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RESEARCH BRIEF

Patients with Cancer Appear More Vulnerable to SARS-COV-2: A Multicenter Study during the COVID-19 Outbreak

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ABSTRACT

The novel COVID-19 outbreak has affected more than 200 countries and territories as of March 2020. Given that patients with cancer are generally more vulnerable to infections, systematic analysis of diverse cohorts of patients with cancer affected by COVID-19 is needed. We performed a multicenter study including 105 patients with cancer and 536 age-matched noncancer patients confirmed with COVID-19. Our results showed COVID-19 patients with cancer had higher risks in all severe outcomes. Patients with hematologic cancer, lung cancer, or with metastatic cancer (stage IV) had the highest frequency of severe events. Patients with nonmetastatic cancer experienced similar frequencies of severe conditions to those observed in patients without cancer. Patients who received surgery had higher risks of having severe events, whereas patients who underwent only radiotherapy did not demonstrate significant differences in severe events when compared with patients without cancer. These findings indicate that patients with cancer appear more vulnerable to SARS-COV-2 outbreak.

SIGNIFICANCE: Because this is the first large cohort study on this topic, our report will provide much-needed information that will benefit patients with cancer globally. As such, we believe it is extremely important that our study be disseminated widely to alert clinicians and patients.

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INTRODUCTION

A new acute respiratory syndrome coronavirus, named SARS-CoV-2 by the World Health Organization (WHO), has rapidly spread around the world since its first reported case in late December 2019 from Wuhan, China (1). As of March 2020, this virus has affected more than 200 countries and territories, infecting more than 800,000 individuals and causing more than 40,000 deaths (2).

With more than 18 million new cases per year globally, cancer affects a significant portion of the population. Individuals affected by cancer are more susceptible to infections due to coexisting chronic diseases, overall poor health status, and systemic immunosuppressive states caused by both cancer and anticancer treatments (3). As a consequence, patients with cancer who are infected by the SARS-CoV-2 coronavirus may experience more difficult outcomes than other populations. Until now, there is still no systematic evaluation of the effects that the SARS-CoV-2 coronavirus has of patients with cancer in a representative population. A recent study reported a higher risk of severe events in patients with cancer when compared with patients without cancer (4); however, the small sample size of SARS-CoV-2 patients with cancer used in the study limited how representative it was of the whole population and made it difficult to conduct more insightful analyses, such as comparing clinical characteristics of patients with different types of cancer, as well as anticancer treatments (5, 6).

Using patient information collected from 14 hospitals in Hubei Province, China, the epicenter of the 2019–2020 COVID-19 outbreak, we describe the clinical characteristics and outcomes [death, intensive care unit (ICU) admission, development of severe/critical symptoms, and utilization of invasive mechanical ventilation] of patients affected by the SARS-CoV-2 coronavirus for 105 hospitalized patients with cancer and 536 patients without cancer. We document our findings for different cancer types and stages, as well as different types of cancer treatments. We believe the information and insights provided in this study will help improve our understanding of the effects of SARS-CoV-2 in patients with cancer.

RESULTS

Patients Characteristics

In total, 105 COVID-19 patients with cancer were enrolled in our study for the time period January 1, 2020, to February 24, 2020, from 14 hospitals in Wuhan, China. COVID-19 patients without cancer matched by the same hospital, hospitalization time, and age were randomly selected as our control group. Our patient population included 339 females and 302 males. Patients with cancer [median = 64.00, interquartile range (IQR) = 14.00], when compared with those without cancer (median = 63.50, IQR = 14.00) had similar age distributions (by design), experienced more in-hospital infections [20 (19.04%) of 105 patients vs. 8 (1.49%) of 536 patients; $P < 0.01$], and had more smoking history [36 (34.28%) of 105 patients vs. 46 (8.58%) of 536 patients; $P < 0.01$], but had no significant differences in sex, other baseline symptoms, and other comorbidities (Table 1). With respect to signs and symptoms upon admission, COVID-19 patients with cancer were similar to those without cancer except for a higher prevalence of chest distress [15 (14.29%) of 105 patients vs. 36 (6.16%) of 536 patients; $P = 0.02$].

Clinical Outcomes

Compared with COVID-19 patients without cancer, patients with cancer had higher observed death rates [OR, 2.34; 95% confidence interval (CI), (1.15–4.77); $P = 0.03$], higher rates of ICU admission [OR, 2.84; 95% CI (1.59–5.08); $P < 0.01$], higher rates of having at least one severe or critical symptom [OR, 2.79; 95% CI, (1.74–4.41); $P < 0.01$], and higher chances of needing invasive mechanical ventilation (Fig. 1A). We also conducted survival analysis on occurrence of any severe condition which included death, ICU admission, having severe symptoms, and utilization of invasive mechanical ventilation (see cumulative incidence curves in Fig. 1B). In general, patients with cancer deteriorated more rapidly than those without cancer. These observations are consistent with logistic regression results (Supplementary Fig. S1), after adjusting for age, sex, smoking, and comorbidities including diabetes, hypertension, and chronic obstructive pulmonary disease (COPD). According to our multivariate logistic regression results, patients with cancer still had an excess OR of 2.17 ($P = 0.06$) for death (Supplementary Fig. S1A), 1.99 ($P < 0.01$) for experiencing any severe symptoms (Supplementary Fig. S1B), 3.13 ($P < 0.01$) for ICU admission (Supplementary Fig. S1C), and 2.71 ($P = 0.04$) for utilization of invasive mechanical ventilation (Supplementary Fig. S1D; Supplementary Table S1). The consistency of observed ORs between the multivariate regression model and unadjusted calculation reassures the association between cancer and severe events even in the presence of other factors such as age differences.

Cancer Types

Information regarding potential risks of severe conditions in SARS-CoV-2 associated with each type of cancer was calculated. We compared different conditions among cancer types (Table 2). Lung cancer was the most frequent cancer type [22 (20.95%) of 105 patients], followed by gastrointestinal cancer [13 (12.38%) of 105 patients], breast cancer [11 (10.48%) of 105 patients], thyroid cancer [11 (10.48%) of 105 patients], and hematologic cancer [9 (8.57%) of 105 patients]. As shown

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Table 1. Characteristics of COVID-19 patients with and without cancer

	COVID-19 patients with cancer ($n = 105$)	COVID-19 patients without cancer ($n = 536$)	*P*
Age (years; median/IQR)	64.00/14.00	63.50/14.00	0.25
Sex			
Male	57/54.72%	245/45.71%	0.11
Female	48/45.28%	291/54.29%	0.11
In-hospital infection	20/19.04%	8/1.49%	<0.01
Smoking	36/34.28%	46/8.58%	<0.01
Comorbidities			
Hypertension	30/28.57%	130/24.25%	0.40
Cardiovascular disease	12/11.43%	39/7.28%	0.17
Diabetes	7/6.67%	29/5.41%	0.64
Cerebrovascular disease	5/4.76%	21/3.92%	0.60
Chronic kidney disease	6/5.71%	22/4.10%	0.44
Chronic liver disease	7/6.67%	35/6.53%	1.00
Signs and symptoms			
Fever	68/64.76%	401/74.81%	0.04
Dry cough	57/52.29%	313/58.40%	0.45
Sputum production	16/15.24%	58/10.82%	0.24
Fatigue	30/28.57%	179/33.40%	0.36
Myalgia	6/5.71%	38/7.09%	0.83
Nausea or vomiting	6/5.71%	41/7.65%	0.68
Chest distress	15/14.29%	36/6.16%	0.02
Headache	7/6.67%	28/5.22%	0.49
Sore throat	11/10.48%	43/8.02%	0.44
Treatments			
Antibiotic treatments	81/77.14%	361/67.35%	0.05
Antiviral treatments	75/71.43%	372/69.40%	0.68
Systemic glucocorticoids	19/18.10%	78/14.55%	0.35
Oxygen therapy	48/45.71%	221/42.02%	0.48
Noninvasive mechanical ventilation	11/10.48%	47/8.77%	0.58
Invasive mechanical ventilation	11/10.48%	15/2.79%	<0.01
Continuous renal replacement therapy	4/3.81%	3/0.56%	<0.01
Extracorporeal membrane oxygenation	3/2.86%	2/0.37%	<0.01
Time since cancer diagnosis to hospitalization			
<3 months	29/27.61%	NA	NA
3–6 months	17/16.19%	NA	NA
6 months–1 year	11/10.47%	NA	NA
1–3 years	19/18.09%	NA	NA
>3 years	19/18.09%	NA	NA
Missing	10/9.52%	NA	NA
Metastatic cancer	17/16.19%	NA	NA
Cancer treatments within 40 days			
Surgery	8/7.62%	NA	NA
Radiotherapy	13/12.38%	NA	NA
Chemotherapy	17/16.19%	NA	NA
Targeted therapy	4/3.81%	NA	NA
Immunotherapy	6/5.71%	NA	NA

Note: Data are presented as median (IRQ) or *n* (%). *P* values denoted the comparison between COVID-19 patients with cancer and without cancer.

Abbreviation: NA, not applicable.

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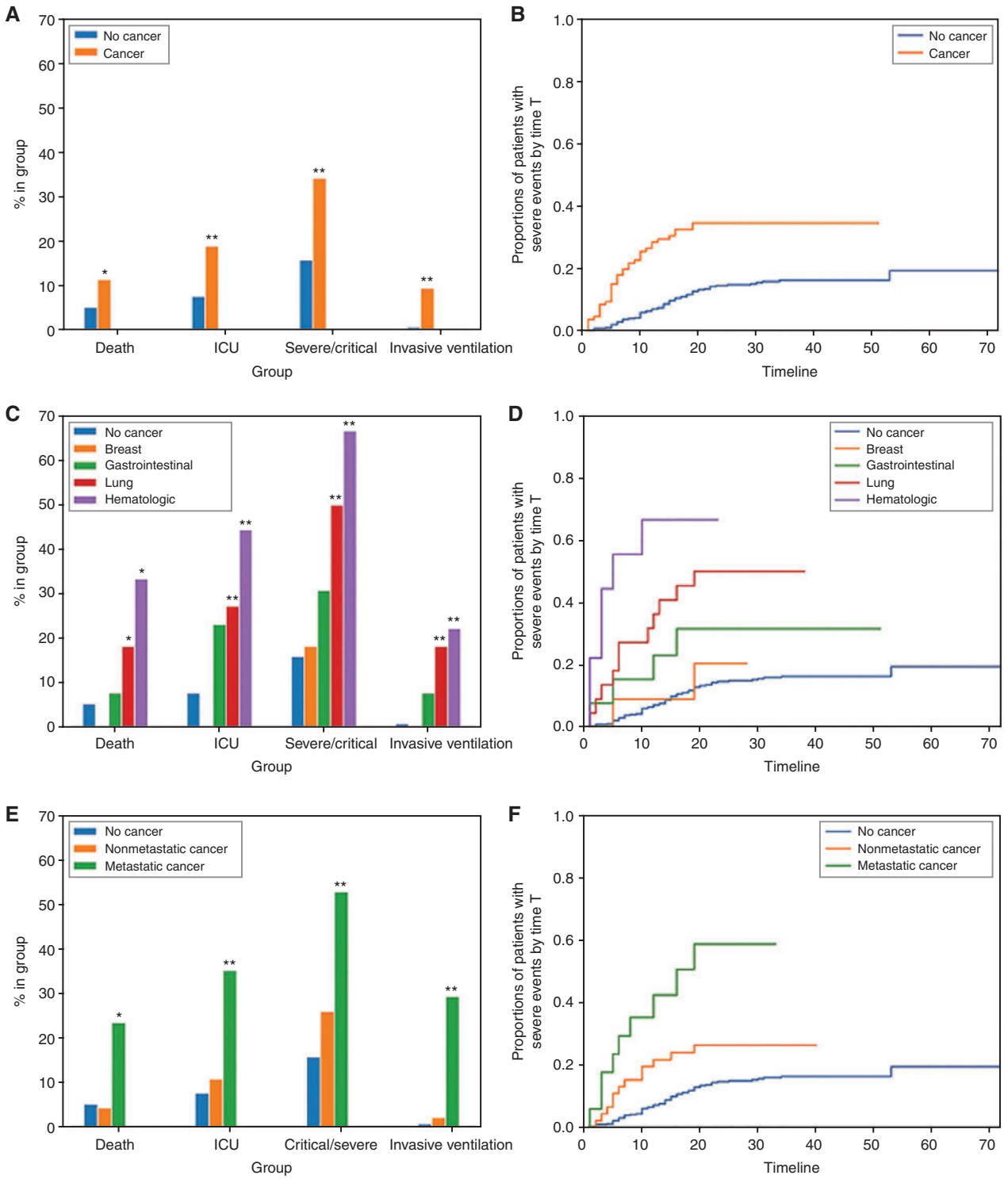

Figure 1. Severe conditions in patients with and without cancer, and patients with different types, stages, and treatments of cancer. Severe conditions include death, ICU admission, having severe/critical symptoms, and usage of invasive mechanical ventilation. Incidence and survival analysis of severe conditions among COVID-19 patients with cancer and without cancer (**A** and **B**), among patients with different types of cancer (**C** and **D**), among patients with metastatic and nonmetastatic cancers (**E** and **F**), (*continued on following page*)

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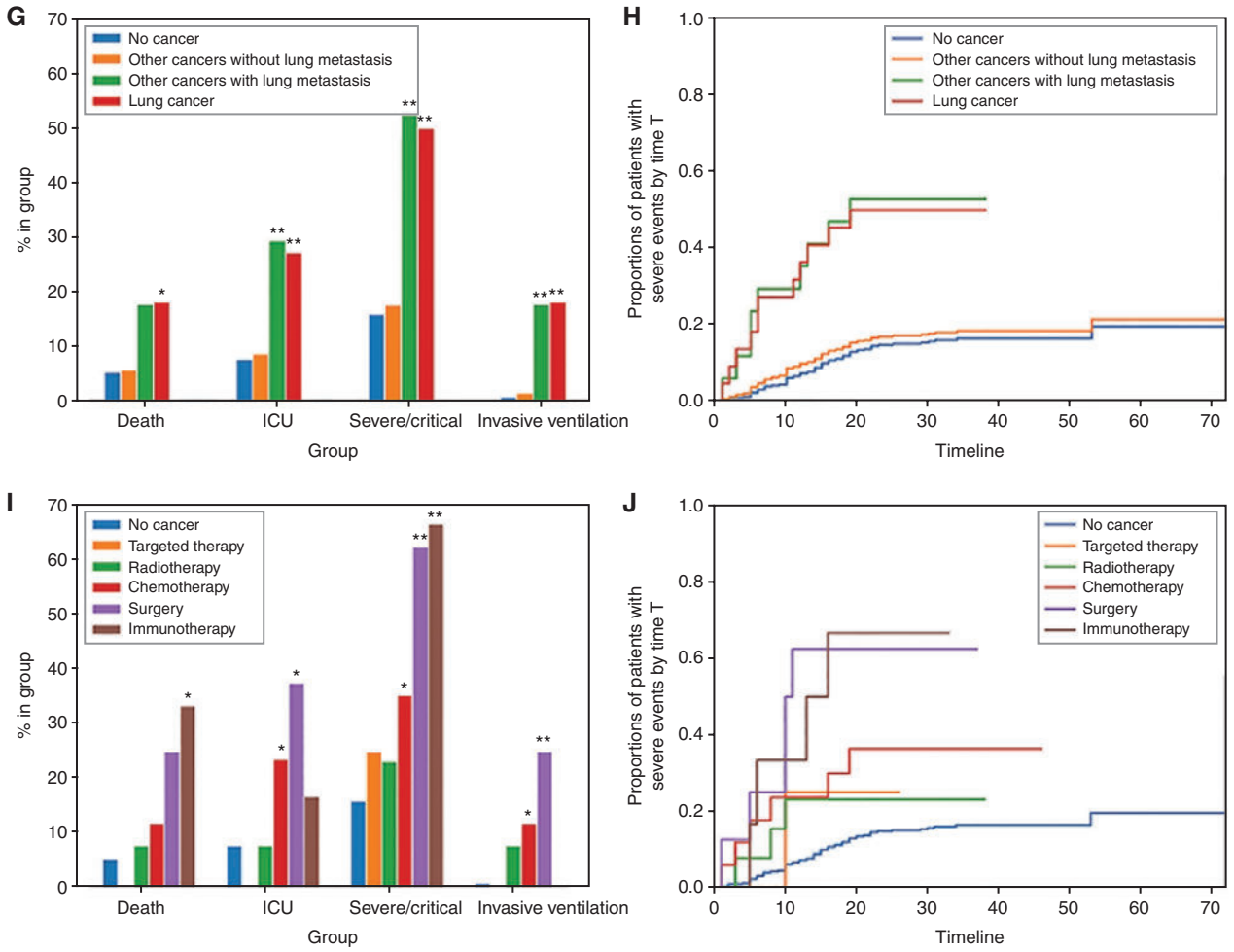

Figure 1. ***(Continued)*** among patients with lung cancer, other cancers than lung with lung metastasis, and other cancers than lung without lung metastasis (**G** and **H**), and patients receiving different types of cancer treatments (**I** and **J**). *P* values indicate differences between cancer subgroups versus patients without cancer. For **A**, **C**, **E**, **G**, **I**, *, $P < 0.05$; **, $P < 0.01$. OR, 95% CI, and *P* values between different subgroups are listed in Supplementary Table S2. For **B**, **D**, **F**, **H**, **J**, HR, 95% CI, and *P* values are listed in Supplementary Table S3.

in Fig. 1C and D and Supplementary Table S2, patients with hematologic cancer including leukemia, lymphoma, and myeloma have a relatively high death rate [3 (33.33%) of 9 patients], high ICU admission rate [4 (44.44%) of 9 patients], high risks of severe/critical symptoms [6 (66.67%) of 9 patients], and high chance of utilization of invasive mechanical ventilation [2 (22.22%) of 9 patients]. Patients with lung cancer had the second-highest risk levels, with death rate [4 (18.18%) of 22 patients], ICU admission rate [6 (27.27%) of 22 patients], risks of severe/critical symptoms [11 (50.00%) of 22 patients], and the chance of utilization of invasive mechanical ventilation [4 (18.18%) of 22 patients; Table 2].

Cancer Stage

We found that patients with metastatic cancer (stage IV) had even higher risks of death [OR, 5.58; 95% CI (1.71–18.23); $P = 0.01$], ICU admission [OR, 6.59; 95% CI (2.32–18.72); $P < 0.01$], having severe conditions [OR, 5.97; 95% CI (2.24–15.91); $P < 0.01$], and use of invasive mechanical ventilation [OR, 55.42; 95% CI (13.21–232.47); $P < 0.01$]. In contrast, patients with nonmetastatic cancer did not demonstrate statistically significant differences compared with patients without cancer, with all $P > 0.05$ (Fig. 1E and F; Supplementary Tables S2 and S3). In addition, when compared with patients without cancer, patients with lung cancer or other cancers with lung metastasis also showed higher risks of death, ICU admission rates, higher critical symptoms, and use of invasive mechanical ventilation, with all *P* values below 0.01, but other cancers without lung metastasis had no statistically significant differences (all *P* values > 0.05; Fig. 1G and H; Supplementary Table S3) when compared with patients without cancer.

Cancer Treatments

Among the 105 COVID-19 patients with cancer in our study, 13 (12.26%) had radiotherapy, 17 (14.15%) received chemotherapy, 8 (7.62%) received surgery, 4 (3.81%) had targeted therapy, and 6 (5.71%) had immunotherapy within 40 days before the onset of COVID-19 symptoms. All of

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Table 2. Severe events in 105 patients with cancer for each type of cancer

Cancer types	Total number	Death *n*%	Average time to death	ICU admission *n*%	Average time to ICU	Critical symptom *n* %	Average time to critical	IMV *n* %	Average time to IMV
Lung cancer	22/20.95%	18.18	16.75/8.17	27.27	10.00/6.82	50.00	8.55/5.71	18.18	14.50/6.98
Gastrointestinal cancer	13/12.38%	7.69	24.0/NA	23.08	9.05/6.16	30.77	8.50/5.85	7.69	22.00/NA
Breast cancer	11/10.48%	0.00	NA/NA	0.00	NA/NA	18.18	12.00/7.00	0.00	NA/NA
Thyroid cancer	11/10.48%	0.00	NA/NA	0.00	NA/NA	9.09	8.00/NA	0.00	NA/NA
Blood cancer	9/8.57%	33.33	19.33/1.89	44.44	2.82/1.80	66.67	3.83/3.08	22.22	9.00/NA
Cervix cancer	6/5.71%	0.00	NA/NA	16.67	4.00/NA	33.33	7.00/3.00	0.00	NA/NA
Esophagus cancer	6/5.71%	16.67	28.00/NA	33.33	9.52/0.50	50.00	7.33/2.05	16.67	16.00/NA
All cancer	105/100%	11.43	19.92/6.13	19.05	6.51/4.16	34.29	7.56/5.2	9.52	14.56/5.68

Note: Only cancer types with more than 5 patients are listed. Numbers are presented as *n*/%; average time to events are presented as mean/SD (days), from initial onset of COVID-19 symptoms to death/ICU admission/critical symptom/IMV.

Abbreviations: NA, not applicable; IMV, invasive mechanical ventilation.

the targeted therapeutic drugs were EGFR–tyrosine kinase inhibitors for treatment of lung cancer, and all of the immunotherapy drugs were PD-1 inhibitors for the treatment of lung cancer. A patient with cancer may have more than one type of therapy. Our observation suggested that patients who received immunotherapy tended to have high rates of death [2 (33.33%) of 6 patients] and high chances of developing critical symptoms [4 (66.67%) of 6 patients]. Patients who received surgery demonstrated higher rates of death [2 (25.00%) of 8 patients], higher chances of ICU admission [3 (37.50%) of 8 patients], higher chances of having severe or critical symptoms [5 (62.50%) of 8 patients], and higher use of invasive ventilation [2 (25.00%) of 8 patients] than other treatments excluding immunotherapy. However, patients with cancer who received radiotherapy did not show statistically significant differences in having any severe events when compared with patients without cancer, with all P values > 0.10 (Fig. 1I and J). Clinical details on the cancer diagnoses and cancer treatments are summarized in Supplementary Table S4.

Timeline of Severe Events

To evaluate the time-dependent evolution of the disease, we conducted the timeline of different events for COVID-19 patients with cancer (Fig. 2A) and COVID-19 patients without cancer (Fig. 2B) with death and other severe events marked in the figure. COVID-19 patients with cancer had a mean length of stay of 27.01 days (SD 9.52) and patients without cancer had a mean length of stay of 17.75 days (SD 8.64); the difference is significant (Wilcoxon test, $P < 0.01$). To better clarify the contributing factors that might influence outcomes, we also included logistic regression of COVID-19 patients with cancer adjusted by immunosuppression levels in Supplementary Table S5. However, no significant association between immunosuppression and severe outcomes was observed from the analysis (with all $P > 0.05$).

DISCUSSION

The findings in this study suggest that patients with cancer infected with SARS-COV-2 tend to have more severe outcomes when compared with patients without cancer. Patients with hematologic cancer, lung cancer, and cancers in metastatic stages demonstrated higher rates of severe events compared with patients without cancer. In addition, patients who underwent cancer surgery showed higher death rates and higher chances of having critical symptoms.

The SARS-COV-2 virus has spread rapidly globally; thus, many countries have not been ready to handle the large volume of people affected by this outbreak due to a lack of knowledge about how this coronavirus affects the general population. To date, reports on the general population infected with SARS-COV-2 suggest elderly males have a higher incidence and death rate (7, 8). Limited information is known about the outcome of patients with cancer who contract this highly communicable disease. Cancer is among the top causes of death. Asia, Europe, and North America have the highest incidence of cancer in the world (9), and at the moment of the writing of this study the SARS-COV-2 virus is mainly spreading in these three areas (referred from https://www.cdc.gov/media/releases/2020/s0226-Covid-19-spread.html; https://www.nytimes.com/2020/02/27/world/coronavirusnews.html). Although COVID-19 patients with cancer may share some epidemiologic features with the general population with this disease, they may also have additional clinical characteristics. Therefore, we conducted this study on patients with cancer with coexisting COVID-19 disease to evaluate the potential effect of COVID-19 on patients with cancer.

On the basis of our analysis, COVID-19 patients with cancer tend to have more severe outcomes when compared with the noncancer population. Although COVID-19 is reported to have a relatively low death rate of 2% to 3% in the general population (10), patients with cancer and COVID-19 not only have a nearly 3-fold increase in the death rate than that

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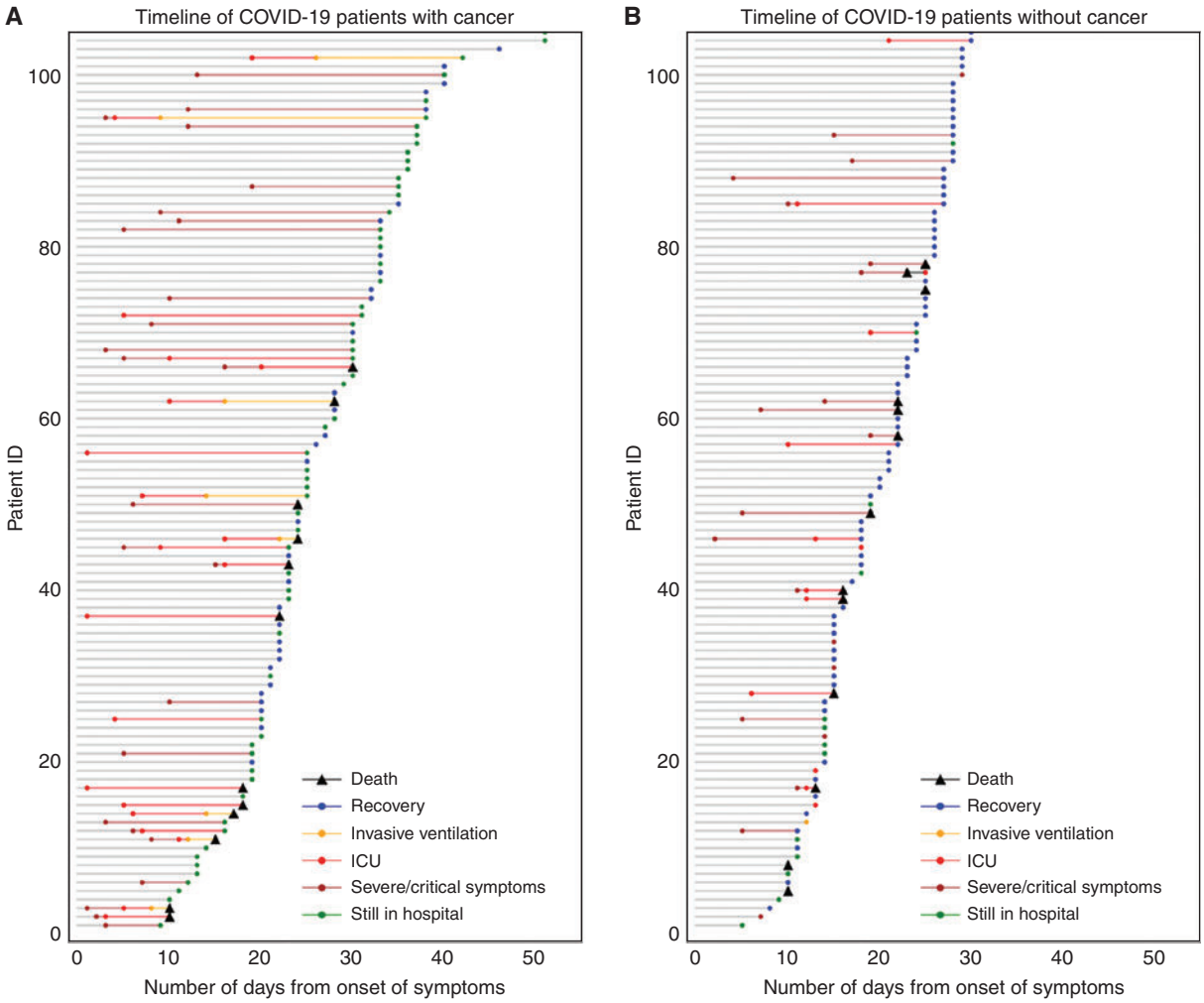

Figure 2. Timeline of events for COVID-19 patients. **A,** Timeline of events in COVID-19 patients with cancer. **B,** Timeline of events in COVID-19 patients without cancer. For visualization purposes, patients without timeline information are excluded and only 105 COVID-19 patients without cancer are shown.

of COVID-19 patients without cancer, but also tend to have much higher severity of their illness. Altogether, these findings suggest that patients with cancer are a much more vulnerable population in the current COVID-19 outbreak. Our findings are consistent with those presented in a previous study based on 18 patients with cancer (4). Because of the limited number of patients with cancer in the previous study, the authors concluded that among patients with cancer, age is the only risk factor for the severity of the illness. On the basis of our data on 105 patients with cancer, we have discovered additional risk factors, including cancer types, cancer stage, and cancer treatments, which may contribute to the severity of the disease among patients with cancer.

Our data demonstrate that the severity of SARS-COV-2 infection in patients is significantly affected by the types of tumors. From our analysis, patients with hematologic cancer have the highest severity and death rates among all patients with cancer, and lung cancer follows second. Patients with hematologic cancer in our study include patients with leukemia, myeloma, and lymphoma, who have a more compromised immune system than patients with solid tumors (11). These patients all had a rapidly deteriorating clinical course once infected with COVID-19. Because malignant or dysfunctional plasma cells, lymphocytes, or white blood cells in general in hematologic malignancies have decreased immunologic function (12–14), this could be the main reason why patients with hematologic cancer have very high severity and death rates. All patients with hematologic cancer are prone to the complications of serious infection (12–14), which can exacerbate the condition which could have worsened in patients with COVID-19. In our study, 55.56% of patients with hematologic cancer had severe immunosuppression, which may be the main reason for deteriorated outcomes. Although the small sample size limits representativity of the observation, we believe our finding can serve as an informative starting point for further investigation when a larger cohort from a wide range of healthcare providers becomes available. Among solid tumors, lung cancer is the highest risk category disease in patients with SARS-COV-2 infection (Fig. 1C). Decreased lung function and severe infection in patients

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with lung cancer could contribute to the worse outcome in this subpopulation (15, 16).

In our analysis, we classified the SARS-COV-2 infection–related high risk factors based on death, severe or critical illness, ICU admission, and the utilization of invasive mechanical ventilation. Using these parameters, we detected a multi-fold increase in risk in the cancer population, in contrast to the noncancer population. If there were primary or metastatic tumors in the lungs, patients were more prone to a deteriorated course in a short time. Intriguingly, when patients with cancer had only early-stage disease without metastasis, we did not observe any difference between the cancer and noncancer population in terms of COVID-19–related death rate or severity (Fig. 1E). The stage of cancer diagnosis seemed to play a significant role in the severity and death rate of COVID-19.

Patients with cancer received a wide range of treatments, and we also found that different types of treatments had different influences on severity and death when these patients contracted COVID-19. Recently, immunotherapy has assumed a very important role in treating tumors, which aids in treatment of cancer by blocking the immune escape of cancer cells. But in our study, in contrast to patients with cancer with other treatments, patients with immunotherapy had the highest death rate and the highest severity of illness, a very puzzling finding. According to pathologic studies on the patients with COVID-19, there were desquamation of pneumocytes and hyaline membrane formation, implying that these patients had acute respiratory distress syndrome (ARDS; ref. 17). ARDS induced by cytokine storm is reported to be the main reason for death of SARS-COV-2–infected patients (18). It is possible that in this setting, immunotherapy induces the release of a large amount of cytokines, which can be toxic to normal cells, including lung epithelial cells (19–21), and therefore lead to a more severe illness. However, in this study the number of patients with immunotherapy was too small; further research with a large case population needs to be conducted in the future.

In addition, COVID-19 patients with cancer who are under active treatment or not under active treatment do not show differences in their outcomes, and there is a significant difference between COVID-19 patients with cancer but not with active treatment and patients without cancer (Supplementary Table S2). These results indicate that COVID-19 patients with both active treatment and just cancer history have a higher risk of developing severe events than noncancer COVID-19 patients. The possible reasons could be due to some known cancer-related complications, for example, anemia, hypoproteinaemia, or dyspnea in early phase of COVID-19 (22). We considered that cancer had a lifetime effect on patients and that cancer survivors always need routine follow-up after primary resection. Therefore, in clinical COVID-19 patient management, equivalent attention needs to be paid to those with cancer whether they are under active therapeutics or not during the outbreak of COVID-19.

This study has several limitations. Although the cohort of COVID-19 patients with cancer is one of the largest in Hubei province, China, the epicenter of the initial outbreak, a larger cohort from the whole country or even from multiple countries will be more representative. Large-scale national and international research collaboration will be necessary to achieve this. At the initial stage of the outbreak, data collection and research activities were not a priority of the hospitals. Therefore, it was not possible to record and collect some data that are potentially informative for our analysis in a timely manner. In addition, due to the urgency of clinical treatment, medical data used in this study were largely disconnected from the patients' historical electronic medical records, which are mostly stored with a different healthcare provider than the medical center providing COVID-19 care. This left us with limited information about each patient.

Our study is the midsize cohort study on this topic and will provide much-needed information on risk factors of this population. We hope that our findings will help countries better protect patients with cancer affected by the ongoing COVID-19 pandemic.

METHODS

Study Design and Patients

We conducted a multicenter study focusing on the clinical characteristics of confirmed cases of COVID-19 patients with cancer in 14 hospitals in Hubei province, China; all of the 14 hospitals served as government-designated hospitals for patients diagnosed with COVID-19 (listed in the Supplementary Data). COVID-19 was diagnosed according to the WHO interim guidance (23). Patients with cancer confirmed with COVID-19 who were hospitalized from January 1, 2020, to February 24, 2020, were enrolled. SARS-CoV-2–infected patients without cancer matched by the same hospital and hospitalization time were randomly selected as our control group. In addition, as age is one of the major predictors of severity of respiratory diseases like COVID-19 (4), we excluded from our analysis 117 younger COVID-19 patients without cancer so that median ages of patients with cancer (median = 64.0, IRQ = 14.00) and patients without cancers (median = 63.5, IQR = 14.00) would be comparable. Four clinical outcomes were monitored up to February 24, 2020, the final date of follow-up. This case series was approved by the Institutional Ethics Board of Zhongnan Hospital of Wuhan University (Wuhan, Hubei, China, No. 2020029). It is worth pointing out that because of limited resources and information available in early stages of this outbreak, sample sizes of some subgroups were small and collection of data for patients with better matched clinical characteristics was not possible. This limited this study design.

Procedures

Medical records of patients were acquired by the data collection team of the above 14 hospitals. A team of physicians who had been taking care of patients with SARS-COV-2 infection reviewed the data. We used a standardized case-report form to collect clinical data. Primary cancer characteristics and detailed treatment information were extracted from past medical records by oncologists in the Hubei Anti-Cancer Association. Data were entered into a computerized database. Cases with insufficient records of previous disease history were excluded. Information collected included demographic data, medical history, comorbidities, symptoms, vital signs, routine blood test, and chest CT scans. Only cancer treatments within 40 days before the onset of COVID-19 symptoms were considered for this study. Each patient's medical record was reviewed by at least two oncologists. Our institutional ethics review board approved the study and waived the need for informed consent.

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End Points and Assessments

There were four primary outcomes analyzed in this study: death, admission into the ICU, development of severe or critical symptoms, and utilization of invasive mechanical ventilation. The clinical definition of severe/critical symptoms follows the 5th edition of the 2019 Novel Coronavirus Disease (COVID-19) Diagnostic Criteria published by the National Health Commission in China, including septic shock, ARDS, acute kidney injury, disseminated intravascular coagulation, and rhabdomyolysis.

Statistical Analysis

The aim of this study was to report clinical outcomes of COVID-19 patients with cancer. For categorical data, percentages of patients in each category were calculated. The Wilcoxon rank sum test was used to compare continuous data, and the Fisher exact test was used to compare categorical data from different categories without multitest adjustment. Multivariate logistic regression was used to estimate ORs and 95% CIs of each factor of interest with outcomes after data was normalized using *Z*-scores. The ORs were adjusted by age, sex, diabetes, hypertension, smoking, and COPD at admission. Time from onset of symptoms to severe outcomes was investigated using survival analysis, with follow-up from initial onset of symptoms until February 24, 2020. Multivariate Cox regression was conducted to estimate the HRs and their corresponding 95% CI. Similar to logistic regression, Cox regression was adjusted by age, sex, diabetes, hypertension, smoking, and COPD at admission. The Kaplan–Meier product-limit estimator was used to conduct survival analysis. All survival analyses were conducted using Lifelines 0.24.0 in Python environment.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: M. Dai, D. Liu, M. Liu, L. Wang, L. Gan, L. Chai, M. Santillana, H. Cai

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