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BRIEF RESEARCH ARTICLE

Covid-19 transmission, outcome and associated risk factors in cancer patients at the first month of the pandemic in a Spanish hospital in Madrid

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Abstract

Background There are no large reported series determining the Covid-19 cancer patient's characteristics. We determine whether differences exist in cumulative incidence and mortality of Covid-19 infection between cancer patients and general population in Madrid.

Material and methods We reviewed 1069 medical records of all cancer patients admitted at Oncology department between Feb 1 and April 7, 2020. We described Covid-19 cumulative incidence, treatment outcome, mortality, and associated risk factors.

Results We detected 45/1069 Covid-19 diagnoses in cancer patients vs 42,450/6,662,000 in total population ($p < 0.00001$). Mortality rate: 19/45 cancer patients vs 5586/42,450 ($p = 0.0001$). Mortality was associated with older median age, adjusted by staging and histology (74 vs 63.5 years old, OR 1.06, $p = 0.03$). Patients who combined hydroxychloroquine and azithromycin presented 3/18 deaths, regardless of age, staging, histology, cancer treatment and comorbidities (OR 0.02, $p = 0.03$).

Conclusion Cancer patients are vulnerable to Covid-19 with an increase in complications. Combined hydroxychloroquine and azithromycin is presented as a good treatment option.

Keywords Covid-19 · Cancer · Metastatic · Mortality · Cumulative incidence

Background

The city of Wuhan, Hubei (China), starred at December 2019 the start of a pandemic without precedents at the modern times. A novel subtype of coronavirus was discovered, with a high capacity of human-to-human transmission and an enormous virulence [1, 2]. The novel coronavirus has a lower lethality than other previously isolated [3]; however, we are objectifying how the virus is capable of developing serious unilateral and bilateral pneumonias and inflammatory responses [4].

The arrival of the virus at Spain took place on January 31st, becoming in one of the most worrying active focus in Europe since early March. A few days later, an intracommunity transmission was detected, declaring the health alert and focusing all the hospital cares on Covid-19 patients.

Currently, Spain, and the region of Madrid is one of the most affected places in the entire world. Cancer patients should continue their diagnoses and treatments due to avoid complications of their previous diseases, as suggested by Cortiula and Curigliano [5, 6]. Their visits should be maintained in all Medical and Radiation Oncology departments, with the consequent increased risk of Covid-19. In a Chinese series, an increase in Covid-19 incidence in oncology population was described, attributing it to the maintenance of visits to the hospital without performing any Covid-19 screening [7]. Another recent study described an increase in more serious cases in cancer patients due to their acquired immunosuppression status, especially those who are receiving

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specific treatment [8]. However, another report described similar characteristics and infection rate, but they detected most infected patients were cancer survivors, without active cancer disease or any recent specific treatment received [9].

In our study, we determine whether exists differences in cumulative incidence and mortality of Covid-19 between cancer patients visiting our Medical Oncology department and general population, in the current epicenter of the pandemic in Europe (Madrid, Spain). We also describe clinical and demographic factors associated with poor prognosis and Covid-19 treatment outcomes in a cohort of cancer patients where an advanced stage predominates.

Methods

We retrospectively review 1069 medical records admitted to Medical Oncology department at Hospital Universitario Infanta Leonor of Madrid, from February 1, 2020, to April 7, 2020. We study cumulative incidence of Covid-19 infection and its mortality in cancer patients.

Covid-19 diagnosis was made based on WHO criteria and/or confirmed by RT-PCR of nasopharyngeal specimens. Severe Covid-19 infection was defined as presence of bilateral pneumonia with CURB-65 scale score ≥ 2/$FiO_2 \geq 35\%$ or admission to an Intensive Care Unit (ICU).

Descriptive analyses are reported as relative frequencies for discrete variables. Continuous variables are reported as mean ± standard deviation (SD) or median and interquartile range (IQR) for normal and not normally distributed variables, respectively. To determine differences on mortality between cancer patients and general population, Fisher's Exact Test were performed. To determine the relationship between clinical and demographic risk factors with mortality, Chi square Test, univariate logistic regression and multivariate logistic regression were performed. Statistical analyses were carried out with STATA SE version 14.1 (StataCorp, College Station, TX, USA). A p value < 0.05 was considered statistically significant.

Results

Forty-five patients were diagnosed with Covid-19 from February 1, 2020, to April 7, 2020, within 1069 cancer patients (4.2%) visited at Medical Oncology department in Hospital Universitario Infanta Leonor in Madrid (Spain). The median follow-up until data cut off was 14 days (range 1–28). The median age was 71 years old (range 34–90). Regarding sex, a higher prevalence of males were detected ($n = 30$, 66.7%). Most patients had metastatic disease ($n = 26$, 57.8%). Most frequent histology were lung cancer ($n = 17$, 37.8%). The overall survivals were similar between patients with active treatment or not active treatment (8 months vs 7 months). All patients who were able to receive treatment for Covid-19 infection received hydroxychloroquine ($n = 37$, 82.2%), most combined with lopinavir/ritonavir ($n = 14$, 31.1%) or azithromycin ($n = 18$, 40.0%). All patients required admission except for 7 patients (84.5%), 29 of them were diagnosed with severe Covid-19 infection (64.4%). All clinical and demographic characteristics, comorbidities and treatment description are shown in Table 1.

The cumulative incidence in our cohort was higher (4.2%) than detected in Madrid: 42,450 over 6,662,000 population at data cut off [10] (0.63%, $p < 0.00001$). Mortality in cancer patients it was amounted to 19 of 45 patients (42.2%), compared to observed in general population, with 5586 deaths among 42,450 Covid-19 patients [9] (13.2%, $p = 0.0001$) and in our hospital, with 1878 covid-19 patients admitted and 192 deaths (10.2%, $p = 0.0001$).

Univariate analyses with differences in clinical and demographic characteristics, comorbidities, Covid-19 symptoms and treatment outcome between survivors and dead's patients are shown in Table 2.

In multivariate analysis, we detected that dead's patients had an older age than survivors (74 versus 63.5 years old), regardless of histology and staging (OR 1.06, CI 1.00–1.12, $p = 0.03$). Combined hydroxychloroquine and azithromycin treatment showed a better outcome, with only 3 deaths among 18 patients under this treatment (12.5%), adjusted by median age, histology, staging, cancer treatment received and hypertension (OR 0.02, CI 0.01–0.73, $p = 0.03$).

Discussion

In our study, we obtained a cumulative incidence of Covid-19 in cancer patients higher than our general population [10]. However, considering the characteristics of our patients, their specific treatments and state of immunosuppression, it is expected to observe a higher incidence of cases. Furthermore, we know that these patients visit frequently the hospital, establishing an added risk of Covid-19.

Our general population had a high fatality rate, with a 13.2% of deaths at data cut off [9]. However, we obtained significant differences within mortality terms in cancer patients, rising up to 42.2% ($p = 0.0001$). When we searched differences in the mortality rate between all Covid-19 patients admitted to our center and our Covid-19 cancer population, we also observed differences, with a mortality rate in our hospital of 9.8% in all Covid-19 patients ($p = 0.0001$).

We believe that our patients could be acquiring nosocomial transmission, as suggested by Yu et al. [7] with up to twice the incidence of cases with respect to general population in China (OR 2.31, CI 1.89–3.02), as described also by Zhang et al. [8] and by Liang et al. [10] with an incidence

Table 1 Clinical and demographic characteristics, outcome, symptoms and treatment of Covid-19 cancer patients

Characteristics	*N*	Percentage (%)
Sex		
Male	30	66.7
Female	15	33.3
Cancer type		
Lung cancer	17	37.8
Breast cancer	6	13.3
Colorectal cancer	6	13.3
Prostate cancer	5	11.1
Other	11	24.5
Cancer staging		
Localized	6	13.3
Locally advanced	13	28.9
Metastatic	26	57.8
Cancer treatment		
No active treatment	13	28.9
Chemotherapy	19	42.2
TKIs	2	4.4
Immunotherapy	1	2.2
New diagnosis	2	4.4
Others	8	17.9
Comorbidities		
Hypertension	23	51.1
Diabetes mellitus	13	28.9
Cardiovascular disease	4	8.8
Chronic kidney disease	3	6.7
COPD	13	28.9
Obesity	6	13.3
Covid-19 diagnosis		
Hospitalization admission	38	84.4
ICU admission	0	0
Home management (discharged from hospital at diagnosis)	7	15.6
Covid-19 outcome		
Dead	19	42.2
Alive	26	57.8
Severe covid-19 infection	29	64.4
Symptoms		
Fever	38	84.4
Cough	39	86.7
Myalgia	10	22.2
Dyspnea	38	84.4
Diarrhea	1	2.2
Covid-19 treatment		
Lopinavir/ritonavir + hydroxychloroquine	10	22.2
Hydroxychloroquine + azithromycin	18	40.0
Lopinavir/ritonavir + hydroxychloroquine + azithromycin	4	8.8
Hydroxichloroquine	2	4.4
Hydroxychloroquine + azithromycin + steroids	2	4.4
Hydroxychloroquine + azithromycin + steroids + tocilizumab	1	2.2

TKIs tyrosine kinase inhibitors, *COPD* chronic obstructive pulmonary disease

Table 2 Clinical and demographic parameters in both subgroup of Covid-19 cancer patients (dead's patients or survivors)

	Survivor patients ($N=26$)	Dead patients ($N=19$)	p value
Age, median	74	63.5	0.01
Male, *n* (%)	16 (61.5)	14 (73.68)	0.39
Cancer characteristics			
Histology			
Lung cancer, *n* (%)	8 (30.8%)	9 (47.3%)	0.20
Cancer treatment			
Chemotherapy, *n* (%)	13 (50.0%)	6 (31.5%)	0.44
Staging			
Metastatic disease, *n* (%)	13 (50.0%)	13 (68.4%)	0.53
Covid-19 characteristics			
Covid-19 treatment			
Hydroxychloroquine + azithromycin, *n* (%)	15 (57.7%)	3 (15.7%)	0.008
Covid-19 symptoms			
Fever, *n* (%)	23 (88.5%)	15 (78.9%)	0.38
Cough, *n* (%)	23 (88.5%)	16 (84.2)	0.67
Severe infection, *n* (%)	12 (46.1%)	17 (89.5%)	0.003
Comorbidities			
Hypertension, *n* (%)	11 (42.3%)	12 (63.1%)	0.16
Diabetes, *n* (%)			
COPD, *n* (%)	8 (30.7%)	5 (26.3%)	0.74
CKD, *n* (%)	4 (15.3%)	2 (10.5%)	0.63
Cardiovascular disease, *n* (%)	2 (7.7%)	1 (5.3%)	0.74
Obesity, *n* (%)	4 (15.3%)	2 (10.5%)	0.63

COPD chronic obstructive pulmonary disease, *CKD* chronic kidney disease

of 1% in cancer patients versus 0.29% in general population in China. We also detected in our study a higher cumulative incidence as in our general population (4.3% vs 0.63%, $p<0.00001$).

In two of these studies, they observed that Covid-19 presented a higher lethality in cancer population [8, 9]. Zhang et al. [8] report a mortality of 28.6% and a severe event rate of 53.6%, as in the study completed by Liang et al. [9], where they described a rate of complications and mortality (39%) higher than the rate detected in all the infected patients in their hospital (8%).

In both studies, the mortality rate is lower than our report. We found a mortality rate in our study of 42.2% of cancer patients. These facts are probably related because the authors included a large cohort of cancer survivors [9], or their cancer staging was not predominantly metastatic [8].

In previously reported studies, it is described that chemotherapy is a risk factor in cancer patients with Covid-19 [6–8]. However, we did not detect an increase in mortality in patients who were receiving this treatment in our cohort. Chemotherapy could be contributing to decrease the inflammation that has been associated with a higher mortality in Covid-19 [4].

Finally, we observed that those cancer patients treated with combined hydroxychloroquine and azithromycin had a better outcome. This fact are not mentioned in the rest of the articles, either due to the absence of data collection [7, 9] or because the drugs outcome is not reported [8]. This is at the moment, to our knowledge, the only report of Covid-19 disease in cancer patients in Europe and the largest series reported including oncology patients.

Conclusion

Covid-19 triggers serious complications in cancer patients, so our efforts should be made to reduce visits to hospital during the pandemic. The severity of the infection at admission and the elderly patients are independents indicators of mortality, and combined treatment with hydroxychloroquine and azithromycin seems a good option in cancer patients.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest for the present work.

Ethical approval The study was approved by the Ethical Committee of our hospital (code: COVID-CANCER-HUIL).

Informed consent The study meets all requirements for informed consent exemption according to the "International Ethical Guidelines for Health-related Research Involving Humans" (CIOMS-WHO 2016).

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