BMC Palliative Care

RESEARCH Open Access

Comparison of the sociodemographic and clinical profiles of cancer patients admitted to a tertiary palliative care unit before and during the COVID-19 pandemic

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Abstract

Objective To compare the sociodemographic and clinical profiles of patients with advanced cancer admitted to a tertiary palliative care unit before and during the COVID-19 pandemic.

Methods This is an analysis of data from patients receiving care before (10/21/2019 to 03/16/2020) and during (09/23/2020 to 08/26/2021) the COVID-19 pandemic. Sociodemographic and clinical data were evaluated. Logistic regression analyses were used, with the odds ratio (OR) and 95% confidence interval (CI) as measures of effect.

Results 673 patients were enrolled (204 in the pre-pandemic period and 469 in the pandemic period). The final logistic regression model demonstrated that patients admitted during the pandemic had a greater chance of having white skin (OR: 1.66 [95% CI: 1.15–2.39]), having a gastrointestinal tract cancer (OR: 2.95 [95% CI: 1.55–5.62]) and in skin, bones, and soft tissue (OR: 2.40 [95% CI: 1.13–5.08]), having received prior radiotherapy (OR: 1.83 [95% CI: 1.26–2.55]), and having a higher global PG-SGA SF score (OR: 1.06 [95% CI: 1.02–1.09]).

Conclusion Ethnicity, nutritional risk, previous radiotherapy, and type of tumor were associated with advanced cancer during the COVID-19 pandemic. It is unclear what impacts the COVID-19 pandemic had on palliative care. This study presented findings based on one tertiary palliative care facility for patients with cancer. Give the limited literature on the subject, our comparative analysis of data serves as a starting point for a debate on this subject. More studies of a similar nature are needed to enable future comparisons and assist planning for other pandemics.

Keywords COVID-19, Palliative care, Neoplasms, Cancer, Therapeutics

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Introduction

Palliative care is defined by the World Health Organization (WHO) as "an approach that improves the quality of life of patients (adults and children) and their families who are facing problems associated with life-threatening illness. It prevents and relieves suffering through the early identification, correct assessment and treatment of pain and other problems, whether physical, psychosocial or spiritual" [1].

As for the recent health emergency, on March 11, 2020, the World Health Organization declared that the outbreak of COVID-19, the disease caused by severe acute respiratory syndrome coronavirus 2 (Sars-CoV-2) had become a pandemic. At first, health systems around the world were overwhelmed by the high demand for intensive care beds because of the severity of the symptoms [2]. The first case in Brazil was recorded on February 25, 2020, in the state of São Paulo, since which time there have been some 38.5 million confirmed cases, resulting in almost 710,000 deaths from the disease, according to Brazilian Ministry of Health data from February 22, 2024 [3].

Little is known about the real impact of the COVID-19 pandemic on the healthcare provided for adult patients with cancer in palliative care. This indicates the need for efforts to be made to understand in greater depth the repercussions of the pandemic on different levels of public health, specifically in Brazil. In the institution where this research was done, there was a general, albeit subjective impression amongst the health workers involved directly in patient care that the profile of the patients admitted to this palliative care facility changed once the pandemic began. People were being hospitalized with a worse functional status and having received less therapeutic care at the other hospitals from the institution.

In order to shed light on the above-mentioned questions and discuss the consequences of the COVID-19 pandemic on palliative care for patients with cancer, this research compares the clinical and sociodemographic profile of patients with advanced cancer treated before and during the COVID-19 pandemic at a tertiary healthcare unit specialized in palliative care.

Methods

This research consists of an observational retrospective cohort study involving the comparative analysis of secondary data collected in October 2023, from a larger project entitled: Association between Symptoms of Nutritional Impact and Inflammatory Markers in Patients with Advanced Cancer. It was carried out at the National Institute for Cancer (INCA), in Rio de Janeiro, Brazil, and was approved by the INCA research ethics committee (#176069919.3.0000.5274) and the Oswaldo Cruz Foundation (Fiocruz) ethics committee (#63157222.0.0000.5240). The institution has been providing palliative care for patients with cancer since 1986, receiving a boost in 1998 with the inauguration of a new unit inspired by the Canadian hospice model. In 2004, when INCA standardized the way it names its health units, this unit was renamed Cancer Hospital IV (CH IV). It has since become a national reference in the teaching, research, and delivery of palliative care for patients with cancer [4].

Data for convenience (available because they were obtained in the larger study) were analyzed from patients receiving care before (10/21/2019 to 03/16/2020) and during (09/23/2020 to 08/26/2021) the COVID-19 pandemic, either at their first outpatient consultation or within 48 h of their first hospitalization at CH IV. The gap between March and September 2020 is because of the guidance issued by the institution to suspend all research and work not directly related to care with the aim of protecting patients and professionals against contracting COVID-19 [5].

The patients selected from the secondary database: were of both sexes; aged ≥ 20; had histopathological confirmation of advanced-stage cancer, irrespective of tumor site; Karnofsky Performance Status (KPS) ≥ 30% [6, 7]; were able to provide the information required for the research, with no apparent mental confusion or cognitive deficit or any exacerbated symptoms (such as intense nausea, dyspnea, pain, fatigue, etc.); and had consented to participate in the study, reading and signing the informed consent form. To minimize bias regarding the impact of SARS-CoV-2 infection on nutritional risk, symptoms presence, and KPS, patients with a confirmed diagnosis at the time of assessment were excluded [5].

Sociodemographic, clinical, and laboratory data were collected from the secondary database. The sociodemographic data collected were: age, sex, skin color, partnership status, and education. The clinical data collected were: principal diagnosis, metastasis, previous antineoplastic treatment, comorbidities, KPS, nutritional risk classification, and prevalence of symptoms (hyporexia, nausea, vomiting, fatigue, pain, mood-related symptoms, such as depression, anxiety, or low spirits), based on the Patient-Generated Subjective Global Assessment Short Form (PG-SGA SF). The time elapsed between triage at the institution and the first evaluation at CH IV, between triage at the institution and death, and between the first evaluation at CH IV and death were also calculated [8].

Statistical analysis

The statistical analyses were conducted using STATA version 13.1. A descriptive analysis of the principle variables was conducted to determine the characteristics of the sample, following classic procedures. The

Kolmogorov-Smirnov test was used to test for normality of distribution.

The numerical variable with normal distribution (PG-SGA SF) was described as mean ± standard deviation; the variables with non-normal distribution (albumin, CRP, and leukocytes) were described as median with interquartile range (IQR). The categorical variables were described as absolute frequency (n) and relative frequency (%). Student's t-test was used to compare the means from each group, and the Mann-Whitney U-test was used to compare the medians from each group. Pearson's chi-squared test or Fisher's exact test were used to compare the categorical variables.

Univariate and multivariate logistic regression analyzes were conducted to assess the chances of presenting certain sociodemographic and clinical characteristics in patients assessed during the COVID-19 pandemic vis-à-vis the pre-COVID-19 period, using odds ratios (OR) and 95% confidence intervals (CI) as measures of effect. To attempt to control potential confounding factors the variables with $p < 0.200$ in the univariate analysis were selected for the multivariate analysis. The final model was designed using the backward forward, the variables with p-value < 0.200 were all included and then removed, one by one, in decreasing order of p-value, leaving only the variables with p-value < 0.50 in the final model. Statistical significance was set at p-value < 0.05.

Results

A total of 673 patients were included in the study: 204 in the pre-pandemic period and 469 in the pandemic period (Fig. 1). Most of the patients were over 60 years old (58.8%), female (58.2%), had non-white skin color (61.1%). The most common primary tumor site was gastrointestinal (GI) tract (22.0%), followed by gynecological (20.5%), and head and neck (15.7%). Statistically significant differences were found between the frequencies of skin color ($p = 0.002$), primary tumor sites ($p = 0.008$), previous radiotherapy ($p = 0.018$) and KPS ($p = 0,037$) of the pre-pandemic and pandemic groups (Table 1; Fig. 2).

Most of the patients assessed were at nutritional risk (PG-SGA SF score ≥ 9). In these patients, hyporexia was the most prevalent nutritional impact symptom (52.0%), followed by nausea (38.0%) and pain (36.3%). The mean PG-SGA SF score and the prevalence of hyporexia ($p = 0.009$), nausea ($p = 0.022$), and vomiting ($p = 0.024$) were higher in the pandemic-period group (Table 2).

There was also a statistically significant difference across the groups for the time that elapsed between triage at the institution and first assessment at CH IV: the time period was greater during the pandemic then before it (576 vs. 446 days; $p = 0.017$) (Fig. 3).

The final logistic regression model (Table 3) revealed that the patients assessed during the pandemic were more likely to have white skin color (OR: 1.66 [95% CI 1.15–239]), a primary tumor site in the GI tract (OR: 2.95 [95% CI 1.55–5.62]) and in skin, bones, and soft

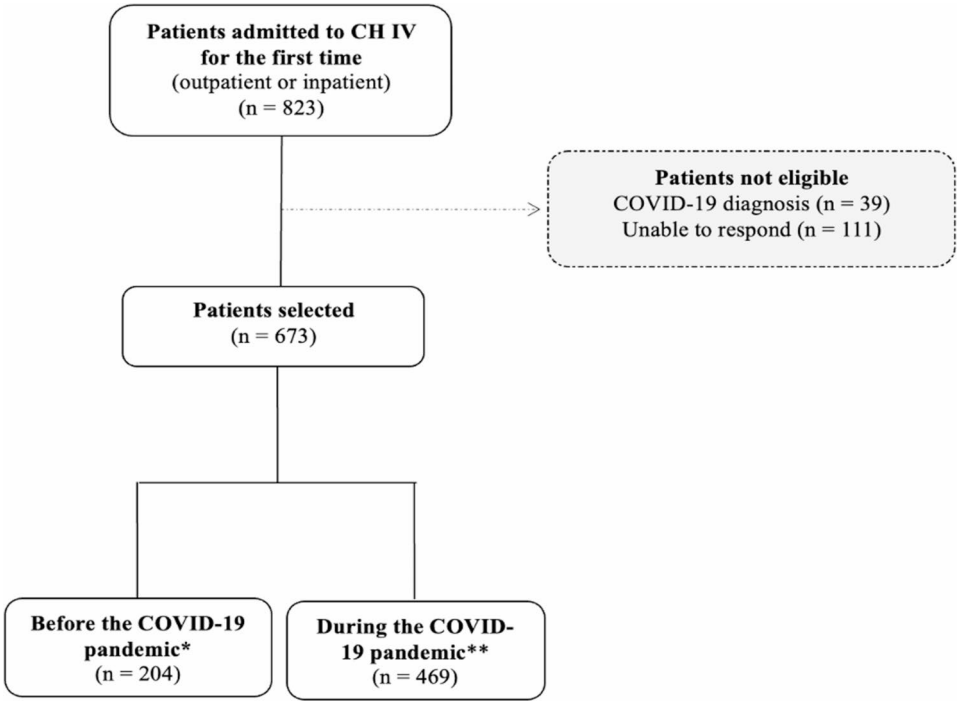

Fig. 1 Flow chart of the selection of study participants. Note CH IV = Cancer Hospital IV (palliative care hospital); n = number of observations; COVID = coronavirus disease. *Selected between October 21, 2019, and March 16, 2020. **Selected between September 23, 2020, and August 26, 2021

Table 1 Sociodemographic and clinical characteristics of patients with advanced cancer in palliative care per evaluation period (before or during the COVID-19 pandemic); *n* = 673

Variables	Total *n* (%)	COVID-19 Pandemic		*p*-value
		Before *n* = 204 (30.3%)	During *n* = 469 (69.7%)	
Age (years)[a]				
< 60	277 (41.2%)	80 (39.4%)	197 (41.9%)	0.544
≥ 60	396 (58.8%)	123 (60.6%)	273 (58.1%)	
Sex[a]				
Male	281 (41.8%)	83 (48.9%)	198 (42.1%)	0.764
Female	392 (58.2%)	120 (59.1%)	272 (57.9%)	
Skin color[a]				
White	262 (38.9%)	61 (30.1%)	201 (42.8%)	**0.002**
Non-white[b]	411 (61.1%)	142 (69.9%)	269 (57.2%)	
Primary tumor site[a]				
Gastrointestinal tract	148 (22.0%)	31 (15.3%)	117 (24.9%)	**0.008**
Gynecological	138 (20.5%)	38 (18.7%)	100 (21.3%)	
Head and neck[c]	106 (15.7%)	35 (17.2%)	71 (15.1%)	
Breast	82 (12.2%)	31 (15.3%)	51 (10.8%)	
Lung	62 (9.2%)	21 (10.3%)	41 (8.7%)	
Skin, bone, and soft tissue	70 (10.4%)	17 (8.4%)	53 (11.3%)	
Others[d]	67 (10.0%)	30 (14.8%)	37 (7.9%)	
Distant metastasis[a]				
No	108 (16.0%)	39 (19.2%)	69 (14.7%)	0.142
Yes	565 (84.0%)	164 (80.8%)	401 (85.3%)	
Prior treatment[a]				
No	108 (16.0%)	35 (17.2%)	73 (15.5%)	0.579
Yes	565 (84.0%)	168 (82.8%)	397 (84.5%)	
Types of prior treatment[a]				
Surgery (yes) [a]	307 (45.6%)	93(45.8%)	214 (45.5%)	0.946
Chemotherapy (yes) [a]	479 (71.2%)	135(66.5%)	344 (73.2%)	0.079
Radiotherapy (yes)[a]	345 (52.3%)	90 (44.3%)	255 (54.3%)	**0.018**

Note: n = number of observations; % = frequency

[a]Number of observations/frequency/X^2

[b]Brown/mulatto/brunette/indigenous/yellow

[c]Oral and nasal cavity, pharynx, larynx, salivary glands, paranasal sinuses, eyes, and thyroid

[d]Leukemia, lymphoma, myeloma, central nervous system, kidney and urinary tract, male genital organs, peritoneum, mediastinum and unrecognized site

tissue (OR: 2.40 [95% CI 1.13–5.08]), have prior radiotherapy (OR: 1.83 95% CI 1.26–2.55]), and have a higher global PG-SGA SF score (OR: 1.06 [95% CI 1.02–-1.09]) (Table 3).

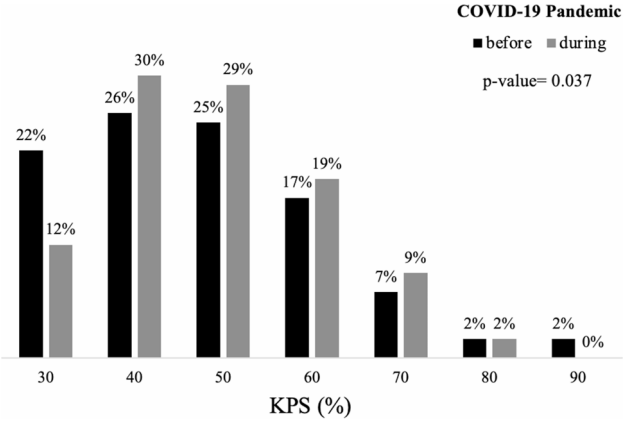

Fig. 2 Karnofsky Performance Status of patients with advanced cancer in palliative care per evaluation period (before or during the COVID-19 pandemic); *n* = 673. Note: KPS = Karnofsky Performance Status

Discussion

This study compared the clinical and sociodemographic profiles of patients with cancer admitted to a specialized palliative care hospital before and during the COVID-19 pandemic.

In the study, there was an overall predominance of patients who were female and aged ≥ 60 years. This is consistent with data on the ageing and feminization of the Brazilian population [9, 10]. Indeed, almost 30% of the study sample consisted of female patients with gynecological and breast tumors.

As for how to interpret the statistically significant difference in skin color (white vs. non-white) between the two periods studied, the higher proportion of white-skinned patients during the pandemic suggests easier access to the healthcare system by patients with white skin, who also tend to have a better socioeconomic status. This finding sheds light on the well-known disparity in access to healthcare services based on race, reinforcing the importance of governmental actions to ensure equity [11]. Besides facing greater reliance on public healthcare systems, black and brown populations are also affected by racism in cancer hospitalization rates. In the U.S., Black patients often receive diagnoses at more advanced stages and have less access to adequate surgical treatments, highlighting significant disparities in cancer care. Addressing these inequalities requires targeted interventions and policies to create a more equitable healthcare system [12–14].

The analysis of primary tumor sites revealed that the most statistically significant difference between the two periods was for the GI tract. Beltran-Arouca similarly found GI tumors in almost one third of a sample during the pandemic, although this figure was not statistically significant [15].

The higher proportion of patients with distant metastases during the pandemic is consistent with the longer

Table 2 Nutritional characteristics of patients with advanced cancer in palliative care per evaluation period (before or during the COVID-19 pandemic); *n* = 673

Variables	Total *n* (%)	COVID-19 Pandemic		*p*-value
		Before *n* = 204 (30.3%)	During *n* = 469 (697%)	
PG-SGA SF (score)[a]	12.3 (6.3)	11.1 (6.0)	12.9 (6.3)	**< 0.001**
PG-SGA SF (score ≥ 9)[b]				
No	212 (31.5%)	73 (36.0%)	139 (29.6%)	0.102
Yes	461 (68.5%)	130 (64.0%)	331 (70.4%)	
Symptoms				
Hyporexia (Yes)[b]	350 (52.0%)	90 (44.3%)	260 (55.3%)	**0.009**
Nausea (Yes)[b]	256 (38.0%)	64 (31.5%)	192 (40.8%)	**0.022**
Vomiting (Yes)[b]	182 (27.0%)	43 (21.2%)	139 (29.6%)	**0.024**
Fatigue (Yes)[b]	204 (30.3%)	59 (29.1%)	145 (30.8%)	0.643
Pain (Yes)[b]	244 (36.3%)	69 (34.0%)	175 (37.2%)	0.422
Mood-related: depression, anxiety, or sadness (Yes)[b]	112 (16.6%)	31 (15.3%)	81 (17.2%)	0.530

Note: n = number of observations; % = frequency; PG-SGA SF = Patient-Generated Subjective Global Assessment Short Form

[a]Mean/standard deviation/Student's t-test

[b]Number of observations/frequency/Pearson's chi-squared test

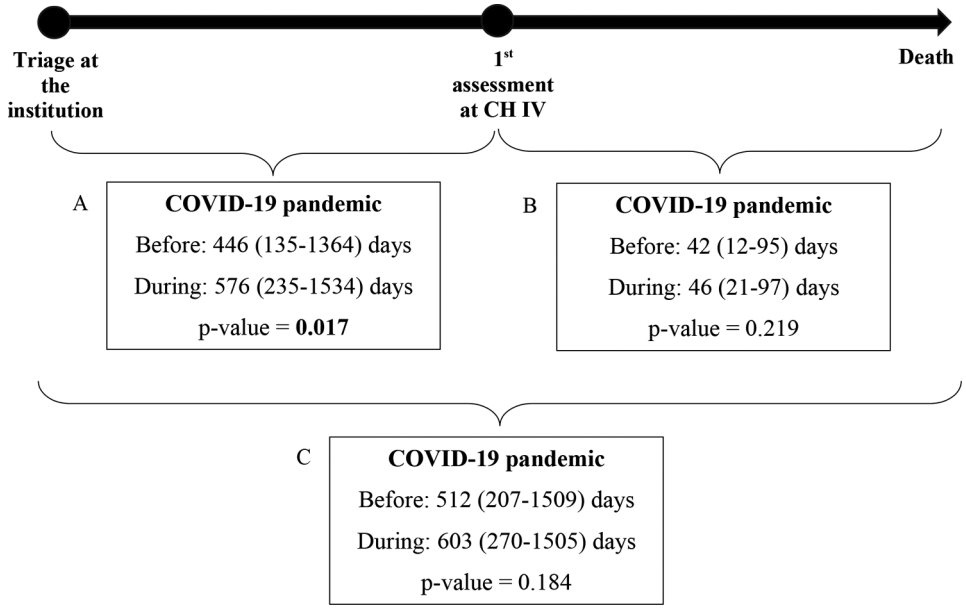

Fig. 3 Time intervals: (**A**) Between triage at the institution and 1st assessment at CH IV; (**B**) Between 1st assessment at CH IV and death; (**C**) Between triage at the institution and death of patients with advanced cancer in palliative care per evaluation period (before or during the COVID-19 pandemic); *n* = 673. Note: CH IV = Cancer Hospital IV. [a] median/interquartile range/Mann-Whitney U-test

period of time between triage at the institution and first evaluation at CH IV, since this would allow the disease to reach a more advanced stage. In Brazil, patients are generally referred for palliative care at a late stage, even though early referral has the effect of improving the quality of life of patients and their families [16, 17].

International guidelines recommend the early integration of palliative care, even alongside curative treatments, to improve quality of life, manage symptoms, and provide comprehensive support to patients and their families. Early involvement by palliative care teams is associated with less aggressive end-of-life care and lower rates of hospital deaths (ASCO Guidelines update). However, oncology patients in Brazil and other countries are still referred to palliative care at advanced stages. This delay is attributed to the misconception that palliative care is exclusively for end-of-life stages, an excessive focus on curative treatments with limited benefits, difficulties in discussing prognoses, and the lack of specialized services [16–20].

The cancer treatment received by the patients remained as usual, except for radiotherapy, which saw a statistically significant increase during the pandemic. There was no difference across the groups for the proportion

Table 3 Factors associated with patients with advanced cancer in palliative care during the COVID-19 pandemic

Variables	During the COVID-19 pandemic			
	Univariate		Multivariate	
	OR (95% CI)	*p*-value[d]	OR (95% CI)	*p*-value[e]
Age ≥ 60 years (ref < 60 years)	0.90 (0.64–1.26)	0.544	-	
Female (ref. male)	0.95 (0.68–1.33)	0.764	-	
White skin color (ref: non-white)[a]	1.74 (1.22–2.47)	0.002	1.66 (1.15–2.39)	**0.006**
Primary tumor site				
GI tract (ref: others[c])	3.06 (1.64–5.71)	**< 0.001**	2.95 (1.55–5.62)	**0.001**
Gynecological (ref: others[c])	2.13 (1.16–3.92)	**0.015**	1.63 (0.86–3.09)	0.133
Head and neck[b] (ref: others[c])	1.64 (0.88–3.08)	0.121	1.18 (0.60–2.32)	0.630
Breast (ref: others[c])	1.33 (0.69–2.57)	0.390	1.17 (0.59–2.34)	0.643
Lung (ref: others[c])	1.58 (0.77–3.23)	0.207	1.49 (0.71–3.13)	0.285
Skin, bones, and soft tissue (ref: others[c])	2.53 (1.22–5.24)	**0.013**	2.40 (1.13–5.08)	**0.023**
Distant metastasis (ref: no)	1.38 (0.90–2.13)	0.143	-	
Prior treatment (ref: no)	1.13 (0.73–1.76)	0.579	-	
Types of prior treatment (ref: no)				
Surgery (ref: no)	0.99 (0.71–1.37)	0.946	-	
Chemotherapy (ref: no)	1.37 (0.96–1.96)	0.079	-	
Radiotherapy (ref: no)	1.49 (1.07–2.07)	**0.018**	1.83 (1.26–2.55)	**0.001**
KPS (%)	1.01 (1.00–1.02)	0.118	-	
PG-SGA SF (score)	1.05 (1.02–1.07)	**0.001**	1.06 (1.02–1.09)	**0.001**
Symptoms				
Hyporexia (ref: no)	1.55 (1.12–2.16)	**0.009**	-	
Nausea (ref: no)	1.50 (1.06–2.12)	**0.023**	-	
Vomiting (ref: no)	1.56 (1.06–2.31)	**0.025**	-	
Fatigue (ref: no)	1.09 (0.76–1.56)	0.643	-	
Pain (ref: no)	1.15 (0.81–1.63)	0.422	-	
Mood-related: depression, anxiety, or sadness (ref: no)	1.25 (0.74–1.35)	0.489	-	
Time between triage at the institution and 1st assessment at CH IV (days)	1.01 (1.01–1.02)	**0.036**	-	
Time between triage at the institution and death (days)	1.00 (0.99–1.00)	0.254	-	
Time between 1st assessment at CH IV and death (days)	0.99 (0.99–1.00)	0.201	-	

Note: OR = odds ratio; CI = confidence interval; GI = gastrointestinal; KPS = Karnofsky Performance Status; PG-SGA SF = Patient-Generated Subjective Global Assessment Short Form; CH IV = Cancer Hospital IV

[a] Brown/mulatto/brunette/indigenous/yellow

[b] Oral and nasal cavity, pharynx, larynx, salivary glands, paranasal sinuses, eyes, and thyroid

[c/] Leukemia, lymphoma, myeloma, central nervous system, kidney and urinary tract, male genital organs, peritoneum, mediastinum and unrecognized site

[d] p-value refers to univariate logistic regression

[e] p-value refers to multiple logistic regression. All variables with $p < 0.200$ in the univariate analysis were selected for the multivariate logistic regression analysis. Variables with $p < 0.050$ retained in the final model

of patients who had received no prior treatment. There are studies that show that standard and hypofractionated radiotherapy were used more during the COVID-19 pandemic, which would explain the increase observed in our cohort [21, 22]. These same studies also point out that hypofractionated radiotherapy had the advantage of reducing the exposure of all those involved to the risk of contracting COVID-19, because of the reduction in the number of sessions. Another factor that is consistent with the higher utilization of radiotherapy is the fact that it is widely used for treating gynecological cancer, which was the form of cancer of almost one in five of the patients in our study. In the palliative context, radiotherapy is effective in relieving symptoms of advanced gynecological cancers, such as pain and bleeding, with low associated toxicity [23].

Another variable that showed a statistically significant difference across the periods was KPS 30%, which was lower during the pandemic. This could be explained by the fact that the proportion of patients with KPS 40–70% was higher during the pandemic, representing individuals with better performance status and the potential to receive outpatient treatment. It could also be the case that the patients with a worse KPS (e.g., 30%) ended up dying during the study period either from cancer or even from COVID-19.

The higher mortality rate among cancer patients with compromised functional status during the pandemic has also been reported in other studies, highlighting an

increased risk of death in cancer patients infected with SARS-CoV-2. The ACHOCC-19 study in Colombia identified higher mortality in patients with an Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 3 or 4 (bedridden for more than 50% of the time or completely bedridden), while studies in Portugal and Catalonia also confirmed an ECOG PS > 2 (out of bed for more than 50% of the time but requiring significant assistance) as an independent risk factor for mortality. These findings underscore the vulnerability of cancer patients with compromised functional status during COVID-19 infection [24–27].

As for PG-SGA SF, although there was no statistically significant difference between the time periods, there was a statistically significant difference among the patients admitted during the pandemic. The patients who were referred after a longer period of time were likely to have the disease at a more advanced stage and with a greater symptom burden, which would translate into higher nutritional risk (PG-SGA SF ≥ 9). There was a higher prevalence of GI symptoms (hyporexia, nausea, and vomiting), probably due to the higher proportion of primary GI tumors.

During the COVID-19 pandemic, oncology patients faced an increased nutritional risk, particularly those with compromised functional status. Nutritional status is a critical factor influencing clinical outcomes in cancer patients, especially during infections such as COVID-19. Moreover, the pandemic exacerbated nutritional challenges due to factors such as disruptions in healthcare services and heightened anxiety, which may lead to hesitancy in seeking treatment, further negatively affecting nutritional status [28–30].

There was a statistically significant difference in the time between triage at the institution and first evaluation at CH IV across the two study periods. This was likely because there were fewer in-person consultations to diagnose advanced cancer during the pandemic, a higher level of absenteeism at routine consultations because of COVID-related restrictions of movement, and the gap between consultations was also increased. The decision to reduce the number of in-person consultations and increase the gap between consultations, making more use of virtual means, was a policy adopted not only at CH IV, but also at all the other services and units at the institution [31, 32].

The strengths of this study include the fact that it is the first to study the research question, which is why there is so little literature on the subject available for comparison, even internationally. Its weaknesses include the facts that it was conducted at a single institution, the discussion of the results was limited by the shortage of comparable studies in the literature, and the gap between the two time periods studied was short. Another potential limitation of this study, given its retrospective nature, is the reduced control over variables, as data collection was not intentional. However, appropriate statistical tests can be used to evaluate the strength of associations among the collected variables.

Conclusion

Ethnicity, primary tumor site, previous radiotherapy, and nutritional risk were all associated with advanced cancer during the COVID-19 pandemic.

It is not yet clear exactly what impacts the COVID-19 pandemic had on palliative care. This study presented findings based on one tertiary care facility specialized in palliative care for patients with cancer. In the absence of a significant body of literature on the subject, our comparative analysis of data serves as a starting point for a debate on this subject. More studies of a similar nature are needed to enable future comparisons with a view to mitigating the impacts caused by the COVID-19 pandemic and improving planning for future pandemics.

As for the observation made by health workers at the palliative care hospital studied here, this research was unable to provide an answer, probably because of the short time lag between the two periods compared. It is possible that a comparison based on longer periods of time could reveal more impacts caused by the COVID-19 pandemic. This work generates results that can guide future studies.

Acknowledgements

The authors gratefully acknowledge the financial support provided by the Graduate Program in Public Health at Sergio Arouca National School of Public Health, Oswaldo Cruz Foundation (PPGSP/ENSP/Fiocruz), which made the publication of this article possible.

Author contributions

B.F.S.R. Roles: Conceptualization, Methodology, Writing – original draft, Writing – review & editing. G.O. Roles: Supervision, Conceptualization, Methodology, Writing – review & editing. V.T.S.L. Roles: Writing – review & editing. L.C.O. Roles: Statistical analysis, Writing – review & editing. K.S.C.R. Roles: Writing – review & editing. S.G.S.M.S. Roles: Supervision, Conceptualization, Methodology, Writing – review & editing.

Funding

Not applicable.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

It was carried out at the National Institute for Cancer (INCA), in Rio de Janeiro, Brazil, and was approved by the INCA research ethics committee (#176069919.3.0000.5274) and the Oswaldo Cruz Foundation (Fiocruz) ethics committee (#63157222.0.0000.5240).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 27 September 2024 / Accepted: 21 January 2025
Published online: 29 January 2025

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