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.

Seminars in Oncology 48 (2021) 145–151

Contents lists available at ScienceDirect

Seminars in Oncology

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

Incidence of COVID-19 in outpatients with cancer receiving active treatment in the context of a pandemic: An Andalusian cohort study ☆

Celia Martín-Bravo [a], Raúl Quirós [c,f], Isabel Blancas [b], Rosa Villatoro-Roldán [a], Marta Robles [a], Julia Alcaide [a,f], Víctor Navarro [a], Diego Pérez [a], Irene Zarcos [a,f], Francisco Rivas-Ruiz [d,f], Elisabeth Pérez-Ruiz [a,e,f,*], Cristina Quero [a]

[a] Oncology Department, Costa del Sol Hospital, Marbella, Spain. A-7, Km 187, 29603 Marbella, Málaga
[b] Oncology Department, San Cecilio Clinical Hospital, Granada, Spain. Avenida del Conocimiento, s/n, 18016 Granada
[c] Medicine Department, Costa del Sol Hospital, Marbella, Spain. A-7, Km 187, 29603 Marbella, Málaga
[d] Research Unit, Costa del Sol Hospital, Marbella, Spain. A-7, Km 187, 29603 Marbella, Málaga
[e] Biomedical Research Institute of Málaga (IBIMA), Málaga, Spain. St. Dr. Miguel Díaz Recio, 28, 29010 Málaga
[f] Research Network on Health Services in Chronic Diseases (REDISSEC), Marbella, Málaga

ARTICLE INFO

Article history:
Received 23 November 2020
Revised 20 January 2021
Accepted 20 January 2021

Keywords:
COVID-19
Cancer
Active treatment
Outpatients
Incidence
Chemotherapy

ABSTRACT

Background: Leading scientific societies have recommended delaying and/or suspending active cancer treatment during the COVID-19 pandemic. Nevertheless, data on this novel infection in patients with a diagnosis of cancer receiving active treatment are scarce and it is unknown if these recommendations could have repercussions on future progress of the disease. The main objective of this study is to learn the COVID-19 incidence rate in outpatients with cancer receiving active treatment.
Methods: This work is a retrospective cohort study that included all patients with a diagnosis of cancer who received active cancer treatment in two Andalusian hospitals between February 26 and May 13, 2020. Variables regarding the patient, tumor, and development of COVID-19 were collected. A descriptive analysis was performed and the cumulative incidence of COVID-19 in these patients was evaluated.
Results: A total of 673 patients were included. The median age was 62 years. There was a low rate of comorbidity and 12.1% had an ECOG >2. Breast cancer was the most common cancer (41%), followed by colorectal and lung cancer. Stage IV cancer was reported in 52.7% of patients. The most common treatment was chemotherapy (53.9%). Treatment was delayed or suspended in 6% of patients. Only three patients developed COVID-19. The cumulative incidence was 0.44% and one person died due to infection.
Conclusions: In the present retrospective cohort study we found a low incidence of COVID-19 infection in patients with cancer receiving active treatment in an outpatient setting. The sociodemographic factors of Andalusia may explain why these results differ from those presented by other colleagues in Spain, but raise questions about whether universal recommendations may put the benefits of antineoplastic therapy at risk.

Introduction

The pandemic caused by the novel coronavirus SARS-CoV-2 [1] is giving rise to unprecedented social and medical measures, especially in at-risk groups such as patients with cancer. These patients, who are more susceptible to infection due to their illness and the treatments they receive, are considered to be at high risk of contracting and dying from COVID-19 [Table 1] [2–7].

Leading scientific societies have recommended that active treatment be delayed or suspended in these patients during the pandemic [8,9]. However, these recommendations are based on small, retrospective studies carried out in China, in which greater

☆ We would like to thank the Research Unit of the Costa del Sol Healthcare Agency for their support in the translation of the manuscript.

* Corresponding author.
E-mail addresses: celiam1994@hotmail.com (C. Martín-Bravo), quiroslopez77@gmail.com (R. Quirós), iblancas@ugr.es (I. Blancas), villatororoldan@gmail.com (R. Villatoro-Roldán), mrobleslasarte@gmail.com (M. Robles), drayulia@hotmail.com (J. Alcaide), victor.navarr1@gmail.com (V. Navarro), dipema2026@gmail.com (D. Pérez), irenezarcos@hotmail.com (I. Zarcos), frivasr@hcs.es (F. Rivas-Ruiz), eliperu@gmail.com (E. Pérez-Ruiz), cquerob@gmail.com (C. Quero).

https://doi.org/10.1053/j.seminoncol.2021.01.002
0093-7754/

Table 1
Summary of literature describing risk of COVID infection in patients with a diagnosis of cancer.

• Author [Year] Reference	• Number of patients • Duration of period of observation in months • Number that developed COVID	• Rik factors • Comorbidities	• Cancer distribution	• Comments
• Robilotti[3] [2000]	• 2,035 patients with cancer tested • Diagnosed at Memorial Sloan Kettering Cancer Center between 10 March to 7 April 2020 • 423 cases of symptomatic COVID-19	• ≥65 years and treatment with immune checkpoint inhibitors predictors for hospitalization and severe disease, whereas receipt of chemotherapy and major surgery were not. • At least one co-morbid condition present in 248 (59%) patients: – Diabetes – Hypertension – Chronic kidney disease – Cardiac disease • Correlated with severe outcomes: – Age – Non-white race – Treatment with ICI • Not associated with a higher risk of complications: – Receipt of chemotherapy within 30 d before COVID-19 diagnosis – Recent major surgery – Metastatic disease • COVID-19 milder among children with cancer	• COVID-19 in 423/2,035 = 21% of patients with a diagnosis of cancer • 56% metastatic solid tumors – Breast (86, 20%) – Colorectal (37, 9%) – Lung (35, 8%) • Hematologic malignancy: – Lymphoma (48, 11%)	• Less about incidence of COVID in patients with cancer than about rate of COVID-19 infection in patients with cancer – Must infer risk factors for infection in cancer patients • Recognized “critical to balance the competing safety considerations of reducing SARS-CoV-2 exposure and cancer treatment continuation”
• Lee[4] [2020]	• Compared adult patients with cancer enrolled in the UK Coronavirus Cancer Monitoring Project (UKCCMP) cohort, with a parallel non-COVID-19 UK cancer control population from the UK Office for National Statistics (ONS, 2017 data) • Patients enrolled in UKCCMP between March 18 and May 8, 2020 • 319 (30.6%) of 1044 patients in the UKCCMP cohort died, 295 (92.5%) of whom had a cause of death recorded as due to COVID-19 • ONS control population is a control cohort comprising all patients with a diagnosis of cancer in 2017	• All-cause CFR in patients with cancer after SARS-CoV-2 infection significantly associated with increasing age [0.10 in patients 40-49 years; 0.48 in ≥80 years • Patients with leukemia, lymphoma, and myeloma had a more severe COVID-19 trajectory compared with patients with solid tumors (rOR 1.57, 95%CI 1.15-2.15; p<0.0043)	• Over-represented in the UKCCMP patient cohort compared with the ONS control population. – Leukemia (OR 2.82, 95%CI 2.21–3.55; p<0.0001) – Myeloma (2.03, 95%CI 1.42–2.83; p=0.0001), – Lymphoma (1.63, 95%CI 1.28–2.06; p<0.000 • Under-represented in the UKCCMP population compared with the control ONS population – Lung cancer – Prostate cancer	• Authors concluded “patients with cancer with different tumor types have differing susceptibility to SARS-CoV-2 infection and COVID-19 phenotypes” • Indirect evidence for susceptibility with cancer. Evidence of vulnerability inferred by looking at distribution in the UKCCMP cohort and the ONS cohort • Over-representation in UKCCMP cohort taken as “perhaps suggestive of an a priori increased susceptibility to viral infection”. • Limitations: Based on patients with symptomatic cancer, high proportion with advanced or metastatic disease ongoing active oncology follow-up.

(*continued on next page*)

Table 1 (*continued*)

• Dai[5] [2020]	• Only 105 patients with cancer; 536 age-matched non-cancer patients • Enrolled on study between January 1, 2020 and February 24, 2020 from 14 hospitals in Wuhan China	• Increased frequency of severe events: – Hematologic cancer – Lung cancer – Metastatic (stage IV) cancer – Recent surgery • Similar frequencies of severe conditions: – Nonmetastatic cancer – Only radiotherapy	• Cancer types: – Lung cancer: 22/105 (20.95%) – Gastrointestinal: 13/105 (12.38%) – Breast cancer: 11/105 (10.48%) – Thyroid cancer: 11/105 (10.48 – Hematologic cancer: 9/105 (8.57%)	• Risk factors are for severity of illness. Risk for getting COVID can only be inferred • Lung cancer is most common cancer in China, and would be over-represented in Chinese patients with COVID-19 and cancer. • Also suggests results may reflect cancer distribution at source
• Grassino[6] [2020]	• Report from the Thoracic Cancers International COVID-19 Collaboration (TERAVOLT) registry, a multicenter observational study • First 200 patients entered into the TERAVOLT registry • Between March 26 and April 12, 2020, data on patients from 42 institutions across eight countries (Italy, Spain, France, Switzerland, Netherlands, USA, UK, and China)	• At time COVID infection: – 74% stage IV disease – 74% on active oncological – 57% on first line with therapy administered a median of 7 days before COVID-19 diagnosis. • Treatment with TKIs decreased risk for hospitalization • Immunotherapy did not worsen outcomes	• Main eligibility criteria were patients with thoracic cancer – Non-small cell lung cancer – Small-cell lung cancer – Mesothelioma – Thymic epithelial tumours – Other pulmonary neuroendocrine neoplasms	• This study did not use a control group -stage IV disease and active treatment possible risk factors for infection • Findings suggest withholding or discontinuing TKIs or immunotherapy for a patient out of fear of COVID-19 might not be warranted
• Wang[7] [2020]	• Case-control analysis of electronic medical records from 73.4 million unique patients from 360 hospitals and 317 000 clinicians across 50 US states to August 14, 2020. The harvest included 2,523,920 diagnosed with at least 1 of 13 common cancers; 273,140 cancer diagnoses occurred within the past year • 16 570 were diagnosed with COVID-19; 1200 with both COVID-19 and cancer. • 53.64% female and 45.67% male • Cancers [total/recent] included – Bladder: 38,890/14,300 – Breast: 663,250/70,580 – Colorectal: 317,580/25,150 – Endometrial: 41,740/7,750 – Kidney: 124 170/12,810 – Leukemias: 137,890/16,930 – Liver: 193,140/15,070 – Lung: 419,050/34,830Melanomas: 198,890/11,490 – NHL: 168,750/26,460 – Pancreatic: 70,950/5,280 – Prostate: 487,560/61,010 – Thyroid: 109,870/14,140	• Significantly increased risk for COVID-19 infection for all 13 cancer types, if recently diagnosed. • Associations adjusted for comorbidities, cancer treatments, transplant procedures, and nursing home stay, alone and together: • African Americans had significantly higher risk for COVID-19 infection than White patients • Racial disparity largest for: – Breast (aOR, 5.44 [95%CI, 4.69-6.31]; $P < .001$) – Prostate (aOR, 5.10 [95% CI, 4.34-5.98]; $P < .001$) – Colorectal (aOR, 3.30 [95% CI, 2.55-4.26]; $P < .001$) – Lung (aOR, 2.53 [95%CI, 2.10-3.06]; $P < .001$). • African Americans more likely infected by COVID-19 than White patients after adjusting for age, sex, and COVID-19 risk factors, with the largest race disparity for breast, prostate, colorectal and lung cancer and weakest but still significant for leukemia. • Women higher risk of COVID-19 than men for colorectal cancer and NHL • Age in general had no association	• Increased risk for COVID-19 infection in: – Recent cancer diagnosis: aOR, 7.14 [95%CI, 6.91-7.39]; $P < .001$ – All cancer diagnosis: aOR, 1.46 [95%CI, 1.42-1.50]; $P < .001$ • Significantly increased risk for COVID-19 infection for all 13 cancer types, if recently diagnosed. • Associations after adjusting for comorbidities, cancer treatments, transplant procedures, and nursing home stay, alone and together: – Leukemia: aOR, 12.16 [95%CI, 11.03-13.40]; $P < .001$, – NHL: aOR, 8.54 [95%CI, 7.80-9.36]; $P < .001$ – Lung: aOR, 7.66 [95%CI, 7.07-8.29]; $P < .001$ – Liver: aOR, 6.49 [95%CI, 5.71-7.38]; $P < .001$ – Breast: aOR, 6.47 [95%CI, 6.06-6.91]; $P < .001$ – Colorectal: aOR, 6.36 [95%CI, 5.71-7.08; $P < .001$ – Pancreatic aOR, 6.26 [95%CI, 4.98-7.87; $P < .001$ – Prostate: aOR, 6.14 [95%CI, 5.72-6.60; $P < .001$ – Bladder: aOR, 5.63 [95%CI, 4.86-6.52; $P < .001$ – Kidney: aOR, 5.33 [95%CI, 4.58-6.21; $P < .001$ – Melanoma: aOR, 5.58 [95%CI, 4.62-6.73; $P < .001$ – Endometrial: aOR, 4.70 [95% CI, 3.79-5.82]; $P < .001$ – Thyroid: aOR, 3.10 [2.47-3.87]; $P < .001$	Retrospective Number of COVID-19 cases in database significantly lower than number of reported cases in US. Age as not a confounding surprising

(*continued on next page*)

Table 1 (*continued*)

• Martín. [2020] [This Study]	• Multicenter retrospective study to investigate COVID-19 incidence rates and morbidity in outpatients with cancer receiving active treatment • Only symptomatic patients tested • 673 patients included • Observation period of 2,5 months.	• Median age 62 years. • Three patients infected - 51, 52 and 76 years old • 3/673 (0.44%) patients who received active cancer treatment developed COVID-19. • Chemotherapy as a risk factor? - 363/673 (53.9%) treated with chemotherapy. 2/3 patients infected with COVID were receiving palliative treatment and in all three, COVID-19 symptoms began within 16 days of last cancer treatment received.	• Cancer distribution: – Breast: 277 (41.2%) – Colorectal: 96 (14.3%) – Lung: 90 (13.4%) – Others: 210 (31.2%)	• Very low incidence of COVID infection raises question as to the real vulnerability of many cancer patients

Abbreviations: aOR, adjusted odds ratio; CFR, case-fatality rate; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; ICI, immune checkpoint inhibitor; NSCLC, non-small cell lung cancer; NHL, non-Hodgkin Lymphoma; ONS, UK Office for National Statistics; OR, odds ratio; SCLC, small cell lung cancer; TKIs, tyrosine kinase inhibitors; UKCCMP, UK Coronavirus Cancer Monitoring Project.

morbidity and mortality was described in cancer patients who developed SARS-CoV-2 infection.

On the one hand, during a pandemic, the potential for benefiting from chemotherapy would remain unchanged, but the risk of harm would be increased to a degree that cannot really be quantified. A study by Liang et al. reported that patients who underwent chemotherapy or surgery during the month prior to being diagnosed with COVID-19 had a numerically higher risk of clinically severe events than those who did not undergo chemotherapy or surgery. They concluded that delaying curative adjuvant chemotherapy could be considered during the pandemic [10].

On the other hand, a few studies have analyzed the risk of SARS-CoV-2 infection in cancer patients. Rogado et al. authored a retrospective study analyzing all the patients admitted to the oncology department of a Madrid hospital for treatment and surveillance during a three-month period during the pandemic [11]. They found that the incidence of infection and mortality was higher in cancer patients than in the general population. Lee et al. published the first prospective study in the UK in which they analyzed mortality due to COVID-19 in cancer patients. Mortality seemed to be driven mainly by age, gender, and comorbidities and not related to active treatment [4].

Nevertheless, no data have been published on the incidence of SARS-CoV-2 infection in patients receiving active treatment on an outpatient basis. Therefore, we have carried out a study on all cancer patients receiving treatment as outpatients in two hospitals in Andalusia, Spain.

Our main objective was to learn the incidence rate of COVID-19 in cancer patients receiving active treatment in an outpatient setting in order to be able to plan treatment schedules on an individual basis for our patients based on the results obtained.

Material and methods

Patients and treatment

A retrospective cohort study was carried out that included all outpatients with cancer treated in two Andalusian hospitals (San Cecilio Clinical University Hospital, Granada, and Costa del Sol Hospital, Marbella). The recruitment period was from February 26, 2020 (the date of the first COVID-19 diagnosis in our autonomous community) to May 13, 2020. Approval was obtained from the Costa del Sol Research Ethics Committee on May 18, 2020.

This study included all patients with solid tumors, in any disease stage, who were currently receiving active treatment. Active treatment was defined as the patient having undergone cancer surgery in the three months prior to inclusion or patients who were receiving chemotherapy, radiotherapy, targeted therapies, or immunotherapy. Patients who were exclusively receiving hormone therapy, who were in follow-up, or who had hematologic tumors were excluded. The data collected included sociodemographic variables, comorbidity, tumor characteristics, whether treatment was received or delayed, and health status at the end of the study period.

SARS-CoV-2 infection was defined as a positive reverse transcription polymerase chain reaction (RT-PCR) assay of a throat or nasal swab. We did not include serology results due to the unequal accessibility and availability of the test among patients. The characteristics related to infection, such as severity, treatment received for it, and whether it resulted in death or not, were also reported.

Statistical analysis

A descriptive analysis was performed using measures of central tendency, dispersion, and position (median and interquartile range) for quantitative variables and frequency distribution for qualitative variables. The cumulative incidence was expressed with its respective 95% confidence interval for the number of infections with respect to the total number of cancer patients as well as the number of delayed or stopped treatments in the total sample. Statistical analyses were performed using SPSS Statistics v. 18.

Table 2
Clinical and pathological characteristics of the patients evaluated.

Characteristics of patients included [N= 673]	N (%)
Hospital	
Costa del Sol	401 (59.6%)
Clínico San Cecilio	272 (40.4%)
Sex	
Female	431 (64.0%)
Male	242 (36.0%)
Hypertension	
Yes	233 (34.6%)
No	440 (65.4%)
Diabetes	
Yes	83 (12.3%)
No	590 (87.7%)
eGFR (MDRD) <60 ml/min	
Yes	42 (6.2%)
No	631 (93.8%)
COPD	
Yes	38 (5.6%)
No	635 (94.4%)
Asthma	
Yes	27 (4.0%)
No	646 (96.0%)
Heart failure	
Yes	6 (0.9%)
No	667 (99.1%)
Ischemic cardiac pathology	
Yes	19 (2.8%)
No	654 (97.2%)
Hospital admission in the previous 3 months	
Yes	146 (21.7%)
No	527 (78.3%)
ECOG	
0	239 (35.5%)
1	353 (52.5%)
2	63 (9.4%)
3	15 (2.2%)
4	3 (0.4%)

Abbreviations: eGFR (MDRD), estimated glomerular filtration rate (**M**odification of **D**iet in **R**enal **D**isease study equation); COPD, chronic obstructive pulmonary disease; ECOG, Eastern Cooperative Oncology Group.

Results

Our study included a total of 673 patients who met all inclusion criteria and no exclusion criteria. The patients' baseline clinical and pathological characteristics are shown in Table 2. Sixty-four percent were women and the median age was 62 years (IQR 49.6-74.3). Comorbidities were infrequent among our patients. Hypertension was present in 34.6% of patients and 12.3% had type 2 diabetes mellitus. A glomerular filtration rate below 60 ml/min was found in 6.2% of patients. Chronic obstructive pulmonary disease (COPD) was present in 5.6%, asthma in 4.0%, and heart disease (heart failure or ischemic cardiopathy) in 3.7% of patients. The majority of patients were in good overall condition (ECOG 0-1 for 88%).

The main characteristics of the cancers are shown in Table 3. Breast cancer was the most common, followed by colorectal cancer and lung cancer. Half of patients had metastases. The most commonly administered treatment was chemotherapy, which was received by 53.9% of patients, followed by hormone therapy combined with other therapies (23.7%), radiotherapy (11.6%), and immunotherapy (10.5%). A total of 30.3% of cases received targeted therapy. Active treatment was delayed or suspended as a consequence of the pandemic in 6% of patients.

Table 3
Characteristics of the tumors.

Characteristics	N (%)
Type of tumor	
Breast	277 (41.2%)
Colorectal	96 (14.3%)
Lung	90 (13.4%)
Others	210 (31.2%)
Stage	
I	65 (9.7%)
II	124 (18.4%)
III	115 (17.1%)
IV	355 (52.7%)
Treatment intention	
Curative	323 (48.0%)
Palliative	350 (52.0%)
Surgery	
Yes	160 (23.8%)
No	513 (76.2%)
Chemotherapy	
Yes	363 (53.9%)
No	310 (46.1%)
Radiotherapy	
Yes	78 (11.6%)
No	595 (88.4%)
Immunotherapy	
Yes	71 (10.5%)
No	602 (89.5%)
Targeted therapies	
Yes	204 (30.3%)
No	469 (69.7%)

During the study period, three patients out of 673 developed COVID-19. Therefore, in our cohort, the cumulative incidence of symptomatic SARS-CoV-2 infection in outpatients with cancer receiving active treatment was 0.44% (95%CI: 0.09-1.3). These patients were young and did not have comorbidities. Two of the three patients were receiving palliative treatment and in all three, the onset of COVID-19 symptoms started within 16 days of the end of the last cancer treatment received. There was one death, and thus the mortality rate among those affected by COVID-19 was 33.3%. The patient who died was receiving palliative chemotherapy. The last cycle was administered 15 days prior to the onset of symptoms and he had an ECOG of 2 in the last cycle. Furthermore, he had undergone cancer surgery in the previous 3 months and had also received other palliative treatments.

Discussion

To the best of our knowledge, our work is the first European cohort of COVID-19 cases among patients with cancer receiving active treatment in the outpatient setting. Just 0.44% of these patients developed COVID-19 and there was one death among the three patients affected. Our cohort was primarily female—due to the fact that the most common tumor was breast cancer (the percentage of patients with lung cancer in the study was very low)—with a median age of 62 years, few comorbidities, and in good general condition. Approximately half of patients were in palliative treatment; 53.9% of those patients were receiving chemotherapy.

The first report to publish data on the prevalence of COVID-19 in cancer patients came from China. All were retrospective in nature and the number of cases was less than 50. Liang et al. [10] reviewed 1,590 cases of patients with COVID-19. Amongst these, 18 (1%) were patients with cancer whose median age was similar to ours, although the majority of those patients were men. They were mainly patients in follow-up who were not receiving treatment (75%). The remaining 25% had received chemotherapy or had undergone surgery in the four weeks prior to being diagnosed with COVID-19. Another retrospective analysis from China published by Zhang et al. [12] analyzed 1,276 patients who had been admitted to the hospital for COVID-19. Of these, 28 were patients with cancer (2.2%). Like the study by Liang et al. [10], the majority were male with a median age that was the same as in our study. That analysis reported that 21.4% of patients with cancer had received some type of treatment in the 14 days prior to the COVID-19 diagnosis. Both studies concluded that patients with cancer who were receiving treatment were at greater risk of adverse events due to COVID-19 than patients with cancer who were not receiving treatment. Mortality, which was only reported in the study by Zhang et al. [12], was 28.6% among patients with cancer, though it was not specified how many of these patients were receiving active treatment.

This pandemic has severely affected the 'old continent,' and as such has allowed for the reporting of more solid—albeit heterogeneous—data on patients with cancer. Lee et al. [4], prospectively analyzed mortality due to COVID-19 in 800 patients diagnosed with cancer who were in active treatment. This study defined patients in active treatment as those who had received any cancer treatment (including surgery, chemotherapy, radiotherapy, hormone therapy, targeted therapy, or immunotherapy) in the previous 12 months. This definition encompasses outpatients, as in our study. They examined the baseline characteristics of these patients and found that 56% were male, a figure similar to the Chinese studies but different to ours. The patients primarily had cancer of the digestive organs (19%), breast cancer (13%), and lung cancer (11%), with metastatic disease found in 43%. Twenty-one percent had no comorbidities and just 33% had received chemotherapy in the four weeks prior to COVID-19 diagnosis (which represents a total of 264 patients receiving outpatient treatment). They did not find greater mortality among patients who had received cancer treatment versus those who had not, a finding that differed from previous publications. They also did not find differences in mortality adjusted for the type of cancer treatment received and concluded that mortality seemed to depend more on advanced age and the presence of comorbidities unrelated to the cancer.

Rogado et al. [11] published the first Spanish study on patients with cancer and COVID-19 in which they retrospectively analyzed 1,069 patients hospitalized in the medical oncology department. They reported an incidence of COVID-19 of 4.2% and a mortality rate among these patients of 42.2%. Those who died tended to be older and whether or not they were receiving treatment or the type of treatment did not appear to play a role. [11] This group of patients with cancer and COVID-19 had a median age of 71 years (somewhat older than those in our study), 57.8% had stage IV disease, 37.8% had lung cancer, and 28.9% were not receiving active treatment [11].

Recently, Yarza et al. [10] published another Spanish study—conducted in the Community of Madrid, and like the study by Rogado et al. [11] — which prospectively analyzed 287 cases of patients with cancer seen in consultation for any reason, related or not to SARS-CoV-2 infection, in the oncological emergency units for patients receiving treatment. All were screened for SARS-CoV-2 either via PCR, radiography, or clinical analysis. Ninety required admission in order to administer in-hospital treatment for COVID-19. Of those 90, the first 63 patients seen in consultation were studied: 52 (83%) had been diagnosed with COVID-19 via PCR (incidence of 18.11% out of the original 287); the remaining 11 (17%) were diagnosed due to findings that were highly clinically and radiologically suspicious. The 63 hospitalized patients had a mean age of 66 years, 46% were women, 82% were receiving treatment for metastatic disease (only 4% were not in active treatment and 50% of the cancer treatments were chemotherapy), and 27% had lung cancer.

Unlike our study, this group [11] analyzed the incidence of SARS-CoV-2 infection among 63 patients with cancer who had COVID-19 seen in consultation for any reason in a hospital where

Table 4
Baseline characteristics of patients and mortality in various published studies.

	Martín-Bravo et al.	Yarza et al.	Rogado et al.	Lee et al.
Hypertension	34.6%	52%	51.1%	31%
Diabetes	12.3%	17%	28.9%	16%
Chronic Kidney Disease	6.2%	8%	6.7%	NA
COPD	9.6%	22%	28.9%	8%
Heart disease	3.7%	19%	8.8	14%
Chronic corticosteroids	10.3%	19%	NR	NR
Mortality	33.34%	25.4%	42.2%	28%

they were screened via PCR (many of them were asymptomatic). This is likely one reason why the incidence found in studies differs considerably, given that in our study, in addition to including all outpatients receiving active treatment, we only performed PCR tests on patients who presented with symptoms or who had radiological findings characteristic of SARS-CoV-2 infection; PCR tests were not performed on asymptomatic patients. In the study by Yarza et al. [13], mortality was 25.4%, compared to 33% (1/3) in our study and much lower than what was reported in another healthcare district in the same autonomous community (Madrid) by Rogado et al [11]. It should be noted that the incidence of COVID-19 in the Community of Madrid has been much higher than in Andalusia [10].

The mortality in patients with cancer has been reported as higher than in patients without cancer with a range between 11.4% and 42.2% [4,5,11–13], depending on the cohort analyzed. Advanced age seems to be an independent factor related to mortality, though non-oncological comorbidity is an aspect to take into account. When comparing non-oncological comorbidities amongst published reports (Table 4), the presence of hypertension, COPD, or cardiovascular disease is high among the cohorts analyzed, which could explain the high rate of mortality among cancer patients.

As with all similar studies we acknowledge the limitations of our analysis and specifically, note several factors that could explain our lower rates of infection including: (1) the fact we only tested patients who were symptomatic, (2) the lower incidence of comorbidities amongst our patients (Table 4), (3) the younger age of our cohort, (4) the lower percentage of patients with a diagnosis of lung cancer, a group that in previous reports has seemed to be more vulnerable likely due to their underlying co-morbidities, but possibly due to the use of immunotherapy [3], and (5) the focus on patients with solid tumors, given the published information suggests patients with hematologic malignancies fare less well [3–5,7].

Although not all studies report the type of cancer treatment and when it is received, it seems that its administration is not directly related to an increase in mortality due to COVID-19, although unfortunately the studies are heterogenous and it is difficult to draw conclusions from them. Furthermore, the delay or suspension of cancer treatment as a measure suggested by the principal scientific societies can have a deleterious effect on disease progression in our patients, an aspect that has not yet been addressed in any study published to date.

In conclusion, despite its limitations our study reveals that the incidence of COVID-19 in cancer patients receiving active treatment can be low, although published information suggests the mortality rate among patients with cancer who become infected is high. More studies are needed in order to shed light on the issues that have been arising during the SARS-CoV-2 pandemic in regard to cancer patients, as they affect the administration of cancer treatment and follow-up on these patients during the receipt of such therapy. Despite the limitations of our analysis, we believe our results raise questions as to the generalizability of existing recommendations. In our opinion, they do not appear applicable to all scenarios and we as have others [14, Wong, this issue] would argue that this must be quickly addressed.

Funding

This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

None.

Acknowledgments

To our patients and their family members, whose cooperation is fundamental in the fight against cancer. To our colleagues in healthcare on the front lines of the battle against COVID-19, whose work and humanity know no limits and who deserve our respect, admiration, and gratitude.

We would like to thank the Research Unit of the Costa del Sol Healthcare Agency for their support in the translation of the manuscript.

References

[1] Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020.
[2] Chen W, Zheng R, Baade PD, et al. Cancer Statistics in China. CA Cancer J Clin. 016 2015;66:115–32.
[3] Robilotti EV, Babady NE, Mead PA, et al. Determinants of COVID-19 Disease Severity in Patients with Cancer. Nat Med 2020;26:1218–23.
[4] Lee LYW, Cazier JB, Starkey T, et al. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. Lancet 2020.
[5] Dai M, Liu D, Liu M, et al. Patients with Cancer Appear More Vulnerable to SARS-CoV-2: A Multicenter Study during the COVID-19 Outbreak. Cancer Discov 2020;10(6):783–91.
[6] Garassino MC, Whisenant JG, Huang L-C, et al. COVID-19 in patients with thoracic malignancies (TERAVOLT): first results of an international, registry-based, cohort study. Lancet Oncol 2020;20:914–22.
[7] Wang Q, Berger NA, Xu R. Analyses of Risk, Racial Disparity, and Outcomes Among US Patients With Cancer and COVID-19 Infection. JAMA Oncol 2020:e206178 Dec 10.
[8] Al-Shamsi HO, Alhazzani W, Alhuraiji A, et al. A Practical Approach to the Management of Cancer Patients During the Novel Coronavirus Disease 2019 (COVID-19) Pandemic: An International Collaborative Group. Oncologist 2020;25(6):e936–45.
[9] Burki TK. Cancer guidelines during the COVID-19 pandemic. Lancet Oncol 2020:629–30. doi:10.1016/S1470-2045(20)30217-5.
[10] Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: A nationwide analysis in China. Lancet Oncol 2020;21:335–7.
[11] Rogado J, Obispo B, Pangua C, et al. Covid-19 transmission, outcome and associated risk factors in cancer patients at the first month of the pandemic in a Spanish hospital in Madrid. Clinical and Translational Oncology 2020.
[12] Zhang L, Zhu F, Xie L, et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. Ann Oncol 2020;31(7):894–901. doi:10.1016/j.annonc.2020.03.296.
[13] Yarza R, Bover M, Paredes D, et al. SARS-CoV-2 infection in cancer patients undergoing active treatment: analysis of clinical features and predictive factors for severe respiratory failure and death. Eur J Cancer 2020;135:242–50. doi:10.1016/j.ejca.2020.06.001.
[14] Wong et al, Seminars in Oncology 2021; 48/1.