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Cancer inpatients with COVID-19: A report from the Brazilian National Cancer Institute

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Abstract

Objective

This study aimed to describe the demographic and clinical characteristics of cancer inpatients with COVID-19 exploring clinical outcomes.

Methods

A retrospective search in the electronic medical records of cancer inpatients admitted to the Brazilian National Cancer Institute from April 30, 2020 to May 26, 2020 granted identification of 181 patients with COVID-19 confirmed by RT-PCR.

Results

The mean age was 55.3 years (SD ± 21.1). Comorbidities were present in 110 (60.8%) cases. The most prevalent solid tumors were breast (40 [22.1%]), gastrointestinal (24 [13.3%]), and gynecological (22 [12.2%]). Among hematological malignancies, lymphoma (20 [11%]) and leukemia (10 [5.5%]) predominated. Metastatic disease accounted for 90 (49.7%) cases. In total, 63 (34.8%) had recently received cytotoxic chemotherapy. The most common complications were respiratory failure (70 [38.7%]), septic shock (40 [22.1%]) and acute kidney injury (33 [18.2%]). A total of 60 (33.1%) patients died due to COVID-19 complications. For solid tumors, the COVID-19-specific mortality rate was 37.7% (52 out of 138 patients) and for hematological malignancies, 23.5% (8 out of 34). According to the univariate analysis COVID-19-specific mortality was significantly associated with age over 75 years (P = .002), metastatic cancer (p <0.001), two or more sites of metastases (P < .001), the presence of lung (P < .001) or bone metastases (P = .001), non-curative treatment or

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best supportive care intent (P < .001), higher C-reactive protein levels (P = .002), admission due to COVID-19 (P = .009), and antibiotics use (P = .02). After multivariate analysis, cases with admission due to symptoms of COVID-19 (P = .027) and with two or more metastatic sites (P < .001) showed a higher risk of COVID-19-specific death.

Conclusion

This is the first Brazilian cohort of cancer patients with COVID-19. The rates of complications and COVID-19-specific death were significantly high.

Introduction

The novel coronavirus, named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) that causes the coronavirus disease 2019 (COVID-19) [1], was first detected in Wuhan, the provincial capital of Hubei, China, in December 2019. SARS-CoV-2 has rapidly spread to many other countries worldwide becoming an unprecedented astounding and devastating pandemic in a short period of time.

Following an exponential upward trend, the increasing number of cases and death toll remain to concern the scientific community around the globe. Currently, more than 13.8 million cases are confirmed worldwide, with more than 593,000 deaths [2]. The first case of COVID-19 in Brazil was detected on February 26, 2020. Standing out worldwide for having one of the steepest epidemiological curves, the country has 2.04 million confirmed cases and more than 77,800 deaths so far [3]. As the most populous areas, the states of São Paulo and Rio de Janeiro have predictably concentrated the highest numbers of cases and deaths. Thus far, Brazil has been considered the new epicenter of the global pandemic [4].

In general, the vast majority of COVID-19 patients develop mild symptoms or remain asymptomatic over the course of the disease. An intermediate group of patients have moderate symptoms requiring hospitalization and some noninvasive intervention. Another group of patients have a more severe course of the disease with desaturation, dyspnea, septic shock, and/or multiple organ dysfunction leading to life-threatening consequences or death [5].

Patients with cancer are more likely to have severe complications and even death when affected by COVID-19 [6–8], mainly due to the effects of the immunosuppressive anticancer treatments, frequent use of corticosteroids, advanced age, comorbidities and pulmonary involvement (primary tumors or secondary lung metastases). Particularly in low- and middle-income countries, COVID-19 has brought a heavy burdening to the public health systems and induced new planning and adjustments in the clinical approach to cancer patients [9].

Based on a few series previously published around the world, data evaluating the impact of COVID-19 outbreak in management and survival of patients with cancer are still very scarce, incomplete, with heterogeneous outcomes and descriptions [10–15]. Brazilian data in this specific field are still unknown due to the lack of publications.

The aim of this report was to describe the demographics, clinical characteristics and laboratory abnormalities of cancer inpatients with COVID-19 admitted to the hospital ward of the Brazilian National Cancer Institute (INCA), exploring factors associated with death.

Methods

Study design and participants

This retrospective cohort was performed through a search on electronic medical records and compiled data of cancer inpatients admitted to INCA with laboratory-confirmed SARS-CoV-2

infection between April 30, 2020 and May 26, 2020. The hospital admission occurred for various medical reasons, including COVID-19 symptoms or any other clinical condition (for those cases with onset of symptoms throughout hospitalization or cancer inpatients who had contact to other COVID-19 cases). Outpatients tested positive for SARS-CoV-2 infection and patients with only non-invasive cancer (or pre-malignant conditions) were not the object of this study.

COVID-19 was diagnosed on the basis of the WHO interim guidance [16], in which confirmation was defined as a positive result on real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay of nasal- and oropharyngeal swab specimens using the U.S. Centers for Disease Control and Prevention (CDC) reagents and protocol [17]. Specimens were collected right after the hospital admission from those patients with COVID-19 symptoms and immediately after clinical suspicion from those admitted to hospital for diverse reasons unrelated to COVID-19.

The study was approved by the National Commission of Ethics in Research (CONEP) and conducted in accordance with the Good Clinical Practice guidelines. Written informed consent was waived due to the retrospective design and the emergency feature of the research. Only anonymized data were analyzed.

Data collection and outcomes

The demographic and clinical characteristics, including tumor site, histological subtype, staging, site of metastases, cancer treatment within the last 60 days, the presence of comorbidities, COVID-19-related clinical signs and symptoms, and laboratory tests at diagnosis and throughout hospitalization were obtained from the electronic medical records. COVID-19-specific clinical treatments were also collected. The variables analyzed in order to feature disease severity were admission to the intensive care unit (ICU), mechanical ventilation, renal failure, hemodialysis, septic shock, and death. Patients transferred out from INCA to another hospital were censored on the date of transfer. Patients who had not been discharged from hospital were censored in the date of the last follow-up on May 31, 2020.

Statistical analysis

The statistical software package SPSS, version 21.0 (São Paulo, Brazil) was used for the analyses performed by accessing the database between June 1st and 6th, 2020. All continuous variables were evaluated by the Kolmogorov-Smirnov test of normality. Categorical variables were shown in percentages or absolute values. The study endpoint was COVID-19-related mortality. Time of follow-up was calculated from the date of swab collection to hospital discharge, death, or censorship of patients who were transferred or still hospitalized at the end of the study.

Risk factors for death were assessed using logistic regression. Crude and adjusted odds ratios (OR) were calculated. Variables with a P-value $< .20$ at the univariate analysis were included in the multivariate model by stepwise forward selection with the entry order based on their level of significance. All P-values $< .05$ were considered statistically significant.

Results

A total of 181 patients had the diagnosis of COVID-19 confirmed at INCA and were considered eligible for this study. The median follow-up for the general population was 5 days (interquartile range, IQR 2–10.3).

The demographic and clinical characteristics are described in detail in Table 1. The mean age was 55.3 years (standard deviation, SD ±21.1) and 92 (50.8%) patients aged 60 or older. Female gender was more prevalent (110 [60.8%]) and 40 patients (22.1%) were former or

Table 1. Baseline demographic and clinical characteristics of the patients.

	N (%)
Variables	
Age, years	
Mean (±SD)	55.3 (±21.1)
Range	1.8–88.0
< 60	89 (49.2)
60–74	67 (37.0)
≥ 75	25 (13.8)
Sex	
Female	110 (60.8)
Male	71 (39.2)
Smoking status	
Never	69 (38.1)
Current	18 (9.9)
Former	22 (12.2)
Missing	72 (39.8)
Comorbidities	
No	46 (25.4)
Yes	110 (60.8)
Missing	25 (13.8)
Main Comorbidities	
Hypertension	77 (42.5)
Diabetes	31 (17.1)
Chronic renal failure	10 (5.5)
COPD/asthma	7 (3.9)
Other*	21 (11.6)
Number of comorbidities	
0	46 (25.4)
1	61 (33.7)
2	28 (15.5)
≥3	21 (11.6)
Missing	25 (13.8)
Long-term systemic corticosteroid use	
No	143 (79.0)
Yes	21 (11.6)
Missing	17 (9.4)
Solid Tumors	
Breast	40 (22.1)
Gastrointestinal	24 (13.3)
Gynecological	22 (12.2)
Urological	17 (9.4)
Central nervous system	13 (7.2)
Head and neck	11 (6.1)
Lung	7 (3.9)
Other	11 (6.1)
Hematological malignancies	
Lymphoma	20 (11.0)
Leukemia	10 (5.5)

(*Continued*)

Table 1. (Continued)

	N (%)
Multiple myeloma	4 (2.2)
Clinical stage	
I—II	27 (14.9)
III	34 (18.8)
IV	90 (49.7)
NA	20 (11.0)
Missing	10 (5.5)
Number of metastatic sites	
No metastasis	61 (33.7)
1	32 (17.7)
2	35 (19.3)
3	13 (7.2)
4	6 (3.3)
5	1 (0.6)
Missing or NA	33 (18.2)
Main sites of metastasis**	
Bone	35 (19.3)
Lymph node	35 (19.3)
Lung	32 (17.7)
Liver	15 (8.3)
Central nervous system	11 (6.1)
Peritoneum	10 (5.5)
Skin	9 (5.0)
Current anticancer therapy (within the last 60 days)**	
Chemotherapy	63 (34.8)
Best supportive care	32 (17.7)
Hormonetherapy	20 (11.0)
Surgery	12 (6.6)
Radiotherapy	10 (5.5)
Immunotherapy/targeted therapy	9 (5.0)
Treatment- naïve patients	16 (8.8)
Cancer status	
No evidence of disease	27 (14.9)
Other	154 (85.1)
Cancer treatment intent	
Non-curative/supportive care	103 (56.9)
Other (adjuvant, neoadjuvant, curative, surveillance)	67 (37.0)
Missing or NA	11 (6.1)
Total	**181**

COPD: chronic obstructive pulmonary disease; NA: not applicable; SD: standard deviation.

*: Congestive heart failure, arrhythmia, ischemic heart disease, cerebrovascular disease, morbid obesity (BMI > 40 Kg/m^2), HIV infection.

**: Patients may have more than one site of metastasis or receive more than one type of anticancer therapy.

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current smokers. Comorbidities were found in 110 (60.8%) cases, of which the most common were hypertension (77 [42.5%]) and diabetes (31 [17.1%]), and 21 (11.6%) patients had three or more comorbidities. Long-term use of corticosteroids was seen in 21 (11.6%) cases.

The most prevalent solid tumors were breast (40 [22.1%]), gastrointestinal (24 [13.3%]), gynecological (22 [12.2%]) and urological (17 [9.4%]). Lung cancer patients made up only 7 (3.9%) cases. Among hematological malignancies, lymphoma (20 [11%]) and leukemia (10 [5.5%]) predominated. A more detailed list of the frequency of cancers by site is detailed in the supporting information section (S1 Table). Patients with metastatic disease accounted for almost half of the cases (90 [49.7%]) and 32 (17.7%) patients had lung metastases. More than a third of the cases (63 [34.8%]) had recently undergone cytotoxic chemotherapy within the last 60 days before the COVID-19 diagnosis, 32 (17.7%) were in best supportive care and 27 (14.9%), in post-treatment clinical surveillance. Only nine patients (5%) were receiving targeted therapy or immunotherapy with checkpoint inhibitors as the current treatment line (Table 1).

Information regarding the conditions of hospital admission and clinical evolution of patients are summarized in Table 2. More than half of the patients (98 [54.1%]) were admitted due to clinical worsening related to COVID-19 and 151 (83.4%) were symptomatic at the time of diagnostic confirmation. The most frequent symptoms were dyspnea (94 [51.9%]), cough (87 [48.1%]) and fever (66 [36.5%]). Admission to the ICU occurred in 32 (17.7%) cases, 130 (71.8%) patients required supplemental oxygen, and 35 (19.3%) cases progressed unfavorably with the need for mechanical ventilation. Ten patients (5.5%) were transferred out from INCA during the course of COVID-19. Fig 1 shows, from the day of swab collection, the timeline of events during hospital stay for COVID-19 patients and highlights that some patients had a rapidly deterioration of their clinical course once infected with SARS-CoV-2.

The most common complications during hospitalization were respiratory failure (70 [38.7%]), septic shock (40 [22.1%]) and acute kidney injury (33 [18.2%]), with 19 (10.5%) patients requiring hemodialysis support. As for laboratory results, the median absolute lymphocytes count was 988/μL (IQR 588–1488), the mean C-reactive protein levels were 19.4 mg/dL (SD ±15.0) and median D-dimer levels were 2099 ng/mL (IQR 909–5948).

Under the clinical diagnosis of a severe acute respiratory syndrome, where influenza infection was considered one of the causative hypotheses and before the final RT-PCR result was confirmed as SARS-CoV-2 infection, oseltamivir was administered to 41 (22.7%) cases. During the course of COVID-19, more than half of the patients (98 [54.1%]) received corticosteroids, 148 (81.8%) were treated with antibiotics (including those against bacterial coinfections), and therapeutic anticoagulation was prescribed to 39 (21.5%) patients. Eight (4.4%) patients received chloroquine and 36 (19.9%), ivermectin.

At the time of analysis, a total of 60 patients (33.1%) had died due to COVID-19. For solid tumors, the COVID-19-specific mortality rate was 37.7% (52/138) and for hematological malignancies (leukemia, lymphoma and multiple myeloma) was 23.5% (8/34). Four out of seven (57.1%) patients with lung cancer died from COVID-19, as well 52.5% (21/40) of breast cancer patients (Fig 2).

As shown in Table 3, mortality related to COVID-19 was significantly associated to older age ($P < .001$ for patients between 60 to 74 years and $P = .002$ for patients aged 75 years or older), metastatic cancer ($P < .001$), two or more sites of metastases ($P < .001$), the presence of lung ($P < .001$) or bone metastases ($P = .001$), non-curative treatment or best supportive care intent ($P < .001$), higher C-reactive protein levels ($P = .002$), admission due to COVID-19 ($P = .009$), and antibiotics use ($P = .02$). Isolated or combined comorbidities and elevated D-dimer levels did not demonstrate increased risk of dying from COVID-19.

Different modalities of cancer therapy, including systemic agents (chemotherapy, hormone therapy, targeted therapy, immunotherapy), surgical procedures or radiotherapy within 60 days before COVID-19 were not associated with mortality. Also, specific therapies during the COVID-19 course, such as oseltamivir, therapeutic anticoagulation, corticosteroids, ivermectin and chloroquine did not influence the risk of death (S2 Table).

Table 2. Patient characteristics at admission and events throughout the hospital stay.

	N (%)
Variables	
Reason for admission	
COVID-19	98 (54.1)
Other	83 (45.9)
Symptoms at COVID-19 diagnosis	
No	18 (9.9)
Yes	151 (83.4)
Missing	12 (6.6)
COVID-19-related symptoms*	
Dyspnea	94 (51.9)
Cough	87 (48.1)
Fever	66 (36.5)
Fatigue	50 (27.6)
Myalgia	49 (27.1)
Diarrhea	25 (13.8)
Nausea/Vomiting	22 (12.2)
Anorexia	15 (8.3)
Headache	8 (4.4)
Anosmia	3 (1.7)
Loss of taste	3 (1.7)
Coryza	3 (1.7)
Sore throat	1 (0.6)
ICU admission	
No	149 (82.3)
Yes	32 (17.7)
Mechanical ventilation	
No	146 (80.7)
Yes	35 (19.3)
Need for supplemental oxygen	
No	51 (28.2)
Yes	130 (71.8)
COVID-19 complications*	
Respiratory failure	70 (38.7)
Septic shock	40 (22.1)
Acute kidney injury	33 (18.2)
Hemodialysis	19 (10.5)
Cardiovascular events	6 (3.3)
Cerebrovascular events	1 (0.6)
Disseminated intravascular coagulation	1 (0.6)
Laboratory tests#,§	
Leukocyte count (n = 179; /μL; median, IQR)	9000 (5890–14300)
Lymphocyte count (n = 179;/μL; median, IQR)	988 (588–1488)
Neutrophil count (n = 179; /μL; median, IQR)	7130 (4015–12024)
Hemoglobin (n = 179; g/dL; mean, IQR)	10.7 (±2.7)
Platelet count (n = 179; /μL; median, ±SD)	243000 (168000–370000)
C-reactive protein (n = 159; mg/dL; mean, ±SD)	19.4 (±15.0)
D-dimer (n = 97; ng/mL; median, IQR)	2099 (909–5948)

(*Continued*)

Table 2. (Continued)

	N (%)
COVID-19-related treatment	
Corticosteroids	
No	80 (44.2)
Yes	98 (54.1)
Missing	3 (1.7)
Antibiotics	
No	33 (18.2)
Yes	148 (81.8)
Oseltamivir	
No	140 (77.3)
Yes	41 (22.7)
Therapeutic anticoagulation	
No	142 (78.5)
Yes	39 (21.5)
Chloroquine	
No	173 (95.6)
Yes	8 (4.4)
Ivermectin	
No	145 (80.1)
Yes	36 (19.9)
Death	
No	112 (61.9)
Yes, from COVID-19	60 (33.1)
Yes, other cause	9 (5.0)
Total	**181**

ICU: intensive care unit; IQR: interquartile range.

*: Patients may have more than one symptom or complication.

#: As continuous variables.

§Reference range as per local laboratory: leukocyte count:4000 to 10000/μL; lymphocyte count:800 to 4500/μL; neutrophil count: 1600 to 7500/μL; hemoglobin: 11.5 to 16.4 g/dL; platelet count:150000 to 400000/μL; C-reactive protein:< 0.5 mg/dL; D-dimer: < 500 ng/mL.

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According to the multivariate analysis patients admitted due to COVID-19 symptoms (OR 2.3, 95% CI—1.1 to 4.9, $P = .027$) and with two (OR 10.0, 95% CI—3.6 to 28.3, $P < .001$) or more metastatic sites (OR 14.8, 95% CI—4.1 to 53.2, $P < .001$) showed a significantly higher risk of COVID-19-specific death.

Discussion

The findings of this cohort highlight, in detail, several significant aspects of the COVID-19 course in patients already diagnosed with cancer. Although the emergency period for case selection was considerably short, due to the large number of cancer patients admitted to INCA with COVID-19, 181 patients were successfully included for analysis. Women had greater representation, more than half of the patients aged 60 years or older and almost a quarter of the patients had also reported smoking. Patients with two or more comorbidities accounted for more than a quarter of the study population as well, in which hypertension and diabetes prevailed.

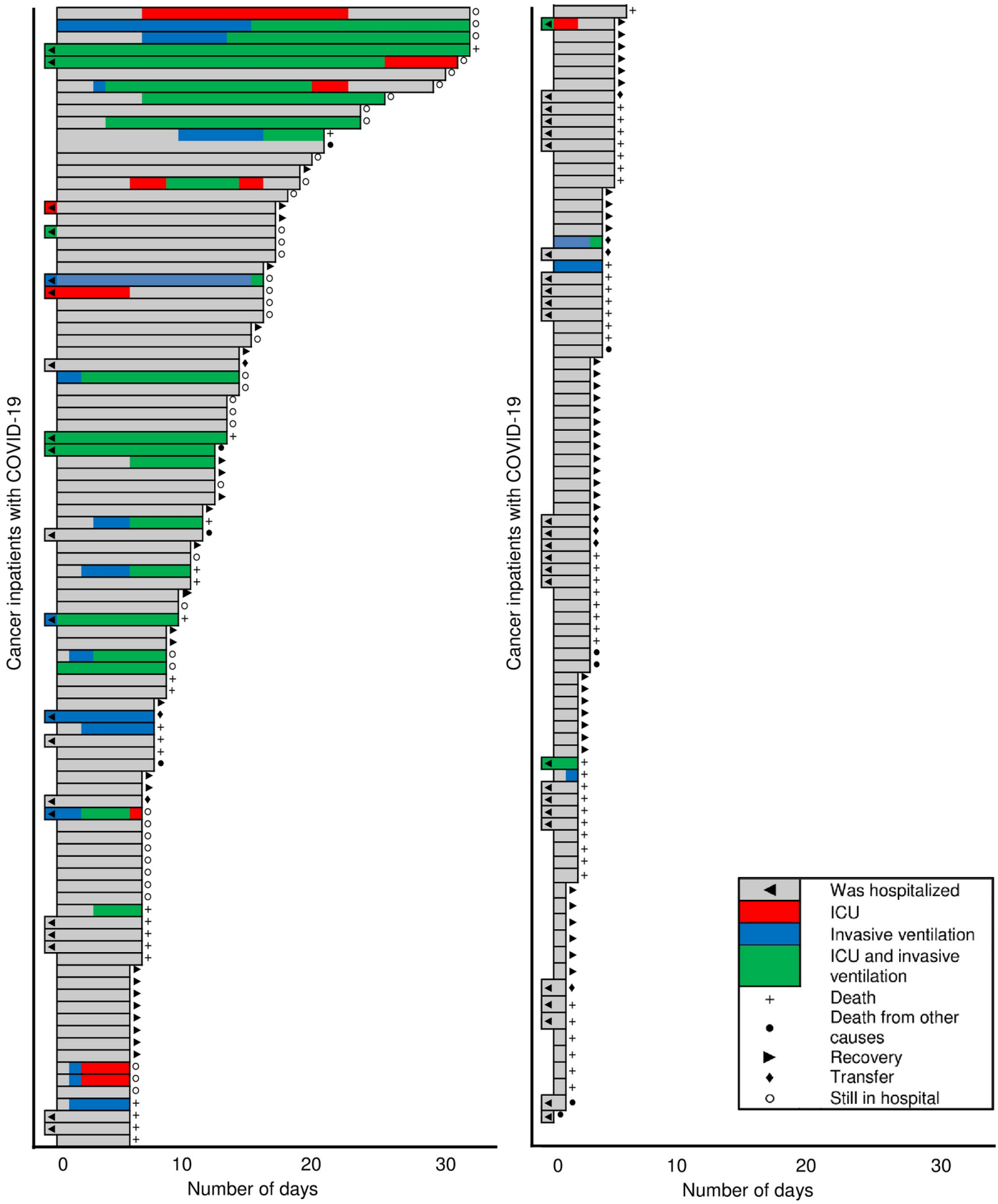
Cancer inpatients with COVID-19
0
10
20
30
Number of days
Cancer inpatients with COVID-19
0
10
20
30
Number of days
Was hospitalized
ICU
Invasive ventilation
ICU and invasive ventilation
Death
Death from other causes
Recovery
Transfer
Still in hospital

Fig 1. Timeline individual cancer inpatients with COVID-19 for events during hospital stay. All cases were represented in the graphic, with some overlaps of timelines.

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Almost half of the patients (83 [45.9%]) were hospitalized due to conditions unrelated to the SARS-CoV-2 infection which can be explained by patients asymptomatic for COVID-19 having been admitted to hospital for other cancer-related clinical complications. An intra-hospital transmission may also be considered, raising an important issue about the remarkable risk of infection to patients admitted for elective procedures. As for the symptoms present at diagnosis, similarly to data of other series [7, 8, 10, 12, 14], in the current cohort, dyspnea, cough and fever were all highly frequent.

The odds of some COVID-related complications were quite similar to the findings reported by Kuderer et al.(14) in an international prospective series in which more than 928 patients were analyzed. The rate of ICU admission of 14% (*versus* 17.7% in the current study) and the mechanical ventilation requirement rate of 12% (*versus* 19.3% in the current study) were also alike in proportional terms. Zhang et al. [6] also showed paralleled data with respect to other variables such as the demand of supplemental oxygen in 78.6% of cases (*versus* 71.8% in the current study).

Early data from non-cancer patients suggested that 14–19% of cases progress with severe complications, such as septic shock, respiratory failure, acute kidney injury and multiple organ failure [5, 15, 18]. In the present study, these rates were much higher, ranging from 18.2 to 38.7%, highlighting the increased likelihood of severe complications in cancer patients. Conversely, cerebrovascular and cardiovascular events were less frequent.

In total, 69 (38.1%) of 181 patients died. Herein, COVID-19-related mortality was considered as the endpoint. Consequently, nine patients who clearly have recovered from COVID-19, and died due to other cancer-related reasons, were excluded from this mortality analysis.

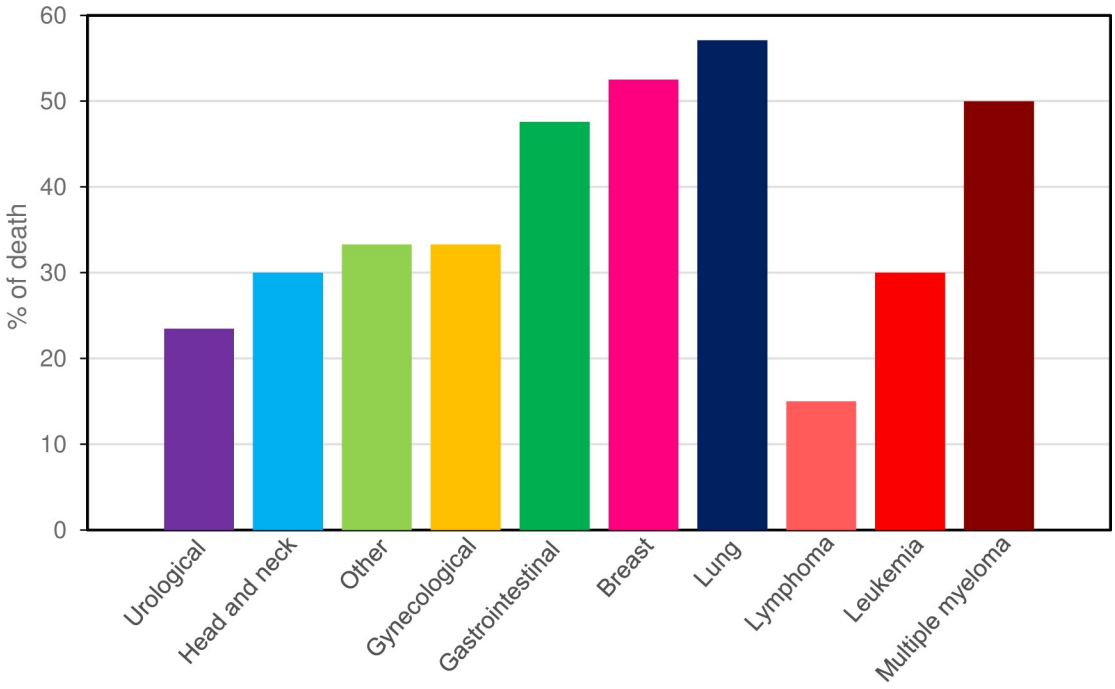

Fig 2. COVID-19-related mortality rate according to the cancer type.

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Table 3. Variables associated to the risk of death from COVID-19*.

Variables	Alive	Death from COVID-19	OR (95%CI)	p-value
Overall population	112	60		
Age, years				
< 60	70 (62.5)	18 (30.0)	1(ref)	..
60–74	32 (28.6)	30 (50.0)	3.6 (1.8–7.5)	**<0.001**
≥75	10 (8.9)	12 (20.0)	4.7 (1.7–12.5)	**0.002**
Sex				
Female	64 (57.1)	41 (68.3)	1.6 (0.8–3.1)	0.153
Male	48 (42.9)	19 (31.7)	1(ref)	..
Comorbidities				
No	29 (25.9)	16 (26.7)	1(ref)	..
Yes	68 (60.7)	34 (56.7)	0.9 (0.4–1.9)	0.793
Missing	15 (13.4)	10 (16.7)	1.2 (0.4–3.3)	0.712
Number of comorbidities				
0	29 (25.9)	16 (26.7)	1(ref)	..
1	44 (39.3)	15 (25.0)	0.6 (0.3–1.4)	0.265
2	16 (14.3)	9 (15.0)	1.0 (0.4–2.8)	0.970
≥3	8 (7.1)	10 (16.7)	2.3 (0.7–6.9)	0.149
Missing	15 (13.4)	10 (16.7)	1.2 (0.4–3.3)	0.712
Type of cancer				
Hematological malignancies	26 (23.2)	8 (13.3)	1(ref)	..
Solid tumors	86 (76.8)	52 (86.7)	2.0 (0.8–4.7)	0.125
Clinical stage				
I—III	49 (43.8)	9 (15.0)	1(ref)	..
IV	42 (37.5)	43 (71.7)	5.6 (2.4–12.8)	**<0.001**
Missing or NA	21 (18.8)	8 (13.3)	2.1 (0.7–6.1)	0.186
Number of metastatic sites				
No metastasis	49 (43.8)	9 (15.0)	1(ref)	..
1	23 (20.5)	9 (15.0)	2.1 (0.7–6.1)	0.157
2	11 (9.8)	21 (35.0)	10.4 (3.8–28.8)	**< 0.001**
≥3	5 (4.5)	13 (21.7)	14.2 (4.0–49.5)	**< 0.001**
Missing or NA	5 (4.5)	13 (21.7)	1.8 (0.6–5.3)	0.275
Lung metastases				
No	80 (71.4)	28 (46.7)	1(ref)	..
Yes	8 (7.1)	24 (40.0)	8.6 (3.5–21.3)	**< 0.001**
Missing	24 (21.4)	8 (13.3)	1.0 (0.4–2.4)	0.916
Bone metastases				
No	76 (67.9)	31 (51.7)	1(ref)	..
Yes	12 (10.7)	21 (35.0)	4.3 (1.9–9.8)	**0.001**
Missing	24 (21.4)	8 (13.3)	0.8 (0.3–2.0)	0.661
Cancer treatment intent				
Other (adjuvant, neoadjuvant, curative, surveillance)	55 (49.1)	11 (18.3)	1(ref)	..
Non-curative/supportive care	49 (43.8)	46 (76.7)	4.7 (2.2–10.1)	**<0.001**
Missing or NA	8 (7.1)	3 (5.0)	1.9 (0.4–8.2)	0.404
Reason for admission				
Other	57 (50.9)	18 (30.0)	1(ref)	..
COVID-19	55 (49.1)	42 (70.0)	2.4 (1.2–4.7)	**0.009**
ICU admission				

(*Continued*)

Table 3. (Continued)

Variables	Alive	Death from COVID-19	OR (95%CI)	p-value
No	89 (79.5)	52 (86.7)	1(ref)	..
Yes	23 (20.5)	8 (13.3)	0.6 (0.2–1.4)	0.245
Mechanical ventilation				
No	90 (80.4)	47 (79.7)	1(ref)	
Yes	22 (19.6)	12 (20.3)	1.0 (0.5–2.3)	0.914
Laboratory tests[§]				
Leukocyte count	..	..	1.0 (1.0–1.0)	0.113
Lymphocyte count	..	..	1.0 (1.0–1.0)	0.271
Neutrophil count	..	..	1.0 (1.0–1.0)	0.071
Hemoglobin	..	..	1.0 (0.8–1.1)	0.424
Platelet count	..	..	1.0 (1.0–1.0)	0.835
C-reactive protein	..	..	1.04 (1.01–1.06)	**0.002**
D-dimer	..	..	1.0 (1.0–1.0)	0.203
Antibiotics				
No	26 (23.2)	5 (8.3)	1(ref)	..
Yes	86 (76.8)	55 (91.7)	3.3 (1.2–9.2)	**0.020**

ICU: intensive care unit; NA: not applicable.

Values in bold are statistically significant.

*:171 patients included, 9 patients who died for other cancer related reasons were excluded from this mortality analysis.

#: Within the last 60 days.

§: As continuous variables.

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Therefore, the overall COVID-19-related mortality rate reached almost one third of the cases (60 [33.1%]), which was higher than that reported by other series with cancer patients [7, 8, 10, 12, 14], and far exceeding the mortality reported for non-cancer patients [5]. It is important to point out that some patients had the definition of non-invasive support after or even before the diagnosis of COVID-19 due to the severity of their advanced malignancies, which may have overestimated the mortality rate. In addition to this, a noticeable number of the analyzed patients (103 [56.9%]) were under non-curative treatment or best supportive care at the time, reflecting the advanced stage of their respective diseases.

Unlike in the multicenter studies recently published by Mehta et al. [10] and Dai et al. [15], the mortality rate was higher in patients with solid tumors than in patients with hematological malignancies, possibly due to the small number of hematological patients in this cohort. But likewise, lung cancer, breast cancer and gastrointestinal cancer stood for the highest numbers of cases progressing to death.

In line with the results published by Kuderer et al. [14], the characteristics associated with clinical fragility, such as being elderly, having advanced stage, a greater number of metastases, pulmonary metastases, non-curative treatment or supportive treatment and symptomatic patients at hospital admission were significantly associated with a higher risk of death. In this same context, the type of anti-cancer treatment received by patients within the previous 60 days did not influence survival outcome.

Except for the association of C-reactive protein with mortality (OR 1.04; p = 0.002), none of the laboratory markers were likely to predict a higher risk of mortality. Other laboratory exams, including inflammatory markers such as lactate, ferritin, fibrinogen, and lactate dehydrogenase were not regularly collected in this cohort, preventing related analyses. A

prospective study in order to evaluate the immune response markers in our cohort of cancer patients with COVID-19 is being currently conducted.

As in the study performed by Kuderer et al. [14], none of the specific therapies prescribed such as antiviral oseltamivir (used for the initial suspicion of influenza infection), therapeutic anticoagulation, ivermectin or chloroquine influenced the risk of death in the current cohort. The strong association between the use of antibiotics and the outcome of death can be explained by the fact that these patients showed a more serious condition than COVID-19, including coinfections.

Lastly, finishing on a positive note, some strengths of the current study can also be recognized. The Brazilian National Cancer Institute is the most important national reference center for the treatment of cancer patients through the Brazilian Public Health System (SUS), with a high admission charge, enabling a quick inclusion of patients for this study.

This was one of the largest series ever undertaken to explore the impacts of SARS-CoV-2 infection specifically in cancer patients. Throughout the analysis, many variables were presented, allowing us to explore the possibility of their association with risk of death. Ultimately, this is the first set of Brazilian data in this field, ever.

Some important limitations are also worth mentioning in this study. As a single-center cohort in a country of continental proportions, such as Brazil, a selection bias may well exist, hindering an external validity. The missing data rate for some variables was considerably high due to the retrospective design of the study. There was no paired sample with non-cancer patients with COVID-19 or cancer patients without COVID-19 to provide a better comparison between the outcomes of morbidity and mortality. Due to the in-hospital follow-up only, there was no report of long-term morbidity. Finally, the general population of the study was very heterogeneous with several types of neoplasia and anti-cancer treatment, making it difficult to design a more reliable portrait by tumor site.

Conclusions

Like other comorbidities, cancer is suggested to be an important prognostic factor for patients with COVID-19, probably due to the greater clinical fragility and the negative impact of immunosuppressive treatments. Despite having formulated early institutional emergency measures, since the onset of the pandemic in Brazil, to reduce the exposure of this group of patients to SARS-CoV-2, INCA had a considerable burden of infected patients in need of hospitalization. The rates of complications and COVID-19-specific death were significantly high.

Supporting information

S1 Table. Data on cancer by site.
(DOCX)

S2 Table. Specific therapies associated to the risk of death from Covid-19.
(DOCX)

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