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Letter to the Editor

Inequity in inequity: Disproportional mortality risk in patients with cancer with COVID-19 in Brazil - a call to action

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The outbreak of respiratory diseases caused by the coronavirus disease 2019 (COVID-19) in Wuhan, China received global attention due to its fast transmission and high lethality, especially among those aged >60 years and with comorbidities.

Approximately seven out of ten deaths by COVID-19 in Latin America occurred in Brazil [1]. More than 450 thousand deaths occurred until the end of May 2021, and only 10% of the Brazilian population was fully vaccinated [2]. Moreover, epidemic behavior in Brazil varied according to characteristics of each region, and inequities were worse in the poorest regions (e.g., northeast and north). Soon, the Brazilian unified health system (SUS) was at risk of collapse due to fast virus transmission, limited national coordination, low testing capacity, and difficulty controlling population transmission.

In patients with cancer, lethality is higher than reported in other studies [3], and the impact of the pandemic on health conditions of these patients is not yet fully understood. Patients with cancer are more vulnerable to COVID-19 and its complications, mainly due to tumoral activity, immunological suppression, antineoplastic treatment, and increased exposure to multiple diagnostic and treatment procedures [4]. Also, heterogeneity and complexity of COVID-19 in patients with cancer are challenging, especially in low-income and developing countries.

Therefore, active strategies to improve oncologic patient care in various contexts during the pandemic are fundamental to recognizing the impact of COVID-19 on patients with cancer. In this context, we conducted a study (research ethics committee of the Instituto de Medicina Integral Prof. Fernando Figueira - CAAE: 34637720.5.0000.5201) in a state of northeastern Brazil to determine lethality and factors associated with fatality in patients with cancer who developed severe acute respiratory syndrome (SARS) due to COVID-19.

The state of Pernambuco has a territorial area of 98,076,021 km [2] and estimated population of 9,616,621 inhabitants (2020) distributed among 185 cities. Patients with cancer aged 20 years or older, with SARS due to COVID-19 (confirmed by reverse transcription-polymerase chain reaction), and notified in FormSUS between March 07, 2020 and May 08, 2021 were included in the study (Fig. 1). Age, sex, race, comorbidities, history and type of cancer, topography of primary tumor, and COVID-19 were included in the analysis. Patients with solid or hematologic tumors or without data regarding cancer type were compared with those with history of cancer. Odds ratio (OR) was calculated for each tumor topography and adjusted OR (aOR) was obtained at final model.

FormSUS database had 41,545 individuals diagnosed with SARS from COVID-19. In total, 756 patients (mean age of 66.3 ± 15.3 years, 51.9% males) were analyzed. Primary tumor topography was not described in 25.5%, 3.2% had history of cancer, 11.6% had hematologic cancer, and 59.7% had solid tumors. Global lethality was 75.8%, and

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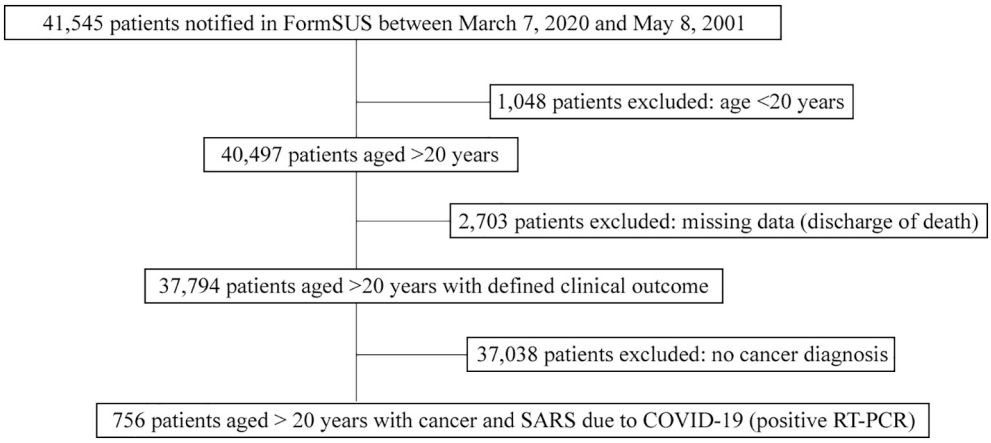

Fig. 1. Flowchart of the FormSUS data used in this study. RT-PCR indicates real-time polymerase chain reaction; SARS indicates severe acute respiratory syndrome.

Table 1
Lethality and mortality risk factors associated with severe acute respiratory syndrome due to COVID-19 in adults with cancer. Data from Health State Secretary of Pernambuco (SES-PE), Brazil, between March 07, 2020 and May 08, 2021.

Cases	Total	Lethality	Univariate Analyses			Multivariate Analyses		
	N = 756	(%)	OR	95%CI	*p*-value	ORa	95% CI	p-value
Age (years)								
Mean ± SD	66·3 ± 15·3	–	1·02	1·01–1·03	**<0·001**	1·02	1·01–1·03	<0·001
Median (IQR)	67 (57·0–78·0)							
Group age (years)	n (%)				**0·015**			
20 to 39	46 (6·1)	67·4	1	–	–	–	–	–
40 to 59	186 (24·6)	68·3	1·04	0·52–2·07	0·908	–	–	–
60 to 79	359 (47·5)	76·6	1·58	0·82–3·07	0·174	–	–	–
80 or more	165 (22·0)	84·8	2·71	1·28–5·73	0·009	–	–	–
Sex								
Female	364 (48·1)	72·5	1	–	–	–	–	–
Male	392 (51·9)	78·8	1·41	1·00–1·96	**0·043**	–	–	–
Race	n (%)		–	–	**<0·001**			
Brown- skinned, black, Asian, Indigenous	460 (60·9)		1	–	–	–	–	–
		74·0						
White	165 (21·8)	86·1	2·11	1·29–3·43	**0·003**	–	–	–
Not described	131 (17·3)	67·1	0·7	0·46–1·06	0·094	–	–	–
Comorbidities			–	–	**0·142**			
Up to one	529 (70·0)	74·3	1	–	–	–	–	–
Two or more	227 (30·0)	79·3	1·32	0·91–1·93	**0·142**	–	–	–
Type of Comorbidities								
Cardiovascular disease (excluding systemic arterial hypertension)	291 (38·5)	76·3	1·04	0·74–1·47	0·802	–	–	–
Diabetes mellitus	154 (20·4)	80·5	1·41	0·91–2·18	**0·126**	–	–	–
Systemic arterial hypertension	68 (9·0)	82·3	1·54	0·81–2·95	**0·189**	–	–	–
Chronic pulmonary disease	62 (8·2)	85·8	1·97	0·95–4·08	**0·068**	2·02	0·96–4·28	0·064
Smoking	44 (5·8)	70·4	0·75	0·38–1·46	0·396	–	–	–
Chronic renal disease	46 (6·1)	73·9	0·9	0·46–1·77	0·759	–	–	–
Chronic neurologic disease	32 (4·23)	84·4	1·76	0·67–4·64	0·253	–	–	–
Overweight	29 (3·8)	62·0	0·51	0·23–1·09	**0·084**	0·5	0·23–1·10	0·087
Other comorbidities	38 (5·0)	76·3	1·03	0·48–2·22	0·939	–	–	–
History and type of cancer								
Cancer history	24 (3·2)	66·7	1	–	–	–	–	–
Location not described	193 (25·5)	78·7	1·85	0·74–4·63	**0·187**	–	–	–
Solid Tumor	451 (59·7)	76·3	1·61	0·67–3·86	0·288	–	–	–
Hematologic cancer	88 (11·6)	69·3	1·13	0·43–2·96	0·804	–	–	–
Topography of primary tumor								
Gastrointestinal system	99 (13·1)	79·8	1·98	0·74–5·26	**0·174**	–	–	–
Urologic	91 (12·0)	79·1	1·89	0·71–5·09	0·205	–	–	–
Breast	89 (11·8)	68·5	1·09	0·42–2·84	0·861	–	–	–
Respiratory system	48 (6·4)	83·3	2·5	0·80–7·81	**0·115**	–	–	–
Gynecological	38 (5·0)	68·4	1·08	0·36–3·22	0·886	–	–	–
Central nervous system	24 (3·2)	83·3	2·5	0·63–9·82	**0·189**	–	–	–
Hematologic cancer	88 (11·6)	69·3	0·69	0·42–1·12	0·133	–	–	–
Other types of cancer	62 (8·2)	73·9	1·44	0·52–3·99	0·486	–	–	–
COVID-19 symptoms								
Cough	466 (61·6)	72·1	0·58	0·40–0·83	**0·003**	0·57	0·40–0·83	0·003
Fever	429 (56·7)	73·0	0·7	0·49–0·98	**0·038**	–	–	–
Oxygen saturation < 95%	494 (65·3)	77·5	1·31	0·93–1·84	**0·126**	–	–	–

SD: standard deviation. IQR: interquartile range. OR: odds ratio. ORa: adjusted odds ratio. CI: confidence interval. *p*-values in bold.

analyses showed age (aOR 1.02; 95% confidence interval [CI] 1.01–1.03; $p < 0.001$) and previous chronic pulmonary disease (aOR 2.02; 95%CI 0.96–4.28; $p = 0.064$) were risk factors for fatality. Being overweight (aOR 0.50; 95%CI 0.23–1.10; $p = 0.087$) and having a cough as a COVID-19 symptom (aOR 0.57; 95% I 0.40–0.83; $p = 0.003$) were protective factors (Table 1).

First, the highest lethality in patients with cancer draws attention because it is disproportionally higher than other studies, even in hospitalized environments [5]. This could be partially explained by characteristics of the studied population (patients with cancer and SARS due to COVID-19), magnitude of the disease, and associated risk factors [5].

Second, we observed that age increased the chance of death by 2% for each year of life, and lethality was higher in patients aged ≥80 years. This age group has the highest growth rate in Brazil and worldwide. However, we believe mortality by cancer in very old individuals tends to decrease or stabilize either by biological phenomenon or lack of notification in cancer registries [6]. Although the COVID-19 pandemic reduced life expectancy by 1.31 years in Brazil [7], the impact of COVID-19 in elderly individuals must also consider interactions among income inequality, poverty, and access to healthcare infrastructure (e.g., availability of physicians and hospital beds).

Aging is associated with a number of comorbidities, including cancer, while chronic diseases are risk factors for severe COVID-19. Although chronic pulmonary diseases are not very frequent comorbidities in COVID-19 patients, they were associated with high lethality in patients with cancer with COVID-19 and the general population [8].

Third, overweight patients with COVID-19 present more severe symptoms and high risk of death [9]; however, this might not be true in patients with cancer. We observed that being overweight was a protective factor, probably because muscle, fat reserve, or both contributed to reducing the impacts of sarcopenia/cachexia, improving prognosis.

Lastly, having a cough as a COVID-19 symptom was also a protective factor for patients with cancer in our study. Perhaps this could be explained because in the presence of cough, the patient may seek medical care early. This symptom is highly prevalent in critically ill patients hospitalized due to COVID-19 [10] and patients with cancer. Therefore, it should be considered an objective alert for patients and caregivers seek healthcare.

Although most patients with cancer and COVID-19 had solid tumors [3], they were not included in the priority vaccination group. On May 28, 2021, the Health Secretary of Pernambuco followed recommendations of the Brazilian Health Ministry, which gave priority for COVID-19 vaccination to patients with cancer aged between 55 and 59 who had chemo- or radiotherapy in the previous six months or had hematologic cancer. [11] Therefore, most patients with cancer with solid tumors or equally vulnerable groups (e.g., patients in palliative care or with other active illnesses) were not vaccinated.

Vulnerability to COVID-19 and complications in patients with cancer were probably due to tumoral activity, immunological suppression, antineoplastic treatment, and increased exposure for multiple diagnostic and treatment procedures [3]. Access, organization of healthcare, and its capacity to promote continuity of safe oncologic care in the pandemic must also be highlighted. The state of Pernambuco has one of the lowest rates of COVID-19 mortality per 100,000 inhabitants in Brazil (attributed to local government efforts) [3]. The highest and disproportional fatality rate among patients with cancer who developed SARS from COVID-19 is possibly due to inequity of conditions and challenges faced by patients with cancer.

Prevention and early access to oncologic and COVID-19 care need to be revisited to reduce inequities. Reorganization of healthcare networks and discussion about possible stigmas and ethical and humanitarian dilemmas related to cancer and aging are also needed. Unfortunately, actions from the Brazilian federal government regarding social distancing recommendations, testing volume, urgency to ensure vaccination, and clinical management differed from most countries and international organizations. Politicization of health and false and distorted information are still obstacles, limiting the fight against COVID-19 in Brazil.

The fight against diseases such as cancer, COVID-19, or both, demands that the healthcare system prioritize humanitarian questions. Therefore, recognition of this unequal fight is needed, especially in developing countries. Further evidence is required to assess the impacts of signs/symptoms, other comorbidities, and tumoral characteristics (e.g., tumor stage, current or past treatment type) in patients with cancer and associations among these important factors and risk of mortality.

Author contributions

Gabrielle R. Sena: Study concepts Study concepts and design, quality control of data and algorithms, data analysis and interpretation, statistical analysis, manuscript preparation, editing and review.

Jurema T. O. Lima: Study concepts Study concepts and design, quality control of data and algorithms, data analysis and interpretation, statistical analysis, manuscript preparation, editing and review.

Maria Julia G. Mello: Study concepts Study concepts and design, quality control of data and algorithms, data analysis and interpretation, statistical analysis, manuscript preparation, editing and review.

Tiago P. F. Lima: Data acquisition and quality control of data and algorithms.

Suely A. Vidal: Data analysis and interpretation.

Mozart J. T. Sales: Data acquisition.

Paulo S. A. Goes: Data acquisition.

Declaration of Competing Interest

The authors have no conflicts of interest to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jgo.2022.05.003.

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