Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Cancer Epidemiology 79 (2022) 102200

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep

Mortality in patients with cancer and SARS-CoV-2 infection: Results from the Argentinean Network of Hospital-Based Cancer Registries

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ARTICLE INFO

Keywords:
COVID-19
Cancer
Mortality
RITA
Argentina

ABSTRACT

Background: Cancer is an important risk factor in patients with COVID-19. We aimed to describe the clinical and demographic characteristics associated with mortality in patients with cancer who were infected with SARS-CoV-2.

Methods: We conducted a retrospective longitudinal study of 1206 patients with confirmed SARS-CoV-2 infection and cancer, registered in the Argentinean Network of Hospital-Based Cancer Registries (RITA) from March 31, 2020 to January 31, 2021. Demographic and clinical differences between survivors and non-survivors were summarized using descriptive statistics. The primary endpoint was all-cause mortality within 30 days of COVID-19 diagnosis. Risk factors for mortality were identified using logistic regression models.

Results: 1206 patients with cancer and confirmed SARS-CoV-2 infection were included, median age was 54 years (interquartile range: 42–65); 793 (65.8%) were female. 1101 (91.3%) had solid tumors and 105(8.7%) had hematological malignancies. The most frequent solid tumor was breast (278, 23.1%), while lymphoma was the main hematological one (59, 4.9%). Cervical cancer was more frequent in survivors, while lung cancer predominated in non-survivors. 275 (22.8%) patients were diagnosed with cancer within the past year. A total of 129 (10.7%) patients died within 30 days after COVID-19 diagnosis, with a case fatality rate of 15.2% (16/105) for hematologic malignancies and 10.3% (113/1101) for solid tumors. Multivariable regression analysis showed that age 60–79 (odds ratio [OR]: 4.69, 95% confidence interval [CI]: 2.72–9.70), age $\geq$ 80 (OR: 12.86, 95%CI: 5.08–32.54), time since cancer diagnosis $<$ 1 year (OR: 2.49, 95%CI: 1.57–3.93) and 1–2 years (OR: 2.20, 95%CI: 1.36–3.57), and lung cancer (OR: 4.35, 95%CI: 2.02–9.36) were risk factors for death.

Conclusion: Patients with cancer and SARS-CoV-2 infection had a high case-fatality rate. Identified risk factors (older age, recent diagnosis and lung type) could guide prevention strategies aimed at reducing the risk of dying from COVID-19 in cancer patients.

1. Introduction

Since the beginning of the SARS-CoV-2 pandemic in Wuhan in December 2019, many studies have shown that the risk of dying from COVID-19 is not uniform among infected patients, but depends on individual characteristics such as sex, age and presence and type of comorbidities. Cancer, a major cause of mortality worldwide, also increases the risk of COVID-19 [1]. There is evidence showing that individuals living with cancer have an increased risk of contracting SARS-CoV-2 infection and developing the disease [1–3]. This can be explained because of their systemic immunosuppressive status, caused by many factors such as the disease itself, the anticancer treatments, the increased immune response to infection secondary to immunomodulatory drugs, [4,5] and the frequent visits to hospitals [3]. In addition, cancer patients are often older and have one or more comorbidities [1, 6], which put them at risk of worse serious outcomes, additional intensive care hospitalization [7] and, eventually, an increased risk of death.

Although there is evidence suggesting that all-cause mortality is higher in COVID-19 patients with cancer than in those without cancer

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https://doi.org/10.1016/j.canep.2022.102200
Received 9 March 2022; Received in revised form 3 June 2022; Accepted 5 June 2022
Available online 8 June 2022

[2,8], mortality risk differs among cancer patients and results are sometimes contradictory. On the one hand, because of the physiological aging process and the greater prevalence of comorbidities in older patients, cancer patients aged 60 and above may have an increased risk of severe outcomes [5,7,9,10–12]. Nevertheless, results from a retrospective cohort [13] and a large meta-analysis [14] showed no increased risk of death in elderly people. On the other hand, while several studies have shown higher mortality from COVID-19 in patients with lung and hematological cancers [2,3,10,11,13,15–17], data from the Cancer Consortium (CCC19) registry [5] and from a cohort of cancer inpatients of the Brazilian National Cancer Institute (INCA) [18], reported no increased in mortality risk among leukemia patients. Moreover, an increased risk was seen in cancer patients diagnosed < 1 year before COVID-19 diagnosis [12,19]; for patients under cancer treatment in the past 3–12 months [18], and with recent chemotherapy [5,20]; contradicting Robilotti and colleagues [7] results, which showed no increased mortality risk among cancer patients treated with chemotherapy or surgery within 30 days before COVID-19 diagnosis.

Because of these heterogeneous results coming from studies with several limitations (small sample sizes, short follow-up period, only hospitalized patients), it is difficult to extract any solid conclusions. In Argentina, studies evaluating COVID-19 mortality in cancer patients are

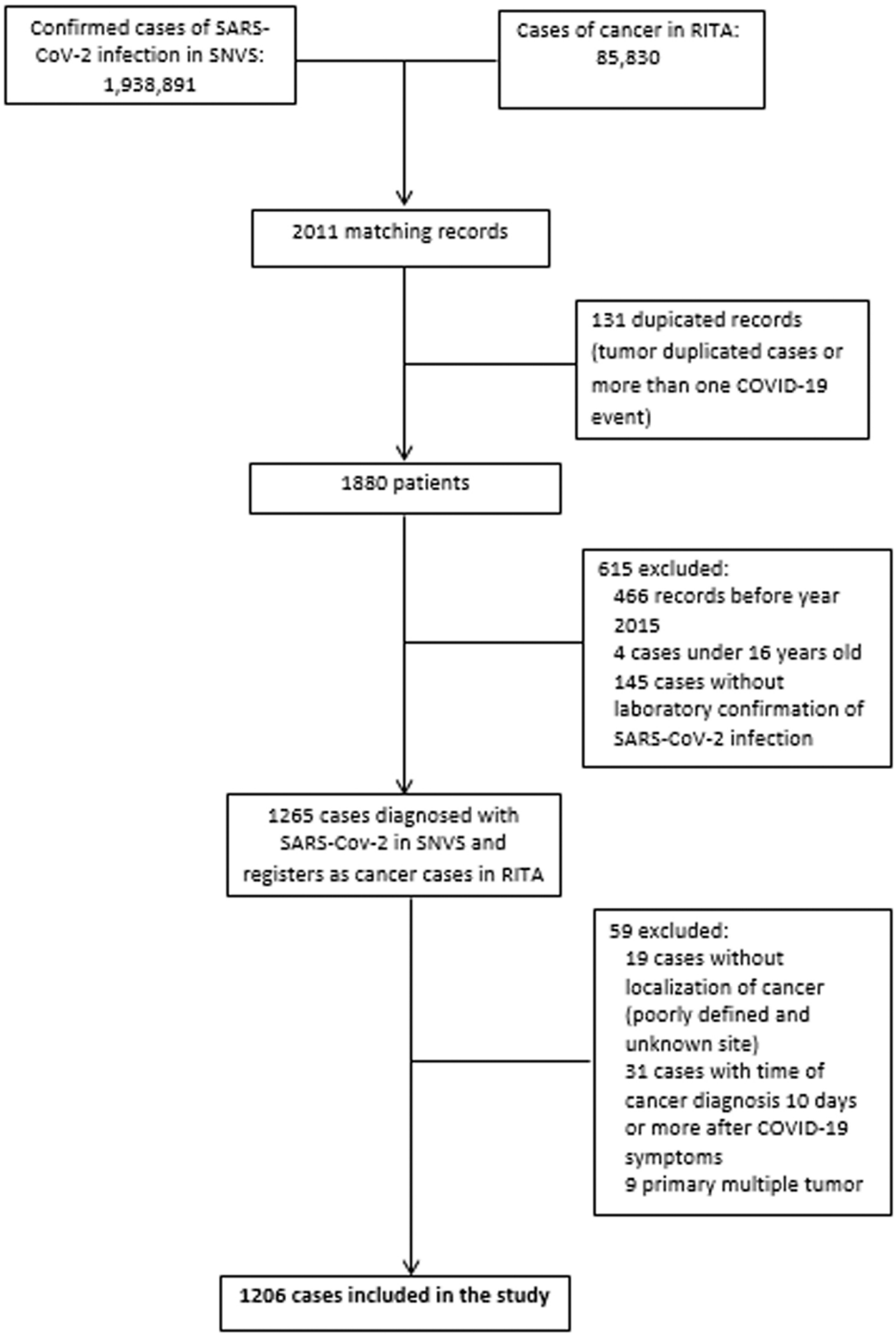

Fig. 1. Study profile.

scarce and involve a small number of patients (75) hospitalized in an oncology institution [21]. Better evidence about COVID-19 infection in cancer patients using local data is a priority for the management of these patients. Therefore, this study aims to describe the clinical and demographic characteristics associated with mortality in a large group of patients with cancer who was infected with SARS-CoV-2.

2. Methods

This retrospective longitudinal study analyzed data from cancer patients with confirmed SARS-CoV-2 infection between March 31, 2020, and January 31, 2021. Data on cancer were obtained from the Argentinean Network of Hospital-Based Cancer Registries (*Registro Institutional de Tumores de Argentina* - RITA), dependent of the National Institute of Cancer (INC). RITA is a national hospital-based cancer registry system created in 2011 and implemented in several public hospitals from 19 (out of 24) provinces. The registry contains administrative and clinical data from all cancer types in a standardized way, used for administration and improvement of quality of care purposes. Data provided by RITA come from hospitals adhered to the registry, which mainly belong to the public health subsystem. Mostly, these hospitals are reference centers within their jurisdiction. As other institutional cancer registries, RITA collects information of all new patients with cancer who are assisted in selected hospitals, which are not representative of the cases that occur in the entire population. Therefore, it is not possible to estimate population incidence. Furthermore, the frequency of registered tumors may reflect the epidemiological profile of the population assisted at a given institution.

Data on all confirmed COVID-19 positive patients were extracted from the National Health Surveillance System (SNVS 2.0), a registry based on mandatory electronic reporting of notifiable events. Linkages were performed using the National Identity Document (DNI) and surname. Recruitment procedure is shown in Fig. 1. Patients came from 34 hospitals distributed in 19 Argentinian provinces in which RITA was implemented. Contributing institutions independently report data from cancer patients through the online electronic database housed at the INC according to the procedures defined in RITA manuals. The cases had follow-up information, and we were able to obtain information on vital status.

Patients eligible for inclusion were people aged sixteen years or older, diagnosed with cancer between January 1, 2015, and January 31, 2021, and with laboratory-confirmed SARS-CoV-2 infection (n = 1880). Exclusion criteria were that SARS-CoV-2 diagnosis preceded the cancer diagnosis by at least 10 days and that tumor site was poorly defined or unknown. In cases of multiple primary tumors and, considering that our unit of analysis was the person (and not the tumor), we decided to exclude the first tumor diagnosed and keep the most recent tumor information. The number of people with more than one diagnosed tumor in the sample was too small (n = 9) and the study did not have enough power to identify differences between groups with and without a history of multiple primary tumors. The vital status of each patient was reviewed 30 days after the diagnosis of SARS-CoV-2 infection. This information was provided by SNVS 2.0 and was confirmed or completed with RITA records.

All procedures were conducted in accordance with the Helsinki Declaration, the International Ethical Guidelines for Health-related Research Involving Humans (2016), and the Personal Data Protection Law No. 25,326, ant the resolution of the Ministry of Health of the Nation No. 1480/11. The study was approved by the Research Ethics Committee of the National Hospital Prof. Alejandro Posadas, under registration number 600 EUPeS0/22/CEIHP.

3. Data collection

We obtained information about demographics, clinical and tumor characteristics, treatments, and vital status from electronic records. We found four cases of inconsistencies between sex and tumor site that were corrected in the system by contacting the registry. Duplicates tumor or COVID-19 event records were eliminated. The variables analyzed were sex, age (categorized as <40, 40–59, 60–79, and ≥80 years old), time since cancer diagnosis (categorized as <1, 1–2, and >2 years), Eastern Cooperative Oncology Group (ECOG) performance status score at cancer diagnosis, cancer stage, cancer type (hematological and solid), and cancer histology. Cancer stage was defined as the early (I–II) or late (III-IV) for solid tumors at cancer diagnosis according to the TNM staging system. The staging for hematological malignancies was not considered because the recommended staging system is different. Histology was classified using the International Classification of Diseases for Oncology, Third Edition (ICD-O3). Tumor sites in the sample included breast (C50), cervix uteri (C53), corpus uteri (C54), colorectal (C18-C20), lung (C34), skin (C44), prostate (C61), urinary tract (C64-C68), testis (C62). Hematological cancer was classified using the morphological codes as follows: lymphoma (959–972), leukemia (980–994), and other hematological (973–976, 998). History of treatment was limited to the first treatment at the institution registering the case.

Variables related to COVID-19 symptoms and clinical manifestations were obtained from the SNVS 2.0 mandatory notification form and included fever, dysgeusia, anosmia, cough, diarrhea, vomiting, pneumonia, respiratory insufficiency, dyspnea, headache, and myalgia.

Data on comorbidities were obtained from RITA records and SNVS 2.0 notification forms. They were grouped as cardiovascular, metabolic (which included diabetes and obesity), respiratory, neurological, chronic kidney, and chronic liver disease, immunosuppression, smoking and pregnancy. The number of comorbidities was grouped as (0, 1–2, ≥3).

The primary endpoint was all-cause mortality, defined as death among patients with cancer and COVID-19 within 30 days of diagnosis of COVID-19.

3.1. Statistical analysis

The hypothesis was that there were differences in demographic and clinical characteristics in patients with cancer history and SARS-CoV-2 infection between survivors and non-survivors. Quantitative variables were presented as medians (IQR), and qualitative variables were presented as frequencies and percentages (only available data were calculated). The median test, Fisher's exact test, χ^2 test, were applied to analyze the differences between groups according to the type of data.

To explore potential risk factors associated with death due to COVID-19 infection in cancer patients, odds ratio (OR) and 95% confidence interval (95%CI) were analyzed using bivariate logistic regression. For the multivariable logistic regression analysis, only those variables with complete data and statistical significance from the bivariate logistic regression analysis ($p < 0.05$) were included. Interaction terms to evaluate the interaction between covariates on mortality risk were also included. The tests used were all two-sided with less than 5% type I error. The differences between groups were considered to be significant when the p-value was less than 0.05. We used IBM SPSS Statistics 21.0 software for statistical analysis.

4. Results

4.1. Description of the population

From March 31 of 2020 to January 31 of 2021, 1880 patients with cancer registered in RITA were notified to the SNVS 2.0 with confirmed diagnoses of SARS-CoV-2 infection. Among these patients, 1206 met the criteria for inclusion and were enrolled (Fig. 1).

4.2. Demographic, clinical, and tumor characteristics for the enrolled population are described in Table 1

Of the 1206 patients with cancer included, 129 (10.7%) had died as of March 03, 2021. 793 (65.8%) patients were female. Median age was 54 years (IQR: 42–65) and 470 (38.9%) patients were aged 60 or older, whereas in the non-survivors group that age range represented 64.4%. The case-fatality rate increased with increasing age, reaching 23.5% in men and 30.3% in women aged 80 or older (Fig. 2).

The median time from cancer diagnosis to the onset of COVID-19 symptoms was 873 days (IQR: 1463–395). 275 (22.8%) patients had been diagnosed with cancer within the past year. Solid tumors were more frequent than hematological ones. The most prevalent solid tumor was breast (278, 23.1%) and cervical (228, 18.9%). Among hematological malignancies, lymphoma (59, 4.9%) and leukemia (27, 2.2%) predominated. Cervical cancer was more frequent in survivors, while lung cancer was more common in non-survivors.

Data of COVID-19 symptoms and clinical manifestation at SARS-CoV-2 diagnosis were available for 664 (55.0%) patients, the most common were cough and fever, followed by headache, myalgia, and fatigue. Compared with survivors, non-survivors were more likely to have dyspnea, chest pain, and pneumonia. Key COVID-19 symptoms like anosmia and dysgeusia were more common in survivors.

Comorbidities data were available in 748 (62%) patients. 477 (63.8%) of them had 1 or 2 comorbidities besides cancer, and 94 (12.6%) had three or more. Cardiovascular disease was the most frequent, followed by metabolic and smoking history (Table 1).

Clinical stage data were available for 453 (41.1%) of the 1101 solid tumors reported. Cancer stage I-II was the most frequent in the cohort (51.0%), while stage III-IV predominated in non-survivors (57.5%). ECOG performance at cancer diagnoses was missing for 462 (38.3%) patients. There were no differences in ECOG scores between survivors and non-survivors. Regarding the history of treatment, data were available for 711 cases (58.9%), with surgery (44.0%) and chemotherapy (32.8%) being the more frequent ones. History of chemotherapy seemed to predominate in non-survivors (47.1%).

We also compared the demographic, clinical and tumor characteristics between patients with solid and hematological cancer (Supplementary material). Case fatality rate was higher in patients with hematological malignancies (15.2%) than in those with solid tumors

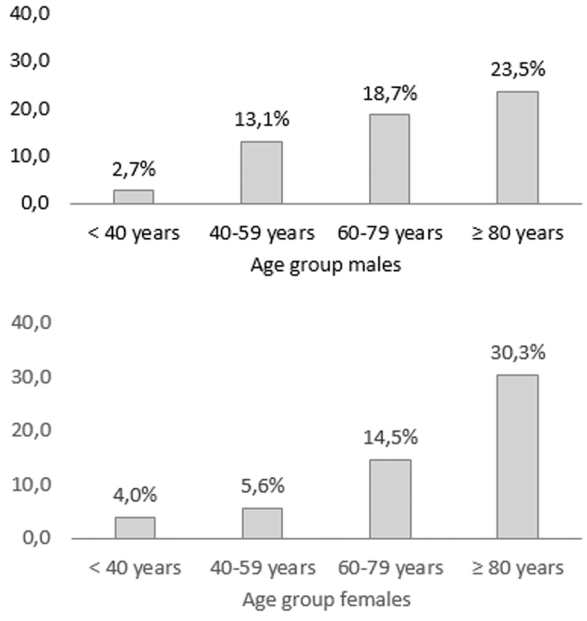

Fig. 2. Case fatality rate in patients with cancer and COVID-19 by sex and age group.

Table 1
Demographic and clinical characteristics in patients with cancer and COVID infection.

Variables	All patients (n = 1206)	Non-survivor (n = 129)	Survivor (n = 1077)	p-value
Sex				0.004
Male	413 (34.2%)	59 (45.7%)	354 (32.9%)	
Female	793 (65.8%)	70 (54.3%)	723 (67.1%)	
Age (median, IQR)	54 (42–65)	64 (56–71)	53 (41–64)	< 0.001
Age group, years				< 0.001
< 40	249 (20.6%)	9 (7.0%)	240 (22.3%)	
40–59	487 (40.4%)	37 (28.7%)	450 (41.8%)	
60–79	420 (34.8%)	69 (53.5%)	351 (32.6%)	
≥ 80	50 (4.1%)	14 (10.9%)	36 (3.3%)	
Cancer type				0.115
Solid tumor	1101 (91.3%)	113 (87.6%)	988 (91.7%)	
Hematological	105 (8.7%)	16 (12.4%)	89 (8.3%)	
Tumor localization				
Solid tumor				
Breast	278 (23.1%)	25 (19.4%)	253 (23.5%)	0.295
Cervical	228 (18.9%)	9 (7.0%)	219 (20.3%)	< 0.001
Colorectal	97 (8.0%)	11 (8.5%)	86 (8.0%)	0.831
Skin	90 (7.5%)	6 (4.7%)	84 (7.8%)	0.198
Prostate	44 (3.6%)	2 (1.6%)	42 (3.9%)	0.221
Kidney and urinary tractor	37 (3.1%)	7 (5.4%)	30 (2.8%)	0.105
Testicle	30 (2.5%)	1 (0.8%)	29 (2.7%)	0.361
Lung	34 (2.8%)	13 (10.1%)	21 (1.9%)	< 0.001
Uterus body	33 (2.7%)	6 (4.7%)	27 (2.5%)	0.155
Other solid†	230 (19.1%)	33 (25.6%)	197 (18.3%)	0.046
Hematological				
Lymphoma	59 (4.9%)	8 (6.2%)	51 (6.2%)	0.466
Leukemia	27 (2.2%)	5 (3.9%)	22 (2.0%)	0.199
Others of RES	19 (1.6%)	3 (2.3%)	16 (1.5%)	0.447
Time since cancer diagnosis				< 0.001
≤ 1 year	275 (22.8%)	50 (38.8%)	225 (20.9%)	
1–2 year	248 (20.6%)	31 (24.0%)	217 (20.1%)	
> 2 year	683 (56.6%)	48 (37.2%)	635 (59.0%)	
Cancer Stage*				0.025
In situ	53/453 (11.7%)	2/40 (5.0%)	51/413 (12.3%)	
I-II	231/453 (51.0%)	15/40 (37.5%)	21/413 (52.3%)	
III-IV	169/453 (37.3%)	23/40 (57.5%)	146/413 (35.4%)	0.190
Non information	648 (58.9%)	73 (64.6%)	575 (58.2%)	
ECOG performance status score*				0.011
0	382/744 (51.3%)	30/73 (41.1%)	352/671 (52.5%)	
1	307/744 (41.3%)	32/73 (43.8%)	275/671 (41.0%)	
2	37/744 (5.0%)	5/73 (6.8%)	32/671 (4.8%)	
3	16/744 (2.2%)	5/73 (6.8%)	11/671 (1.6%)	
4	2/744 (0.3%)	1/73 (1.4%)	1/671 (0.1%)	
Non information	462 (38.3%)	56 (43.4%)	406 (37.7%)	0.207
ECOG performance status score in last year*				0.071

(continued on next page)

Table 1 (*continued*)

Variables	All patients (n = 1206)	Non-survivor (n = 129)	Survivor (n = 1077)	p-value
0	87/162 (53.7%)	11/26 (42.3%)	76/136 (55.9%)	
1	61/162 (37.7%)	10/26 (38.5%)	51/136 (37.5%)	
2	5/162 (3.1%)	3/26 (11.5%)	2/136 (3.1%)	
3	8/162 (4.9%)	2/26 (7.7%)	6/136 (4.9%)	
4	1/162 (0.6%)	0/26 (0%)	1/136 (0.6%)	
Non information	113 (41.1%)	24 (48.0%)	89 (39.6%)	0.272
Comorbidities*				
Cardiovascular disease	308/748 (41.2%)	46/100 (46.0%)	262/648 (40.4%)	0.292
Metabolic disease	226/748 (30.1%)	36/100 (36.0%)	190/648 (29.3%)	0.176
Smoking	216/748 (28.8%)	32/100 (32.0%)	188/648 (28.2%)	0.439
Respiratory disease	73/748 (9.8%)	15/100 (15.0%)	58/648 (9.0%)	0.058
Immunosuppression	50/748 (6.7%)	7/100 (7.0%)	43/648 (6.6%)	0.892
Renal disease	46/748 (6.1%)	10/100 (10.0%)	36/648 (5.6%)	0.085
Neurological disease	19/748 (2.5%)	5/100 (5.0%)	14/648 (2.2%)	0.160
Liver disease	13/748 (1.7%)	4/100 (4.0%)	9/648 (1.4%)	0.083
Pregnancy	5/748 (0.7%)	1/100 (1.0%)	4/648 (0.6%)	0.513
Non information	458 (38.0%)	29 (22.5%)	429 (39.8%)	< 0.001
Number of comorbidities*				0.003
0	177/748 (23.7%)	20/100 (20.0%)	157/648 (24.2%)	
1–2	477/7484 (63.8%)	57/100 (57.0%)	420/648 (64.8%)	
> 3	94/748 (12.6%)	23/100 (23.0%)	71/648 (11.0%)	
COVID-19 manifestations*				
Cough	376/664 (56.6%)	48/78 (61.5%)	328/586 (56.0%)	0.351
Fever	365/664 (55.0%)	46/78 (59.0%)	319/586 (54.4%)	0.449
Headache	276/664 (41.6%)	13/78 (16.7%)	263/586 (44.9%)	< 0.001
Myalgia	231/664 (34.8%)	22/78 (28.2%)	209/586 (35.7%)	0.194
General discomfort	213/664 (32.1%)	20/78 (25.6%)	193/586 (32.9%)	0.195
Odynophagia	210/664 (31.6%)	10/78 (12.8%)	200/586 (34.1%)	0.001
Anosmia	133/664 (20.0%)	2/78 (2.6%)	131/586 (22.4%)	< 0.001
Dyspnea	111/664 (16.7%)	33/78 (42.3%)	78/586 (13.3%)	< 0.001
Diarrhea	93/664 (14.0%)	10/78 (12.8%)	83/586 (14.2%)	0.748
Dysgeusia	84/664 (12.7%)	3/78 (3.8%)	81/586 (13.8%)	0.013
Arthralgia	62/664 (9.3%)	8/78 (10.3%)	54/586 (9.2%)	0.766
Chest pain	50/664 (7.5%)	11/78 (14.1%)	39/586 (6.7%)	0.019
Respiratory insufficiency	48/664 (7.2%)	16/78 (20.5%)	32/586 (5.5%)	< 0.001
Vomiting	44/664 (6.6%)	7/78 (9.0%)	37/586 (6.2%)	0.375
Abdominal pain	31/664 (4.7%)	5/78 (6.4%)	26/586 (4.4%)	0.395
Pneumonia	31/664 (4.7%)	8/78 (10.3%)	23/586 (3.9%)	0.021
Non information	543 (44.9%)	47 (38.2%)	496 (45.7%)	0.115
History of treatments*				
Surgery	313/711 (44.0%)	28/70 (40.0%)	285/641 (44.5%)	0.475
Chemotherapy	233/711 (32.8%)	33/70 (47.1%)	200/641 (31.2%)	0.007
Radiotherapy	91/711 (12.8%)	5/70 (7.1%)	86/641 (13.4%)	0.136
Hormonotherapy	52/711 (7.3%)	3/70 (4.3%)	49/641 (7.6%)	0.305
Immunotherapy	4 /711 (0.6%)	0/70 (0%)	4/641 (0.6%)	1.000
Other treatments	18/711 (2.5%)	1/70 (1.4%)	17/641 (2.7%)	1.000
Non information	495 (41.0%)	59 (45.7%)	436 (40.5%)	0.252
Treatments within 4 weeks before symptoms onset*				
All	23/700 (3.3%)	7/69 (10.1%)	16/631 (2.5%)	0.005
Surgery	14/23 (60.9%)	6/7 (85.7%)	8/16 (50.0%)	0.116
Chemotherapy	6/23 (26.1%)	1/7 (14.3%)	5/16 (31.3%)	0.612
Radiotherapy	3/23 (13.0%)	0/7 (0%)	3/16 (18.8%)	0.526
Treatments within last year before symptoms onset*				
All	159/700 (22.7%)	30/69 (43.5%)	129/631 (20.4%)	< 0.001
Surgery	77/159 (48.4%)	13/30 (43.3%)	64/129 (49.6%)	0.535
Chemotherapy	57/159 (35.8%)	14/30 (46.7%)	43/129 (33.3%)	0.170
Radiotherapy	13/159 (8.2%)	1/30 (3.3%)	12/129 (9.3%)	0.465
Hormonotherapy	8/159 (5.0%)	1/30 (3.3%)	7/129 (5.4%)	1.000
Other treatments	4/159 (2.5%)	1/30 (3.3%)	3/129 (2.3%)	0.571

Data are n (%) or IQR = interquartile rate. RES= reticular endothelial system. † Other solids: thyroid, brain, stomach, ovary, melanoma, bladder, pancreas, unspecified uterus, soft tissue malignant tumor liver and intrahepatic bile ducts, larynx, gallbladder and intrahepatic bile ducts, bone, esophagus, other thoracic organs, anus, nostril, sinuses, middle ear, mouth, parotid, salivary glands, tongue, amygdala, other malignant tumors of the female genitalia, nasopharynx, oropharynx, pharynx and poorly defined lip and mouth, small intestine, other digestives, eye, penis. *From available data.

(10.3%), although the difference was not statistically significant. Patients with solid tumor were more frequently females (751/1101, 68.2%), while hematological malignancies predominated in males (63/105, 60.0%). Cardiovascular disease history was more frequent in patients with solid tumors than in those with hematological malignancies (294/680, 43.2% vs 14/68, 20.6%), as well as metabolic disease history (214/680, 31.5% vs 12/68, 17.6%).

Conversely, immunosuppression history predominated in hematological malignancies (13/68, 19.1% vs 37/680, 5.4%). From 666 patients with solid tumors and information about treatment, 313 (44.0%) had history of surgery, while 42 (93.3%) of 45 with hematological malignancies had history of chemotherapy. Regarding history of treatment within the last year before the onset of COVID-19 symptoms, 77 (52.0%) of 148 patients with solid tumor had surgery compared with none of the patients with hematological malignancies, and 11 (100%) of

patients with hematological malignancies received chemotherapy compared with 46 (31.1%) of 148 with solid tumors.

The association between demographic and clinical factors and death among patients with cancer and COVID-19 is summarized in Table 2. Results show that male sex, age older than 40, type of cancer (lung), and time since cancer diagnosis (less than two years) increased the risk of death; while cancer stage, number of comorbidities, respiratory symptoms and ECOG performance status did not show a statistically significant difference. Statistically significant variables with completed data were included in the multivariable regression analysis (Table 2).

Results showed that age 60–79 (OR: 4.69 [95%CI: 2.72–9.70]) and ≥ 80 (OR: 12.86 [95%CI: 5.08–32.54]), time since cancer diagnosis less than 1 year (OR: 2.49 [95%CI: 1.57–3.93]) and 1–2 years (OR: 2.20 [95%CI: 1.36–3.57]), and lung cancer (OR: 4.35 [95%CI: 2.02–9.36]) were associated with increased odds of death. There was no interaction effect between the selected variables (Supplementary material).

5. Discussion

To our knowledge, this is the first large report describing the clinical features and risk factors for mortality among patients with cancer diagnosed with SARS-Cov-2 in Argentina during the first year of the pandemic. By integrating data from cancer registries (RITA, INC) with data on COVID-19 from the national surveillance system (SNVS 2.0), we found that patients with cancer are at higher risk of mortality once diagnosed with COVID-19. Furthermore, the risk of dying increased with age and was greater in patients older than 60 years, when time since cancer diagnosis was more recent (less than two years), and in those with lung cancer, but not with hematological malignancies.

Our findings show an overall case-fatality rate of 10.2%, nearly four-fold higher than the CFR observed in the Argentine general population (2.7%) [22], and similar to those reported by a Brazilian cancer center (12.4%) [10], by the Cancer Consortium database (CCC19) (13%) [5], and by the PRE-COVID-19 study (10%) [23]. In contrast, it is lower than the observed in Hubei (20%) [13], and by the UK Coronavirus Cancer Monitoring Project (UKCCMP) (28%) [24]. Reasons for these findings are unclear, but these two latter studies are based on hospitalized patients, enrolling more severe cases. Patients from the UKCCMP tend to be older, with a greater probability to require hospitalization and having adverse events. Conversely, our case-fatality is considerably higher than that found by Williams [25], who used the infection fatality rate in order to correct for the ascertainment bias (when only more ill patients are tested for the disease). Our data demonstrate that the risk of death in patients with cancer and COVID-19 increases substantially with age. This result is consistent with previous studies showing that age is a key determinant of the prognosis among patients with COVID-19 and cancer [5,7,10–12,24]. An early report from China did not find significant differences in age between survivors and non- survivors, probably because the study already included an elderly population [13]. Interestingly, in comparison with the general population, elderly patients with cancer may not be at increased risk of death when infected with COVID-19 [14], which implies that the presence of cancer may not

Table 2
Logistic regression models. Risk factors associated with death in cancer patients with SARS-CoV-2 infection (n = 1206).

Variables	Univariable OR (IC95%)	p value	Multivariable OR (IC95%)	p value
Sex				
Female	1 (Ref)	…	…	…
Male	1.72 (1.19–2.49)	0.004	1.34 (0.89–1.98)	0.152
Age range, years				
≤ 40	1 (Ref)	…	…	…
40–59	2.19 (1.04–4.62)	0.049	2.13 (1.01–4.53)	0.054
60–79	5.24 (2.57–10.70)	< 0.001	4.69 (2.72–9.70)	< 0.001
> 80	10.37 (4.18–25.70)	< 0.001	12.86 (5.08–32.54)	< 0.001
Time since cancer diagnosis				
> 2 years	1 (Ref)	…	…	…
1–2 years	1.89 (1.17–3.04)	0.009	2.20 (1.36–3.57)	0.001
≤ 1 year	2.94 (1.92–4.49)	< 0.001	2.49 (1.57–3.93)	< 0.001
Tumor localization				
Other cancer	1 (Ref)	…	…	…
Lung	5.63 (2.75–11.55)	< 0.001	4.35 (2.02–9.36)	< 0.001
Cancer stage				
In situ	1 (Ref)	…		
I-II	1.77 (0.39–7.99)	0.457		
III-IV	4.02 (0.91–17.64)	0.065		
Number of comorbidities				
0	1 (Ref)	…		
1–2	1.07 (0.62–1.83)	0.819		
> 3	2.54 (1.31–4.93)	0.006		
Symptoms				
Dyspnea	4.78 (2.87–7.94)	< 0.001		
Respiratory insufficiency	4.47 (2.32–8.60)	< 0.001		
Chest pain	2.30 (1.13–4.71)	0.022		
Pneumonia	2.80 (1.21–6.49)	0.017		
Anosmia	0.09 (0.02–0.38)	0.001		
Dysgeusia	0.25 (0.08–0.81)	0.021		
Odynophagia	0.28 (0.14–0.56)	< 0.001		
Headache	0.25 (0.13–0.45)	< 0.001		
ECOG performance status score				
0	1 (Ref)	…		
1	1.37 (0.81–2.30)	0.243		
2	1.83 (0.66–5.05)	0.241		
3	5.33 (1.73–16.36)	0.003		
4	11.73 (0.72–192.33)	0.084		
Chemotherapy				
No	1(Ref)	…		
Yes	1.97 (1.19–3.24)	0.008		

further increase the already poor prognosis among elderly people.

As other studies indicate, mortality is significantly affected by the type of tumor [2,3,10,11,13,15–17]. From our analysis, patients with lung cancer have the highest death rates among all patients. Decreased lung function and severe infection in patients may contribute to the worse outcome in this subgroup [2]. As other studies have shown [5,18, 21], we did not find increased risk of death in patients with leukemia or other hematological malignancies. Patients with hematologic cancer, especially leukemia and myeloma, are more often treated with more myelosuppressive therapy and are severely immunocompromised because of underlying disease, so they may potentially be more susceptible to cytokine-mediated inflammation [11]. Despite the fact that the case-fatality rate was higher in patients with hematological malignancies, our study did not have enough power to show statistical significance. As Mehta et al. [26] have shown, results may reflect the prognosis of main cancer types at the country. In Argentina, the annual mortality (ratio of annual deaths/new diagnosis) is the highest for lung cancer (88.6%) and is also high for hematological malignancies (55.8%) [27], suggesting that COVID-19 infection may increase the mortality risk associated with the type of cancer itself. Consistent with other studies [12,18,25], we observed an increased risk of death for patients recently diagnosed with cancer, which supports the fact that patients with active or progressive disease, as they have increased levels of immunosuppression (intrinsic or by cancer treatment), have a worse outcome [5].

The strengths of this study include sample size, study length and database linkage. The use of COVID-19 data from the National Health Surveillance System allowed us to match laboratory-confirmed SARS-CoV-2 cases from our cancer registry over a sustained period of time and obtain a considerable number of cases for analysis. During this period, several waves occurred, which determined the availability of hospital technical and human resources, as well as the ICU ventilation capacity that could have affected the risk of mortality [28]. We used laboratory-confirmed cases to avoid possible confounding by other infections. However, it depends on the sensitivity of the PCR diagnostic test, and it is likely that the number of cancer patients affected with COVID has been underestimated [23]. Also, reported cases varied depending on the availability of testing, and it is expected that patients with mild or asymptomatic disease had not been tested and were, therefore, not included in this study. Other limitations include the incomplete documentation for many variables of interest, which does not allow us to evaluate the effect of treatment, comorbidities, and other measures of severity of disease such as hospitalization or need for intensive care.

Our results have to be interpreted in the health care context of Argentina. Despite Argentina has universal access to health, the health system is fragmented in terms of financing and service delivery into three subsectors: the public subsector (national, provincial, and municipal), the social security subsector, and the private health subsector. Such fragmentation has been proposed as one of the causes of inequalities in health care [29]. In this line, studies have shown that the lack of health insurance is one of the factors explaining inequalities in cancer mortality [30] and cancer screening underuse in Argentina [31, 32]. As RITA is mainly implemented in public hospitals, which assist mostly low-income people with (only) the public coverage, it may result in a selection bias and cases registered could experience worse health outcomes than insured cases. However, in our sample, the proportion of people without formal health coverage was 39%, and with social security 44%, similar to the general population (according to the 2010 Population Census).

During the first year of the pandemic, isolation measures in Argentina were strict, and professional societies discouraged unnecessary visits to hospitals to prevent cancer patients from developing COVID. In turn, changes in cancer care could have caused delays in treatment, and a reduction in early cancer diagnosis, which might result in excess deaths from cancer in the future [33].

6. Conclusions

In conclusion, patients with cancer who develop COVID-19 have a high case-fatality rate. Clinicians should pay special attention to those subgroups of cancer patients that showed a major vulnerability, such as those over 60 years of age, with lung cancer, and recently diagnosed. The risk factors identified emphasize the need to develop specific strategies aimed at reducing the risk of dying from COVID-19. Also, imperative efforts should be made to improve the quality of cancer registries.

CRediT authorship contribution statement

Gisel L. Fattore: Project administration, Conception and study design, Methodology, Interpretation of data, Writing – original draft. **Natalia S. Aráoz Olivos**: Methodology, Formal analysis and interpretation of data, Writing – review & editing. **Jose E. Carrizo Olalla:** Interpretation of data, Writing – review & editing, Visualization. **Lara Gomez**: Conception and study design, Data collection, Writing – review & editing. **Agustina Flamenco Marucco**: Data collection, Formal analysis and interpretation of data, Writing – review & editing. **María Paz Rojas Mena**: Data collection, Formal analysis and interpretation of data, Writing – review & editing.

Acknowledgments

We thank all registrars involved in data collection and registration in RITA, the National Epidemiology Direction who provided the COVID data, and Antonia Rodríguez (National Program for the Prevention and Early Detection of Colorectal Cancer, National Cancer Institute), and Mariana Haereber who provided language help.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.canep.2022.102200.

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