Impact of Inflammatory Markers on the Prognosis of Patients with Cancer Admitted to the National Cancer Institute with SARS-CoV-2 in the First Wave of the Pandemic in Brazil

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Impacto de Marcadores Inflamatórios no Prognóstico de Pacientes Oncológicos Internados no Instituto Nacional de Câncer com SARS-CoV-2 na Primeira Onda da Pandemia no Brasil

Impacto de los Marcadores Inflamatorios en el Pronóstico de Pacientes con Cáncer Ingresados en el Instituto Nacional del Cáncer con SARS-CoV-2 en la Primera Ola de la Pandemia en el Brasil

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ABSTRACT

Introduction: The intense inflammatory process triggered by COVID-19 has been pointed out by several authors. **Objective:** To evaluate the impact of inflammatory markers on the prognosis of patients with solid tumors hospitalized with SARS-CoV-2/COVID-19 in the first wave of the pandemic in Brazil. **Method:** A cohort study of patients >18 years old with cancer, hospitalized at a public cancer treatment reference center, with SARS-CoV-2/COVID-19 from March to September 2020. The following inflammatory markers were analyzed: neutrophil-lymphocyte ratio (NLR), derivation of the neutrophil-lymphocyte ratio (dNLR) and platelet-lymphocyte ratio (PLR). The outcome of this study was death during hospitalization. The association between the independent variables and the outcome was analyzed using univariate and multiple logistic regression. **Results:** Of the 185 patients, most were aged < 65 years (61.1%), had performance status (PS) ≥ 2 (82.4%) and were in cancer treatment (80.0%). Breast cancer was the most frequent tumor (26.5%). For the majority of the cases, the length of hospital stay was ≥ 5 days (59.5%) and occurred in the intensive treatment unit (84.3%). During hospitalization, 86 (46.5%) patients progressed to death. In the adjusted analysis only high NLR (≥ 4.44) was associated with the risk of death (OR 3.54; 95% CI; 1.68 - 7.46; p = 0.001). **Conclusion:** NLR proved to be an important prognostic marker, and levels above its median value were related to an increased risk of death during hospitalization.

Key words: COVID-19; SARS-CoV-2; neoplasms; biomarkers; hospital mortality.

RESUMO

Introdução: O intenso processo inflamatório desencadeado pela covid-19 tem sido apontado por diversos autores. **Objetivo:** Avaliar o impacto de marcadores inflamatórios no prognóstico de pacientes com tumores sólidos internados com SARS-CoV-2/covid-19 na primeira onda da pandemia no Brasil. **Método:** Estudo de coorte com pacientes maiores de 18 anos com câncer, internados em um centro público de referência no tratamento oncológico, com SARS-CoV-2/covid-19, no período de março a setembro de 2020. Os seguintes marcadores inflamatórios foram analisados: razão neutrófilo-linfócito (RNL), derivação da razão neutrófilo-linfócito (dRNL) e razão plaqueta-linfócito (RPL). Foi considerado desfecho deste estudo a ocorrência de óbito durante a internação hospitalar. A associação entre as variáveis independentes e o desfecho foi analisada por meio de regressão logística univariada e múltipla. **Resultados:** Dos 185 pacientes, a maioria apresentava idade < 65 anos (61,1%), *performance status* (PS) ≥ 2 (82,4%) e estavam em tratamento oncológico (80,0%). O câncer de mama foi o tumor mais frequente (26,5%). Para a maior parte dos casos, o tempo de internação foi ≥ 5 dias (59,5%) e ocorreu em unidade de tratamento intensivo (84,3%). Durante a internação, 86 (46,5%) pacientes evoluíram para óbito. Na análise ajustada, apenas a RNL elevada (≥ 4,44) esteve associada ao risco de morrer (OR 3,54; IC 95%; 1,68 - 7,46; *p* = 0,001). **Conclusão:** A RNL se mostrou um importante marcador prognóstico, e níveis acima do seu valor mediano estiveram relacionados ao aumento do risco de morte durante a internação hospitalar.

Palavras-chave: COVID-19; SARS-CoV-2; neoplasias; biomarcadores; mortalidade hospitalar.

RESUMEN

Introducción: El papel de la inflamación desencadenada por la COVID-19 ha sido señalado por varios autores. **Objetivo:** Evaluar el impacto de los marcadores inflamatorios en el pronóstico de pacientes con tumores sólidos hospitalizados por SARS-CoV-2/COVID-19 en la primera ola de la pandemia en el Brasil. **Método:** Estudio de cohorte con pacientes >18 años con cáncer, ingresados en un centro público de referencia en el tratamiento del cáncer, con SARS-CoV-2/COVID-19 de marzo a septiembre de 2020. Se evaluaron los siguientes marcadores inflamatorios: relación neutrófilos-linfocitos (RNL), derivación de la relación neutrófilos-linfocitos (dRNL) y relación plaquetas-linfocitos (RPL). Se consideró como desenlace de este estudio la ocurrencia de muerte durante la hospitalización. La asociación entre las variables independientes y el desenlace se analizó mediante regresión logística univariada y múltiple. **Resultados:** De los 185 pacientes hospitalizados, la mayoría tenía una edad < 65 años (61,1%), un *performance status* (PS) ≥ 2 (82,4%) y estaban en tratamiento oncológico (80,0 %). El cáncer de mama fue el tumor más frecuente (26,5%). Para la mayoría de los casos, el tiempo de hospitalización fue ≥ 5 días (59,5%) y ocurrió en la unidad de tratamiento intensivo (84,3%). Durante la hospitalización, 86 (46,5%) pacientes terminaron falleciendo. En el análisis ajustado, solo una RNL alta (≥ 4,44) se asoció con el riesgo de muerte (OR 3,54; IC 95%; 1,68 - 7,46; p = 0,001). **Conclusión:** La RNL demostró ser un importante marcador pronóstico, y los niveles por encima de su valor medio se relacionaron con un mayor riesgo de muerte durante la hospitalización.

Palabras clave: COVID-19; SARS-CoV-2; neoplasias; biomarcadores; mortalidad hospitalaria.

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INTRODUCTION

In December 2019, a cluster of pneumonia cases caused by a newly identified type of coronavirus was reported in Wuhan, Hubei Province, China. This was initially named as novel coronavirus (2019-nCoV) on 12 January 2020 by the World Health Organization (WHO). A few months later, after the exponential increase in cases worldwide, more specifically on February 11, 2020, severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2) was designated coronavirus disease 2019 (COVID-19) by the who International Viral Taxonomy Commitee[1]. Soon after, the disease was declared by the WHO a public health emergency of international importance on January 30, 2020[2]. From the beginning of the pandemic until June 2023, more than 694.6 million confirmed cases of COVID-19 and 6.9 million deaths were recorded worldwide. In Brazil, which occupied the 5th position in the world in number of occurrences, 37.8 million cases and 705.37 thousand deaths from the disease were recorded[3]. A study[4] that analyzed data from the Influenza Epidemiological Surveillance Information System (SIVEP-Gripe), which records cases hospitalized in Brazil for severe acute respiratory infections (SARI), pointed out that, at the time of the first wave of the disease in the country (from February 25, 2020 to November 5, 2020), 325,857 cases were recorded, with 113,432 deaths, which corresponds to a mortality rate of 34.81%.

Cancer patients are more likely to present complications and progress to death when affected by COVID-19. A pioneering study conducted at the National Cancer Institute (INCA), Rio de Janeiro,Brazil[5], involving 181 cancer patients affected by COVID-19 in the first months of the pandemic, showed that 60 (33.1%) patients died due to complications of COVID-19. The lethality was significantly higher in patients aged over 75 years ($p = 0.002$), metastatic cancer ($p < 0.001$), two or more sites of metastases ($p < 0.001$), lung metastases ($p < 0.001$) or bone metastases ($p = 0.001$), non-curative treatment or supportive treatment ($p < 0.001$), high levels of C-reactive protein ($p = 0.002$), hospitalization due to COVID-19 ($p = 0.009$) and use of antibiotics ($p = 0.02$). In this study, after multivariate analysis, cases admitted due to symptoms of COVID-19 ($p = 0.027$) and with two or more sites of metastasis ($p < 0.001$) had a higher risk of dying from COVID-19. A systematic review with meta-analysis[6] that included 81 studies, involving 61,532 cancer patients, showed that between 4% and 61% died from complications of COVID-19. Patients with cancer and SARS-CoV-2 infection had a higher risk of death than patients without cancer. In addition, when compared to controls, younger patients with lung cancer and hematological cancer had a worse prognosis[6].

Recently, hematological inflammatory biomarkers such as neutrophil-lymphocyte ratio (NLR), neutrophil-lymphocyte ratio derivation (dNLR), and platelet-lymphocyte ratio (PLR) have been associated with prognosis in patients with oncological, cardiovascular, and infectious diseases[7]. In COVID-19, these markers can be a useful tool for risk determination and optimal utilization of limited health resources. Several authors have pointed to the importance of NLR as a potential prognostic tool in COVID-19. However, there is no consensus on its association with disease severity and risk of death[8]. Several Brazilian studies have analyzed the importance of these markers as predictors of severity or death in patients with COVID-19[9-15]. However, to date, no national study has evaluated its usefulness in cancer patients.

This study aims to evaluate the impact of inflammatory markers on the prognosis of patients with solid tumors hospitalized with SARS-CoV-2/COVID-19 in the first wave of the pandemic in Brazil.

METHOD

A retrospective cohort study with cancer patients older than 18 years, admitted to Inca units, from March to September 2020, with SARS-CoV-2/COVID-19 infection.

Participants included in the study met the following criteria: patients who tested positive for SARS-CoV-2 in the real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay on material collected by nasal or oropharyngeal *swab*; hospitalization between March 1, 2020, and September 30, 2020. Patients with hematological cancer and no available complete blood count result were excluded from the study. Samples were collected at hospital admission in patients with symptoms of COVID-19 or immediately after clinical suspicion in patients hospitalized for reasons unrelated to COVID-19.

The information was obtained from the electronic and physical medical records of the patients. The sociodemographic and lifestyle characteristics used were sex, race/skin color, age (categorized as: < 65 years or ≥ 65 years), marital status (categorized as: with or without a partner), education (categorized as: < 8 years or ≥ 8 years), alcohol and tobacco consumption (current situation and preponderant occurrence throughout life). Among the clinical factors potentially associated with death, the following were collected: presence of metastasis, body mass index (BMI) (categorized as: eutrophic or other categories), Charlson comorbidity

index, systemic arterial hypertension and primary tumor site (categorized as: breast, gynecological, abdomen, bone and connective tissue, prostate, head and neck, lung and central nervous system (CNS)). The factors related to hospitalization for COVID-19 analyzed were: previous hospitalization for other causes, hospitalization in the intensive care unit (ICU), total hospitalization time (categorized by the median value in: ≥ 5 days or < 5 days), oncological treatment phase at hospital admission (treatment-naïve or treatment at some point in life), performance status (PS) in hospitalization (categorized in: 0 or 1 or ≥ 2), cardiovascular events, hemodialysis, ventilatory support (none, use of supplemental O_2 or invasive mechanical ventilation (IMV)) and inflammatory markers (categorized by the median value in: NLR < 7.8 or ≥ 7.8), PLR (< 340.4 or ≥ 340.4) and dNLR (< 4.4 or ≥ 4.4).

Inflammatory markers were obtained from the result of the complete blood count routinely collected, using the following equations: NLR = absolute neutrophil count/absolute lymphocyte count; dNLR = absolute neutrophil count (absolute leukocyte count - absolute neutrophil count); PLR = absolute platelet count/absolute lymphocyte count. Death during hospitalization was considered as outcome.

Descriptive analysis of the study population was performed using measures of central tendency (median) and dispersion (interquartile range) for continuous variables, and frequency distribution for categorical variables. The association between independent variables and death was verified by univariate and multiple logistic regression, considering values of $p < 0.05$ as significant. The SPSS program version 23.0[16] was used to perform the statistical analyzes.

This study was approved by the Research Ethics Committee (REC) under opinion number 3.992.183 (CAAE: 30910020.8.0000.5274) on 04/27/2020, according to Resolution nº. 466, of 2012[17] of the National Health Council (NHC).

RESULTS

185 hospitalized patients were included during the study period. In all, 86 (46.5%) died during hospitalization.

The sociodemographic and lifestyle factors associated with the risk of death during hospitalization due to SARS-CoV-2/COVID-19 are shown in Table 1. Most were white (47%), female (62.7%), aged < 65 years (61.1%), without a partner (55.2%), with ≥ 8 years of schooling (65.7%), consumed alcohol (53.0%) or tobacco (51.3%) and was resident in the city of Rio de Janeiro (50.3%). Elderly patients had a higher risk of death compared to younger patients (OR = 2.20; 95% CI; 1.20 - 4.01; p = 0.010) (Table 1).

Most patients had non-metastatic disease (70.6%), were overweight or obese (68.3%), had no comorbidities (53.3%) or systemic arterial hypertension (55.0%), and the most frequent underlying disease was breast cancer (26.5%). These factors were not statistically associated with death in this population (Table 2).

Most patients had been previously hospitalized for other causes (58.4%), and required ICU admission (84.3%), with hospital stay of five days or more (59.5%), at some stage of cancer treatment (80.0%), with PS ≥ 2 (82.4%), without cardiovascular events (94.6%) or need for hemodialysis (87.5%). Ventilatory support was used by most patients, being supplementation of O_2 (23.2%) and IMV (28.6%). Among the factors related to hospital admission, those *admitted* to the ICU (p = 0.001), with a total length of stay of less than five days (p = *0.003)*, with PS ≥ 2 (p = 0.036), with a history of cardiovascular events (p = 0.045), on hemodialysis (p = 0.020) and with *ventilatory* support (p < 0.001) were associated with a higher risk of death during hospitalization. Regarding inflammatory markers, in the univariate analysis, an increased risk was observed when NLR ≥ 7.78 (p < 0.001) and dNLR ≥ 4.44 (p < 0.001) (Table 3).

In the multiple analysis, after adjustment for ventilatory support, presence of cardiovascular events and comorbidities, among the inflammatory markers, only NLR was independently associated with death during hospitalization. Patients with NLR ≥ 4.44 had a 3.54 -fold increased risk of death compared to those with NLR < 4.44 (OR = 3.54; 95% CI 1.68 - 7.46, p = 0.001) (Table 4).

DISCUSSION

This study analyzed 185 patients with solid tumors who presented COVID-19 at hospital admission or immediately after clinical suspicion in those already hospitalized for reasons unrelated to COVID-19. The cases refer to the first wave of the pandemic in Brazil. Patients with higher NLR values at the time of diagnosis of COVID-19 were more severe, with an almost four times higher risk of death during hospitalization, when compared to those with lower values of this marker. In addition, PLR did not show a statistically significant association with the risk of dying and dNLR showed an association only in the univariate analysis, losing significance in the adjusted analysis.

Other international studies have pointed to the usefulness of various inflammatory indices to predict

Table 1. Sociodemographic and lifestyle factors associated with the risk of death during hospitalization from SARS-CoV-2/COVID-19 (N=185)

Variable	N (%)	Death during hospitalization		OR (95% CI)	*p*
		Yes (%)	No (%)		
Sex/Gender					
Female	116 (62.7)	54 (62.8%)	62 (62.6)	Reference	
Male	69 (37.3)	32 (37.2%)	37 (37.4)	0.99 (0.55 – 1.81)	0.982
Race/color/ethnicity:					
White	86 (47.0)	44 (51.2)	42 (42.9)	Reference	
Non-white	99 (53.0)	42 (48.8)	56 (57.1)	0.72 (0.40 – 1.28)	.0.260
Age					
<65 years old	113 (61.1)	44 (51.2)	69 (69.7)	Reference	
≥ 65 years old	72 (38.9)	42 (48.8)	30 (30.3)	2.20 (1.20 – 4.01)	**00.010**
Marital Status					
Without a partner	100 (55.2)	51 (60.7)	49 (50.5%)	Reference	
With a partner	81 (44.8)	33 (39.3)	48 (49.5)	0.66 (0.37 – 1.19)	0.170
Education					
≥8 years of school	115 (65.7)	55 (67.1)	60 (64.5)	Reference	
<8 years of study	60 (34.3%)	27 (32.9)	33 (35.5)	0.89 (0.48 – 1.67)	0.722
Alcohol consumption					
No	79 (53.0)	39 (54.2)	40 (51.9)	Reference	
Yes (contact with alcohol at some point)	70 (47.0)	33 (45.8)	37 (48.1)	0.82 (0.48 – 1.74)	0.786
Tobacco consumption					
No	81 (51.3)	35 (47.9%)	46 (54.1)	Reference	
Yes (contact with tobacco at some point)	77 (48.7)	39 (45.9)	38 (52.1)	1.28 (2.40 - 0.68)	0.439
Place of residence					
City of Rio de Janeiro	93 (50.3)	45 (52.3)	48 (48.5%)	Reference	
Other cities	92 (49.7)	40 (47.7)	51 (51.5)	0.86 (0.48 – 1.53)	0.602

Captions: OR = *odds ratio*; CI = confidence interval.

Note: The statistically significant variable is highlighted in bold.

mortality in patients with COVID-19[4-6]. In Brazil, similarly, the absolute number of leukocytes[9,14], neutrophils[9,14], lymphocytes[9,11,14], basophils[11], hematocrit[11], hemoglobin1[4], NLR[9,11,15], dNLR[15], PLR[11-14], neutrophil-platelet ratio (NPR)[11,15], monocyte-lymphocyte ratio (MLR)[9] and systemic inflammation index (SII)[11,15] have been predictors of severity, need for ICU admission or death in different scenarios[9,11-15]. In contrast, one study showed that NLR was not associated with disease severity or death[10]. It is important to highlight that none of these studies included patients exclusively with cancer and COVID-19 and that, with regard to NLR, there is no uniformity among these authors in the definition of the cutoff points used: 6.13[9], 9.94[11], or as a continuous variable[15]. In this study, which exclusively included patients with solid tumors, the median value (4.44) was used as the cutoff point, which may have underestimated the risk of death. In a systematic literature review including 21 international studies involving cancer patients, the cutoff points for predicting mortality ranged from 3,19-11,75[8].

Similarly to the current study, other authors observed that increased dNLR and PLR values were not independent factors associated with death. However, NLR was also not a predictor of death, and only SII[18] remained in the adjusted analysis model.

In the present study, bivariate analysis showed that the risk of dying was influenced by factors classically described as associated with the prognosis of patients with COVID-19, such as age ≥ 65 years, current ICU stay, total length of stay < 5 days, PS ≥ 2, presence of cardiovascular

Table 2. Clinical factors associated with death (N=185)

Variable	N (%)	Death on admission		OR (95% CI)	*p*
		Yes (%)	No (%)		
Metastasis					
M0	120 (70.6)	49 (64.5)	71 (75.5)	Reference	
M1	50 (29.4)	27 (35.5)	23 (24.5)	1.70 (0.88 – 3.31)	0,117
BMI					
Eutrophic	46 (31.7)	21 (33.9)	32 (38,6)	Reference	
Overweight or obese	99 (68.3)	41 (66.1)	51 (61.4)	1.23 (0.62 – 2.43)	0.562
Comorbidity (Charlson)					
No comorbidity	96 (53.3)	21 (25.0)	37 (38.5)	Reference	
With comorbidity	84 (46.7)	63 (75.0)	59 (61.5)	1.88 (0.99 – 3.58)	0.054
Arterial hypertension					
No	99 (55.0)	42 50.0	57 (59.4)	Reference	
Yes	81 (45.0)	42 50.0	39 (40.6)	1.46 (0.81 – 2.34)	0.208
Primary tumor type					
Breast	49 (26.5)	23 (26.7)	26 (26.3)	Not calculated	0.786
Gynecologic cancer*	32 (17.3)	14 (16.3)	18 (18.2)		
Abdomen**	40 (22.2)	21 (24.4)	20 (20.2)		
Bone and connective tissue***	20 (10.8)	9 (10.5)	11 (11.1)		
Prostate	17 (9.2)	7 (8.1%)	10 (10.1)		
Head and neck cancer****	15 (8.1)	5 (5.8)	10 (10.1)		
Lung	8 (4.3)	6 (7.0)	2 (2.0)		
CNS	3 (1.6)	1 (1.2)	2 (2.0)		

Captions: OR = *odds ratio*; CI = confidence interval; BMI = body mass index; CNS = central nervous system.

(*) cervix (21); uterine body (8); vulva (2); ovary (1).
(**) intestine (20); stomach (5); bladder (4); liver (3); anal canal (2); pancreas (2); kidneys (1); bile ducts (1); peritoneum (2); retroperitoneum (1).
(***) non-melanoma skin (8); soft tissue (6); bone (4); melanoma skin (2).
(****) larynx (8); thyroid (3); tonsil (1); mouth (1); nasopharynx (1); oropharynx (1).

events, hemodialysis and need for ventilatory support. However, in the adjusted analysis, these variables lost statistical significance and were not retained in the logistic regression model.

Some limitations of this research should be highlighted. First, this is a retrospective study and data were collected based on the hospital's physical and electronic medical records. Second, having been performed with patients from a single institution and the relatively small sample size may have impacted the results and limited their generalization. Third, although the blood counts used were those collected at the time of admission for COVID-19 or as close as possible to the date of their detection, patients could be at distinct stages of cancer. Finally, although the results of this study refer exclusively to the first wave of the pandemic in Brazil, different variants of the coronavirus may have influenced the prognosis. On the other hand, this is the first Brazilian study to investigate the prognostic roles of systemic inflammation indices based on blood cell counts in patients with solid tumors and COVID-19.

CONCLUSION

In this study, high NLR values showed prognostic ability to predict death during hospitalization of patients with solid tumors and COVID-19.

CONTRIBUTIONS

All the authors contributed substantially to the study design, analysis and/or interpretation of the data, wording and/or critical review. They approved the final version to be published.

Table 3. Factors related to admission to INCA associated with the risk of death during hospitalization due to SARS-CoV-2/COVID-19 (N=185)

Variable	N (%)	Death on admission		OR (95% CI)	*p*
		Yes (%)	No (%)		
Previous hospitalization for other causes					
No	77 (41.6)	9 (57.0)	59 (59.6)	Reference	
Yes	18 (58.4)	37 (43.0)	40 (40.4)	1.11 (0.62 – 2.00)	0.719
Current hospitalization - ICU					
No	29 (15.7)	64 (74.4)	92 (92.9)	Reference	
Yes	156 (84.3)	22 (25.6)	7 (7.1)	4.52 (1.82 – 11.21)	**0.001**
Total length of hospital stays					
5 days or more	110 (59.5)	61 (70.9)	49 (49.5)	Reference	
< 5 days	75 (40.5)	25 (29.1)	(50-50.5)	2.49 (4.58 - 1.35)	**0.003**
Cancer treatment phase					
Therapy Naïve	37 (20.0)	14 (16.3)	23 (23.2)	Reference	
In any treatment	148 (80.0)	72 (83.7)	76 (76.8)	1.56 (0.74 – 3.26)	0.240
PS					
PS 0 or 1	21 (17.6)	7 (10.8)	14 (25.9)	Reference	
PS ≥ 2	98 (82.4)	58 (89.2)	40 (74.1)	2.90 (1.07 – 7.83)	**0.036**
Cardiovascular events					
No	175 (94.6)	77 (90.6)	97 (98.0)	Reference	
Yes	10 (5.4)	8 (9.4)	2 (2.0)	5.04 (1.04 – 24.42)	**0.045**
Hemodialysis					
No	161 (87.5)	69 (81.2)	92 (92.9)	Reference	
Yes	23 (12.5)	16 (18.8)	7 (7.1)	3.05 (1.19 – 7.81)	**0.020**
Ventilatory support					
None	89 (48.1)	6 (7.0)	47 (47.5)	Reference	
Supplemental O2	43 (23.2)	47 (54.7)	42 (42.4)	8.77 (3.40 – 22.58)	**<0.001**
Invasive mechanical ventilation	53 (28.6)	33 (38.4%)	10 (10.1)	25.85 (8.56 – 78.10)	**<0.001**
Neutrophil-lymphocyte ratio					
< 7.79	91 (50.0)	30 (35.3)	61 (62.9)	Reference	
≥ 7.79	91 (50.0)	55 (64.7)	36 (37.1)	3.11 (01.69 – 5.70)	**<0.001**
Platelet-lymphocyte ratio					
< 340.45	91 (50.0)	38 (44.7)	53 (54.6)	Reference	
≥ 340.45	91 (50.0)	47 (55.3)	44 (45.4)	1.49 (0.83 – 2.67)	0.182
Derivation of neutrophil-lymphocyte ratio					
< 4.44	91 (50.0)	28 (32.9)	63 (64.9)	Reference	
≥ 4.44	91 (50.0)	57 (67.1)	34 (35.1%)	3.77 (2.04 – 6.98)	**<0.001**

Captions: OR = *odds ratio*; CI = confidence interval; ICU = intensive care unit; PS = performance status.

Note: The statistically significant variables are highlighted in bold.

Table 4. Adjusted analysis of the impact of inflammatory markers on the risk of death during hospitalization due to COVID-19 (N=185)

Variable	OR (95% CI)	*p*
Neutrophil-lymphocyte ratio		
< 4.44	Reference	
≥ 4.44	3.54(1.68-7.46)	**0.001**

Captions: OR = *odds ratio*; CI = confidence interval.

Note: Adjusted for ventilatory support, presence of cardiovascular events and presence of comorbidities. The statistically significant variable is highlighted in bold.

DECLARATION OF CONFLICT OF INTERESTS

The author Anke Bergmann declares a potential conflict of interest due to the condition of being the scientific editor of the Brazilian Journal of Cancerology of INCA. The other authors do not have a conflict of interest.

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