deep plane, delivering 0.5 mL of Restylane Define® (Galderma) per side to improve mandibular contour continuity.

All procedures were performed by the same experienced surgeon using identical anatomical landmarks and injection techniques. Specific commercial products are mentioned solely for technical reproducibility, and do not imply endorsements.

Data collection and definitions

Data were collected through individual semi-structured interviews conducted in a private setting either immediately after the procedure or during follow-up appointments. The interview guide explored perceptions of facial appearance, psychosocial impact of the intervention, and experiences related to gender dysphoria, self-esteem, institutional support, and access to public policy.

The Satisfaction with Facial Appearance Overall Scale (SFAOS), a subscale of the FACE-Q,[9] is a psychometrically validated tool developed to assess how satisfied individuals are with the general appearance of their faces. The SFAOS consists of a set of items that prompt participants to rate their satisfaction with facial attributes, such as symmetry, balance, and overall appearance, at different times of the day. Responses were collected using a 4-point Likert scale ranging from "very dissatisfied" to "very satisfied." This quantitative approach complements the qualitative data by providing a structured measure of subjective appearance-related outcomes.[9]

The Beck Anxiety Inventory (BAI) is a widely used, psychometrically validated instrument designed to measure the severity of anxiety symptoms in clinical and research settings. It consists of 21 self-report items that describe common somatic and cognitive symptoms of anxiety, such as numbness, dizziness, fear of the worst occurrence, or difficulty in breathing. Each item was rated on a 4-point scale ranging from 0 ("not at all") to 3 ("severely"), referring to how much the symptom bothered the respondent during

the past week. The total score ranges from 0 to 63, with interpretive guidelines classifying the scores into minimal (0–10), mild (11–19), moderate (20–30), and severe (31–63) anxiety levels. This tool allows for a nuanced understanding of emotional states that may intersect with gender dysphoria and identity affirmation processes.[10]

Statistical analysis

Quantitative data were analyzed descriptively to assess within-participant changes between baseline and 30-day follow-up. Mean change scores (Δ) were calculated as 30-day score minus baseline score for both the BAI and the FACE-Q Satisfaction with SFAOS. The 95% confidence intervals (CI) for the mean paired differences were calculated to estimate the precision of the change. Standardized mean change was calculated using Cohen's dz ($dz = t/\sqrt{n}$) to quantify the magnitude of within-participant effects. Given the small sample size and exploratory design, emphasis was placed on magnitude and precision rather than on confirmatory hypothesis testing. Analyses were performed using SPSS software (version 18.0; SPSS Inc., Chicago).

Qualitative analysis

All interviews were audio-recorded, fully transcribed, and analyzed using thematic content analysis according to Bardin's framework.[8] This methodological approach consists of three structured phases: (1) pre-analysis, involving a floating reading of the material and constitution of the corpus; (2) exploration of the material, including identification of meaning units, coding, and progressive categorization; and (3) treatment and interpretation of results, in which themes were consolidated and analytically articulated.

Interviews were conducted sequentially and the analysis was conducted concurrently with data collection. After each interview, the transcripts were read in full and initially coded to identify recurring meaning units related to facial perception, dysphoria, psychosocial impact, and institutional experiences. The codes were iteratively refined through constant comparisons across interviews, leading to the consolidation of thematic cores.

Thematic saturation-guided recruitment was operationally defined as the point at which subsequent interviews no longer generated new codes or conceptual categories, and the thematic structure remained analytically stable.

Coding and categorization were conducted by the primary researcher with iterative discussions of emerging themes within the research team to enhance interpretive coherence and analytical transparency.

To ensure methodological rigor and transparency in qualitative reporting, this study followed the Consolidated Criteria for Reporting Qualitative Research (COREQ).[11]

Ethical considerations

The study adhered to all ethical principles outlined in Resolution No. 466/2012 of the Brazilian National Health Council and was approved by the Research Ethics Committee of the Universidade Federal da Bahia (UFBA) (approval number 6.469.528).

RESULTS

Six transmasculine individuals participated in the study. The mean age was 34.17 years (SD = 12.49). Five participants were single and one reported being in a relationship. Four had completed higher education and two had completed high school. Five participants were employed, but all reported monthly incomes below the Brazilian minimum wage. Four participants reported engaging in regular physical activity, and one (16.7%) was identified as a smoker. All participants engaged in regular psychological follow-up at the time of the study. One participant had a previous diagnosis of severe anxiety disorder.

Anxiety symptoms

The mean BAI score decreased from 11.33 (SD = 10.84) at baseline to 8 (SD = 6.72) after 30 days. The mean within-participant change (Δ) was −3.33 points, corresponding to a standardized mean change (Cohen's dz) of 0.77, indicating a moderate-to-large within-participant reduction in anxiety symptoms.

Although variability across participants was observed, the overall direction of change was toward lower anxiety at follow-up. Considering the limited sample size and short-term assessment, these findings were interpreted as exploratory rather than confirmatory evidence.

Satisfaction with facial appearance

Consistent within-participant improvements were observed across all FACE-Q satisfaction scores in the facial appearance domains at 30 days (**Table 1**). The mean change scores (Δ) ranged from +1.17 to +2.17 points, indicating higher satisfaction at follow-up compared with baseline.

The standardized mean changes (Cohen's dz) ranged from 1.19 to 5.31, reflecting substantial within-participant effects across domains. The largest standardized change was observed in the "appearance in photographs" domain, reflecting a highly consistent within-participant improvement.

Given the small purposive sample and exploratory design, effect sizes were presented to describe the magnitude of within-participant changes rather than to support confirmatory inference.

Across domains, descriptive inspection of response distributions demonstrated a shift from predominantly dissatisfaction categories at baseline to predominantly "somewhat satisfied" or "very satisfied" responses at 30 days (**Figures 1 and 2**).

From the initial skimming and content coding of the interviews, five thematic cores emerged to structure the analysis: (1) facial dysphoria and self-perception; (2) impact on self-esteem and social relationships; (3) support and care during the transition process; (4) minimally invasive procedures as an alternative to surgery; and (5) invisibility of transmasculine persons in public policies and within the Brazilian Unified Health System (SUS). These themes served as the basis for the qualitative analysis and are presented in **Table 2**.

DISCUSSION

The findings of this exploratory study suggest that nonsurgical facial harmonization with hyaluronic acid may be associated with short-term improvements in self-perceived facial satisfaction and psychosocial comfort among transmasculine participants. For the quantitative component, within-participant change estimates indicated consistent improvements across the FACE-Q satisfaction domains and a trend toward reduced anxiety symptoms. These quantitative results are presented as complementary magnitude estimates (Δ, 95% CI: and standardized mean change) rather than confirmatory evidence, and are interpreted alongside qualitative narratives that contextualize perceived changes in dysphoria-related distress, self-esteem, and social confidence. This aligns with existing literature that highlights the face as a central element in gender recognition and identity validation, especially among transmasculine individuals.[3] Although anxiety scores showed a trend toward reduction, variability was observed and changes should be interpreted with caution. Taken together, the qualitative narratives and exploratory quantitative change estimates suggest that minimally invasive facial interventions may contribute to perceived psychosocial comfort and identity congruence in the short-term. Given the limited sample size and

Table 1. Within-participant changes in FACE-Q satisfaction with facial appearance domains from baseline to 30 days (n = 6)

Domain	Baseline Mean (SD)	30-Day Mean (SD)	Mean Change (Δ)	95% CI of Δ	Cohen's dz
Facial symmetry	1.5 (0.55)	3.17 (0.75)	+1.67	0.58–2.75	1.61
Facial harmony	1.5 (0.55)	3.33 (0.82)	+1.83	0.61–3.06	1.57
Facial proportion	1.5 (0.55)	3.17 (0.75)	+1.67	0.58–2.75	1.61
End-of-day appearance	1.17 (0.41)	3 (1.1)	+1.83	0.8–2.87	1.86
Freshness	1.83 (0.98)	3 (1.1)	+1.17	0.14–2.2	1.19
Rested appearance	1.67 (0.82)	2.83 (0.98)	+1.17	0.14–2.2	1.19
Profile view	1.5 (0.55)	2.83 (0.98)	+1.33	0.48–2.19	1.63
Appearance in photographs	1.17 (0.41)	3.33 (0.52)	+2.17	1.74–2.6	5.31

Values are presented as means (standard deviations). Mean change (Δ) was calculated as 30-day score minus baseline score. Positive Δ values indicate higher satisfaction at follow-up. Δ = mean within-participant change (30-day minus baseline). 95% CI = 95% confidence interval of the mean paired difference. Cohen's dz represents the standardized mean change for paired samples (dz = t/√n). Effect sizes were reported to describe the magnitude of change in this exploratory study.

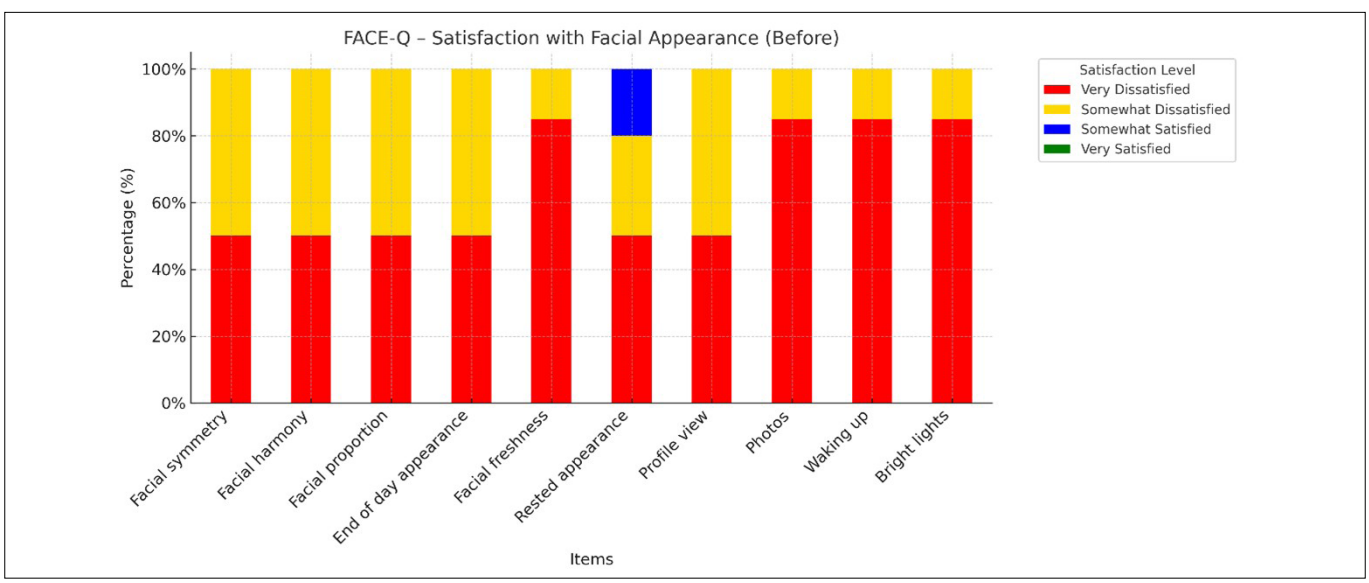

Figure 1. Distribution of satisfaction levels with facial appearance before the procedure according to the FACE-Q instrument (n = 6).

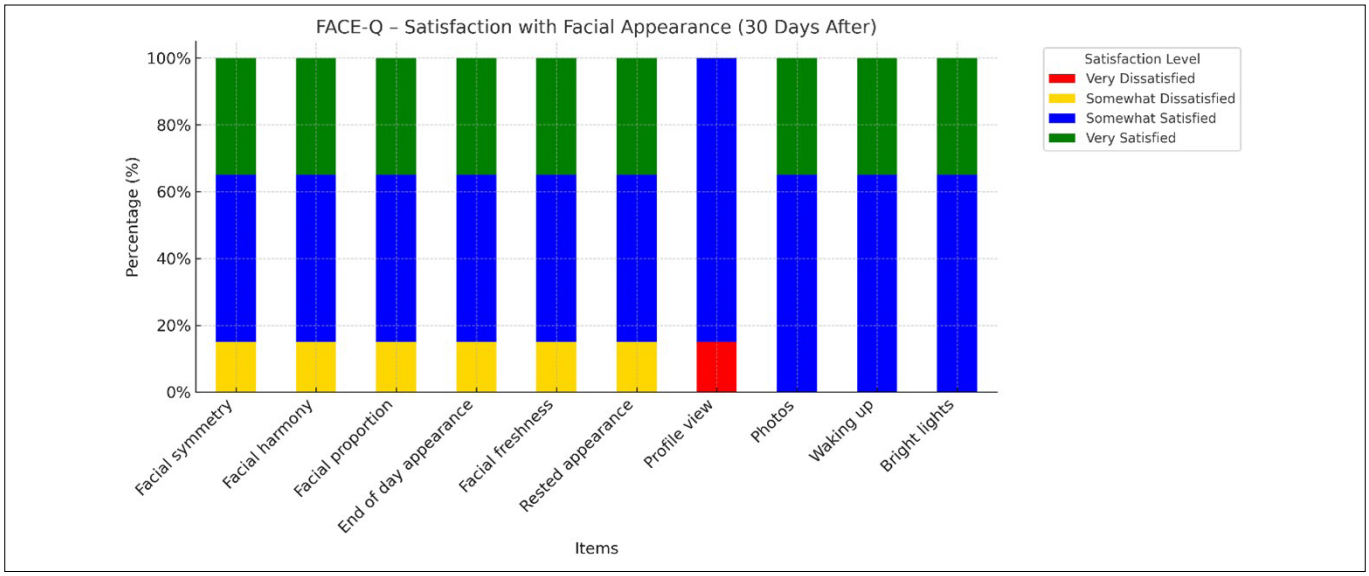

Figure 2. Distribution of satisfaction levels with facial appearance 30 days after the procedure according to the FACE-Q instrument (n = 6).

Table 2. Thematic cores, descriptions, and illustrative quotes from participants

Thematic core	Analytical description	Illustrative quotes
Facial dysphoria and self-perception	Dissatisfaction with specific facial features – particularly the jawline, chin, and facial symmetry – emerged as a core marker of dysphoria. Participants expressed emotional discomfort when seeing themselves in the mirror, with aesthetic incongruities reinforcing the distress associated with gender dysphoria. Subtle facial adjustments were described as directly alleviating this discomfort.	"Every time I looked in the mirror, I felt really uncomfortable. Mainly because of my jaw asymmetry." "The chin area always made me feel very insecure, especially in photos." "My jaw was crooked, and now I can see both sides in a harmonious way."
Impact on self-esteem and social relationships	Participants reported increased self-confidence and improved social interactions after the procedure. They began to feel more comfortable in public spaces, in photographs, and in interpersonal relationships. Being perceived by others in a way that aligned with their gender identity significantly contributed to their psychological well-being.	"After the procedure, I felt more confident going out, talking to people, looking them in the eye." "I stopped avoiding photos and started feeling more like myself in social settings." "People started saying I looked more masculine, and that made me feel really good."
Support and care during the transition	The availability of supportive relationships – whether familial, peer-based, or institutional – was pivotal during the transition process. Emotional and psychological support, as well as respectful and attentive care, were experienced as affirming and therapeutic. The procedure itself was described not just as clinical but as a form of care and affection.	"I have support from my family, I receive psychological counseling, and I use hormones regularly." "I didn't receive support during my transition, but I found help from friends." "There's general resistance from my family, but my mother supported me." "This care felt like a gesture of affection to me."
Minimally invasive procedures as an alternative to surgery	All participants endorsed the hyaluronic acid procedure as a safe and effective option. Its non-permanent and reversible nature was valued, especially for those who were not ready for surgical interventions. These procedures were framed not as superficial beautification, but as tools for authentic identity expression and improved mental health.	"I think it's a faster, less painful process, and the result is amazing." "This type of procedure can help a lot of people." "It may seem like a small thing to others, but this small detail completely changed our self-esteem." "Beyond improving my self-esteem, this procedure made me feel seen."
Invisibility of transmasculine persons in public policies and the Brazilian Unified Health System	Participants highlighted the systemic invisibility of transmasculine persons in health policies and public narratives. Many reported mental health challenges linked to social marginalization. They emphasized that access to aesthetic procedures within the public health system would not only improve individual well-being but also symbolize broader social recognition of transmasculine identities.	"Transmasculine persons are an invisible group within the trans population." "It's common among us to experience anxiety, stress, and depression." "We transmasculine persons go through violent situations that often don't make the news." "This isn't aesthetics for vanity. It's identity affirmation. It's mental health." "This procedure is necessary because the person needs it for their affirmation."

follow-up period, these findings should be understood as preliminary and hypothesis-generating rather than confirmatory.

The findings of this study suggest that nonsurgical facial harmonization using hyaluronic acid may be associated with perceived improvements in emotional well-being, self-esteem, and identity congruence among transmasculine persons. Facial dysphoria, particularly concerning the jawline, chin, and facial symmetry, emerged as a central source of psychological distress in participants' narratives, aligning with international evidence that underscores the face as a critical site for gender dysphoria, owing to its influence on social gender recognition.[2,5]

These results are consistent with those of recent studies that describe nonsurgical procedures as promising or potentially useful approaches within gender-affirming care, particularly for transmasculine individuals who face barriers to surgical access or prefer less invasive alternatives.[1,6] In this context, the incorporation of such practices into public health systems may align with the principles of autonomy, accessibility, and equity in gender-affirming care.

The high levels of dissatisfaction captured by the FACE-Q instrument were consistent with the participants' narratives and echo findings in the literature, showing that while hormone therapy induces systemic bodily changes, it has a limited impact on craniofacial bone structure. In this context, injectable fillers, particularly hyaluronic acid, have been described as minimally invasive and adjustable options that allow gradual and individualized facial masculinization.[2,6]

Participants described perceived improvements in self-esteem following the procedures, as reflected in their verbal reports, and reported changes in daily behavior such as increased comfort with being photographed and engaging socially. These observations are consistent with those of previous studies suggesting associations between appearance-related changes and self-image or dysphoria-related distress.[1,6] Some participants also reported reduced anxiety and enhanced feelings of safety, which may indicate a link between facial harmonization and perceived psychological well-being, an area that remains underexplored in research involving transmasculine populations.

Institutional and familial support emerged as important contextual elements in participants' experiences. Those who reported supportive relationships with either family members or healthcare teams reported more positive and affirmative transition processes. These narratives highlight the importance of healthcare environments that are not only technically competent, but also emotionally responsive and affirming.[1]

A preference for minimally invasive procedures over surgical options was evident in participants' narratives. They emphasized the reversibility, adjustability, and natural-appearing results associated with hyaluronic acid injections, aspects that align with patient-centered care principles that prioritize autonomy and individualized trajectories of gender affirmation.[1,2] The possibility of gradual, non-permanent changes was described as particularly meaningful for individuals who wish to adapt their appearance over time. Such flexibility may accommodate evolving gender expression and reduce concerns related to the permanence of surgical interventions, features valued by the participants in this study.

From an anatomical perspective, the lower third of the face plays a prominent role in gender recognition, particularly in relation to the mandibular contour and chin projection. The clinical literature describes the use of hyaluronic acid and other dermal fillers as minimally invasive approaches to enhance the mandibular angle definition and lower facial projection in transgender patients.[5,6] These techniques have been reported as strategies for facial masculinization through targeted augmentation of the mandibular body and chin. In our study, the participants' narratives indicated that modifications in the jawline and chin were especially meaningful in everyday contexts, such as photographs and social interactions, contributing to a perceived sense of gender congruence. The adjustability and reversibility of injectable fillers are advantageous, particularly for individuals who are navigating evolving gender expressions or facing structural barriers to surgical access. In public health settings, where access to surgery may be limited, such minimally invasive options may represent an additional pathway within gender-affirming care, reinforcing the importance of individualized and gender-sensitive approaches in aesthetic and dermatological practice.

Some studies have suggested that transgender men may present more varied or less predictable preferences regarding facial appearance than other gender-diverse populations.[3] In this context, preferences may favor more neutral or less strongly gendered features, reflecting the complexity and heterogeneity of gender identity experiences. Within this framework, the adaptability of injectable fillers such as hyaluronic acid may be perceived as advantageous because they allow for gradual and individualized modifications aligned with patient-defined goals.

These findings are consistent with an integrative review[4] that described associations between nonsurgical procedures and improvements in self-confidence and quality of life among transgender individuals. The review also emphasizes the limited availability of robust clinical evidence and highlights the need for clearer guidance and best-practice frameworks to inform the responsible implementation of these techniques.

Recent clinical studies have described treatment considerations for facial masculinization in transgender patients using injectable fillers.[2] These reports illustrate how nonsurgical procedures such as hyaluronic acid injections have been applied to enhance mandibular angle definition and lower facial projection. In the cited clinical cases, volumizing fillers were used to achieve a broader and more angular contour consistent with patients' aesthetic goals.[2] While our study was exploratory and qualitative in nature, participants'

narratives describing increased comfort with their appearance and reduced dysphoria were consistent with these clinical observations. The non-permanent and adjustable nature of injectable treatments may offer flexibility to individuals seeking gradual and personalized gender-affirming modifications.

By situating our qualitative findings within the existing international clinical literature, nonsurgical facial harmonization can be understood as a potentially relevant component of gender-affirming care that carries both technical and psychosocial dimensions. Although exploratory, the participants' accounts suggest that access to such interventions in public healthcare settings may hold symbolic and experiential significance beyond aesthetic changes.

Narratives on the relative invisibility of transmasculine individuals in public health policies highlight broader structural challenges within the Brazilian Unified Health System (SUS). While our findings cannot inform policy directly, they underscore the importance of continued research and dialogue regarding the scope and organization of gender-affirming services, including non-surgical approaches.

Limitations

This study should be interpreted within the context of an exploratory mixed-method design. The small purposive sample (n = 6), recruited from a single public gender-affirming outpatient clinic, may limit the transferability to other healthcare settings or populations. However, the qualitative core component prioritized the depth of lived experience and contextual understanding over statistical representativeness, which was consistent with its exploratory objectives.

The absence of a control group and a 30-day follow-up restrict conclusions regarding long-term durability or comparative effectiveness. The quantitative component was intentionally designed to be complementary and descriptive, focusing on the within-participant magnitude of change and precision estimates rather than confirmatory hypothesis testing. These short-term quantitative indicators were integrated with qualitative narratives to provide contextualized interpretations rather than causal inferences.

Although all participants were engaged in ongoing psychological follow-up and only one reported a prior diagnosis of a more severe anxiety disorder, transition-related and clinical variables, such as the duration of social transition or prior gender-affirming procedures, were not systematically collected in a standardized form and may have contributed to individual variability in experiences. Future studies may benefit from incorporating a more structured characterization of these factors.

The analytic procedures followed Bardin's structured content analysis framework, with explicit operationalization of thematic saturation and concurrent analysis. Within this epistemological approach, rigor was supported through systematic categorization and transparent reporting of the analytic phases.

Despite these limitations, this study represents one of the first structured empirical investigations of non-surgical facial masculinization conducted within a public healthcare context in Brazil. Integrating qualitative narratives with exploratory quantitative change estimates contributes contextually grounded evidence to an underexplored domain of transmasculine health and offers a foundation for larger, longitudinal, and comparative investigations.

CONCLUSION

In this exploratory study conducted in a public gender-affirming outpatient clinic, transmasculine participants reported reduced facial dysphoria, improved self-perception, and greater social confidence following nonsurgical facial harmonization with hyaluronic acid. Complementary quantitative measures showed consistent short-term improvements in facial satisfaction domains and a trend toward reduced anxiety symptoms.

Given the small sample size, the absence of a control group, and the 30-day follow-up, these findings should be interpreted as preliminary and context-specific. Nevertheless, they highlight the potential psychosocial relevance of minimally invasive facial interventions within broader gender-affirming care pathways. Future studies with larger sample sizes, longer follow-up periods, and comparative designs are required to evaluate the durability, safety, and generalizability of the results.

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FINE, a novel laboratory-based frailty index for elderly patients: a retrospective descriptive study

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ABSTRACT

BACKGROUND: Frailty in older adults is a multifactorial geriatric syndrome associated with inflammation, malnutrition, and hematological decline. Objective and easily applicable laboratory-based indices may complement clinical frailty assessment by providing rapid and low-cost screening tools, particularly in primary care and resource-limited settings.

OBJECTIVES: To develop a simple laboratory-based frailty screening index (FINE, Frailty Index for the Elderly) using C-reactive protein (CRP), albumin, hemoglobin, and sex, and to evaluate its association with the Clinical Frailty Scale (CFS) in older adults.

DESIGN AND SETTING: A retrospective descriptive study conducted using electronic health records of individuals aged 80 years and older.

METHODS: Data from 322 older adults were analyzed. Their FINE scores were calculated by assigning 0 or 1 point to CRP, albumin, hemoglobin, and sex based on clinically accepted reference thresholds, yielding a total score ranging from 0 to 4. Frailty was assessed using pre-recorded CFS scores. Associations between FINE scores, CFS, and individual biomarkers were examined. The screening performance was evaluated using receiver operating characteristic (ROC) curve analysis.

RESULTS: The mean age of participants was 84.9 ± 4.0 years, and 55.6% were female. The prevalence rate of frailty was 46.6%. FINE scores exhibited a positive correlation with CFS and CRP levels, and a negative correlation with albumin and hemoglobin levels ($p < 0.005$). ROC analysis demonstrated a statistically significant but moderate discriminatory ability for frailty (area under the curve = 0.642; 95% confidence interval: 0.582–0.703). At a cut-off value of ≥ 0.5, FINE scores demonstrated high sensitivity (89.3%) but low specificity (22.1%).

CONCLUSION: The FINE score is a simple, rapid, and low-cost laboratory-based frailty screening tool that is significantly associated with clinical frailty and key biological processes underlying frailty. Although low specificity limits its use as a diagnostic instrument, it may serve as a practical first-step screening approach in primary care and resource-limited settings. Further multicenter prospective studies are required to validate these findings.

INTRODUCTION

Frailty is a multidimensional geriatric syndrome characterized by progressive decline in physiological reserves and increased vulnerability to internal and external stressors. It is closely associated with adverse health outcomes including falls, hospitalization, functional dependency, institutionalization, and mortality. The biological mechanisms underlying frailty include chronic low-grade inflammation, immune system dysregulation, malnutrition, and hematological impairment.[1,2]

The Clinical Frailty Scale (CFS) is one of the most widely used tools for assessing frailty in clinical practice. It provides a rapid global assessment based on functional status and clinical judgment.[3] Although such clinical scales are easy to apply, they may have limitations, such as variability due to cognitive bias of the evaluator. Given the rapid increase in the older population, more objective, quantitative, and reproducible methods are needed to determine frailty.[4]

Laboratory biomarkers have recently gained attention as potential indicators of frailty. Elevated levels of inflammatory markers such as C-reactive protein (CRP), reduced serum albumin levels, and decreased hemoglobin concentrations have consistently been associated with frailty and adverse geriatric outcomes.[5–7] These biomarkers reflect key pathophysiological domains of frailty, including systemic inflammation, nutritional status, and hematological reserve, and are routinely measured in clinical practice.

In addition, frailty is more common in women than in men and frailty scores are higher in women; this difference has been attributed to biological and socioeconomic factors such as lifespan,

physical limitations, hormonal changes, and levels of social support.[8,9] While sex itself is not a biological marker, it may modify the expression and clinical manifestations of frailty.

Several laboratory-based frailty indices have been proposed. However, many of these models rely on a large number of laboratory variables, which may limit their feasibility and routine use in everyday clinical settings.[10] Therefore, a simple, laboratory-based frailty screening tool that prioritizes accessibility, rapid calculation, and applicability in primary care and resource-limited environments is highly needed.

In this context, we developed the Frailty Index for the Elderly (FINE), a concise laboratory-based score derived from three routinely available biomarkers (CRP, albumin, and hemoglobin), and a sex component. Rather than replacing comprehensive clinical frailty assessments, the FINE score is intended to be a screening-oriented tool to help identify older individuals who may benefit from further geriatric evaluation. In this study, we sought to examine the association between the FINE score and clinical frailty as assessed using the CFS, evaluate its screening performance using receiver operating characteristic (ROC) analysis, and explore its potential utility in adults aged 80 years and above.

OBJECTIVE

The primary objective of this study was to develop a simple, laboratory-based frailty index (FINE) using CRP, albumin, hemoglobin, and sex and to evaluate its association with CFS in older adults.

METHODS

Study design and population

This retrospective, single-center study included individuals aged 80 years and older who were evaluated at the Healthy Aging Unit and were followed for at least one year. Inclusion criteria were as follows: ≥ 80 years old, at least one complete blood count and biochemical test performed, and the presence of CFS data in their medical records. Participants' clinical data and laboratory parameters were reviewed, and their relationships with frailty were evaluated.

Demographic characteristics (age and sex), comorbidity status, and clinical observations of the participants were obtained from the patient records system. The laboratory parameters evaluated as biomarkers were CRP (mg/L), albumin (g/dL), and hemoglobin (g/dL).

All biochemical data were obtained from initial blood samples collected at the time of admission from the study participants. Laboratory data from a single time point were analyzed for each individual. Measurements were performed in the hospital laboratory using automated analyzers.

This was a retrospective, descriptive file review study. The study was conducted in accordance with the Declaration of Helsinki and approved by the Niğde Ömer Halisdemir Üniversitesi Research Ethics Review Committee (Approval No 2025/22). Patient identity information was kept confidential and used only for scientific purposes.

Data collection and definitions

FINE scores were established using three biomarkers (CRP, albumin, and hemoglobin) and sex. To enhance clinical interpretability and external applicability, cut-off values for each biomarker were determined based on commonly accepted clinical reference thresholds routinely used in geriatric practice, rather than being statistically derived from the study population. Values below or above threshold values were assigned 0 or 1 point, respectively, and a total FINE score ranging from 0 to 4 was calculated for each participant (**Table 1**). Higher scores indicated increased biological frailty. Sex was included as a component of the score based on a well-established epidemiological evidence indicating well-established epidemiological evidence women, reflecting population-level biological vulnerability.

Clinical frailty assessment

The level of clinical frailty was assessed using CFS scores, which were previously entered into the patient records system. The CFS is a widely used and highly valid measure of frailty that rates individuals on a scale from 1 (very fit) to 9 (terminally ill).[11,12] Frailty was operationally defined as a CFS score ≥ 5, corresponding to at least mild frailty, while scores of 1–4 were considered non-frail.

Statistical analysis

Data analysis was performed using IBM SPSS Statistics for Windows, version 25.0 (Armonk, New York). The normality of continuous data was assessed using the Kolmogorov–Smirnov test. Normally distributed continuous data are presented as means ± standard deviation, non-normally distributed data

Table 1. FINE score = CRP + albumin+ hemoglobin + sex

Parameter	Value	Point
CRP	≤ 5 mg/L	0
	> 5 mg/L	1
Albumin	≥ 35 g/L	0
	< 35 g/L	1
Hemoglobin	≥ 12 g/dL (female) ≥ 13 g/dL(male)	0
	Lower than	1
Sex	Male	0
	Female	1

FINE, Frailty Index for the Elderly; CRP, C-reactive protein.

as median (minimum-maximum), and categorical variables as frequency and percentage. For comparisons between two groups of continuous data, the Mann–Whitney *U* test was used for independent groups, and the Kruskal–Wallis test was employed for comparisons between three groups. The Games–Howell test was used for post-hoc analysis to determine statistical significance between the groups. As conditions for parametric tests were not met, Spearman's rank correlation analysis was used to examine the relationships. ROC curve analysis was applied to determine the diagnostic accuracy and to identify the most appropriate cut-off points for the variables. Within the scope of the ROC analysis, sensitivity and specificity were evaluated at different test threshold values. The area under the ROC curve (AUC) was calculated to evaluate the classification success of the model. In all statistical analyses, statistical significance is set at a p-value of < 0.05. Due to the retrospective study design and sample size, formal internal and external validation analyses were not performed.

RESULTS

The average age of the participants was 84.86 ± 4.01 years, and 55.6% were female. The most common chronic diseases were cardiovascular (45.8%), endocrine (16.2%), and gastrointestinal (10.4%) disorders. The average scores of the CFS, Katz Activities of Daily Living Scale (Katz ADL), and Lawton Instrumental Activities of Daily Living (Lawton IADL) Scale are presented in **Table 2**.

Of all the participants, 46.6% were assessed as frail. According to Katz ADL scores, 60.6% of participants were partially dependent, whereas according to the Lawton IADL score, this percentage was 95.7%. **Table 3** shows the distribution of frailty status according to the calculated mean FINE scores and determined cut-off values.

A significant positive correlation was identified between the participants' CFS scores and both CRP and FINE scores, whereas albumin and hemoglobin levels were negatively correlated ($p < 0.005$). Katz ADL scores were negatively correlated with CRP and FINE scores and positively correlated with albumin and hemoglobin values ($p < 0.005$). Similarly, Lawton IADL scores were negatively correlated with CRP and FINE scores and positively correlated with albumin and hemoglobin levels ($p < 0.005$) (**Table 4**).

Table 2. Clinical and functional assessment score averages

	Mean + SD	Median (min–max)
Age	84.86 ± 4.01	84(80–102)
CFS score	4.4 ± 1.41	4(1–9)
Katz ADL	4.78 ± 1.48	5(0–6)
Lawton IADL	6 ± 2.35	7(0–9)
CRP(mg/L)	8.87 ± 19.93	2.85(0.1–143.8)
Albumin (g/L)	40.92 ± 4.11	41(22–50)
Hemoglobin (g/dL)	12.74 ± 1.82	12.8(6.9–17.3)
FINE score	1.38 ± 0.93	1(0–4)

FINE, Frailty Index for the Elderly; CFS, Clinical Frailty Scale; ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living; CRP, C-reactive protein.

Table 3. Distribution of fragility based on participant features and FINE scores

		N	%
Gender	Female	179	55.6
	Male	143	44.4
Frailty status according to CFS	Terminally ill	1	0.3
	Living with very severe frailty	6	1.9
	Living with severe frailty	8	2.5
	Living with moderate frailty	53	16.5
	Living with mild moderate frailty	82	25.5
	Living with very mild frailty	94	29.2
	Managing well	57	17.7
	Fit	8	2.5
	Very fit	13	4
Presence of frailty based on CFS	Fragile	150	46.6
	Not fragile	172	53.4
Dependency status according to Katz ADL score	Independent	118	36.6
	Moderate impairment	195	60.6
	Very dependent	9	2.8
Dependency status according to Lawton IADL score	Independent	1	0.3
	Moderate impairment	308	95.7
	Very dependent	13	4
Anemic condition	Anemia present	191	59.3
	Anemia absent	131	40.7
Presence of chronic disease	Cardio vascular system disease	232	45.8
	Endocrine system disease	82	16.2
	Neurologic disease	46	9
	Gastro intestinal system disease	53	10.4
	Respiratory system disease	42	8.3
	Rheumatologic disease	17	3.3
	Other diseases	8	1.5
	No chronic disease	26	5.1
FINE score-based fragility	FINE score ≥ 0.5 (fragile)	268	83,2
	FINE score < 0.5 (not fragile)	54	16,8

FINE, Frailty Index for the Elderly; CFS, Clinical Frailty Scale; ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living.

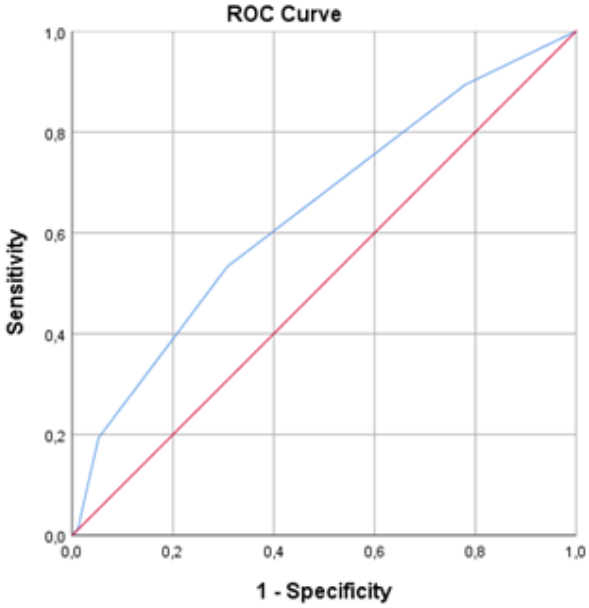
Table 4. Correlations between clinical and functional scales and laboratory parameters

		Age	CFS	Katz ADL	Lawton IADL
CRP (mg/L)	r	−0.029	0.155	−0.136	−0.134
	P*	0.606	0.005	0.015	0.016
Albumin (g/L)	r	−0.19	−0.327	0.238	0.342
	p*	0.001	< 0.001	< 0.001	< 0.001
Hemoglobin (g/dL)	r	−0.074	−0.164	0.199	0.174
	P*	0.185	0.003	< 0.001	0.002
FINE	r	0.068	0.314	−0.319	−0.26
	P*	0.225	< 0.001	< 0.001	< 0.001

* Spearman's correlation test; CRP, C-reactive protein.

Frail participants had higher CRP levels and lower albumin and hemoglobin levels. A significant difference was found between the participants' dependency status, as measured by their Katz ADL scores, and their albumin and hemoglobin levels. The post-hoc analysis revealed that the albumin and hemoglobin levels of fully independent participants were higher than those of participants with moderate impairment (**Table 5**).

As shown in **Table 6**, the FINE score was statistically significant in distinguishing frailty ($p < 0.001$). The AUC for diagnosing the presence of frailty with the FINE score was 0.642 (95% CI, 0.582–0.703). (**Figure 1**). At a cutoff value of ≥ 0.50, the sensitivity of FINE for predicting the presence of frailty was 89.3% and its specificity was 22.1%.



FINE, Frailty Index for the Elderly; ROC, receiver operating curve.

Figure 1. ROC curve analyses of FINE.

DISCUSSION

The FINE score developed in this study represents a practical and feasible laboratory-based approach for frailty screening in older adults. Based on only three routinely available biomarkers and sex, the FINE score demonstrated a significant association with clinical frailty, as assessed by the CFS in individuals

Table 5. Comparison of laboratory values according to frailty and dependency status

	CRP (mg/L)		Albumin (g/L)		Hemoglobin (g/dL)	
	Median (min-max)	p	Median (min-max)	p	Median (min-max)	p
Gender						
Female	2.70 (0.20–143.8)	0.763[a]	42 (26–48)	0.123[a]	12.4 (6.9–16.4)	**< 0.001[a]**
Male	3 (0.1–129.3)		41 (22–50)		13.3 (9.1–17.3)	
Presence of frailty based on CFS						
Fragile	3.35 (0.3–143.8)	**0.033[a]**	40 (22–48)	**< 0.001[a]**	12.5 (6.9–17)	**0.006[a]**
Not fragile	2.3 (0.1–132.3)		42 (26–50)		13 (8.4–17.3)	
Dependency status according to Katz ADL						
Independent	2.3 (0.1–97.5)	0.164[b]	42 (26–50)	**0.036[c] (a–b)**	13.08 (8.4–17.3)	**0.030[c] (a–b)**
Moderate impairment	3.1 (0.2–143.8)		41 (22–48)		12.6 (6.9–17)	
Very dependent	3.2 (1.2–14.2)		38 (28–46)		13.1 (9.7–14)	
Dependency status according to Lawton IADL						
Independent and moderate impairment	2.8 (0.1–143.8)	0.678[a]	42 (22–50)	0.081[a]	12.8 (6.9–17.3)	0.45[a]
Very dependent	3.9 (0.6–14.2)		40 (28–46)		13.1 (9.7–14)	

a Mann–Whitney U test;b Kruscal–Wallis test;c Games–Howel Test; FINE, Frailty Index for the Elderly; CFS, Clinical Frailty Scale; ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living; CRP, C-reactive protein.

Table 6. Discriminative power of FINE scores in frailty diagnosis (ROC analysis)

	AUC	95% CI	Cut-off	Sensitivity (%)	Specificity (%)	p
FINE	0.642	0.582–0.703	≥ 0.5	89.3	22.1	< 0.001

aged ≥ 80 years. The AUC values obtained in the ROC analysis demonstrated that the FINE score provided meaningful accuracy in distinguishing biological frailty levels. These findings support those of previous studies, suggesting that frailty screening in older adults can be performed using simple biomarkers.[12,13]

Frailty is strongly linked to biological processes such as systemic inflammation, nutritional deterioration, and hematological decline.[14] The three key biomarkers used in our study (CRP, albumin, and hemoglobin) represent the pathophysiological components of frailty. Numerous studies have shown that CRP levels are significantly elevated in frail individuals, indicating that systemic inflammation contributes to increased physiological frailty in older adults.[5,15] These findings underscore the pathophysiological significance of including CRP in the FINE scoring system. Similarly, low albumin levels are directly associated with both frailty and mortality and are considered an indicator of overall health in older individuals.[16,17] Hemoglobin levels are associated with both nutritional status and physical capacity in older adults. Reduced oxygen-carrying capacity in anemic individuals may lead to functional loss and an increased risk of falls.[18] According to the Toulouse cohort study, a 1 g/dL increase in hemoglobin was associated with a 14% reduction in the risk of frailty (OR = 0.86; $p < 0.005$).[19] These results support the association between low hemoglobin levels, loss of physiological reserve, and functional impairment. In this context, the ability of the FINE score to combine these three parameters into a simplified structure reflecting both the biological frailty burden and systemic physiological reserve is an important contribution.

Various laboratory-based frailty indices have been proposed. For example, models such as FI-LAB use dozens of parameters, which limit their applicability in daily practice.[20,21] In a study of 26,554 patients in France, the bFRAil score was used and was based on CRP, hemoglobin, albumin, vitamin D, age, and sex. The bFRAil score demonstrated a strong diagnostic performance, with an AUC of 0.78.[22] However, calculating this score is complex and time-consuming. Compared with more complex laboratory frailty indices, FINE prioritizes feasibility and accessibility. This simplicity may be particularly advantageous in primary care, home healthcare, and settings with limited resources.

The discriminatory performance of FINE was moderate (AUC, 0.642), suggesting that it should be viewed as a screening-oriented tool rather than as a diagnostic instrument. Its high sensitivity (89.3%) supports its potential role in identifying individuals who may benefit from comprehensive geriatric assessment. These features make FINE a fast, low-cost, and widely accessible approach to assessing frailty. It enables frailty screening using only routine laboratory data without the need for complex physical tests or time-consuming functional assessments. The FINE score stands out as a practical and applicable tool, particularly in primary care services, home healthcare, and clinical settings with limited resources. Through the integrated use of biological markers, age-specific pathophysiological processes such as systemic inflammation, nutritional status, and hematological reserve can be objectively assessed.

This study had certain limitations. The retrospective, single-center design limits generalizability, and potential confounders such as comorbidity burden and functional dependency were not analytically adjusted for. In addition, no external validation was performed. Future multicenter prospective studies are needed to validate the predictive value of FINE and assess its association with longitudinal clinical outcomes.

CONCLUSION

FINE is a simple, low-cost, laboratory-based frailty screening tool that demonstrates a significant association with clinical frailty in older adults. Although not intended as a diagnostic instrument, it may serve as a practical first-step screening approach to identify individuals at increased risk of frailty. Future multicenter prospective studies are warranted to validate its predictive and prognostic value for clinical outcomes.

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Telenutrition promoting equity of access in the SUS: a descriptive study

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ABSTRACT

BACKGROUND: In the area of nutrition, telehealth regulations were established on October 22, 2023, through Resolution No. 760, which defines and regulates telenutrition as a form of care and/or provision of services in food and nutrition through Information and Communication Technologies.

OBJECTIVES: To present the profile of telenutrition users in the TeleNordeste-BP project. Design and setting: Descriptive study carried out by hospital BP – A Beneficência Portuguesa de São Paulo.

METHODS: All services were provided through teleconsultation with nutritionists from the TeleNordeste project between May and December 2023.

RESULTS: Of the 884 services, 873 (98.8%) were tele-interconsultation. The distribution of services by state was: 430 (48.6%) from Maranhão; 301 (34%) from Alagoas and 153 (17.3%) are from patients from Piauí. Among the services provided, 671 (75.9%) users were female and 213 (24.1%) were male; the average age was 39.54 years (standard deviation +/– 19.9). Most adult patients were overweight: 135 (25.9%) were classified as overweight, 121 (23.2%) as grade 1 obese, 100 (19.2%) as grade 2 obese, and 66 (12.6%) as grade 3 obese.

CONCLUSION: chronic non-communicable diseases (NCDs) were the main reasons for seeking nutritional services, with more than 90% of the main reasons for consultation. Access to the telenutrition service offered by the TeleNordeste-BP project not only impacted the patient in ensuring access to nutritional care but also enabled the increase of Vigilância Alimentar e Nutricional (VAN).

INTRODUCTION

The evolution of information systems and communication technologies has fostered healthcare development and addressed a major challenge in the provision of accessible, affordable, and high-quality healthcare services. Geographical barriers are no longer a limiting factor in accessing new resources and technologies.[1–3] In the field of nutrition, telehealth showed some movements in 2009; however, it was from the COVID-19 pandemic that the discussion about its regulation took shape,[4] and on October 22, 2023, the Conselho Federal de Nutrição published Resolution No. 760 defined and regulated telenutrition as a form of care and/or provision of services in food and nutrition through Information and Communication Technologies.[5]

Considering the technological resources and expanded access to healthcare enabled by telehealth, Hospital BP – A Beneficência Portuguesa de São Paulo, in partnership with the Brazilian Ministry of Health through the Programa de Apoio ao Desenvolvimento Institucional do Sistema Único de Saúde (Proadi-SUS), implemented the TeleNordeste Project,[6] in the states of Alagoas, Maranhão, and Piauí over a three-year period from 2021 to 2023. The project provided synchronous teleinterconsultations across multiple specialties to support Primary Health Care (PHC) services in 360 participating municipalities.

The inclusion of nutritionists in the TeleNordeste Project was designed to support the healthcare model and work processes through integration with Healthcare Networks, enabling the dietary monitoring of patients. Telenutrition facilitates access to nutritional therapy, while teleconsultations shared with other healthcare professionals promote a model of continuing education, including professional support, training, and coordinated care for users of the Unified Health System (SUS).

Within the project, the role of telenutrition was guided by the principles of the Política Nacional de Alimentação e Nutrição (PNAN), encompassing the organization of nutritional care; promotion of adequate and healthy eating; food and nutrition surveillance; participation and social control; and research, innovation, and knowledge production in food and nutrition, while respecting the essential and derived attributes of PHC.[7]

In this context, the present descriptive study aims to characterize the profile of users assisted by nutrition services within the TeleNordeste-BP project, considering the reasons for care, nutritional status by age group, clinical outcomes, and user satisfaction.

METHODS

This study adhered to the Strengthening of the Reporting of Observational Studies in Epidemiology (STROBE) Statement.[8]

Study design

Descriptive study analyzing variables collected during nutrition teleinterconsultations within the TeleNordeste Project.

Local

This research was developed by Hospital BP – A Beneficência Portuguesa de São Paulo through the Programa de Apoio ao Desenvolvimento Institucional do Sistema Único de Saúde (Proadi-SUS), in partnership with the Brazilian Ministry of Health, as part of the implementation of the Specialized Medical Assistance Project in the Northeast region of Brazil via telemedicine (TeleNordeste-BP). The project was registered under NUP 25000.170151/2021-65 and operated in three states in the Brazilian Northeast: Alagoas, Maranhão, and Piauí.

Study period

Data collection was conducted from May to December 2023.

Inclusion and exclusion criteria

All nutrition teleinterconsultations conducted by the TeleNordeste Project during the study period were included.

Variables

Variables were recorded during consultations and extracted from patients' electronic medical records for subsequent analysis. The variables considered included consultation outcomes (resolution indicators, communication flow, and coordination with points of the Health Care Network); types of consultations provided (teleinterconsultations; triangulated consultations involving a primary care nutritionist, a primary care healthcare professional, and the patient; and teleconsultations for clinical case discussion between a nutritionist and a primary care healthcare professional); demographic and anthropometric data (sex, age, weight, and height); and project evaluation through satisfaction surveys using the Net Promoter Score (NPS)[9,10] administered to users and healthcare professionals in the region.

Data analysis

Statistical analyses were performed using PSPP-GNU® statistical software (GNU General Public License, version 3, June 29, 2007). Continuous variables with a normal distribution were expressed as means and standard deviations, whereas continuous variables with a non-normal distribution were presented as medians and interquartile ranges. Categorical variables were reported as absolute frequencies and percentages. A 95% confidence interval (95% CI) considered significant when $p < 0.05$.

Research ethics committee approval

The study protocol was reviewed and approved by the Research Ethics Committee of Hospital BP – A Beneficência Portuguesa de São Paulo (CAAE No. 72813923.6.0000.5483), with a waiver of informed consent.

RESULTS

Data from 884 consultations were analyzed, of which 873 (98.8%) were conducted as teleinterconsultations and 11 (1.2%) were teleconsultations without the presence of the patient. The distribution of consultations by state was as follows: 430 (48.6%) from Maranhão, 301 (34%) from Alagoas, and 153 (17.3%) from Piauí. Among the consultations performed, 671 users (75.9%) were female and 213 (24.1%) were male, with a mean age of 39.54 years (standard deviation ± 19.9). Nutritional care was offered to users across all stages of life. Of the 884 patients treated, age data were missing for three patients (0.3%). The greatest demand was observed among adults, accounting for 577 consultations (65.3%), followed by elderly patients with 146 consultations (16.5%). Care for adolescents accounted for 83 users (9.4%), children for 56 (6.3%), and infants for 19 users (2.1%) (**Table 1**).

Most patients treated had chronic non-communicable diseases. Of the total, 265 patients (30.0%) had diabetes mellitus, 227 (25.7%) had systemic arterial hypertension, and 204 (23.1%) had dyslipidemia. Seventy-seven patients (8.7%) had both diabetes and hypertension, while 55 (6.2%) presented with the three associated conditions: hypertension, diabetes, and dyslipidemia. Among the patients treated, 68 (7.7%) were pregnant. Regarding consultation outcomes, only 16 patients (1.8%) were discharged after the first consultation, while 848 users (95.9%) required follow-up consultations, and 20 patients (2.3%) were referred to another specialist or point within the healthcare network. With respect to user satisfaction, 264 responses were obtained for the Net Promoter Score (NPS), of which 241 (91.7%) were promoters, 15 (5.7%) were neutral, and 7 (2.7%) were detractors (**Table 1**).

Table 1. Characterization of the study population

Total	884 (100%)
Gender*	
Female	671 (75.9%)
Male	213 (24.1%)
*Age (years)***	39,54 (+/−19,9)
Age group*	
Infant	19 (2.1%)
Child	56 (6.3%)
Teenager	83 (9.4%)
Adult	577 (6.,3%)
Elderly	146 (16.5%)
States*	
Alagoas	301 (34%)
Maranhão	430 (48.6%)
Piauí	153 (17.3%)
Type of service*	
Teleconsultation	11 (1.2%)
Teleinterconsultation	873 (98.8%)
Main diagnoses*	
Systemic Arterial Hypertension (SAH)	227 (25.7%)
Diabetes Mellitus (DM)	265 (30%)
Dyslipidemia (DLP)	204 (23.1%)
SAH + DM	77 (8.71%)
SAH + DM + DLP	55 (6.22%)
Outcome of care*	
Follow-up in the PHC unit	16 (1.8%)
Referral to another specialist	20 (2.3%)
Return	848 (95.9%)
NPS*	89
Total responses	264 (100%)
Promoters	242 (91.7%)
Neutrals	15 (5.7%)
Detractors	7 (2.7%)

(*) Data are presented in absolute numbers and percentages; (**) means and standard deviations; and (***) medians and interquartile ranges.

Table 2 presents the nutritional status of users according to age group. Among children under 10 years of age, 6 (8.1%) were classified as underweight, 46 (62.2%) as normal weight, 6 (8.1%) as overweight, and 14 (18.9%) as obese; data were missing for 2 children (2.7%). In the 10–20 year age group, nearly half of the adolescents treated (35; 47.3%) were classified as obese, 12 (16.2%) as overweight, 16 (21.6%) as normal weight, and 7 as underweight. Among the 68 pregnant women assisted, 31 (45.6%) were classified as obese, 20 (29.4%) as overweight, 13 (19.1%) as eutrophic, and 4 (5.9%) as underweight. A total of 522 consultations were provided to adults, of which data for 19 users (3.6%) could not be analyzed. Most adult users were overweight or obese: 135 (25.9%) were classified as overweight, 121 (23.2%) as having grade 1 obesity, 100 (19.2%) as having grade 2 obesity, and 66 (12.6%) as having grade 3 obesity.

Among the elderly population, 146 consultations were conducted, with 85 users (58.2%) classified as overweight, 39 (26.7%) as eutrophic, and 12 (8.2%) as underweight; data were missing for 10 users (6.8%) (**Table 2**).

In Alagoas, 88 municipalities (86.3%) had nutritionist services, with 245 nutritionists registered in Primary Health Care (PHC). TeleNordeste provided nutrition teleinterconsultations in 19 municipalities in the state, three of which (15.8%) did not have nutritionists. In Maranhão, 177 municipalities (81.6%) had nutritionists, with 406 professionals registered in PHC. TeleNordeste provided services in 39 municipalities, nine of which (23.1%) did not have nutritionists. In Piauí, 159 municipalities (70.9%) had nutritionists registered in the National Registry of Health Establishments (CNES), with 281 professionals working in PHC. TeleNordeste delivered nutritional services in 30 municipalities, seven of which (23.3%) did not have nutritionists (**Table 3**).

Table 2. Nutritional status by age group

Population	Children/teenagers (years)		Pregnant women	Adults	Elderly
Age range	0–10	10–20	≥ 10	≥ 20	≥ 60
Weight (kg)	15.9 (17.65)***	68,32 (28.88)**	74.55 (24.35)***	78 (27.3)***	69.86 (15.82)**
Height (m)	1.03 (0.42)***	1.55 (0.15)***	1.57 (0.06)***	1.57 (0.12)***	1.55 (0.11)***
BMI	16.35 (5.85)***	27.37 (9.41)**	29.9 (9.6)***	31.4 (10.2)***	28.78 (2.66)**
N total*	74 (100%)	74 (100%)	68 (100%)	522 (100%)	146 (100%)
Nutritional status*					
Underweight	6 (8.1%)	7 (9.5%)	4 (5.9%)	17 (3.3%)	12 (8.2%)
Eutrophic	46 (62.2%)	16 (21.6%)	13 (19.1%)	64 (12.3%)	39 (26.7%)
Overweight	6 (8.1%)	12 (16.2%)	20 (29.4%)	135 (25.9%)	85 (58.2%)
Obesity	14 (18.9%)	35 (47.3%)	31 (45.6%)	N/A	N/A
ND	2 (2.7%)	4 (5.4%)	0 (0%)	19 (3.6%)	10 (6.8%)
Obesity I	N/A	N/A	N/A	121 (23.2%)	N/A
Obesity II	N/A	N/A	N/A	100 (19.2%)	N/A
Obesity III	N/A	N/A	N/A	66 (12.6%)	N/A

(*) Data are presented in absolute numbers and percentages; (**) means and standard deviations; and (***) medians and interquartile ranges. ND, not defined; N/A, not applicable.

Table 3. Distribution of coverage of nutritionist assistance in the territory

	State		
	Alagoas	**Maranhão**	**Piauí**
Estimated population (inhabitants IBGE)*	3,220,104	7,010,960	3,271,199
Number of Municipalities (IBGE)*	102 (100%)	217 (100%)	224 (100%)
Municipalities with Nutritionists*	88 (86.3%)	177 (81.6%)	159 (70.9%)
Nutritionists in Primary Health Care	245 (100%)	406 (100%)	281 (100%)
Nutritionists in Specialized Health Care	393 (100%)	611 (100%)	309 (100%)
Municipalities served by TeleNordeste*	19 (100%)	39 (100%)	30 (100%)
No nutritionist in the municipality	3 (15.8%)	9 (23.1%)	7 (23.3%)
With a nutritionist in the municipality	16 (84.2%)	30 (76.9%)	23 (76.6%)

(*) Data are presented in absolute numbers or percentages.

DISCUSSION

Chronic non-communicable diseases (NCDs) were the primary reasons for seeking nutrition services, accounting for more than 90% of the main reasons for consultation. This finding is consistent with national data indicating that NCDs affect approximately 52% of individuals aged 18 years and older, with hypertension, back problems, depression, and diabetes being the most prevalent conditions.[11] Evidence from the literature further indicates that cardiovascular diseases, diabetes, chronic kidney disease, and certain cancers are among the 10 leading causes of premature death (ages 30–69), and that diet represents a key modifiable risk factor.[12] Therefore, nutritional care focused on the promotion, prevention, and control of NCDs constitutes a timely and relevant intervention for the region.

Another important finding of this study was the higher demand for teleinterconsultations among women, who accounted for 671 consultations (75.9%), with 61.3% of adult users classified as overweight or obese. In recent years, obesity prevalence among adults has more than doubled, increasing from 12.2% to 26.8%, while the prevalence of overweight individuals rose from 43.3% to 61.7% in 2019, disproportionately affecting women.[13] A cross-sectional study by Brum et al.,[14] published in 2025 and based on Vigitel data from 2006 to 2021, reported that compared with 2006, the prevalence in 2021 increased by 152% for BMI ≥ 45, 120% for BMI ≥ 40, and 104% for BMI ≥ 35. In contrast, BMI ≥ 30 increased by 66%, underscoring the growing burden of severe obesity and its implications for healthcare systems due to increased care demands.

Regarding children and adolescents, our study found that among children under 10 years of age, 18.9% were obese, and among those aged 10–20 years, 47.3% were obese. The prevention and treatment of childhood obesity has been a public health problem with growing numbers worldwide, increasing the risk of developing NCDs at this stage of life and in adulthood. According to data from the Ministry of Health, in 2020, 5.4% of children under 2 years of age monitored in PHC were severely underweight, and 15.5% were overweight or obese. The early introduction of solid foods, the provision of ultra-processed foods to this population, and socioeconomic factors have influenced this prevalence. Among infants aged 6–24 months, 44% had received ultra-processed foods.[15]

Among adolescents aged 15–17 years, the prevalence of overweight was 19.4%, corresponding to an estimated total of 1.8 million people, and was higher among female adolescents (22.9%) than among male adolescents (16%). Regarding the obesity indicator, the pattern was similar to that observed for overweight, with prevalence being higher among female adolescents (approximately 8%) than among male adolescents (5.4%).[11] The objective of nutrition actions among children should not only focus on improvements in anthropometric indices but also on behavioral changes.[15] Considering the increase in obesity in Brazil, health policies aimed at preventing and treating obesity are necessary, and the study carried out by Flores-Ortiz et al.,[16] published in 2019, suggests that such policies are especially needed in the capitals of the North, Northeast, and Central-West regions, where the greatest increases in the prevalence of overweight and obesity have occurred in the country.

The telehealth nutritional care of the TeleNordeste-BP project was structured based on the premises of in-person care and the presence of a professional from the territory, which assisted in the collection of reliable patient data, mainly anthropometric data. This enabled an assessment of the food and nutritional profile of the local population and its determining factors, supporting PHC in one of the guidelines of the Política Nacional de Alimentação e Nutrição (PNAN) for structuring health and nutrition indicators that guide the formulation of public health policies and local nutritional care actions, through the continuous description and prediction of trends in the food and nutrition situation and its determining factors.[17]

Another relevant aspect regarding the presence of nutritionists in PHC was highlighted in a review conducted by Casas-Agustench et al.[18] in 2020, which noted that incorporating nutritionists into primary care settings, or increasing their presence, would provide access to more qualified health professionals to carry out nutritional treatment, representing a more cost-effective intervention in terms of health expenditures. Considering that in 2018 the total costs of hypertension, diabetes, and obesity in the SUS reached R$ 3.45 billion, and that 72% of these costs were

attributable to individuals aged 30–69 years and 56% to women, the estimates of costs associated with chronic diseases related to inadequate nutrition highlight the economic impact of these conditions on the SUS[12] and the importance of multidisciplinary actions aimed at lifestyle modification and health care.

In our study, according to the NPS assessment, the majority of users (91.7%) were promoters, and the NPS score was 89, indicating an excellent result. This finding is consistent with data in the literature showing that most patients perceive improved access to care[19,20] and support the continuation of telehealth consultations in the future due to benefits such as reduced travel, lower costs, and guaranteed access to qualified care.[20]

Regarding adherence to telenutrition services, care was provided in 88 (16.2%) of the 543 municipalities across the states of Alagoas, Maranhão, and Piauí. Adherence of municipalities to the TeleNordeste-BP project, the composition of local healthcare teams, and difficulties related to connectivity or access to technological devices may have influenced the number of municipalities that participated. Another important point is that approximately one in four municipalities that used the nutrition service did not have nutritionists in Primary Health Care, and the TeleNordeste-BP project enabled access to nutritional care for many users in these locations.

Limitations

The results are subject to limitations related to the individual datasets used and the information recorded in the medical records, as well as to biases inherent in a retrospective study design. The number of nutritionists by region was estimated based on data extracted from the CNES database in March 2025.

CONCLUSION

Chronic non-communicable diseases (NCDs) were the main reasons for seeking telenutrition services. Considering the socioeconomic impact involved, offering telenutrition consultations to SUS users is a relevant strategy for health promotion and prevention. Access to the telenutrition service offered by the TeleNordeste-BP project not only impacted patients by ensuring access to nutritional care but also enabled increased Vigilância Alimentar e Nutricional (VAN) in the municipalities served, providing data and evidence to support broader actions and public policies, such as regulating food advertising to children, taxing ultra-processed foods, and implementing intersectoral actions aimed at reducing food insecurity.

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Impact of physical activity associated with bariatric surgery on systemic arterial hypertension control: a systematic review

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ABSTRACT

BACKGROUND: Obesity is a highly prevalent condition frequently associated with systemic arterial hypertension (SAH). Bariatric surgery (BS) is an effective strategy for weight loss and has been shown to improve blood pressure (BP) control, whereas physical activity (PA) is recognized as an important adjuvant therapy for treatment of SAH. Nevertheless, evidence regarding the combined impact of BS and PA on BP reduction remains inconsistent.

OBJECTIVES: This review aimed to evaluate whether BS combined with PA contributes to additional BP reduction in individuals with obesity.

METHODS: The review followed PRISMA guidelines and was registered in PROSPERO (CRD42024628299). Eligible studies included randomized controlled trials, cohort and cross-sectional studies involving adults who underwent BS, with or without PA. Searches were performed in CENTRAL, PubMed, LILACS, and BVS. Methodological quality was assessed using the RoB2 and JBI tools, and the certainty of evidence was graded according to GRADE.

RESULTS: Of the 406 records screened, nine studies were included (n = 504 participants). BS alone was associated with significant reductions in BP. When PA was combined with BS, additional reductions were reported; however, the findings were heterogeneous and supported by low to very low certainty of evidence. The follow-up duration across studies ranged from 4 months to 5 years.

CONCLUSION: The combination of BS and PA provides modest but clinically relevant benefits in BP reduction. However, the limited number of studies and short follow-up periods preclude definitive conclusions. High-quality, long-term randomized clinical trials are warranted to clarify the role of PA in optimizing BP control after BS.

CLINICAL TRIAL OR SYSTEMATIC REVIEW REGISTRATION: The review followed PRISMA guidelines and was registered in PROSPERO (CRD42024628299).

INTRODUCTION

Obesity represents one of the most pressing public health challenges worldwide. According to the Pan American Health Organization, approximately one in every eight individuals is affected, corresponding to over 1 billion people currently living with the condition.[1]

Beyond its high prevalence, obesity substantially increases the risk of systemic arterial hypertension (SAH) and contributes to the overall cardiovascular burden. It is associated with dyslipidemia, atrial fibrillation, heart failure, stroke, insulin resistance, and other cardiometabolic alterations, all of which are strongly linked to higher all-cause mortality.[1]

Elevated blood pressure (BP) in overweight individuals or individuals with obesity results from multiple mechanisms. The key factors include renal compression by perirenal/intrarenal fat, impaired sodium excretion; insulin resistance, hyperinsulinemia, and obstructive sleep apnea.[2] Additional contributors include heightened sympathetic and renin-angiotensin-aldosterone system activity, altered baro- and chemoreceptor function, chronic adipokine-mediated inflammation, and hyperuricemia linked to high-fructose intake, which promotes oxidative stress and endothelial dysfunction.[3–5] These mechanisms highlight the role of visceral obesity in SAH, indicating that excess weight plays a central role.

In this context, bariatric surgery (BS) emerges as an alternative to address these frequently coexisting comorbidities, obesity and SAH. Beyond weight loss, patients undergoing this procedure experience a significant decrease in systolic blood pressure (SBP) and diastolic blood pressure (DBP).[6] Furthermore, studies have shown that BS also promotes a significant decrease in mean arterial pressure (MAP).

Several studies have compared BS with drug therapy in patients with hypertension and have showed significant benefits: BS leads to a greater reduction in the use of antihypertensive medication in the medium- and long-term compared to drug therapy alone.[7,8]

In contrast, physical activity (PA) is a widely recognized intervention for cardiovascular and cardiorespiratory benefits,[9] and is a crucial option for patients with obesity and SAH. However, candidates for BS are less physically active and engage in fewer minutes of PA per day than the general population. Furthermore, they show lower adherence rates to PA,[10] which limits the benefits of this measure.

Studies have indicated that participation in PA after BS is associated with improvements in muscle strength and cardiorespiratory and physical functions.[11,12] Published reviews have suggested that PA as an adjunct to BS is associated with improved weight loss and quality of life,[13] as well as improved BP levels.[14]

OBJECTIVE

Although several studies have addressed the benefits of PA combined with BS,[15–18] evidence remains inconsistent. Furthermore, there is a scarcity of high-quality studies that specifically evaluate whether PA enhances BP reduction in this context. Given this gap in knowledge, the objective of this study was to assess, through a systematic review, whether PA combined with BS contributes to BP reduction in people with obesity.

METHODS

Protocol and registration

This systematic review was conducted in accordance with the Cochrane Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO: CRD42024628299).

Inclusion criteria

Studies were selected based on the following inclusion criteria: (1) randomized controlled trials, cross-sectional studies, and cohort studies including adult patients (≥ 18 years) who underwent BS, with no restrictions regarding drug therapy for comorbidities; and (2) no restrictions on the year of publication or language.

Exclusion criteria

The exclusion criteria were as follows: (1) systematic reviews or studies using secondary data; and (2) studies involving individuals with neurological and/or psychiatric impairments.

Search and data extraction strategy

The final search for studies evaluating the effects of BS, whether associated with PA or not, was conducted on December 18, 2024, in the following databases: Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, LILACS, and the Virtual Health Library (BVS). The PICOS framework guided the research question: In patients who underwent BS, does PA help reduce BP levels? The inclusion criteria were as follows: (population: patients who underwent BS; intervention: practice of PA; comparison: patients who underwent BS without PA; outcome: reduction of SBP and DBP). The keywords and Medical Subject Headings (MeSH) terms were "physical activity," "exercise," "blood pressure," "hypertension," and "bariatric surgery." Two authors, independently and blindly, assessed the studies in two stages. In the first stage, titles, abstracts, and duplicate studies were screened for eligibility using the Rayyan QCRI application (Qatar Computing Research Institute, Doha). Subsequently, the full texts were evaluated for eligibility. Disagreements were resolved by consensus or by a third reviewer. Data extracted included the authors, country, year, sample size, study design, objectives, intervention type, assessed parameters, treatment duration, and results.

Risk of bias assessment

Methodological quality was assessed using the Cochrane Risk-of-Bias 2 (Rob 2) tool, developed for randomized clinical trials, and the Joanna Briggs Institute (JBI) Risk-of-Bias tool, developed to analyze the risk of bias in cross-sectional and cohort studies. Bias domains included randomization, deviations from intended interventions, outcome measurement, missing outcome data, and selection of reported results, which were classified as low, with some concerns, or high. Disagreements were resolved by discussion.

The certainty of evidence regarding the impact of PA on BP reduction after BS was assessed using the GRADEpro Guideline Development Tool (software), considering risk of bias, inconsistency, indirectness, imprecision, and publication bias. Evidence quality was classified as high, moderate, low, or very low.

RESULTS

Characteristics of the included studies

Participant and outcome assessor blinding were not feasible for the proposed intervention (PA), which may have compromised the risk of bias assessment, as performance bias was considered

high. Consequently, the certainty of the evidence was rated as very low to low according to the GRADE approach (Grading of Recommendations Assessment, Development, and Evaluation) (**Table 1**).

A total of 406 studies were identified through the search strategy (Figure 1). After screening the titles and abstracts, 269 articles were retained, of which seventeen were considered potentially eligible for full-text review; eight were subsequently excluded for not meeting the eligibility criteria. Ultimately, nine studies were included in this systematic review (**Figure 1** and **Table 2**).

The included studies, published between 2006 and 2024, were conducted in Brazil (n = 3), Iran (n = 1), Italy (n = 1), Spain (n = 1), Poland (n = 1), Canada (n = 1), and Denmark (n = 1), encompassing a total of 504 participants, of whom 368 were women (73%). Four studies compared the combined effects of BS and PA.

The studies were divided into subgroups: four evaluated BS associated with or without supervised PA, and five assessed body changes after BS and their effects on hypertension, specifically SBP and DBP (**Table 3**).

Body and metabolic changes after bariatric surgery

In the study by Keleidari et al.,[19] 35 individuals with obesity underwent BS and were followed for 6 months. Significant reductions in SBP and DBP were observed (SBP: from 124.4 ± 7.8 mmHg to 116.6 ± 5.6 mmHg; DBP: from 79.8 ± 5 mmHg to 76.8 ± 5.3 mmHg) ($p < 0.05$), with a mean decrease of 4.6 mmHg in MAP.

In the study by Serés et al.,[20] 31 patients with morbid obesity were followed for one year after undergoing BS. SBP decreased from 135 ± 18 to 127 ± 17 mmHg ($p = 0.07$), whereas DBP showed a more pronounced reduction, from 87 ± 11 to 77 ± 12 mmHg ($p < 0.001$). During maximal effort, SBP remained unchanged, whereas DBP decreased significantly. The MAP decreased both at rest and during maximum effort (103–93.7 mmHg and 127.3–123.7 mmHg).

Pereira et al.,[11,21] followed 78 patients undergoing BS, grouped according to the postoperative time (BS2:1–2 years; BS4:2–4 years; BS6:4–6 years; BS+6:6–10 years) and assessed comorbidities using the ACRO score, an adapted cardiorespiratory fitness score for obesity, developed to evaluate functional capacity before and after BS. All groups showed improvement in obesity-related conditions, particularly in hypertension. The proportion of participants with

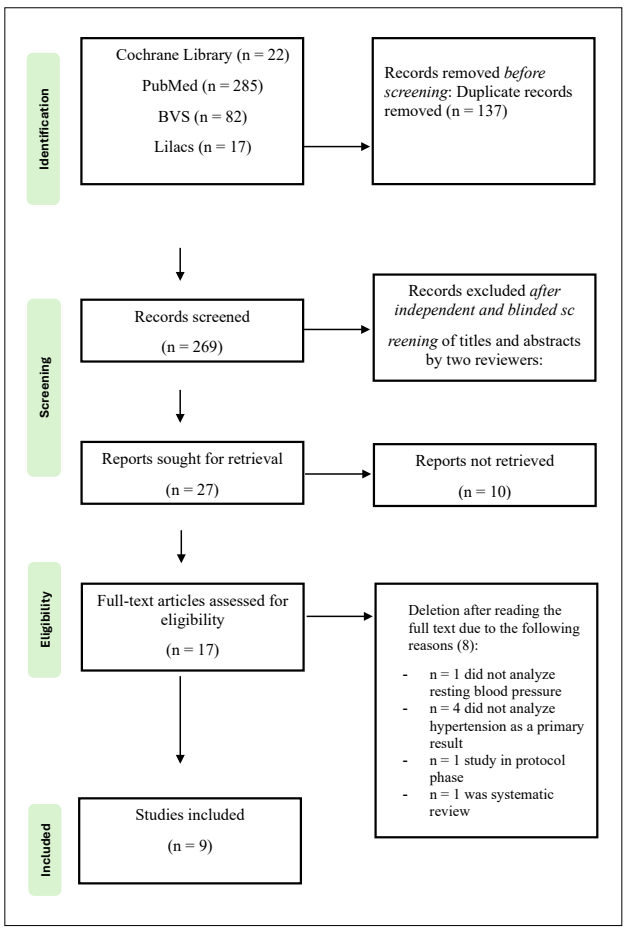

Figure 1. Primary flowchart of the study selection process for inclusion in the systematic review.

Table 1. Analysis of risk of bias using GRADE

Certainty assessment							Nº of patients			Effect			
Nº of studies	Study design	Risk of bias	Inconsistency	Indirect evidence	Imprecision	Other considerations	bariatric surgery and physical exercise	Patiens without physical exercise		Relative (95% CI)	Absolute (95% CI)	Certainty	Importance
Cohort													
4		Observational study	Not serious	Not serious	Serious		Serious	None	0/250	0/250	Not estimable	Very low	CRITICAL
Clinical trials													
3		Randomized clinical trials	Not serious	Not serious	Serious		Serious	None	0/70	0/70	Not estimable	Low	CRITICAL
Cross-sectional													
2		Observational studies	Not serious	Not serious	Not serious		Serious	None	0/32	39/0	Not estimable	Very low	CRITICAL

controlled hypertension (ACRO ≤ 2) increased from 8.3% to 66.6% in BS2, from 64.2% to 92.8% in BS4, from 40.9% to 81.8% in BS6, and from 23.3% to 86.6% in BS+6, indicating sustained improvement in BP control over time.

Jankiewicz-Wilka et al.,[22] evaluated 28 patients with morbid obesity and metabolic syndrome after BS with a follow-up of up to 48 months. After 24 months, a significant reduction in body mass index (BMI), waist circumference, and BP was observed, with a gradual decrease over time ($p < 0.05$ for SBP and $p < 0.01$ for DBP), although absolute BP values were not reported.

In contrast, Valezi et al.,[23] analyzed 43 patients with class III obesity before and 12 months after Roux-en-Y gastric bypass (RYGB). Significant reductions were observed in body weight (from 116.5 ± 21.5 kg to 80 ± 15.9 kg), BMI (from 41.8 ± 4.4 kg/m² to 28.4 ± 3.8 kg/m²), and SBP from 130 mmHg to 120 mmHg ($p < 0.001$), while DBP remained unchanged ($p > 0.05$). The MAP decreased from 96.7 mmHg to 93.3 mmHg. The follow-up periods in surgical-only studies ranged from 2 weeks to 24 months.

Body and metabolic changes in bariatric surgery associated with physical activity

Moriconi et al.,[24] evaluated the impact of PA on BP control in individuals with and without type 2 diabetes mellitus (T2DM). The intervention included ≥ 150 min/week of moderate-intensity aerobic activity plus strength training. After five years, active participants with T2DM showed lower SAH prevalence (33% versus 62%; $p = 0.0043$), reductions in SBP, DBP, and MAP (approximately 102–92 mmHg), and decreased antihypertensive

Table 2. Characteristics of the studies included in the systematic review

Author/year	Study design	Sample (n)	Age range/average age	Intervention/physical activity	Follow-up period
Keleidari et al., 2016	Cross-sectional	35	31,45 ± 8, 84 years	Not specified	6 months
Serés et al., 2006	Prospective	31	38 ± 8 years	Not specified	1 year
Moriconi et al., 2024	Observational, 5 years	148	54 ± 9 years (DM2); 45 ± 10 years (without DM2)	≥ 150 min per week of moderate aerobic activity + 2–3 sessions of muscle strengthtening	5 years
Mundbjerg et al., 2018	Randomized controlled clinical trial	60	42,3 ± 9, 1 years	Supervised training twice per week, 40 min (15 min cycling, 10 min Upper limb strength, 15 min free exercise)	2 years
Pereira et al., 2019	Retrospective cross-sectional	78	37–45 years	Not specified	1 year
Jankiewicz-Wika et al., 2011	Prospective cross-sectional	28	43,7 ± 10 years (20–59 years)	Not specified	2 years
Belzile et al., 2023	Randomized clinical trial	59	42 years	Supervised training 3 times per week for 12 weeks, 60 min (35 min aerobic + 25 min strength exercise)	1 year
Valezi et al., 2011	Observatoinal, longitudinal, analytical, prospective	43	35,9 ± 12, 2 years	Not specified	1 year
Castello et al., 2010	Prospective randomized controlled	21	20–45 years	Aerobic treadmill training, 36 sessions for 12 weeks (60 min on alternate days)	4 months

Table 3. Variations of blood pressure after bariatric surgery

Study	Time	Group	Pre SBP	Post SBP	Δ SBP	Pre DBP	Post DBP	Δ DBP	Observations
Keleidari et al., 2016	6 months	–	124.4 ± 7.8	116.6 ± 5.6	–7.8	79.8 ± 5	76.8 ± 5.3	–3	Significant reduction
Serés et al., 2006	12 months	–	135 ± 18	127 ± 17	–8	87 ± 11	77 ± 12	–10	Reduction after 1 year
Moriconi et al., 2024	5 years	PA	137 ± 6	122 ± 9	–15	84 ± 6	75 ± 7	–9	Sustained reductoin
Mundbjerg et al., 2018	12 months	Intervention	–	–	–	–	–4.8*	–	Reduction in DBP
Pereira et al., 2019	Up to 6 months	BS2 to BS+6	–	–	–	–	–	–	Only reported body weight
Jankiewicz-Wika et al., 2011	24 months	–	↓	↓	↓	↓	↓	↓	BP values were not reported
Belzile et al., 2023	3–12 months	–	–	–	–	–	–	–	Clinical remission of hypertension
Valezi et al., 2011	12 months	–	–	–	–7,7%	–	–	NS	Reduction only in SBP; DBP with no changes
Castello et al., 2010	12 weeks	Intervention	150 ± 7.1	146.6 ± 4	–3.4	88.8 ± 2.4	85 ± 3	–3.8	Effect only on intervention

Δ *SBP/DBP*: difference between the pre- and postoperative values (absolute value); ↓ indicates a significant reduction without exact numerical data;
* Mundbjerg et al., 2018: only DBP showed a significant difference (–4.8 mmHg in the intervention group); SBP remained stable; Pereira et al., 2019: focused on weight loss and did not report BP; Belzile et al., 2023: clinical improvement in hypertension, but without numerical data.

medication use (73% to 33% in the active group versus 78.7% to 62.3% in the control group). Among participants without T2DM, SAH prevalence was also lower in active individuals (6.9% versus 28%), with levels sustained throughout the follow-up. Overall, PA was consistently associated with lower BP values, independent of medication use ($p < 0.001$).

Mundbjerg et al.,[25] evaluated a supervised PA program in 44 participants after BS and divided them into intervention and control groups. The intervention combined aerobic and resistance training for 26 weeks. After 24 months, no significant difference in SBP was observed; however, DBP was significantly lower in the intervention group (difference of 4.8 mmHg; $p = 0.034$), indicating a sustained benefit of PA. The MAP decreased from approximately 103 mmHg to 94 mmHg, reflecting clinically relevant hemodynamic improvement.

In a randomized study including 59 patients with severe obesity who underwent BS, the participants were assigned to a control or a 12-week supervised exercise program. Baseline SAH prevalence was similar between both groups (36.8% in the control group and 42.5% in the intervention group; $p = 0.62$). Most comorbidity resolutions, including hypertension, occurred within the first three months post-surgery, with no significant differences between groups thereafter ($p > 0.05$).[26]

Castello et al.,[27] randomized 21 women to control or supervised 12 weeks of aerobic training after BS. SBP was 150 ± 7.1 mmHg in the control group and 146.6 ± 4 mmHg after intervention, while DBP was 88.8 ± 2.4 mmHg and 85 ± 3 mmHg, respectively. Both groups showed a significant reduction in DBP. The MAP was 109 mmHg in the control group and 105.5 mmHg in the intervention group.

Regarding methodological quality, three randomized trials were assessed using the RoB2 tool (Figure 2) developed by Cochrane for randomized clinical trials, while the remaining six studies were assessed using the JBI tool, which provides standardized instruments for evaluating different study designs in systematic reviews. Regarding randomized clinical trials, according to the RoB2 tool, two studies had a low risk of bias, while one had a moderate risk. Analysis using the JBI platform revealed that one study had a reliability rating of 90.9 %, while four studies had 72.7% and one had a 63.6%.

DISCUSSION

To our knowledge, this is the first review to provide evidence synthesis examining the effectiveness of PA combined with BS in reducing SAH, thereby addressing an important gap in the literature.

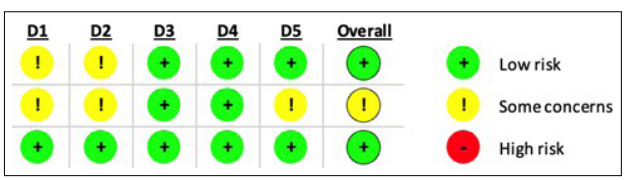

Figure 2. Analysis of risk of bias using the platform RoB-2.

This review included three randomized clinical trials,[25–27] two cross-sectional studies,[19,21] and four cohort studies.[20,22–24] Among these, three trials[25–27] and one cohort study[24] specifically evaluated the effect of PA on BP, whereas the remaining studies analyzed the effects of BS alone.

Although BP changes before and after BS were assessed, few studies reported post-intervention values in sufficient details, thus preventing a meta-analysis as outlined in the protocol.

Overall, the findings regarding the impact of PA on BP reduction after BS were inconsistent. Belzile et al.,[26] reported that comorbidity resolution occurred mainly shortly after surgery, with no additional benefit from PA ($p > 0.05$). Conversely, Mundbjerg et al.[25] identified a significant reduction in DBP in the PA group after 24 months, with a difference of 4.8 mmHg compared to the control group ($p = 0.034$).

Castello et al.,[27] despite analyzing the results only four months after BS,[28] observed a significant reduction in SBP in both groups. However, a significant reduction in DBP was recorded only in the PA group. Moriconi et al.[24] consistently reported lower BP values among patients who engaged in PA in all analyzed periods ($p < 0.001$).

Quality of evidence

The risk of bias assessment revealed recurrent limitations, including inadequate randomization and the impossibility of blinding owing to the nature of PA interventions. Insufficient methodological details made it difficult to assess bias, leading to a downgrading of the evidence using the GRADE tool. Additionally, small sample sizes (22–148 participants) and the limited number of studies specifically evaluating PA[24–27] further reduced the robustness of the findings.

Agreements and disagreements with other studies or reviews

There was no consistency among the studies regarding whether PA helped reduce BP when combined with BS.

Few studies have directly evaluated the impact of PA on BP after BS, which limited the available data and required cautious interpretation.

BS induces important physiological changes, with BP reduction frequently observed. Serés et al.[20] and Huang et al.[29] reported greater reductions in DBP than in SBP, the latter often without statistical significance.

This pattern may reflect the higher sensitivity of DBP to early metabolic and vascular changes. According to the American Heart Association,[28] DBP decreases earlier due to reduced peripheral resistance and inflammation, whereas SBP depends on slower changes in arterial compliance and stiffness.[28]

Similarly, Van Brussel et al.[30] highlighted that DBP responds more rapidly to hemodynamic variations, whereas SBP reflects later structural adaptations.

Conversely, Valezi et al.[23] observed a stable DBP with changes in SBP only. The mechanisms explaining the isolated decrease in SBP include increased arterial compliance and reduced systolic pressure peaks, without vasodilation of the microcirculation.[31] Further analysis of this study outcome suggests that one possible explanation is that baseline DBP was already within normal limits, which may have limited the observation of a significant decrease.

Three studies demonstrated reductions in both SBP and DBP.[19,21,22] The long follow-up period in the Jankiewicz-Wilka et al. study[22] allowed the observation of sustained metabolic and hemodynamic effects, while higher baseline BP levels across these studies may have favored reductions in both parameters.

Regarding PA, of the four studies evaluated, one showed no post-intervention changes;[26] one showed changes in both parameters;[24] and two showed changes in DBP only.[25,27]

Evidence suggests that most BP benefits occur after BS in the short term, with a limited additional impact from supervised PA. Belzile et al.[26] observed the resolution of hypertension mainly in the immediate postoperative period, without further changes after PA introduction. Similarly, Chen Hu et al.[32] attributed BP and BMI reductions primarily to BS rather than PA.

Consistent with these findings, Carretero-Ruiz et al.,[33] found no significant reductions in BP associated with PA in bariatric patients. Despite the overall beneficial effects of BS, the association between PA and BP control in the immediate postoperative period has not yielded consistent results.

Castello et al.[27] initiated PA interventions early, immediately after BS, which may have influenced the results; in contrast, Ren et al.[14] reported significant BP reductions when PA was initiated one year after surgery.

In other studies, BP reduction has been observed in both SBP and DBP values. Moriconi et al.[24] reported significant reductions in SAH in both patients with and without T2DM, whereas Ren et al.,[14] showed greater weight loss and lower BP among physically active patients.

In contrast, other studies have reported significant changes only in DBP following supervised PA. Castello et al.[27] observed reductions mainly in DBP compared with SBP. Mundbjerg et al.[25] found that, 24 months after surgery and with regular exercise practice, changes occurred primarily in DBP. This may be explained by the fact that Castello's intervention was short-term and of moderate intensity, which tends to affect peripheral resistance (related to DBP) more than central arterial compliance (related to SBP).

The long-term BP effects after BS vary with follow-up duration. Climent et al.,[34] investigated the impact of BS on BP across different follow-up periods. In the short term (less than three years), BS showed a strong association with SAH remission. However, the results in the medium term (3–5 years) and long term (more than five years) were less consistent and demonstrated modest effect sizes.

One included study with a 36-month follow-up showed that 68.1% of hypertensive patients achieved BP remission in the first postoperative year; however, 21.9% experienced recurrence by three years. Similar relapse patterns were reported by Bäckdahl et al. ,[35] in the GATEWAY trial, a randomized clinical trial that evaluated the effect of BS in patients with pharmacologically controlled SAH, in which 80% of patients undergoing BS reduced antihypertensive use at 12 months, compared with 13% in the control group. BP reduction occurred early and stabilized around the sixth month, while a five-year follow-up revealed hypertension recurrence in approximately 20% of patients.

Among the studies included, Castello et al.[27] had the shortest follow-up, with only four months after BS, whereas Jankiewicz-Wilka et al.[22] had the longest follow-up period (two years). Thus, none assessed medium- or long-term effects, limiting conclusions regarding durability and potentially underestimating recurrence rates.

CONCLUSION

Current evidence indicates that BS combined with PA may promote modest yet clinically relevant reduction in BP. However, the limited number of studies, methodological heterogeneity, and short follow-up periods preclude definitive conclusions, highlighting the need for larger, high-quality studies.

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Health outcomes and medical response during a military deployment in Iraq: a prospective observational study of morbidity, treatments, and evacuations

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ABSTRACT

BACKGROUND: Overseas military deployment poses a significant healthcare challenge, requiring the prevention of morbidity associated with physical strain and the environment, as well as the provision of effective medical care to ensure operational continuity in operations.

OBJECTIVES: To describe and analyze the medical care activity during the deployment of the Spanish contingent from the General Command of Ceuta at the Union III base (Baghdad) and to evaluate the recorded morbidity, applied treatments, and the need for medical evacuation.

STUDY DESIGN AND SETTINGS: A prospective, observational, and analytical study was conducted during the deployment between May and November 2025 at the Union III military base in Baghdad.

METHODS: All medical encounters recorded by the deployed medical services were included. Demographic and clinical variables as well as the applied treatment, need for follow-up, and evacuation, were analyzed. Statistical analysis included descriptive statistics and association tests, with a p value < 0.05 considered significant.

RESULTS: In total, 506 medical encounters were recorded. Traumatic injuries were the most frequent reason for consultation (25.7%), followed by infectious (20.9%) and digestive (17.2%) conditions. Most cases were resolved at Role 1 level, with a low evacuation rate (3.4%) and a high degree of local resolution.

CONCLUSIONS: The deployed medical support demonstrated a high resolutive capacity, with a predominance of non-combat-related pathologies and a low need for evacuation. These results highlight the importance of maintaining effective medical structures and reinforcing preventive measures to reduce morbidity during future deployments.

INTRODUCTION

Overseas military deployments are an essential component of the preparation, availability, and operational effectiveness of the armed forces, with purposes beyond a mere deterrent presence. In Iraq, under the umbrella of the NATO Mission Iraq (NMI), a non-combatant multinational mission aimed at advising and strengthening Iraqi defense and security institutions, Spanish personnel deployed at the Union III base (Green Zone, Baghdad) perform functions such as facility security, guard duties, escorts, personnel protection, allied training, and logistical support in the theater of operations.[1,2] These operational tasks require maintenance of unit cohesion and a tiered medical support system that guarantees triage, initial treatment, and evacuation according to the allied doctrine of Roles 1 or 2 and evacuation pathways.[3]

The Baghdad setting, characterized by high temperatures, low humidity, suspended dust, and sustained physical loads (carrying equipment, prolonged guard duties, transfers between bases, escorts, and shooting exercises), imposes significant physiological demands. Scientific evidence places acclimatization, hydration, and workload control as pillars to mitigate heat illness and preserve force performance.[4,5] Additionally, specific preparation for load carriage is associated with a reduction in overuse morbidity and the risk of musculoskeletal injuries.[5]

Furthermore, in the context of life on base, frequent transitions between air-conditioned interiors and hot, dusty exteriors favor the appearance of respiratory infections and certain skin conditions, potentially impacting operational continuity. In recent missions in Afghanistan and Iraq, it has been documented that disease and non-battle injuries (DNBI) account for a substantial

portion of healthcare demand and represent a relevant proportion of medical evacuations with high resolution in the first echelon.[6,7]

Beyond their operational and healthcare dimensions, military deployments involve substantial economic investments and rigorous logistical planning. According to NATO data, in 2024, military expenditure in allied countries amounted to nearly $ 1,506 million, representing an average of 2.2% of the Alliance's GDP; meanwhile, Spain allocated approximately 1.24% of its GDP to defense spending that year (~17,2 million €).[8,9] This highlights that operations depend not only on personnel and operational resources, but also on demanding and efficient budgetary management.

Literature from theaters of operations reinforces this framework. Recent studies have demonstrated that in austere environments, traumatic injuries can be managed locally with simple devices and clear referral/evacuation criteria;[10] likewise, endemic infectious pathologies in deployed personnel, such as mucosal leishmaniasis, require protocols activatable from the area and continuity of care,[11] while telemedicine programs offer 24/7 expert support and improve MEDEVAC/CASEVAC decision-making.[12] Similarly, the casuistry of forward surgical teams (Role 2 forward) provides intervention thresholds for extremity injuries in comparable scenarios.[13]

Prospective real-time morbidity data from Role 1 medical activities in allied deployments are scarce, making this study one of the few structured analyses of morbidity patterns and evacuation requirements in a desert operational environment.

Therefore, the objective of this study was to describe and analyze all medical attendances recorded during the deployment of the Spanish contingent at the Union III base (Baghdad) (May 26–November 26, 2025), evaluating the frequency of diagnostic categories; the applied treatments and their degree of local resolution; the proportion and reasons for evacuation; and the associations between type of condition, unit profile, and rank.

While the existing literature provides a solid framework for DNBI patterns and medical support in combat zones, there is a need for detailed, prospective data from contemporary, non-combat advisory missions set in urban environments, such as Baghdad's Green Zone. Such settings present unique challenges in which physiological strain and base-living conditions are the primary risk factors, unlike high-intensity combat or remote austere outposts.

METHODS

Design and participants

This study was conducted according to the STROBE criteria (STROBE Statement–Checklist of items that should be included in Observational Studies in Epidemiology) and was approved by the Ethics Committee on Medicinal Products of the Central Defense Hospital Gómez Ulla (CEIm-HCDGU).

This prospective, observational, and analytical study was conducted during the deployment of the Spanish contingent from the General Command of Ceuta at Union III (Green Zone, Baghdad) between May 26 and November 26, 2025. All medical encounter attendances recorded by the deployed medical service for the personnel of the said contingent were consecutively included, applying a non-probabilistic convenience sampling that exclusively covered the attended population from the Ceuta contingent. The participating units were: Legión, Regulares, Caballería, Artillería, Cuartel General, Ingenieros, and Unidad Logística No. 23 (ULOG23). Information was collected by the medical team attached to the base security missions, escort/support for training, and logistical sustainment, guaranteeing immediate care and systematic documentation of each healthcare event.

Data collection and definitions

Inclusion criteria: All Spanish military personnel of the Ceuta contingent who required medical attention in operations and whose cases were recorded by the deployed medical services. The exclusion criteria were attendances corresponding to personnel not belonging to the Ceuta contingent, or incomplete records without formal documentation of care.

The following variables were recorded:

- Attendance number (unique identifier).

Rank (enlisted, non-commissioned officer, or officer).

- Unit of origin.
- Sex (male/female).
- Diagnostic area (Traumatology, Infectious, Digestive, Dermatology, Allergology, Dentistry, Neurology, Ophthalmology, ENT, Podiatry, Urology, Cardiology, Pulmonology, Nephrology).
- Diagnosis (clinical description).
- Applied treatment.
- Follow-up (yes/no) after the first assessment.
- Evacuation (yes/no) and referral destination when applicable.

Data collection was prospective and used standardized forms completed by medical personnel during the mission. For analytical purposes, each encounter was treated as an independent observation, in line with established approaches to morbidity surveillance within military epidemiology. Subsequently, the records were digitized for analysis.

The study received a favorable evaluation from CEIm-HCDGU (registration no. 67/25). The data were obtained from an operational healthcare database and were treated anonymously and confidentially, without personal identification information, in accordance with the General Data Protection Regulation and Organic Law No. 3/2018 on Personal Data Protection and the guarantee of digital rights.

Statistical analysis

Data were processed using SPSS version 28 (IBM Corp., Armonk, New York). Absolute and relative frequencies (%) were calculated for all the variables. Inferential analysis was performed using Pearson's chi-square test to assess the associations between categorical variables. All tests were two-tailed, and statistical significance was set at $p < 0.05$.

RESULTS

During the study period, 506 medical attendances were recorded, corresponding exclusively to the military personnel of the Ceuta contingent deployed at the Union III base (Baghdad). Each record was considered as an independent event; therefore, the same service member could generate more than one healthcare episode during the study period. Most attendances were men (482, 95.3%), while 24 (4.7%) were women. The distributions by rank and unit are presented in **Table 1**.

Traumatic conditions constituted the most frequent reason for consultation, with 130 cases (25.7%), followed by infectious (106, 20.9%) and digestive (87, 17.2%) conditions. This was followed by dermatological diseases (n = 45, 8.9%) and allergological conditions (n = 29, 5.7%). Other areas with lower incidences were dentistry (26, 5.1%), neurology (23, 4.5%), ophthalmology (19, 3.8%), otorhinolaryngology (14, 2.8%), podiatry (11, 2.2%), urology (10, 2%), and cardiology (4, 0.8%), as well as isolated pulmonology and nephrology (1 case each, 0.2%). The global distribution by diagnostic area is summarized in **Table 2** and represented graphically in **Figure 1**.

Regarding origin, most attendances were from Regulares (153 cases, 30.2%), followed by Legión (132 cases, 26.1%). The next was Cuartel General with 103 cases (20.4%), while Caballería registered 81 attendances (16.0%). Logistic support units (ULOG/ULOG23) included 22 cases (4.3%), and Artillería included 14 cases (2.8%). Finally, a single case corresponding to Ingenieros was recorded (0.2%). This distribution reflects the operational weight of each unit and the intensity of its tasks during deployment in Baghdad (**Figure 2**).

Table 1. General characteristics of the sample: sex, rank, and unit of origin; n and %

Variable	Category	n	%
Sex	Male	482	95.3
	Female	24	4.7
Military rank	Enlisted	310	61.3
	Non-Commissioned Officer	92	18.2
	Officer	104	20.6
Unit of origin	Regulares	153	30.2
	Legión	132	26.1
	Cuartel General	103	20.4
	Caballería	81	16
	ULOG/ULOG23	22	4.3
	Artillería	14	2.8
	Ingenieros	1	0.2
Total attendances	–	**506**	**100**

Table 2. Distribution of attendances by diagnostic area; n and %

Diagnostic Area	n	%
Traumatology	130	25.7
Infectious	106	20.9
Digestive	87	17.2
Dermatology	45	8.9
Allergology	29	5.7
Dentistry	26	5.1
Neurology	23	4.5
Ophthalmology	19	3.8
Otorhinolaryngology	14	2.8
Podiatry	11	2.2
Urology	10	2
Cardiology	4	0.8
Pulmonology	1	0.2
Nephrology	1	0.2
Total	**506**	**100**

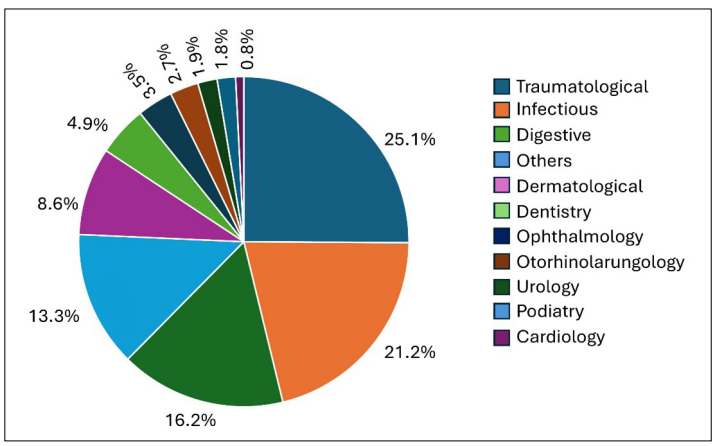

Figure 1. Percentage distribution of attendances by diagnostic area.

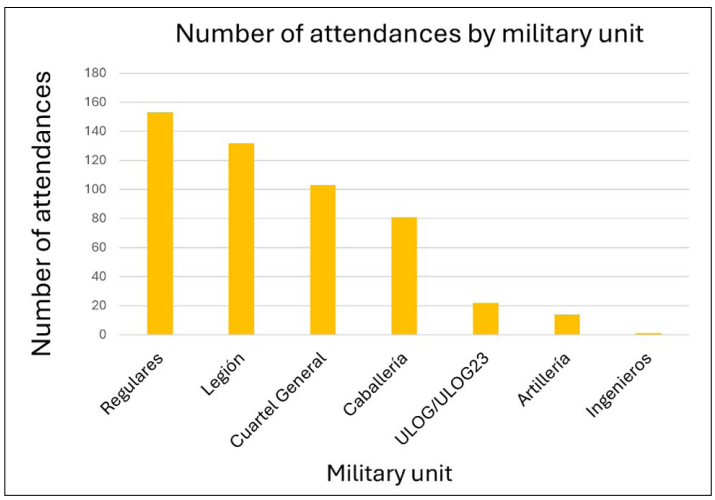

Figure 2. Number of attendances by military unit.

Inferential analysis showed that the relationship between unit of origin and type of condition was statistically significant ($\chi^2 = 277.66$; df = 182; $p < 0.001$), indicating that morbidity patterns varied relevantly among the different units of the contingent. Units with a higher physical load and direct participation in security and escorting tasks (mainly Regulares, Legión, and Caballería) presented a higher proportion of traumatic injuries, whereas units with a more administrative or support component, such as Cuartel General and ULOG23, showed a broader distribution of digestive, infectious, and dermatological pathologies. Artillería and Ingenieros, with a lower number of cases, reflected more heterogeneous healthcare profiles, but with less epidemiological weight in the overall contingent.

Regarding military rank, most attendances corresponded to enlisted personnel, with 310 cases (61.3%), followed by officers with 104 cases (20.6%) and non-commissioned officers with 92 cases (18.2%). Inferential analysis did not show a significant association between rank and type of condition ($\chi^2 = 36.46$; df = 28; $p = 0.131$), indicating that enlisted personnel, non-commissioned officers, and officers presented a similar morbidity pattern, without relevant differences in the distribution of diagnostic areas based on rank.

Regarding clinical evolution, 99 cases (19.6%) required at least one follow-up, whereas 407 cases (80.4%) were resolved in a single medical act. Most attendances were managed entirely in the area, with 18 evacuations (3.4%) to higher echelons (reference hospitals, civilian clinics, or specialist consultations, mainly dentistry and telemedicine). Inferential analysis showed that the relationship between diagnostic area and evacuation was highly significant ($\chi^2 = 96.19$; df = 14; $p < 0.001$), indicating that the clinical reason clearly conditioned the need for referral. The areas that generated the highest number of evacuations were dentistry, certain traumatic conditions requiring advanced imaging tests, and some isolated cases of cardiology and respiratory pathology. In contrast, most digestive, dermatological, allergological, and mild neurological pathologies were managed completely in Role 1, without requiring MEDEVAC or external consultations. **Table 3** records exclusively the diagnostic areas that generated at least one evacuation during the study period.

As is shown in **Table 4**, a total of 861 therapeutic interventions were recorded because many episodes required treatment combinations. Simple analgesics constituted the most commonly used group with 137 interventions (15.9%), followed by nonsteroidal anti-inflammatory

Table 3. Evacuations by diagnostic area (only areas with at least one evacuation are shown)

Diagnostic area	Total cases	Evacuated	% Evacuation	Role 2E	Dentist	Telemedicine
Traumatology	130	5	3.8%	4	0	1
Infectious	106	2	1.9%	1	0	1
Digestive	87	2	2.3%	1	0	1
Dermatology	45	1	2.2%	0	0	1
Dentistry	26	6	23.1%	0	6	0
Urology	10	1	10%	0	0	1
Cardiology	4	1	25%	1	0	0
Total (only areas with ≥ 1 evacuation)	**408**	**18**	**4.4%**	**7**	**6**	**5**

Note: The remaining diagnostic areas (neurology, ophthalmology, otorhinolaryngology, podiatry, pulmonology, and nephrology) recorded no evacuations during the study period.

Table 4. Therapeutic interventions grouped by pharmacological families / type of measure; n and % of total interventions

Therapeutic Category	n	%	Examples Included
Simple Analgesics	137	15.9%	Paracetamol, metamizol, nolotil
Systemic NSAIDs	122	14.2%	Ibuprofen, diclofenac, naproxen, dexketoprofen
Fluid Therapy	69	8%	Oral rehydration salts, saline, ringer's lactate, glucose
Topical anti-inflammatories	52	6%	Diclofenac gel, lidocaine patches
Digestive/antispasmodics	52	6%	Hyoscine butylbromide, omeprazole, loperamide
Systemic antibiotics	49	5.7%	Amoxicillin/clavulanate, azithromycin, ciprofloxacin
Physiotherapy/physical measures	36	4.2%	Physiotherapy, stretching, functional bandage, cryotherapy
Respiratory (mucolytics/sprays)	34	4%	Acetylcysteine, oxymetazoline
Antiseptics/local wound care	30	3.5%	Povidone-iodine, chlorhexidine
Corticosteroids (topical and systemic)	23	2.7%	Prednisone, hydrocortisone
Antihistamines	23	2.7%	Cetirizine, ebastine
Antiemetics	13	1.5%	Ondansetron, metoclopramide
Antifungals	8	0.9%	Miconazole, KETOCONAZOLE
Psychotherapy/anxiolytics	8	0.9%	Diazepam
Antivirals	4	0.5%	Acyclovir
Urological	3	0.3%	Tamsulosin
Total	**861**	**100%**	**–**

drugs (NSAIDs), with 122 interventions (14.2%). Fluid therapy (oral or intravenous serum) was administered on 69 occasions (8%), digestive treatments and antispasmodics reached 52 interventions (6%), as did topical anti-inflammatory drugs (52, 6%).

Systemic antibiotics were used in 49 interventions (5.7%), mainly for respiratory, dermatological, and dental infections. Physiotherapy and physical measures (functional bandages, stretching, cryotherapy, and directed rest) comprised 36 interventions (4.2%), while respiratory treatments (mucolytics and nasal sprays) comprised 34 interventions (4%).

The other groups used antiseptics and local wound care less frequently (30, 3.5%), topical and systemic corticosteroids (23, 2.7%), antihistamines (23, 2.7%), antiemetics (13, 1.5%), antifungals (8, 0.9%), and psychotropic drugs (8, 0.9%). The use of antivirals was occasional (n = 4; 0.5%), and urological treatments were exceptional (n = 3; 0.3%).

DISCUSSION

The results of this study revealed a morbidity pattern typical of military deployments in desert environments with high operational loads, dominated by musculoskeletal injuries, respiratory infections, and digestive disorders. This profile is consistent with that described in previous operations in Iraq and Afghanistan, where DNBI represent 60–70% of the total healthcare demand and constitute the main cause of loss of operational capacity.[14,15] Similar morbidity distributions have also been reported in contemporary deployments in Lebanon (UNIFIL), Mali (EUTM), and the wider Sahel region, where non-combat conditions, environmental exposure, and sustained operational tempo continue to drive DNBI as the principal source of healthcare utilization.[13,15,26]

In our series, traumatic injuries represented 25.7% of the total attendances, which is consistent with previous studies indicating that patrols, prolonged guard duties, sustained physical load, and continuous use of protective equipment increase the risk of overuse musculoskeletal injuries in deployments in hot zones.[16,17] Although this proportion is lower than that described in high-intensity maneuvers, where it can exceed 45–50%,[18] it is expected that in a more static scenario such as Union III, overload syndromes, low back pain, and mild sprains predominate compared to acute trauma associated with intense training. This distribution coincides with the musculoskeletal injury patterns described by Knapik et al.[19] and Jones et al.,[16] who relate accumulated fatigue and prolonged effort to a higher incidence of lumbar pain and lower extremity injuries. These findings reinforce the need for targeted musculoskeletal injury-prevention programs, including load-management strategies, pre-deployment conditioning, and routine physiotherapy availability, to mitigate cumulative fatigue effects in Role 1 environments.[5,16,17,19]

Infectious diseases accounted for 20.9% of consultations, mostly corresponding to upper respiratory tract infections. This proportion is comparable to that described in previous deployments in Iraq and Afghanistan, where respiratory illnesses constitute one of the main causes of DNBI, representing between one-fifth and one-fourth of the healthcare demand in operations. Factors such as abrupt thermal changes between air-conditioned environments and extremely hot exteriors, coexistence in closed spaces, and continuous exposure to suspended dust have been identified as key predisposing elements for this type of pathology.[20] This pattern has also been documented in series from the Armed Forces Health Surveillance Division (AFHSD), which attributes a key role to thermal contrast and mucosal dryness in predisposing to uncomplicated pharyngitis and bronchitis.[21]

Digestive disorders, the third most frequent category (17.2%), stood out above the usual rate of exercise in the national territory, which is consistent with the operational environment of Baghdad. Previous studies have shown that changes in dietary habits, variable water chlorination, thermal stress, and dehydration predispose personnel to gastroenteritis, abdominal cramps, and functional constipation in deployed personnel.[22,23] Similarly, dermatological alterations (8.9%) were frequent in dry climates, where sweat retained by the continuous use of equipment and friction favored the appearance of irritative dermatitis, mycoses, and folliculitis.

One of the most relevant findings was the statistically significant difference between military units and diagnostic areas. Units more exposed to physical and security tasks – Regulares, Legión, and Caballería – had the highest proportion of traumatic cases, whereas Cuartel General and Logistic Unit (ULOG) presented a more diversified spectrum, with a predominance of digestive, respiratory, and dermatological pathologies. This pattern is consistent with the literature describing a higher burden of DNBI in combat units than in support units in relation to physical intensity, mission type, and environmental exposure during deployment.[14]

In contrast, no significant differences were observed by military rank, which coincides with previous studies indicating that in prolonged operational deployments, health risk is determined mainly by the function performed and operational exposure rather than by hierarchical rank.[20]

Regarding evacuation, a significant association was identified between the diagnostic area and the need for referral. Evacuations to Role 2E, to the American clinic in Union III, or via telemedicine from Hospital Gómez Ulla were mainly concentrated in dentistry, traumatology, and cardiology, which usually require complementary tests that are not available in Role 1 or specialist evaluation. The evacuation rate in the present study, well below 10%, is consistent with previous literature, where more than 85–90% of DNBI

cases are resolved at the first healthcare echelon.[24,25] This high degree of local resolution reflects the adequate capacity of the deployed medical team and the effectiveness of triage according to the allied doctrine.

The analysis of treatments showed a typical Role 1 care pattern, with the wide use of nonsteroidal anti-inflammatory drugs, simple analgesics, fluid therapy, antibiotics for respiratory or skin infections, and frequent use of physiotherapy and functional measures. The high proportion of combined interventions evidences the clinical variability of cases and the need for multimodal approaches, something already described in previous operations where mixed symptoms (pain + overload + dehydration + mild infections) are common.[26] Together, these results mirror trends observed in contemporary deployments in the Sahel, Lebanon, and Eastern Europe, enhancing the broader contextual relevance of the findings.[13,15,26]

This study has several operational implications. First, it reinforces the importance of injury prevention programs for overload, hydration control in hot environments, and adequate acclimatization, all of which are fundamental pillars to decreasing morbidity in desert zones.[4,5] Second, it highlights the value of telemedicine in the theater of operations, where it is not always possible to have specialists, aligning with recent experiences that have demonstrated that teleconsultation reduces unnecessary evacuations and improves the continuity of care.[27]

Finally, the data underscore the need to adapt healthcare resources to the actual observed morbidity profile, especially by reinforcing the capacity to manage digestive, respiratory, and dermatological pathologies, and maintaining fast evacuation pathways for dentistry, traumatology, and cardiology.

Overall, the results of this work confirm that most morbidities in Union III are concentrated in non-combat-related conditions, generally mild and manageable at Role 1, but have a significant operational impact if not addressed early. Adequate healthcare planning, anticipation of climate-specific risks, personnel training, and the availability of diagnostic and treatment equipment adapted to the environment constitute key elements in guaranteeing the sustained operability of the contingent.

This study has several limitations that should be considered. First, its observational and single-center design, while reflecting the reality of a specific deployment, limits the generalizability of the findings and prevents the establishment of causal relationships. Second, there is a potential for under-reporting of minor conditions that personnel might have self-treated or not considered severe enough to seek medical attention. Third, the study period (May to November) coincided with the hottest months in Iraq, which likely influenced the incidence of heat-related, dermatological, and certain infectious pathologies; therefore, the morbidity pattern described may not be fully representative of annual cycles. Despite these limitations, the data provide a valid and detailed snapshot of healthcare demands and medical response capacity during contemporary military deployment in this theater of operation.

CONCLUSIONS

The morbidity of the Spanish contingent deployed in Union III was concentrated in non-combat-related conditions, mainly traumatic, infectious, and digestive conditions, in line with those described in other deployments in desert environments. Significant differences were observed in the disease pattern according to the unit of origin, with a higher burden of musculoskeletal pathology in Regulares, Legión, and Caballería and a more diversified profile (digestive, respiratory, and dermatological) in Cuartel General and ULOG, underscoring the need to adapt preventive measures and healthcare resources to the mission type of each unit. Military rank (enlisted, non-commissioned officer, officer) was not significantly associated with the type of condition, suggesting that, in this operational scenario, risk exposure is determined mainly by function and unit rather than by rank. These findings may inform future medical planning, preventive strategies, and resource allocation aimed at optimizing Role 1 healthcare support and sustaining operational readiness for overseas military deployment.

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Is photobiomodulation therapy free from racial bias?: a narrative review of skin pigmentation

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ABSTRACT

BACKGROUND: Photobiomodulation therapy (PBMT) has been extensively researched for tissue repair, pain relief, and muscle recovery. However, melanin, a primary skin chromophore, can impede photon penetration into darker skin, potentially diminishing the efficacy of PBMT. Despite this, clinical protocols and guidelines seldom account for skin pigmentation when setting parameters, possibly exacerbating racial disparities in healthcare.

OBJECTIVE: To examine the effect of melanin on the efficacy of PBMT and highlight the necessity for personalized strategies that account for skin pigmentation.

DESIGN AND SETTING: Short communication conducted at the Universidade de São Paulo (USP), Ribeirão Preto, São Paulo.

METHODS: A narrative review of PBMT mechanisms, light–tissue interactions, and the impact of melanin absorption on treatment outcomes was conducted.

RESULTS: The clinical outcomes of PBMT depend on the technical parameters (wavelength, energy, and dose) and skin pigmentation. Darker skin tones with higher melanin content may lead to reduced photon penetration effectiveness. However, most studies and protocols do not consider this variable. Only a few clinical trials have categorized outcomes by skin tone, exposing a notable knowledge gap.

CONCLUSION: Melanin plays a crucial role in PBMT response, and overlooking skin pigmentation in research and clinical practice could perpetuate disparities. Enhanced and tailored protocols are essential to optimize PBMT outcomes among diverse populations.

INTRODUCTION

Photobiomodulation therapy (PBMT) has been widely studied for its effects on tissue repair, analgesia, and muscle recovery;[1] however, its mechanisms are only partially understood. The process involves the absorption of photons by mitochondrial chromophores, which leads to ATP synthesis, the modulation of reactive species, and subsequent signaling pathways.[2] The therapeutic effectiveness of PBMT is affected by various physical and biological factors. Parameters such as wavelength, power, and energy play a critical role in determining the interaction of light with tissues. The therapeutic outcome is dependent on both technical (wavelength, power, and energy) and biological factors. In the "optical window" (600–1100 nm), light transmission is optimized, although chromophores such as melanin, hemoglobin, and water significantly affect the propagation of photons.[3,4]

Melanin is particularly significant due to its wide absorption spectrum, potentially restricting light penetration in darker skin tones. Optical studies[5,6] have shown that device characteristics and tissue properties can unpredictably affect penetration, raising concerns about standardization. Despite this, prominent guidelines such as those from the World Association for Photobiomodulation Therapy (2010, 2022) currently do not differentiate dosing parameters based on skin pigmentation. In regions with predominantly Black or Brown populations, this oversight may worsen inequities. Furthermore, limited clinical studies have categorized participants by skin type, resulting in the underrepresentation of melanodermic individuals in the literature.

IS MELANIN THE MAIN CULPRIT?

In PBMT, chromophores absorb light to initiate biological responses. Key endogenous chromophores found in human tissues comprise melanin, hemoglobin, water, and

cytochrome c-oxidase.[2] Melanin is particularly noteworthy due to its robust and broad-spectrum absorption, particularly across the visible and near-infrared spectra (600–900 nm) commonly employed in PBMT. While melanin plays a crucial role in protecting the skin from photodamage, it also acts as a substantial optical impediment.[7] In individuals with darker skin tones, heightened melanin levels can absorb a significant portion of incoming photons, thereby diminishing the energy penetrating deeper tissues and potentially reducing the therapeutic efficacy.[3]

Importantly, melanin concentration and distribution vary among individuals and across anatomical regions. However, these factors are rarely considered in standard PBMT protocols. This oversight can lead to mismatches between the planned and delivered energy, resulting in suboptimal or inconsistent outcomes, particularly in melanodermic populations. Optical studies have confirmed that melanin significantly affects light distribution and penetration depth.[7]

The wide absorption spectrum of melanin enables it to absorb a significant amount of incident light, reducing the availability of photons for therapeutic chromophores. However, its role extends beyond simple attenuation of incident fluence. Upon excitation, melanin can trigger photochemical reactions that generate heat and multiple reactive oxygen and nitrogen species (ROS/RNS), including singlet oxygen, hydrogen peroxide, superoxide, hydroxyl radicals, and nitric oxide derivatives. These pathways reflect the dual photobiology of melanin: protective in certain circumstances but reactive and potentially harmful in others.[2,8] This dual nature is particularly pertinent when adjusting parameters to enhance the penetration of PBMT into darker skin. While increasing the fluence, irradiance, or exposure time can offset superficial absorption, these adjustments also raise the amount of energy deposited in the melanin-rich epidermis. This elevation escalates the risk of thermal burden, localized heat buildup, and heightened ROS/RNS production, which may clinically present as discomfort, erythema, or superficial injury.[8]

The issue at hand is not whether to increase PBMT parameters, but how to execute them safely. Evidence from optical modeling and clinical studies advocates for several strategies: giving preference to longer wavelengths (e.g., 800–900 nm and 1.064 nm), which exhibit reduced melanin absorption; utilizing larger spot sizes to lessen epidermal burden and enhance depth penetration; monitoring initial sensory cues such as warmth or tingling, which manifest at lower fluences in darker phototypes; and implementing gradual rather than sudden fluence increments. In summary, melanin does not impede PBMT but serves as a crucial dosimetric factor. Incorporating its optical behavior into treatment planning is essential for maximizing efficacy while maintaining safety.

LIGHT IS LIGHT? RETHINKING STANDARDIZATION IN OPTICAL THERAPIES

Despite advances in PBMT, uncertainties persist when these protocols are applied to diverse populations. Optical technologies encounter inherent limitations, such as device variability, disparities between programmed and delivered parameters, and the biological diversity of human skin. Factors like melanin content, tissue thickness, and individual optical responses are frequently overlooked in clinical practice and research.

A systematic review of 461 trials on cosmetic laser- and light-based therapies identified structural bias.[9] While many trials included phototypes IV–VI, few analyzed outcomes based on skin type, compromising their relevance to darker-skinned populations. Conditions like post-inflammatory hyperpigmentation frequently preclude higher phototypes from primary laser treatments due to variable efficacy and a higher risk of adverse effects. Despite the promise of techniques such as fractional photothermolysis and Nd:YAG when used judiciously, the literature is still fragmented and heavily dependent on subjective skin classification scales.[10]

Taken together, these gaps emphasize the need to reassess whether the current PBMT approaches sufficiently account for individual variability. As Enwemeka[11] noted, "light is light," but biological diversity requires moving beyond technical precision to clinically inclusive applications.

WHAT SHOULD BE CONSIDERED WITH CAUTION?

Patient responses to PBMT vary depending on pigmentation, tissue composition, and perception thresholds. Individuals with darker phototypes may experience warmth or discomfort at lower fluences. Sartor et al.[12] demonstrated that individuals with higher phototypes perceived PBMT stimuli sooner, even with standardized parameters, highlighting the importance of carefully adjusting energy density and duration to prevent adverse effects. Tattoos and other pigment alterations can change cutaneous perception, complicating treatment planning.

Experimental models[4] and in vivo optical studies[6] further confirmed the reduced penetration at 660 nm in darker skin compared with lighter tones, with wavelength-dependent differences (e.g., 14 versus 21 mm for 660 nm; 20 versus 26 mm for 830 nm). Equipment variability adds further inconsistencies. These findings challenge one-size-fits-all protocols; clinicians must assess the pigmentation, anatomical site, and tissue thickness to adapt the parameters. Insights from dermatological laser therapy suggest that PBMT should adopt a pigmentation-based calibration to enhance its safety and efficacy. This naturally leads to the challenge of individualized dosimetry in PBMT. How can we accurately measure and adjust the treatment parameters to consider variations in melanin concentration, tissue optical properties, and other patient-specific

factors? Addressing this issue is crucial for advancing photobiomodulation into a personalized therapeutic modality.

WHERE DO WE GO FROM HERE? A CALL FOR INDIVIDUALIZED DOSIMETRY

The notion that PBMT is universally effective regardless of skin tone is oversimplified. Individuals with higher melanin concentrations may receive subtherapeutic fluences if protocols are not adjusted, leading to concerns about effectiveness and fairness. Future studies should adopt individualized dosimetry, consider skin phototype as a key factor, and involve participants from all Fitzpatrick categories. Computational models can aid in refining treatment strategies. Clinicians should adjust the wavelength, power, and exposure according to individual patient characteristics. The integration of pigmentation-sensitive dosimetry is crucial for the progress of PBMT in personalized treatment.

CONCLUSION

Melanin is a crucial factor influencing the results of PBMT. Standardized protocols that ignore the risk of skin pigmentation lead to disparities in treatment efficacy and safety. Integrating pigmentation assessment and individualized dosimetry into research and clinical practice is essential for advancing PBMT into a more effective, safe, and inclusive therapeutic modality.

CLINICAL RELEVANCE

- PBMT outcomes vary with skin pigmentation, emphasizing the necessity for individualized dosimetry.
- Adjustment of parameters for melanin improved safety and efficacy.
- Pigmentation-aware protocols ensure consistent, equitable treatment.

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E-cigarette use in Brazil—prevalence and associated factors in a national cross-sectional study of 16,093 adults: a short communication

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ABSTRACT

BACKGROUND: Monitoring tobacco consumption is important for supporting national and global agendas and commitments.

OBJECTIVE: To analyze the prevalence and sociodemographic and geographic factors associated with e-cigarette use in Brazil, using data from Vigitel 2023.

DESIGN AND SETTING: Cross-sectional analytical study was conducted using secondary data from Vigitel 2023.

METHODS: Sociodemographic characteristics (sex, age, education, and ethnicity), geographic location, and e-cigarette use were analyzed. Descriptive analyses were performed using Chi-squared and Mann–Whitney *U*-tests. Additionally, weighted multivariable logistic regression models were used to examine independent associations between sociodemographic factors and current e-cigarette use. Post-stratification weights were applied, and adjusted odds ratios (aOR) with 95% confidence intervals (95% CI) were estimated.

RESULTS: Among 16,093 adults, the prevalence of current e-cigarette use was 5.55%. In the adjusted model, younger age was strongly associated with use (aOR per year increase = 0.93; 95% CI 0.92–0.94; $p < 1$). Men had higher odds of use than women (aOR = 1.34; 95% CI 1.12–1.6; $p < 0.01$). Educational level was not independently associated with usage. Caucasian individuals had higher odds compared to mixed-race individuals (aOR = 1.29; 95% CI 1.05–1.58; $p = 0.015$). Residents of the southern region showed increased odds (aOR = 1.48; 95% CI 1.1–1.99).

CONCLUSION: Current e-cigarette use in Brazil is independently associated with younger age, male sex, Caucasian ethnicity, and residence in southern Brazil. These findings underscore the importance of strengthening public policies that regulate and control these devices as well as educational campaigns targeting high-risk groups.

INTRODUCTION

Smoking is responsible for approximately eight million deaths annually. Of these deaths, approximately seven million are due to direct tobacco consumption and approximately 1.2 million are a consequence of exposure to secondhand tobacco smoke. Therefore, smoking is considered a serious global public health problem and a risk factor for diseases such as lung cancer, chronic obstructive pulmonary disease, myocardial infarction, stroke, type 2 diabetes, hypertension, infertility, oral health issues, and premature skin aging.[1]

Nicotine, the main psychoactive substance in cigarettes, strongly contributes to respiratory diseases such as chronic obstructive pulmonary disease and asthma, and cardiovascular problems such as atherosclerosis and stroke. Nicotine also affects the digestive system, causing gastroesophageal reflux, peptic ulcers, and liver cirrhosis. It also affects the genitourinary system, causing erectile dysfunction and infertility.[2]

E-cigarettes, also known as electronic smoking devices, have many names including vapors, hookah pens, e-hookahs, e-cigars, personal vaporizers, and mods. Although these drugs have begun to act as alternatives to smoking cessation, they pose significant public health risks. The incorrect perception that e-cigarettes are harmless has contributed to their popularity, particularly among young people.[3,4]

The use of e-cigarettes exposes the body to chemicals such as nicotine, formaldehyde, acetaldehyde, acrolein, and diacetyl, as well as heavy metals such as nickel, cadmium, and chromium.

These compounds include carcinogens and cytotoxic substances that cause lung and cardiovascular diseases. Furthermore, electronic cigarette use is concerning because it can lead to the consumption of other tobacco products, particularly among adolescents and young adults.[5]

A study conducted by the Heart Institute (involving 400 e-cigarette users in São Paulo, Brazil) found that their nicotine levels were up to six times higher than those of conventional cigarette smokers who smoked an average of 20 cigarettes per day. This suggests that e-cigarettes pose a greater risk of addiction.

Additionally, the Covitel report, which surveyed 9,000 people via telephone about the risk factors for chronic noncommunicable diseases during the pandemic, indicated that the prevalence of e-cigarette use in Brazil was 8% in the first quarter of 2023, primarily among those aged 18–24.[1]

Although national surveys such as the Brazilian National School Health Survey (PeNSE) and the Covitel study have reported the prevalence of e-cigarette experimentation and use in specific populations, particularly adolescents and young adults, there is still limited evidence based on nationally standardized surveillance systems that allow comparisons across all Brazilian state capitals. Moreover, most Brazilian studies have focused on adolescents, university students, or convenience samples, and few have explored the sociodemographic and geographic distribution of e-cigarette use in the adult population using population-based data.[3,4]

Internationally, surveillance systems, such as the Behavioral Risk Factor Surveillance System in the United States and similar national health surveys in Europe, have provided consistent monitoring of e-cigarette use trends and associated factors. However, comparable analyses of chronic disease risk factors using Brazil's official surveillance system are scarce.[6]

Therefore, analyzing Vigitel 2023 data provides an opportunity to fill this gap by offering updated, population-based estimates of e-cigarette use among adults living in all Brazilian state capitals and identifying associated sociodemographic and regional factors. This information is essential to guide regulatory policies and targeted public health interventions.[7]

OBJECTIVE

Therefore, given the limited adult population-based evidence derived from Brazil's official surveillance systems and the need for updated nationwide data, this study sought to analyze the prevalence and sociodemographic and geographic factors associated with e-cigarette use in Brazil, using data from Vigitel 2023.

METHODS

This was a cross-sectional analytical study using secondary data from the Surveillance of Risk and Protective Factors for Chronic Diseases by Telephone Survey (Vigitel) 2023.[8] Vigitel is an annual, population-based survey conducted by the Brazilian Ministry of Health through telephone interviews with adults (aged 18 and older) living in the capitals of Brazil's 26 states and the Federal District. This study was conducted in accordance with the principles of the Declaration of Helsinki. The data used in this study are publicly available, and it was not possible to access identifying information concerning the participants. Furthermore, this study adhered to Resolution No. 510 of the 2016 National Health Council (Brazil).[8]

The 2023 Vigitel sample consisted of 16,093 respondents with 800 interviews conducted in each capital city, equally divided between landlines and cell phones. Vigitel's methodology employs statistical weighting to adjust the sample distribution to the adult population living in households with telephone access, using data from the Brazilian Institute of Geography and Statistics' Demographic Census.[8] The data used in this study are publicly available, and it is not possible to access identifying information about the participants. Furthermore, this study adhered to Resolution Number 510 of the 2016 National Health Council (Brazil).[8]

A total of 16,093 respondents were included in the analysis. Current e-cigarette use was defined as daily or occasional use of electronic nicotine delivery devices.

The independent sociodemographic variables included sex (male/female), age (years), education level (high school, college, or postgraduate), and ethnicity/color (Caucasian, black, mixed, or other).

The city of residence (26 state capitals and the Federal District) was used for descriptive analyses. For multivariate analyses, the city of residence was grouped into five macro-regions (North, Northeast, Southeast, South, and Central-West) to improve model stability and interpretability.

Descriptive analyses were conducted to estimate the prevalence and compare groups using the Chi-squared and Mann–Whitney *U*-tests. Subsequently, weighted multivariable logistic regression models were used to assess the independent associations between sociodemographic variables and current e-cigarette use. Post-stratification (raking) weights were applied to account for the Vigitel sampling design. Adjusted odds ratios (aOR) and 95% confidence intervals (95% CI) were calculated. All variables were included in the final model. Statistical significance was set at $p < 0.05$.

RESULTS

Among the 16,093 adults interviewed in 2023, 5.55% reported current e-cigarette usage. In the descriptive analyses, significant differences were observed according to sex, age, ethnicity/color, and city of residence (**Tables 1 and 2**). In the weighted multivariable logistic regression model (**Table 3**), younger age remained strongly associated with e-cigarette use (aOR per year increase = 0.93; 95% CI 0.92–0.94; $p < 1$). Men had

Table 1. Factors associated with the use of electronic cigarettes (n = 16,093)

Variables	Electronic Cigarette			Test*
	No	Yes	Total	
	15,200 (94.45%)	893 (5.55%)	16,093 (100%)	
Sex				< 1
Male	5,806 (38.2%)	510 (57.11%)	6,316 (39.25%)	
Female	9,394 (61.8%)	383 (42.89%)	9,777 (60.75%)	
Age (mean ± SD)	47.07 (± 16.85)	31.37 (± 11.94)	46.20 (± 17)	< 1
Education Level				0.12
High school	7,601 (50.01%)	443 (49.61%)	8,044 (49.98%)	
College degree	5,773 (37.98%)	361 (40.43%)	6,134 (38.12%)	
Graduate degree	1,826 (12.01%)	89 (9.97%)	1,915 (11.9%)	
Race/Color				< 1
White	5,892 (38.76%)	408 (45.69%)	6,300 (39.15%)	
Black	1,611 (10.6%)	82 (9.18%)	1,693 (10.52%)	
Asian	175 (1.15%)	13 (1.46%)	188 (1.17%)	
Mixed-race (pardo)	7,008 (46.11%)	363 (40.65%)	7,371 (45.8%)	
Indigenous	142 (0.93%)	10 (1.12%)	152 (0.94%)	
Other	254 (1.67%)	9 (1.01%)	263 (1.63%)	
Doesn't know	77 (0.51%)	7 (0.78%)	84 (0.52%)	
Prefer not to answer	41 (0.27%)	1 (0.11%)	42 (0.26%)	

* Mann–Whitney ***U***-test was used for quantitative variables (age and education level) or Chi-squared test was used for categorical variables (sex, ethnicity, and city).

Table 2. Factors associated with electronic cigarette use in Brazil's regions (n = 16,093)

Variables	Electronic Cigarette			Test*
	No.	Yes	Total	
	15,200 (94.45%)	893 (5.55%)	16,093 (100%)	
City				< 1
Aracaju	581 (3.82%)	11 (1.23%)	592 (3.68%)	
Belém	582 (3.83%)	23 (2.58%)	605 (3.76%)	
Belo Horizonte	537 (3.53%)	28 (3.14%)	565 (3.51%)	
Boa Vista	597 (3.93%)	41 (4.59%)	638 (3.96%)	
Campo Grande	478 (3.14%)	47 (5.26%)	525 (3.26%)	
Cuiabá	557 (3.66%)	42 (4.7%)	599 (3.72%)	
Curitiba	515 (3.39%)	63 (7.05%)	578 (3.59%)	
Florianópolis	549 (3.61%)	62 (6.94%)	611 (3.8%)	
Fortaleza	545 (3.59%)	21 (2.35%)	566 (3.52%)	
Goiânia	529 (3.48%)	44 (4.93%)	573 (3.56%)	
João Pessoa	599 (3.94%)	13 (1.46%)	612 (3.8%)	
Macapá	631 (4.15%)	15 (1.68%)	646 (4.01%)	
Maceió	563 (3.7%)	27 (3.02%)	590 (3.67%)	
Manaus	618 (4.07%)	19 (2.13%)	637 (3.96%)	
Natal	556 (3.66%)	36 (4.03%)	592 (3.68%)	
Palmas	616 (4.05%)	35 (3.92%)	651 (4.05%)	
Porto Alegre	535 (3.52%)	36 (4.03%)	571 (3.55%)	
Porto Velho	542 (3.57%)	32 (3.58%)	574 (3.57%)	
Recife	575 (3.78%)	18 (2.02%)	593 (3.68%)	
Rio Branco	532 (3.5%)	31 (3.47%)	563 (3.5%)	
Rio de Janeiro	576 (3.79%)	30 (3.36%)	606 (3.77%)	
Salvador	590 (3.88%)	16 (1.79%)	606 (3.77%)	
São Luís	599 (3.94%)	27 (3.02%)	626 (3.89%)	
São Paulo	487 (3.2%)	59 (6.61%)	546 (3.39%)	
Teresina	560 (3.68%)	32 (3.58%)	592 (3.68%)	
Vitória	589 (3.88%)	26 (2.91%)	615 (3.82%)	
Brasília	562 (3.7%)	59 (6.61%)	621 (3.86%)	

* Mann–Whitney ***U***-test was used for quantitative variables (age and education level) or Chi-squared test was used for categorical variables (sex, ethnicity, and city).

34% higher odds of use than women ((aOR = 1.34; 95% CI 1.12–1.6; $p < 0.01$). Caucasian individuals showed higher odds compared to mixed-ethnicity individuals (aOR = 1.29; 95% CI 1.05–1.58; $p = 0.015$). Regionally, residents of the South had higher odds of use (aOR = 1.48; 95% CI 1.1–1.99), while residents of the northeast showed lower odds compared to the north region (aOR = 0.74; 95% CI 0.55–0.98).

DISCUSSION

The findings of this study indicate that while e-cigarette use in Brazil is still restricted to a portion of the population, it is primarily concentrated among young people with a significantly lower average age than non-users. These results expand on the previous Brazilian evidence by providing updated estimates based on a nationally standardized surveillance system covering all state capitals, thereby complementing the findings of school-based and pandemic-period surveys.

The inverse association between age and e-cigarette use indicated that younger adults were disproportionately affected. This highlights the emergence of a new generation exposed to nicotine without prior experience with conventional smoking, which makes this group particularly vulnerable to addiction.[9–11]

After adjusting for potential confounders, younger age remained the strongest predictor of e-cigarette use. Male sex and Caucasian ethnicity were independently associated with higher odds of use, whereas educational level was not significantly associated after adjustment. Regional disparities persist, particularly in the South region.[12,13]

In terms of geographic distribution, e-cigarette use was most prevalent in Curitiba, São Paulo, and the Federal District, with statistically significant differences observed among these locations. These findings support the notion that large cities, with their economic and social dynamics, can act as hubs for disseminating new nicotine products and influencing consumption behavior.[9]

Despite the 2009 ban imposed by the National Health Surveillance Agency (Agência Nacional de Vigilância Sanitária), reinforced in 2024, e-cigarette use continues to grow among young people, indicating that current strategies are insufficient to curb this trend. Furthermore, the smuggling and illegal marketing of these products poses additional challenges, requiring increased oversight and strengthened public control policies.[8]

E-cigarette use in Brazil raises significant public health concerns, particularly given the false perception that these devices are less harmful than conventional cigarettes. Although e-cigarettes eliminate tobacco combustion, they still expose users to high concentrations of nicotine, heavy metals, and toxic compounds in aerosols generated by vaporization.[14]

Furthermore, attractive flavors and modern designs contribute to the popularity of these products among young people, creating an environment that encourages the early initiation and development of nicotine dependence. Evidence also shows that e-cigarette use can lead to conventional smoking. Thus, the use of these devices not only challenges the healthcare system, but also threatens the progress of historic anti-smoking policy in Brazil.[10,11]

Another important factor is the economic impact of smoking, which extends beyond health issues. The WHO warns that tobacco product use contributes to poverty by diverting essential financial resources such as those allocated to food and housing. While e-cigarette use appears to be associated with younger, Caucasian, and more educated men, conventional cigarette use has different characteristics.

The National Health Survey revealed that approximately 10% of Brazilians spend money on tobacco products and tend to have lower income and education levels than non-smokers. The National Cancer Institute indicates that cigarette smoking accounts for approximately 8% of per capita household income in Brazil. This finding highlights the relationship between tobacco spending and the limited resources required for other necessities. This contributes to a cycle of socioeconomic vulnerability that exacerbates public health problems and limits access to adequate care.[13]

Therefore, to improve the effectiveness of existing public policies, it is important to recognize that strategies for reducing the use of both types of cigarettes must differ. Brazil has adopted measures in response to this scenario, such as the Strategic Action Plan to Combat Chronic Noncommunicable Diseases (2011–2022). This plan aims to reduce smoking prevalence by 30%. However, as this target was not fully achieved, the commitment was renewed in the plan to combat noncommunicable diseases and injuries (2021–2030), which was launched in 2022. Smoking reduction is

Table 3. Weighted multivariable logistic regression analysis of current e-cigarette use, Vigitel 2023 (n = 16,093)

Variable	Adjusted OR	95% CI	*p* value
Age (per year increase)	0.93	0.92–0.94	< 0.01
Sex			
Male (vs female)	1.34	1.12–1.6	< 0.01
Education Level			
College (vs ≤ high school)	1.18	0.97–1.44	0.09
Postgraduate (vs ≤ high school)	0.88	0.62–1.24	0.46
Race/Color			
White (vs mixed-race)	1.29	1.05–1.58	0.015
Black (vs mixed-race)	0.91	0.66–1.26	0.58
Other (vs mixed-race)	1.12	0.73–1.72	0.6
Region			
Northeast (vs North)	0.74	0.55–0.98	0.038
Southeast (vs North)	1.21	0.93–1.57	0.15
South (vs North)	1.48	1.10–1.99	0.01
Center-West (vs North)	1.33	0.99–1.79	0.056

Model adjusted for age, sex, education level, ethnicity, and macroregion. Post-stratification weights (pesorakes) were applied. Reference categories: female; ≤ high school; mixed-ethnicity; North region. OR, odds ratio; CI, confidence interval.

a central objective of this plan. The plan emphasizes the necessity of stronger public policies, particularly considering the increased use of e-cigarettes, which are still considered a "less harmful" alternative to traditional cigarettes.[12]

Despite the National Health Surveillance Agency's bans since 2009, the use of electronic smoking devices continues to increase, suggesting that the current monitoring and control strategies are ineffective. Furthermore, the use of flavorings in cigarettes and the smuggling of these products are critical issues requiring a more intensive approach.[13]

Therefore, it is essential to redirect public policies toward e-cigarettes and intensify educational initiatives focused on health literacy for self-care, especially in regions and groups where e-cigarette use is most prevalent. Therefore, strengthening educational campaigns with an emphasis on demystifying the benefits of e-cigarettes is crucial for preventing the growth of e-cigarette use among young people and reducing the social and economic impact of smoking in Brazil.[13]

The results of Vigitel 2023 provide a solid foundation for understanding the profile of e-cigarette users in Brazil and can contribute to strengthening public policy. Continuous monitoring of factors associated with the use of these substances and implementation of educational interventions are essential to address the challenges posed by chronic, noncommunicable diseases in Brazil.[9,14]

In summary, the growth in e-cigarette use in Brazil, especially among young people, highlights the urgent need to strengthen health education initiatives as a central axis of prevention strategies. Investing in qualified, accessible, and ongoing information is essential to curb this trend and protect new generations from the risks associated with early nicotine exposure and the development of addiction.

CONCLUSION

In Brazil, current e-cigarette use was independently associated with younger age, male sex, Caucasian ethnicity, and residence in the southern region. These findings highlight the need for targeted public health policies and continuous surveillance using population-based monitoring systems. Therefore, it is imperative to strengthen public policies that limit access to e-cigarettes and expand educational initiatives to inform people concerning the associated health risks. In addition, monitoring the prevalence and determinants of e-cigarette use should be a priority in public health agendas to support preventive measures aligned with national and international tobacco control goals.

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Analysis of the outcome and costs of lower back pain should not only rely on electronic data but also use real-world experiences

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Dear Editors,

We enjoyed reading the article by Zanuto et al.[1] on the costs, classification, and effects of physical activity on lower back pain in 198 patients analyzed using the Nordic and Baecke questionnaire at baseline and 6, 12, and 18 months later. Lower back pain was associated with female sex and young age and incurred high costs for medical consultations, while cycling was much cheaper. Although this study is noteworthy, several points must be discussed.

First, the data were partly extracted from the electronic medical records of the included patients. However, electronic data have the disadvantage that data may be missing, the extracted data may be inconsistent, it is not easy to check the accuracy of the data, and desirable new data can no longer be generated. It is important to know how many patients had to be excluded because of missing or incorrect data.

The second issue is the discrepancy between the aims of the study (analyzing the cost of chronic lower back pain and its correlates in adults during an 18-month follow-up period) and the assessment of musculoskeletal symptoms such as pain, formication, or numbness in the neck, shoulder, upper back, elbows, and wrists/hands. These body regions cannot be considered to be related to the lower back; therefore, patients with symptoms related to the upper limbs, neck, and upper back should be excluded from the analysis. The inclusion of this data may massively bias the results, especially in cases in which no other symptoms in the lower spine have been reported in addition to these symptoms. Patients with these types of symptoms should be excluded from the study.

Third, the cost of diagnostic and therapeutic management was calculated by reviewing the demand for services in medical records. However, it is possible that patients obtain their analgesic medication via the Internet or the black market. In addition, many patients resort to alternative treatments, which are also not recorded in the medical records. Therefore, their costs do not appear in the medical records, suggesting that the true cost of treating chronic lower back pain is much higher. If lower back pain is a psychosomatic manifestation of depression and is treated with psychotherapy, these costs will also not appear in the total costs.

Fourth, it was unclear why television viewing was included in the analysis of physical activity. Watching television usually takes place while sitting or lying down and is hardly associated with physical activity. Therefore, this item should be excluded from the Baecke questionnaire.

Fifth, the actual cause of the lower back pain was not included in the analysis. Lower back pain due to plasmacytoma, bone metastases, or spinal cord stroke may lead to results different from those of lower back pain due to viral infection, stress, or Elsberg's syndrome. Because the study results are highly dependent on the underlying cause of the lower back pain, the etiology should be considered in the analysis.

In summary, lower back pain should not be confused with neck pain, and the cause of lower back pain should be included in analyses when performing longitudinal studies.

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Christiaan Neethling Barnard — A controversial figure: Courage, innovation, and the global impact of the world's first human heart transplant

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In the early hours of May 26, 1968, Professor Euryclides de Jesus Zerbini and his associates performed the first human heart transplantation in Brazil. Years prior, the possibility of such operation had been proposed to him twice; however, he had considered it premature.

In December 3, 1967, Dr. Christiaan Neethling Barnard performed the first human-to-human heart transplantation worldwide. The following day, Dr. Zerbini began a series of meetings to prepare his team. As in several centers worldwide, the Brazilian team decided to pursue transplantation inspired by Barnard's achievement.[1]

Dr. Barnard was born in November 8, 1922, in the rural town of Beaufort West, South Africa, approximately 300 miles from Cape Town. He later moved to Cape Town to study Medicine at the University of Cape Town and worked in other towns before returning to Groote Schuur Hospital (GSH).[2]

He was later awarded a scholarship to the University of Minnesota in Minneapolis, United States, under the leadership of the renowned Professor Owen Wangensteen. There, he observed the pioneering use of cardiopulmonary bypass by Walton Lillehei and Richard Varco.

After 30 months in the United States, most of that time spent far from his family, as he was married to a nurse and had two young children, Dr. Barnard returned to Cape Town. He brought a heart-lung machine funded by a grant from the U.S. National Institutes of Health (NIH), and immediately initiated an open-heart surgery program at GSH.

In the early 1960s, he considered heart transplantation. In January 1964, Dr. James Hardy performed the first cardiac xenotransplantation in a human using a chimpanzee heart.[3] In addition to performing orthotopic heart transplants in dogs with his younger brother, Dr. Marius Barnard. He also traveled to the United States for 3 months to work with Dr. David Hume in Richmond, Virginia, gaining experience in immunosuppression for kidney transplantation. Coincidentally, Dr. Richard Lower recently transferred from Stanford to the same service, where he began an experimental heart transplantation program similar to that led by Dr. Norman Shumway at Stanford.

By late 1967, three American surgeons had announced their readiness to perform a heart transplant, or nearly attempted one: Dr. Shumway at Stanford, Dr. Lower in Richmond, and Dr. Adrian Kantrowitz at Maimonides Hospital in New York City.

After returning from Richmond, Dr. Barnard and Professor Velva Schrire, Chief of Cardiology at the GSH, selected the candidates for transplantation. Due to concerns that performing the first transplant in a non-white recipient during the apartheid era could be misinterpreted as experimenting on non-white patients, they decided that both the donor and recipient must be Caucasian. The recipient was a 53-year-old man with ischemic cardiomyopathy.

On the afternoon of Saturday, December 2, 1967, a 25-year-old woman, named Denise Darvall, was struck by a drinker and brought to GSH. After brain death was confirmed, her father consented to the donation of her heart and kidneys.

The transplantation was performed with the donor and recipient in adjacent operating rooms. As criteria for brain death had not yet been established, the team waited for the donor heart to stop beating before perfusing it via the heart-lung machine.

At the end of the procedure, after removing the aortic cross-clamp, Dr. Barnard attempted twice to wean the patient off the cardiopulmonary bypass, succeeding on the third attempt. The operation concluded at 6:15 a.m. on December 3, 1967.[2]

In the three Brazilian transplants Dr. Zerbini performed between 1968 and 1969, the heart was similarly perfused after circulatory arrest by inserting a cannula into the innominate artery and connecting it to a heart-lung machine.

Today, the original GSH building houses the Museum of the First Heart Transplant. The museum features a complete reconstruction of the operating rooms, Washkansky's recovery room, and Dr. Barnard's office, with numerous fascinating historical photographs.

A major early controversy arose after the surgery. As three American surgeons were on the verge of performing the first transplant (Shumway, Lower, and Kantrowitz), some accused Barnard of being reckless or insufficiently prepared. However, solid evidence showed that he had mastered surgical techniques in dogs and was trained in immunosuppression in Richmond. Ultimately, Barnard dared.[1,2]

Although Washkansky survived only 18 days, Barnard's achievements reverberated worldwide. His second patient, Philip Blaiberg, survived 19 months.

Barnard immediately became an international celebrity. He was received by the Mayor of New York City and appeared on American television with Adrian Kantrowitz and Michael DeBakey. He also traveled to Europe, where he met Sophia Loren and later claimed to have had an affair with actor Gina Lollobrigida.[1]

After divorcing his first wife, he married two younger, wealthy women, fathering two children with each of his three wives. Although cardiovascular surgery at GSH continued under his associates, including his brother Marius Barnard, constant international engagements increasingly removed him from daily clinical practice, and his personal life became a target of criticism.

Despite these developments, the challenges of early graft failure and severe rejection in the pre-cyclosporine era prompted Barnard and his junior Belgian colleague, Jacques Losman, to develop a heterotopic heart transplantation model in 1975. Although rarely used today, this technique played an important role.

Barnard retired early from GSH at age 61, citing arthritis. He has dedicated himself to public speaking, writing, and controversial involvement with a cosmetics company.

In June 2000, Prof. Alain Carpentier organized a congress in Paris, inviting all surviving pioneers and a group of "grand invités." During closing dinner at the Eiffel Tower, as I was looking for a table with a good view of Paris, someone waved at me. Upon approaching, I barely recognized Dr. Barnard, who had undergone nasal graft reconstruction following cancer. He told me, 'I am living in the best city in the world, Vienna, and taking care of the Christian Barnard Foundation.' The patient died on September 2, 2001, from an asthma attack while swimming in a hotel pool in Paphos, Cyprus.

How will Christiaan Barnard be remembered in retrospect? He will be remembered as the surgeon who had the courage to perform the world's first human heart transplant. To avoid criticism, he insisted on waiting for the donor heart to stop beating, a decision later introduced heterotopic heart transplantation, an innovative technique well-suited to the pre-cyclosporine era. Unfortunately, his personal life and public behavior led some colleagues to view him as a "playboy."

Therefore, in my opinion, these aspects should not detract from the contributions of this fascinating and charismatic individual, whom I had the privilege of meeting.

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3. a statement that the study protocol was endorsed by an Internal Review Board (Ethics Committee), including the date and number of the approval (in the case of original articles). This is required for absolutely all studies involving human subjects or patient data (such as medical records), in accordance with the Committee on Publication Ethics (COPE) guidelines, and even for case reports. A copy of the approval document must be submitted to the Journal;
4. each author should indicate a valid, up-to-date email address for contact;
5. a list of a minimum of five potential referees outside of the authors' institutions, who could be invited, at the Editor-in-Chief's discretion, to evaluate the manuscript.

General guidelines for original articles

The following are considered to be full-text original articles: clinical trials; cohort, case-control, prevalence, incidence, accuracy and cost-effectiveness studies; case series (i.e. case reports on more than three patients analyzed together); and systematic reviews with or without meta-analysis. These types of article should be written with a maximum of 3,500 words (from the introduction to the end of the conclusion).

Typical main headings in the text include Introduction, Methods, Results, Discussion and Conclusion. The authors can and should use short subheadings too, especially those concerning the reporting guideline items.

Trial and systematic review registration policy

São Paulo Medical Journal supports the clinical trial registration policies of the World Health Organization (WHO) and the International Committee of Medical Journal Editors (ICMJE) and recognizes the importance of these initiatives for registration and international dissemination of information on randomized clinical trials, with open access. Thus, since 2008, manuscripts on clinical trials are accepted for publication if they have received an identification number from one of the public clinical trial registration database (such as ClinicalTrials.gov and/or REBEC and/or the World Health Organization; the options are stated at http://www.icmje.org). The identification number should be declared at the end of the abstract. Articles describing systematic reviews must provide the protocol registration number from a reliable database, such as PROSPERO, Open Science Framework, Cochrane, Joanna Briggs and others. Articles presenting clinical trials or systematic reviews without registration protocols will be promptly rejected without peer review.

Results from cases with DNA sequences must be deposited in appropriate public databases. The protocol number or URL can be requested at any time during the editorial review. Publication of other research data in public repositories is also recommended, since it contributes towards replicability of research, increases article visibility and possibly improves access to health information.

Sample size

All studies published in SPMJ must present a description of how the sample size was arrived at. If it was a convenience or purposive sample, the authors must declare so and explain the characteristics of this sample and recruitment method. For clinical trials, for instance, it is mandatory to inform each of the three main values used to calculate sample size:

- power (usually 80% or more);
- level of significance (usually 0.05 or lower);
- clinically meaningful difference (effect size targeted), according to the main outcome measurement.

Regardless of study results (if "positive" or "negative"), the journal will probably reject articles of trials using underpowered samples, when sample size has not been properly calculated or the calculation has not been fully described as indicated above.

Abbreviations, acronyms and products

Abbreviations and acronyms must not be used, even those in everyday use, unless they are defined when first used in the text. However, authors should avoid them for clarity whenever possible. Drugs or medications must be referred to using their generic names (without capital letters), with avoidance of casual mention of commercial or brand names.

Interventions

All drugs, including anesthetics, should be followed by the dosage and posology used.

Any product cited in the Methods section, such as diagnostic or therapeutic equipment, tests, reagents, instruments, utensils, prostheses, orthoses and intraoperative devices, must be described together with the manufacturer's name and place (city and country) of manufacture in parentheses. The version of the software used should be mentioned.

Any other interventions, such as exercises, psychological assessments or educational sessions, should be described in enough details to allow reproducibility. The Journal recommends that the TIDieR reporting guidelines should be used to describe interventions, both in clinical trials and in observational studies.[13]

Supplementary material

Because supplementary material comprises documents that do not form part of the text of the manuscript, São Paulo Medical Journal will not publish it. The authors should cite an access link that allows readers to view the supplementary material.

Short communications

Short communications are reports on the results from ongoing studies or studies that have recently been concluded for which urgent publication is important. They should be structured in the same way as original articles. The authors of this kind of communication should explain, in the covering letter, why they believe that publication is urgent. Short communications and case reports must be limited to 1,000 words (from the introduction to the end of the conclusion).

Case reports, case series, narrative reviews and letters to the editor

Starting in June 2018, only individual case reports dealing with situations of public health emergencies will be accepted by *São Paulo Medical Journal*. Case reports that had already been accepted for publication up to May 2018 will still be published in a timely manner.

After initial evaluation of scope by the editor-in-chief, case reports, case series and narrative reviews will be considered for peer-review evaluation only when accompanied by a systematic search of the literature, in which relevant studies found (based on their level of evidence) are presented and discussed.[12] The search strategy for each database and the number of articles obtained from each database should be shown in a table. This is mandatory for all case reports, case series and narrative reviews submitted for publication. Failure to provide the search description will lead to rejection before peer review.

The access route to the electronic databases used should be stated (for example, PubMed, OVID, Elsevier or Bireme). For the search strategies, MeSH terms must be used for Medline, LILACS, and Cochrane Library. DeCS terms must be used for LILACS. EMTREE terms must be used for Embase. Also, for LILACS, the search strategy must be conducted using English (MeSH), Spanish (DeCS) and Portuguese (DeCS) terms concomitantly. The search strategies must be presented exactly as they were used during the search, including parentheses, quotation marks and Boolean operators (AND, OR, and NOT). The search dates should be indicated in the text or in the table.

Patients have the right to privacy. Submission of case reports and case series must contain a declaration that all patients gave their consent to have their cases reported (even for patients cared for in public institutions), in text and images (photographs or imaging examination reproductions). The Journal will take care to cover any anatomical part or examination section that might allow patient identification. For deceased patients whose relatives cannot be contacted, the authors should consult the Editor-in-Chief. All case reports and case series must be evaluated and approved by an ethics committee.

Case reports should be reported in accordance with the CARE Statement,[7] including a timeline of interventions. They should be structured in the same way as original articles.

Case reports must not be submitted as letters. Letters to the editor address articles that have been published in the *São Paulo Medical Journal* or may deal with health issues of interest. In the category of letters to the editor, the text has a free format, but must not exceed 500 words and five references.

FORMAT: FOR ALL TYPES OF ARTICLES

Title page

The title page must contain the following items:

1. Type of paper (original article, review or updating article, short communication or letter to the editor);
2. Title of the paper in English, which should be brief but informative, and should mention the study design.[14] Clinical trial, cohort, cross-sectional or case-control study, and systematic review are the most common study designs. Note: the study design declared in the title should be the same in the methods and in the abstract;
3. Full name of each author. The editorial policy of the *São Paulo Medical Journal* is that abbreviations of authors' names must not be used; therefore, we ask that names be stated in full, without using abbreviations;
4. Place or institution where the work was developed, city and country;
5. Each author should indicate the way his/her name should be used in indexing. For example: for "João Costa Andrade", the indexed name could be "Costa-Andrade J." or "Andrade JC", as preferred;
6. The author's professional background (Physician, Pharmacist, Nurse, Dietitian or another professional description, or Undergraduate Student); and his/her position currently held (for

example, Master's or Doctoral Student, Assistant Professor, Associate Professor or Professor), in the department and institution where he/she works, and the city and country (affiliations);

7. Each author should present his/her ORCID identification number (as obtained from HYPERLINK "http://www.orcid.org/" www.orcid.org);
8. Each author must inform his contribution, preferably following the CRediT system (see above in Authorship);
9. Date and venue of the event at which the paper was presented, if applicable, such as congresses, seminars or dissertation or thesis presentations.
10. Sources of financial support for the study, bursaries or funding for purchasing or donation of equipment or drugs. The protocol number for the funding must be presented with the name of the issuing institution. For Brazilian authors, all grants that can be considered to be related to production of the study must be declared, such as fellowships for undergraduate, master's and doctoral students; along with possible support for postgraduate programs (such as CAPES) and for the authors individually, such as awards for established investigators (productivity; CNPq), accompanied by the respective grant numbers.
11. Description of any conflicts of interest held by the authors (see above).
12. Complete postal address, e-mail address and telephone number of the author to be contacted about the publication process in the Journal (the "corresponding author"). This author should also indicate a postal address, e-mail address and telephone number that can be published together with the article. *São Paulo Medical Journal* recommends that an office address (rather than a residential address) should be informed for publication.

Second page: abstract and keywords

The second page must include the title and a structured abstract in English with a maximum of 250 words. References must not be cited in the abstract.

The following headings must be used in the structured abstract:

- Background – Describe the context and rationale for the study;
- Objectives - Describe the study aims. These aims need to be concordant with the study objectives in the main text of the article, and with the conclusions;
- Design and setting – Declare the study design correctly, and the setting (type of institution or center and geographical location);
- Methods – Describe the methods briefly. It is not necessary to give all the details on statistics in the abstract;
- Results – Report the primary results;
- Conclusions – Make a succinct statement about data interpretation, answering the research question presented previously. Check that this is concordant with the conclusions in the main text of the article;
- Clinical Trial or Systematic Review Registration – Mandatory for clinical trials and systematic reviews; optional for observational studies. List the URL, as well as the Unique Identifier, on the publicly accessible website on which the trial is registered.
- MeSH Terms - Three to five keywords in English must be chosen from the Medical Subject Headings (MeSH) list of Index Medicus, which is available at http://www.ncbi.nlm.nih.gov/sites/entrez?db=mesh.These terms will help librarians to quickly index the article.
- Author keywords - The authors should also add three to six "author keywords" that they think express the main article themes. These keywords should be different from the MeSH terms and preferably different from words already used in the title and abstract, so as to improve the discoverability of the article by readers doing a search in PubMed. They provide an additional chance for the article to be retrieved, read and cited. Combinations of words and variations (different wording or plurals, for example) are encouraged.

References

For any manuscript, all statements in the text that do not result from the study presented for publication in the *São Paulo Medical Journal* but from other studies must be accompanied by a quotation of the source of the data. All statements regarding health statistics and epidemiological data should generally be followed by references to the sources that generated this information, even if the data are only available electronically.

São Paulo Medical Journal uses the reference style known as the "Vancouver style," as recommended by the International Committee of Medical Journal Editors (ICMJE). Follow the instructions and examples at www.icmje.org, item "References", for the format.

In the text, the references must be numbered in the order of citation. The citation numbers must be inserted after periods/full stops or commas in sentences, and in superscript (without parentheses or square brackets). References cited in the legends of tables and figures must maintain sequence with the references mentioned in the text.

In the list of references, all the authors must be listed if there are up to and including five authors; if there are six or more, the first three should be cited, followed by the expression "et al." For books, the city of publication and the name of the publishing house are mandatory. For texts published on the internet, the complete uniform resource locator (URL) or address is necessary (not only the main home page of a website or link), so that by copying the complete address into a computer internet browser, the Journal's readers will be taken to the exact document cited, and not to a general website.

At the end of each reference, please insert the "PMID" number (for papers indexed in PubMed) and the link to the "DOI" number if available.

Authors are responsible for providing a complete and accurate list of references. All references cited in the text must appear in the reference list, and every item in the reference list must be cited in the text. Also, citations must be in the correct sequence.

Manuscripts that do not follow these guidelines for references will be returned to the authors for adjustments.

The reference list should be inserted after the conclusions and before the tables and figures.

Figures and tables

Images must be submitted at a minimum size that is reproducible in the printed edition. Figures should be sent at a resolution of 300 DPI and minimum size of 2,500 pixels (width) and be recorded in ".jpg" or ".tif" format. Images submitted in inadequate formats will not be accepted.

Images must not be embedded inside Microsoft PowerPoint or Microsoft Word documents, because this reduces the image size. Authors must send the images separately, outside of .doc or .ppt documents. Failure to send the original images at appropriate sizes leads to paper rejection before peer review.

Flowcharts are an exception: these must be drawn in an editable document (such as Microsoft Word or PowerPoint), and should not be sent as an image that can't be changed.

Figures such as bars of line graphs should be accompanied by the tables of data from which they have been generated (for example, sending them in the Microsoft Excel spreadsheets, and not as image files). This allows the Journal to correct legends and titles if necessary, and to format the graphs according to the Journal's style. Graphs generated from software such as SPSS or RevMan must be generated at the appropriate size, so that they can be printed (see above). Authors must provide internal legends/captions in correct English.

All the figures and tables should be cited in the text. All figures and tables must contain legends or titles that precisely describe their content and the context or sample from which the information was obtained (i.e. what the results presented are and what the kind of sample or setting was). The reader should be able to understand the content of the figures and tables simply by reading the titles (without the need to consult the text), i.e. titles should be complete. Acronyms or abbreviations in figure and table titles are not acceptable. If it is necessary to use acronyms or abbreviations inside a table or figure (for better formatting), they must be spelled out in a legend below the table or figure.

For figures relating to microscopic findings (i.e. histopathological results), a scale must be embedded in the image to indicate the magnification used (just like in a map scale). The staining agents (in histology or immunohistochemistry evaluations) should be specified in the figure legend.

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[3]Verifique com o consultor as opções de planos com reembolso.Planos de saúde empresarial, conforme as regras da ANS. Informações resumidas.

A comercialização dos planos respeita a área de abrangência dos produtos e das respectivas operadoras. A disponibilidade dos produtos pode variar de acordo com a região e a entidade de classe com a qual os proponentes mantêm o vínculo.

Os planos podem ser coparticipados. Para conhecer a tabela completa de procedimentos e valores de coparticipação, consulte a operadora.

Todas as informações referentes aos planos, incluindo condições, preços, rede de prestadores e sua abrangência geográfica, são de responsabilidade exclusiva das respectivas operadoras de saúde e poderão estar sujeitas a alterações por parte delas, mesmo após a contratação do plano, respeitadas as disposições contratuais e legais (Lei no 9.656/98). Janeiro.

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