RESEARCH ARTICLE

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Overall Survival in Breast Cancer Patients: Analysis of a 27-Year Historical Cohort

Marina Elias Rocha[1]*, Rosemar Macedo Sousa Rahal[1], Leonardo Ribeiro Soares[1], José Carlos Oliveira[2], Ruffo Freitas Junior[1,3]

Abstract

Background: This study aimed to analyzed overall survival and prognostic factors in a 27-year historical cohort of women with breast cancer in the Brazilian city of Goiânia. **Methods:** This retrospective cohort study used data from the population-based cancer registry in Goiânia, Goiás, Brazil, to evaluate overall survival between 1988 and 2015. Survival curves were constructed using the Kaplan-Meier method and compared with the log-rank test. Multivariate Cox regression analysis was performed to evaluate predictors of survival, with significance established at $p<0.05$. **Results:** The most common age group among the 7,395 women included in this study was 50-69 years (45.4%). The majority had localized breast cancer (62.4%) and the luminal A subtype (50.1%). The median survival was 122 months, with a 5-year overall survival rate of 83.1% and a 10-year overall survival rate of 65.5%. When evaluating ethnicity, survival was found to be greater for among white women compared to black women (mean of 120 months versus 110 months). In the Cox regression analysis, the following factors were found to be associated with decreased overall survival: age >70 years (HR: 1.33; $p<0.001$), histologic grade III (HR: 1.21; $p=0.042$), estrogen receptor-negative breast cancer (HR: 1.26; $p=0.010$), progesterone receptor-negative breast cancer (HR: 1.47; $p=0.041$), triple-negative subtype (HR: 2.36; $p=0.008$) and regional disease extension (HR: 1.73; $p=0.023$) or metastasis (HR: 2.67; $p=0.012$). **Conclusion:** During the study period, the overall survival rate in this cohort of women with breast cancer was 83.1% at five years and 65.5% at ten years. Different clinical, biological and tumor-related factors significantly affected prognosis in this population.

Keywords: Breast cancer- women's health- survival analysis- epidemiology

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Introduction

Breast cancer poses a significant challenge to global health, both due to its high incidence and mortality [1-3]. An estimated 73,610 new cases are expected for Brazil as a whole between 2023 and 2025, corresponding to an approximate rate of 66.54 new cases per 100,000 women over this three-year period. In 2020 alone, 17,825 deaths occurred, representing a mortality rate of 16.47 deaths per 100,000 women [3-5].

The high mortality rate from breast cancer in Brazil, as in other developing countries, is attributed to a combination of factors, particularly the lack of strategies aimed at early detection and treatment access barriers [6]. These aspects and the complexity of the subject were widely discussed in the AMAZONA study, which provided solid evidence of the impact of financial limitations in breast cancer survival rates within the Brazilian National Health System (SUS) when compared to the supplementary health sector [7, 8].

The proportion of the Brazilian population that depends on the SUS is as high as 80% [3, 9]. However, due to constraints in the public sector, breast cancer in this large segment of the population tends to be diagnosed when tumors are already locally advanced or metastatic. This delay in diagnosis affects the outcome of the disease and has a further significant impact on resource management within the public healthcare sector [6].

Few population-based studies have described breast cancer survival in low- and middle-income countries. Taking into consideration a 27-year database from a population-based cancer registry that received an uninterrupted flow of information, this study aimed to analyze overall survival and its associated factors in women diagnosed with breast cancer in midwestern Brazil.

Materials and Methods

This retrospective cohort study was conducted using data from the Goiânia population-based cancer registry. The target population consisted of women living in the city of Goiânia, Goiás, Brazil who were diagnosed with breast cancer between 1988 and 2015.

*[1]Advanced Center for Breast Diagnosis (CORA), Federal University of Goiás, Goiânia, GO, Brazil. [2]Goiânia Population-Based Cancer Registry, Goiás Anticancer Association, Goiânia, GO, Brazil. [3]Araújo Jorge Hospital, Goiás Association for the Combat of Cancer (ACCG), Goiânia, GO, Brazil. *For Correspondence: marinaeliasrochaenf@gmail.com*

Goiânia population-based cancer registry

Data were extracted from the cancer registry onto a form that encompassed sociodemographic aspects, making full use of the data contained in the registers. Whenever the variables collected required supplementary information or confirmation, the patient's records were accessed.

Study population

The total number of breast cancer cases registered between January 1988 and December 2015 amounted to 9,176 patients. Since duplicated cases, cases of breast cancer in males, cases from the municipality of Aparecida de Goiânia (greater metropolitan region) and cases of breast cancer in situ registered during the same period were excluded, the final study sample consisted of 7,395 patients.

Variables

The following variables were evaluated: age at the moment of diagnosis (classified as <50 years, 50-69 years or ≥70 years); ethnicity (self-reported as white, of mixed race or black); histologic grade according to the Bloom-Richardson grading system (grade I, II or III), histological tumor type (invasive ductal, invasive lobular or others); and extension of the disease (localized, regional extension or metastasis). The immunohistochemical expression of the estrogen (ER) and progesterone (PR) receptors was considered positive or negative as reported by each laboratory. HER2 expression was considered positive when the degree of positivity was expressed as 3+ or when confirmed by immunofluorescence. Tumor subtype was determined in accordance with the recommendations of the 15th St. Gallen International Breast Cancer Conference [10].

Survival analysis

In the survival analysis, the cut-off date for the time of follow-up or active search for the women was established as August 24, 2023. First, the data available in the registry database and/or in the patient's records were recovered. To complete the data with information on patients' vital status, a search was performed in the national death records, at the websites of the electoral register and the Municipal Department of Health and Social Care.

Statistical analysis

The database was constructed using Excel, version 2010 (Microsoft Corporation, Redmond, WA, USA). The frequencies of all the variables were calculated and an analysis of central tendency was performed to determine the mean age of the participants.

The statistical analysis of the data was performed using SPSS (Statistical Package for Social Sciences), version 2010. Data normality was verified using the Kolmogorov-Smirnov test. The patients' profiles were described using absolute (n) and relative frequencies (%) for the categorical variables and medians with minimum and maximum values for the continuous variables. Survival curves were constructed using the Kaplan-Meier method. The log-rank test was used for comparison between groups, taking the following variables into consideration: age group, histological type of tumor, histologic grade, immunohistochemical expression of ER, PR and HER2, tumor subtype, and extension of the disease. Multivariate Cox regression analysis was performed for the outcome (overall survival), adding the time of survival as a covariable. The final model was obtained using backward elimination, assuming a conditional inclusion probability of 0.05 to 0.10 for each predictor variable being included. Significance level was set at 5% for the entire statistical analysis ($p<0.05$).

Ethical aspects

The protocol of the present study was approved by the internal review boards of the Araújo Jorge Hospital (protocol number 1.629.547) and the Teaching Hospital of the Federal University of Goiás (protocol number 1.596.198).

Results

Over the 27-year period analyzed, a total of 9,176 patients were diagnosed with breast cancer. After application of the exclusion criteria, 7,395 patients remained in the study, resulting in an overall 5-year survival rate of 83.1% and a 10-year survival rate of 65.5% (Figure 1).

As shown in Table 1, 45.4% of the women with breast cancer were in the 50-69-year age group; in 53% of cases the woman's marital status was classified as being "in a stable relationship"; and 58.4% reported themselves as white. Regarding their clinical profile, 62.4% had localized breast cancer, while 90.6% had an invasive ductal carcinoma and 60.1% had a grade II tumor. In 50.1% of cases, tumor subtype was luminal A.

Table 2 shows survival time according to the different descriptive variables, with the median values highlighted. Median survival for the entire sample was 122 months. The factors shown to affect overall survival were age, ethnicity, tumor grade, extension of the disease and tumor subtype. Table 3 shows the association between the outcome overall survival and the predictors as evaluated according to a Cox multiple regression model. A statistically significant association was found between age at diagnosis and the outcome in all five of the models proposed.

Age at diagnosis was found to be significantly associated with an accumulated risk of death from breast cancer in women of 50 to 69 years of age (HR: 0.58; 95%CI: 0.52 – 0.63). Regarding ethnicity, women who self-reported as black had an HR of 1.33 (95%CI: 0.88 – 1.59). Grade I tumors proved to be a protective factor, with an HR of 0.70. The tumor subtype luminal A was found to represent a significant protective factor (HR: 0.25), while triple-negative tumors represented a risk factor (HR: 2.36). Finally, having the localized form of the disease was the strongest protective factor for overall survival compared to regional and metastatic disease, which had the highest risk factors for death.

Figure 2 shows the survival curves (in months) according to the factors found to be statistically significant: age group, ethnicity, tumor grade, extension of the disease, tumor subtype and ER-positivity. The log rank

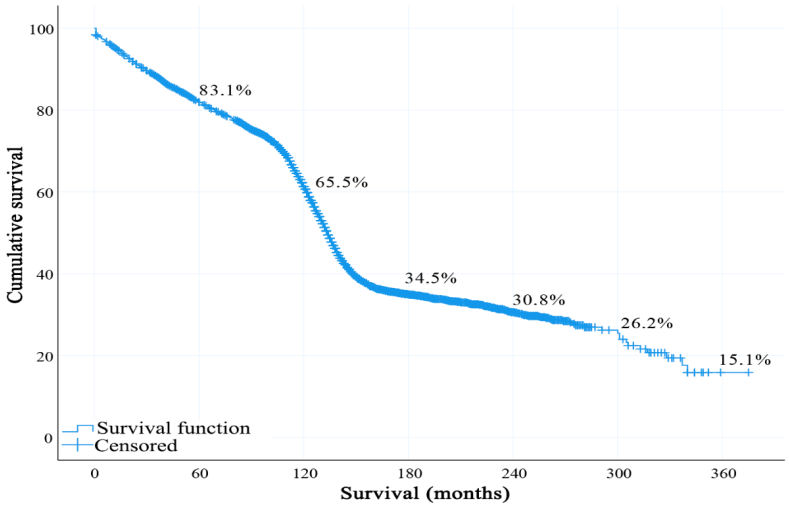

Figure 1. Overall Survival in Women with Breast Cancer

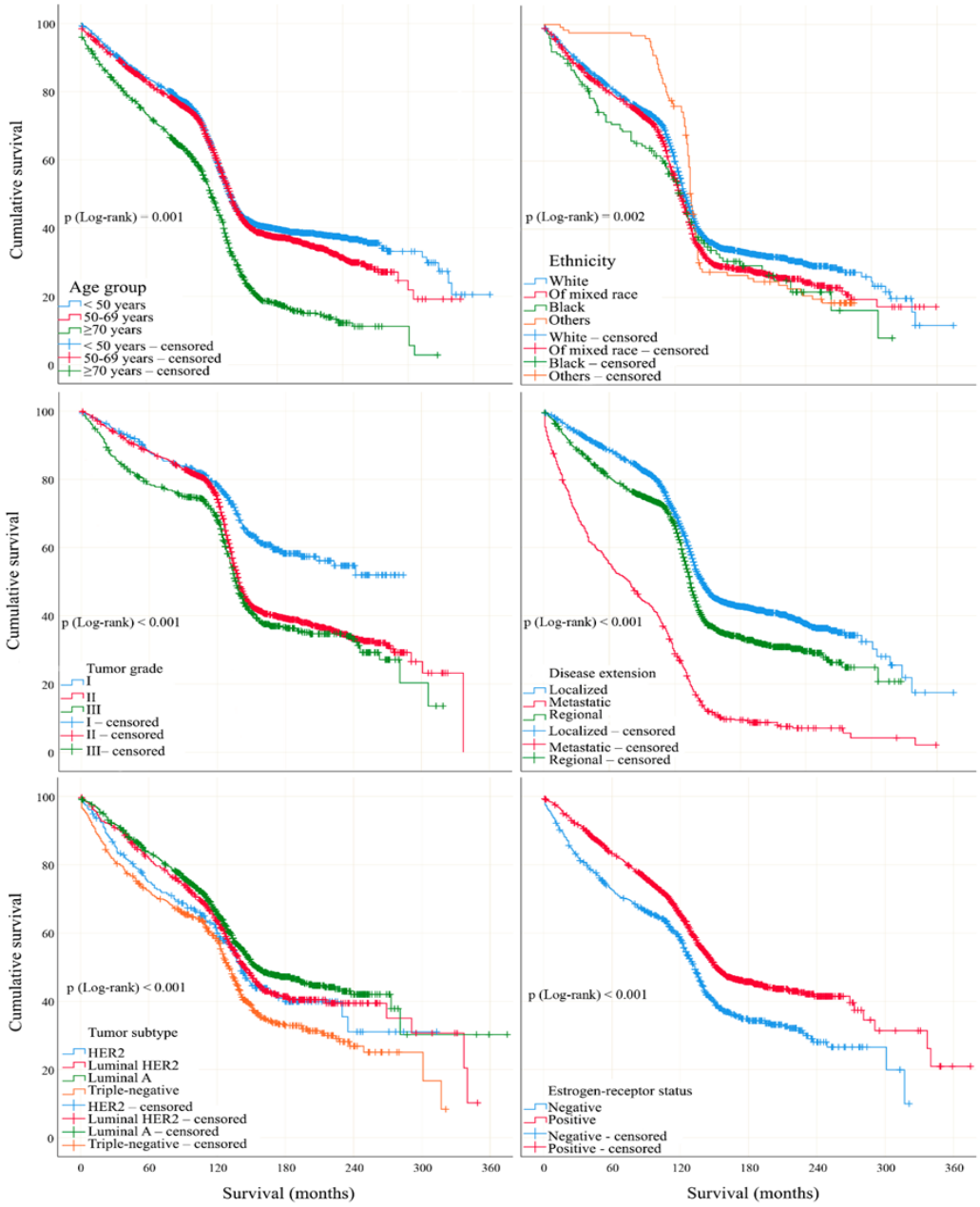

Figure 2. Breast Cancer Survival Curves as a Function of Age Group, Ethnicity, Tumor Grade, Disease Extension, Tumor Subtype and Estrogen Receptor Status.

Table 1. Sociodemographic Profile of the Study Sample of Women with Breast Cancer

Characteristics	n	%
Age Group		
< 50 years	2,876	39.4
50-69 years	3,319	45.4
≥70 years	1,109	15.2
Marital status		
Married	730	17.1
Divorced	159	3.7
In a stable relationship	2,257	53.0
Single	910	21.4
Widowed	204	4.8
Ethnicity		
White	2,817	58.4
Other	123	2.6
Of mixed race	1,725	35.8
Black	156	3.2
Disease extension		
Localized	3,679	62.4
Regional	1,6	27.1
Metastatic	621	10.5
Tumor type		
Invasive ductal	6,702	90.6
Invasive lobular	284	3.8
Other	409	5.5
Tumor grade		
I	494	16.3
II	1,82	60.1
III	692	22.9
Laterality		
Right	2,983	48.8
Left	3,076	48.8
Treatment		
No	48	1.6
Yes	2,999	98.4
Estrogen receptor		
Negative	874	29.2
Positive	2,115	70.8
Progesterone Receptor		
Negative	1,133	37.9
Positive	1,856	62.1
HER2		
Negative	2,09	70.3
Positive	884	29.7
Tumor subtype		
HER2	254	8.5
Luminal HER2	632	21.3
Luminal A	1,489	50.1
Triple-negative	597	20.1
Vital status		
Deceased	4,036	58.0
Living	2,919	42.0

n, absolute frequency; %, relative frequency

p-value for age group was 0.001, indicating that survival decreases with age, particularly for the group of patients over 50 years of age. Furthermore, as shown, a significant association was found between ethnicity and survival (log rank p=0.002).

Discussion

This study presents one of the most robust analyses of breast cancer survival in Brazil and is based on consolidated data from a population-based cancer registry covering a 27-year period (1988-2015). A review of the registry database revealed a total of 9,176 patients with breast cancer, with 7,395 of these being included in this study. Five- and ten-year overall survival was, respectively, 83.1% and 65.5%, with a median survival of 122 months. This increase in survival in the Brazilian population is remarkable compared to the 1995-1999 and 2005-2009 periods for which 5-year survival rates were 78% and 87%, respectively [3]. Similar results were found in other studies conducted in Brazil. In the state of Rio Grande do Sul, a hospital-based cohort study reported a 5-year survival rate of 87.7% and a 10-year survival rate of 78.7% [11]. In the AC Camargo Breast Cancer Referral Center in São Paulo, a study involving over 5,000 patients showed an increase in overall survival from 83% to 90% in the period from 2000 to 2012 [12]. In the state of Acre, data from a high-complex oncology unit in the state capital, Rio Branco, showed a 5-year survival rate of 87.3% between 2007 and 2012 [13]. Taken together, these data reflect the stabilization of the survival curves in the country, both in the north and in the south and southeast despite certain geographical and socioeconomic variations between these regions.

Likewise, breast cancer survival has also increased in the majority of developed countries. In the United States, data from the Surveillance, Epidemiology, and End Results (SEER) Program showed a survival rate of 90.8% for the 2013-2019 period [1, 14]. A similar survival rate has also been reported in Australia [1, 14]. Conversely, survival rates are lower in countries such as Malaysia (68%), India (60%), Mongolia (57%), South Africa (53%) and in the province of Shandong in China (69%) [8, 14, 15]. These differences are associated with early diagnosis of the disease and, principally, with advances in treatment including access to locoregional therapies and systemic drugs [14-16]. In Brazil, for example, there was a delay of almost 10 years (from 2005 to 2013) in the incorporation of adjuvant Trastuzumab into the public health system; with an estimated 5,223 deaths resulting from this delay [16].

In the present study, the predominant age group

Table 2. Descriptive Statistics on Breast Cancer Survival Time in Months, According to each Predictive Factor

	Mean	Standard Deviation	Median	Minimum	Maximum
Age Group					
< 50 years	127.40	66.63	124.00	1.00	375.00
50-69 years	122.10	64.04	123.00	1.00	348.00
≥70 years	100.86	60.80	110.00	1.00	327.00
Marital status					
Married	80.71	47.63	86.00	1.00	201.00
Divorced	92.20	44.97	96.00	1.00	196.00
In a stable relationship	133.23	65.87	131.00	1.00	344.00
Single	109.70	64.00	118.00	1.00	349.00
Widowed	73.24	46.02	84.00	1.00	231.00
Ethnicity					
White	119.77	64.79	120.00	1.00	375.00
Other	153.63	61.55	134.00	15.00	284.00
Of mixed race	112.19	62.95	114.00	1.00	359.00
Black	110.56	72.75	114.00	1.00	319.00
Disease extension					
Localized	131.72	62.88	128.00	1.00	375.00
Regional	121.91	65.19	126.00	1.00	327.00
Metastatic	80.97	64.18	77.50	1.00	359.00
Tumor type					
Invasive ductal	120.56	64.52	121.00	1.00	375.00
Invasive lobular	131.82	62.35	133.00	1.00	306.00
Others	118.23	73.39	126.00	1.00	349.00
Tumor grade					
I	135.27	59.92	137.00	1.00	284.00
II	136.19	62.35	132.00	1.00	337.00
III	121.65	67.33	127.00	1.00	319.00
Treatment					
No	75.73	41.53	94.00	6.00	139.00
Yes	106.73	63.49	106.00	1.00	340.00
Estrogen receptor					
Negative	109.81	68.20	120.00	1.00	321.00
Positive	120.98	61.52	123.00	1.00	375.00
Progesterone receptor					
Negative	111.73	68.03	120.00	1.00	375.00
Positive	121.35	60.72	123.00	1.00	349.00
HER status					
Negative	117.81	63.55	122.00	1.00	375.00
Positive	117.88	64.52	123.00	1.00	349.00
Tumor subtype					
HER2	112.04	66.45	120.00	1.00	313.00
Luminal HER	120.07	63.61	124.00	1.00	349.00
Luminal A	121.11	60.92	123.00	1.00	375.00
Triple-negative	110.05	69.04	121.00	1.00	321.00

was 50-69 years, representing 45.4% of the cases, with a median survival of 123 months for this group. This median value was similar for the group of women under 50 years of age, who represented 39.4% of the sample studied. These findings corroborate data from the literature [17-19]. In the women over 70 years of age, median survival was 110 months, and this was probably related to clinical comorbidities, advanced stages of the disease and restrictions in access to the gold-standard treatment [20].

In Brazil, data on ethnicity are defined based on self-

Table 3. Cox Multiple Regression between Overall Survival and Predictors in Women with Breast Cancer

	HR	95%CI		p-value
		Lower limit	Upper limit	
Age at diagnosis				
< 50 years	0.60	0.56	0.67	0.001
50 - 69 years	0.58	0.52	0.63	0.008
≥70 years	1.33	1.05	2.01	<0.001
Ethnicity				
White	0.68	0.37	0.80	0.025
Of mixed race	0.77	0.67	1.76	0.310
Black	1.33	0.88	1.59	0.719
Tumor type				
Invasive lobular	0.28	0.09	0.90	0.332
Invasive ductal	0.30	0.07	1.18	0.842
Others	1.35	1.09	2.11	0.021
Tumor grade				
I	0.70	0.35	0.97	0.038
II	1.32	1.10	1.66	0.021
III	1.21	1.14	2.74	0.042
ER/PR/HER				
ER-negative	1.26	1.21	2.09	0.010
PR-negative	1.47	1.07	1.64	0.041
HER-negative	0.29	0.11	1.06	0.121
Tumor subtype				
Luminal A	0.25	0.09	0.69	0.039
Luminal *HER2*	0.21	0.44	1.10	0.769
HER2	0.21	0.15	1.02	0.651
Triple-negative	2.36	1.43	4.84	0.008
Disease extension				
Localized	0.29	0.08	0.93	0.039
Regional	1.73	1.14	1.98	0.023
Metastatic	2.67	2.43	5.11	0.012

HR, Hazard ratio; CI, confidence interval; ER, estrogen receptor; PR, progesterone receptor; HER, *HER2* status

reported skin color [21]. Most individuals in this sample (58.4%) considered themselves to be white and survival was greater in this group compared to those who self-reported their ethnicity as being of mixed race or black. In the multivariate analysis, being black was associated with a greater risk of death, which corroborates the extensive literature on the subject [3, 6, 17, 19, 22]. Issues regarding access to healthcare services due to cultural and socioeconomic problems could influence this finding. In addition, the possibility cannot be ruled out that there may be biological and tumor-related factors intrinsic to this population [23, 24].

Confirming data in the literature regarding tumor subtype, this study found that overall survival and progression-free survival are poorer in women with triple-negative tumors, these being the most aggressive, with higher rates of distant recurrence [25-28]. This emphasizes the importance of public policies in secondary prevention and breast cancer screening, enabling diagnosis to be made early and improving long term prognosis [29]. Likewise, clinical staging was confirmed as an important prognostic factor in breast cancer, with a reduction in overall survival in the patients diagnosed with locally advanced and/or metastatic disease [30]. In this respect and in agreement with the literature, patients with regional extension of the disease or metastases had poorer survival [25-28].

Socioeconomic inequalities directly impact breast cancer survival, as they determine clinical staging at diagnosis, adherence to therapeutic treatment, and continuity of care. Women in vulnerable contexts, with low income, low education levels, and living in rural areas, often arrive at services in advanced stages, with limited access to innovative therapies and greater exposure to financial risks. This scenario translates into lower overall and specific survival rates, demonstrating that socioeconomic status is not only a risk factor for disease development but also a critical determinant of the likelihood of cure or long-term disease control [31-33].

The limitations of this study include its retrospective design and those inherent to population-based studies.

To mitigate these limitations, patient survival was investigated individually on various search platforms, thus increasing the robustness of the data presented. Furthermore, whenever data were missing from the registry database, a search was performed directly in the relevant patient records at the referring institute to minimize missing data.

In conclusion, during the analysis period, the 5-year overall survival rate of women with breast cancer was 83.1%, with a 10-year overall survival rate of 65.5%. The factors that affected prognosis were age group, ethnicity, tumor type, histologic grade, estrogen and progesterone receptor positivity, tumor subtype and the extension of the disease.

Author Contribution Statement

MER, LRS, RMSR, JCO and RFJ conceived the original idea for this study. MER, LRS, RMSR, JCO and RFJ conducted the research. MER, LRS, RMSR, JCO and RFJ interpreted the results and wrote the first draft of the manuscript. All the authors contributed to revising the manuscript and approved the final version.

Acknowledgements

Approval

The present study was previously approved by the internal review boards of the Araújo Jorge Hospital (reference # 1.629.547) and the Teaching Hospital of the Federal University of Goiás (reference # 1.596.198).

Ethical Declaration

The present study was previously approved by the internal review boards of the Araújo Jorge Hospital (reference # 1.629.547) and the Teaching Hospital of the Federal University of Goiás (reference # 1.596.198).

Data Availability

The data that supports the findings of this study are available from the corresponding author upon reasonable request.

Conflict of Interest

None.

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