

## RESEARCH COMMUNICATION

# One-year mortality and consequences of COVID-19 in cancer patients: A cohort study

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## Abstract

The 1-year mortality and health consequences of COVID-19 in cancer patients are relatively underexplored. In this multicenter cohort study, 166 COVID-19 patients with cancer were compared with 498 non-cancer COVID-19 patients and 498 non-COVID cancer patients. The 1-year all-cause mortality and hospital mortality rates in Cancer COVID-19 Cohort (30% and 20%) were significantly higher than those in COVID-19 Cohort (9% and 8%, both  $P < .001$ ) and Cancer Cohort (16% and 2%, both  $P < 0.001$ ). The 12-month all-cause post-discharge mortality rate in survival discharged Cancer COVID-19 Cohort (8%) was higher than that in COVID-19 Cohort (0.4%,  $P < .001$ ) but similar to that in Cancer Cohort (15%,  $P = .084$ ). The incidence of sequelae in Cancer COVID-19 Cohort (23%, 26/114) is similar to that in COVID-19 Cohort (30%, 130/432,  $P = .13$ ). The 1-year all-cause mortality was high among patients with hematologic malignancies (59%), followed by those who have nasopharyngeal, brain, and skin tumors (45%), digestive system neoplasm (43%), and lung cancers (32%). The rate was moderate among patients with genitourinary (14%), female genital (13%), breast (11%), and thyroid tumors (0). COVID-19 patients with cancer showed a high rate of in-hospital mortality and 1-year all-cause

**Abbreviations:** COVID-19, Coronavirus disease 2019; RT-PCR, Reverse Transcriptase Polymerase Chain Reaction; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; WHO, World Health Organization; IQR, Interquartile range; CI, Confidence interval; RR, Relative Risk; HR, Hazard Ratio; USA, The United States of America; UK, United Kingdom; LDH, Lactic dehydrogenase; HFNC, High low nasal cannula; NIV, Non-invasive ventilation; IMV, Invasive mechanical ventilation; ECMO, Extracorporeal membrane oxygenation; ALT, Alanine transaminase; AST, Aspartate transaminase; CRRT, Continuous renal replacement therapy; RR, Respiratory rate; FiO<sub>2</sub>, Fraction of inspired oxygen; PaO<sub>2</sub>, Partial pressure of oxygen; PEEP, Positive end-expiratory pressure; CPAP, Continuous positive airway pressure; ICU, Intensive care unit; DVT, Deep vein thrombosis; eGFR, Estimated glomerular filtration rate; PE, Pulmonary embolism; COPD, Chronic obstructive pulmonary disease; CHD, Coronary heart disease; APTT, Activated partial thromboplastin time.

Chen Chai, Xiaojun Feng, Meixia Lu, Shoupeng Li, Kui Chen, and Hongxiang Wang have contributed equally to this study.

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mortality, but the 12-month all-cause post-discharge mortality rate in survival discharged cancer COVID-19 patients was similar to that in Cancer Cohort. Comparing to COVID-19 Cohort, risk stratification showed that hematologic, nasopharyngeal, brain, digestive system, and lung tumors were high risk (44% vs 9%,  $P < 0.001$ ), while genitourinary, female genital, breast, and thyroid tumors had moderate risk (10% vs 9%,  $P = .85$ ) in COVID-19 Cancer Cohort. Different tumor subtypes had different effects on COVID-19. But if cancer patients with COVID-19 manage to survive their COVID-19 infections, then long-term mortality appears to be similar to the cancer patients without COVID-19, and their long-term clinical sequelae were similar to the COVID-19 patients without cancer.

#### KEYWORDS

Cancer, consequences, coronavirus disease 2019, mortality, risk factors

## 1 | INTRODUCTION

As of 30 March 2021, the number of COVID-19 cases and deaths continued to rise with 127.3 million cumulative cases and 2.8 million deaths globally.<sup>1</sup> The global cancer burden is estimated to have risen to 19.3 million new cases and 10.0 million deaths in 2020.<sup>2</sup> Some initial reports suggested that patients with an active malignancy might be more likely to contract SARS-CoV-2 and have an increased risk of short-term mortality.<sup>3–6</sup>

However, these initial reports were restricted by the follow-up time.<sup>6</sup> As some patients remained hospitalized for some time, longer-term follow-up is needed to better understand the effect of COVID-19 on cancer patients.<sup>3,6,7</sup> Cancer encompasses a diverse array of primary tumor subtypes with different outcomes.<sup>8,9</sup> To the best of our knowledge, there are no reports to study the long-term prognosis of cancer patients with COVID-19, and few studies compare them with cancer patients without COVID-19 as well as different tumor subtypes.

Herein, 166 cancer patients with COVID-19, 498 COVID-19 patients without cancer, and 498 cancer patients without COVID-19 were compared. All of the patients were from the four hospitals in Wuhan, a COVID-19 “hot spot” in China. All survival patients were

followed up for at least 12 months after hospital admission.

## 2 | METHODS

### 2.1 | Study design and patients

In this multicenter ambidirectional comparative cohort study, we enrolled sequential cancer patients who were admitted with COVID-19 (Cancer COVID-19 Cohort) to the four hospitals in Wuhan, Hubei Province, China, the epicenter of the first COVID-19 pandemic, between January 1, 2020, and March 18, 2020 (Table S1). Eligibility criteria for enrollment were laboratory confirmation of SARS-CoV-2 virus infection by RT-PCR test and hospitalized patients with active cancer (Table S2). COVID-19 disease severity was defined according to World Health Organization (WHO) guidelines.<sup>10</sup> Primary tumor subtypes were classified by the WHO Classification of Tumors series.<sup>11</sup> Each COVID-19 patient with cancer was matched to patients without cancer from the same COVID-19-positive population (COVID-19 Cohort) in a ratio of 1:3 based on age ( $\pm 5$  years) and sex. The patients served as uninfected controls were chosen at a ratio of

1:3 (based on age, gender, and cancer subtype) from cancer patients admitted to the same four hospitals between 1 January 2019 and 17 March 2020. All data were de-identified. This study was done in accordance with the STROBE statement.<sup>12</sup>

## 2.2 | Study variables and outcomes

We define the acute phase as the time between symptom onset and hospital discharge. Data were collected on site by trained coordinators manually reviewing the electronic medical records and importing them into a secure online database using a standardized case report form (supplementary case report form, Data S1). Demographic characteristics, coexisting conditions, presenting symptoms, vital signs, biochemical findings, treatment practices, and a variety of hospital outcome data were collected. To ensure the enrollment of an unbiased population, the eligible patients were consecutively recruited from each site from 1 January 2020 to 17 March 2020.

All survivors who had been discharged from the hospital were selected into the follow-up study to observe their health consequences in recovery from COVID-19 (supplementary follow-up studies, Data S1). Some patients were followed up in the outpatient clinic and asked to complete a series of questionnaires. We followed up with the patients until death or 18 February 2021, whichever came first.

The primary outcomes included the 1-year all-cause mortality rate and sequelae. Secondary outcomes included the hospital mortality rate, the length of hospital stay, and the 12-month all-cause post-discharge mortality rate.

## 2.3 | Statistical analysis

We aimed to generate a representative sample of cancer patients with COVID-19 by starting with at least 5500 COVID-19 patients and 40 900 cancer patients from the four hospitals (Figure S1). To describe baseline characteristics, treatment, and outcomes, we prespecified the following covariates for inclusion in the models. Descriptive statistics were used to describe the baseline data of the patients. Categorical variables were presented as percentages. Continuous variables were expressed as mean  $\pm$  SD if they were normally distributed or as median (IQR) if they were not. Proportions for categorical variables were compared using the  $\chi^2$  test.

The Kaplan–Meier method with log-rank test was used for comparing survival curves between Cancer

COVID-19 Cohort and control groups. Cox proportional hazards regression was used to investigate the effect of several risk factors on survival. Univariable and multivariable analyses between 1-year mortality and risk factors were performed. The risk factor variables were included in the stepwise Cox proportional hazards regression. A backward stepwise technique was used to evaluate all potential univariable correlates ( $P < .05$ ) and create a multivariable model containing variables with  $P < .05$ .

Analyses were performed using SPSS Statistics 26.0 software (International Business Machines Corp, IBM) and Graph Pad Prism (Version 8.0.2, GraphPad Software, Inc.).

## 3 | RESULTS

### 3.1 | Patient characteristics at baseline

The median age of the 166 hospitalized cancer COVID-19 patients was 65 (59–70) years old and 49% (82/166) of the patients were male (Table 1). The patients consist of different primary tumor subtypes following WHO classification criteria (Table 2).<sup>13</sup> Among the patients, most cancers were of the digestive system (25%, 42/166), followed by the lung (15%, 25/166), and genitourinary (13%, 22/166). In terms of primary organ tumor, lung cancer was the most common cancer type (15%, 25/166), followed by breast cancer (11%, 19/166), and colon cancer (11%, 18/166).

At baseline, the demographics characteristics of the patients were well-balanced in all three cohorts (Table 1). Comorbidities among Cancer COVID-19 Cohort were generally similar to those among COVID-19 Cohort. But comparing to Cancer Cohort, Cancer COVID-19 Cohort was more likely to have a history of diabetes (9% vs 15%,  $P = .07$ ), hyperlipidemia (7% vs 20%,  $P < .001$ ), hyperuricemia (3% vs 10%,  $P < .001$ ), and chronic obstructive pulmonary diseases (COPD; 1% vs 7%,  $P = .001$ ), supporting the risks of these underlying conditions for contracting COVID-19.

In terms of COVID-19 symptoms, patients in Cancer COVID-19 Cohort were more likely to have expectoration (36% vs 21%,  $P < .001$ ), dyspnea (24% vs 16%,  $P = .017$ ), and consciousness disorder (11% vs 4%,  $P = .001$ ) than those in COVID-19 Cohort, but less likely to have a sore throat (7% vs 14%,  $P = .024$ ) or dry cough (43% vs 53%,  $P = .031$ ; Table 1). Cancer COVID-19 Cohort had more severe complications such as respiratory failure (16% vs 10%,  $P = .045$ ), acute kidney injury (18% vs 8%,  $P = .001$ ), and acute liver injury (32% vs 22%,  $P = .011$ ) than COVID-19 Cohort (Table 1).

TABLE 1 Characteristics of Cancer COVID-19 Cohort, COVID-19 Cohort, and Cancer Cohort

	Patients, no. (%)		<i>P</i> value <sup>a</sup>	Cancer Cohort (n = 498)	<i>P</i> value <sup>b</sup>
	Cancer COVID-19 Cohort (n = 166)	COVID-19 Cohort (n = 498)			
<b>Demographics</b>					
Age, median (IQR), y	65 (59–70)	65 (59–70)	1.000	66 (58–73)	.49
<b>Sex</b>					
Female	84 (51)	252 (51)	1.000	252 (51)	1.000
Male	82 (49)	246 (49)		246 (49)	
<b>Comorbidities</b>					
Current smoking	8 (5)	14 (3)	.211	127 (26)	<.001
Hypertension	55 (33)	171 (34)	.777	135 (27)	.137
Diabetes	24 (15)	104 (21)	.069	47 (9)	.07
Hyperlipidemia	33 (20)	76 (15)	.164	34 (7)	<.001
Hyperuricemia	16 (10)	42 (8)	.634	14 (3)	<.001
Coronary heart disease	12 (7)	40 (8)	.739	53 (11)	.2
Cerebrovascular disease	4 (2)	18 (4)	.453	14 (3)	1.000
COPD	11 (7)	25 (5)	.429	7 (1)	.001
Chronic kidney disease	3 (2)	11 (2)	1.000	7 (1)	1.000
Chronic liver disease	5 (3)	7 (1)	.313	28 (6)	.18
Arrhythmia	8 (5)	18 (4)	.488	27 (5)	.764
<b>Symptoms at admission</b>					
Fever	118 (71)	363 (73)	.652	NA	NA
Chills	26 (16)	88 (18)	.552	NA	NA
Headache or dizzy	26 (16)	79 (16)	.951	NA	NA
Myalgias	26 (16)	104 (21)	.142	NA	NA
Fatigue	88 (53)	253 (51)	.622	NA	NA
Rhinorrhea	10 (6)	20 (4)	.281	NA	NA
Sore throat	12 (7)	69 (14)	.024	NA	NA
Dry cough	72 (43)	264 (53)	.031	NA	NA
Expectoration	60 (36)	105 (21)	<.001	NA	NA
Hemoptysis	10 (6)	7 (1)	.003	NA	NA
Chest congestion	70 (42)	203 (41)	.75	NA	NA
Dyspnea	40 (24)	79 (16)	.017	NA	NA
Nausea or vomiting	21 (13)	45 (9)	.178	NA	NA
Abdominal pain	8 (5)	15 (3)	.27	NA	NA
Diarrhea	31 (19)	101 (20)	.653	NA	NA
Consciousness disorder	18 (11)	20 (4)	.001	NA	NA
<b>Complications</b>					
Respiratory failure	27 (16)	52 (10)	.045	NA	NA
Acute cardiac injury	3 (2)	2 (0)	.195	NA	NA
Acute kidney injury	29 (18)	41 (8)	.001	NA	NA
Acute liver injury	53 (32)	110 (22)	.011	NA	NA
Prothrombotic coagulopathy	2 (1)	4 (1)	1.000	NA	NA
Electrolytic disturbance	28 (17)	63 (13)	.171	NA	NA
In-hospital infection	6 (4)	16 (3)	.802	NA	NA

(Continues)

TABLE 1 (Continued)

	Patients, no. (%)		<i>P</i> value <sup>a</sup>	Patients, no. (%)	
	Cancer COVID-19 Cohort (n = 166)	COVID-19 Cohort (n = 498)		Cancer Cohort (n = 498)	<i>P</i> value <sup>b</sup>
Treatment					
Antiviral drug	108 (65)	359 (72)	.086	NA	NA
Intravenous antibiotics	88 (53)	224 (45)	.073	NA	NA
Intravenous antifungal	20 (12)	36 (7)	.053	NA	NA
Anticoagulation	50 (30)	37 (7)	<.001	NA	NA
Intravenous corticosteroids	44 (27)	70 (14)	<.001	NA	NA

<sup>a</sup>Cancer COVID-19 Cohort vs COVID-19 Cohort.

<sup>b</sup>Cancer COVID-19 Cohort vs Cancer Cohort.

### 3.2 | One-year all-cause mortality

The median follow-up time from the point of hospital admission was 12.2 (IQR 12.1–12.6) months (Table 3 and Figure 1A). In the Cox proportional hazards regression analysis, 30% (49/166) of the patients in Cancer COVID-19 Cohort died within 12 months. The mortality was 9% (44/498) in COVID-19 Cohort (relative risk/RR = 0.29; 95% CI 0.19 to 0.44,  $P < .001$ ), for an absolute risk difference of –19 percentage points (95% CI –13 to –29,  $P < .001$ ). And that was 16% (80/498) in Cancer Cohort (RR, 0.43; 95% CI 0.30 to 0.62,  $P < .001$ ), for an absolute risk difference of –13 percentage points (95% CI –9 to –19,  $P < .001$ ). Results were similar in the adjusted analysis. Figure 1A shows the main difference between Cancer COVID-19 Cohort and Cancer Cohort was in the first 2 months, with mortality of 20% (34/166) and 4% (20/498,  $P < .001$ ) in each cohort, respectively.

### 3.3 | One-year health consequences

At the 1-year follow-up, 56 cancer COVID-19 patients were excluded because 49 patients died and seven patients could not be reached, and 70 COVID-19 patients were excluded because 44 patients died and 26 patients lost contact. As a result, 114 cancer COVID-19 patients and 432 COVID-19 participants were enrolled for the questionnaire interview. In this follow-up investigation, the rate of having at least one symptom was 23% (26/114) in Cancer COVID-19 Cohort, generally similar to that in COVID-19 Cohort (30%; 130/432,  $P = .13$ ). Interestingly, patients in Cancer COVID-19 Cohort were slightly likely to have fatigue (4% vs 12%,  $P = .016$ ), chest congestion (3% vs 9%,  $P = .027$ ), and anxiety (0 vs 5%,  $P = .021$ ) than those in COVID-19 Cohort (Table 3).

### 3.4 | Hospital mortality

The median length of hospital stay in Cancer COVID-19 Cohort (25 days; IQR 15–33 days) was longer than that in COVID-19 Cohort (21 days; IQR 11–28 days;  $P = .005$ ; Table S4). Patients in Cancer COVID-19 Cohort were more likely to develop severe COVID-19 than those in COVID-19 Cohort (36% vs 20%,  $P < .001$ ; Table 3). Cancer COVID-19 Cohort also required significantly more mechanical ventilation than COVID-19 Cohort (14% vs 6%,  $P < .001$ ). Regarding the hospital mortality, 20% (34/166) patients in Cancer COVID-19 Cohort died in hospital, 8% (42/498) were found in COVID-19 Cohort (RR 0.36; 95% CI 0.22 to 0.59,  $P < .001$ ), and 2% (8/498) were observed in Cancer Cohort (RR 0.10; 95% CI 0.05 to 0.19,  $P < .001$ ).

### 3.5 | Twelve-month post-discharge mortality

The median follow-up time of cancer COVID-19 patients after discharge was 11.2 (IQR 10.8–11.6) months among those who were alive (Table 3 and Figure 1B). The 12-month all-cause post-discharge mortality rate was 11% (15/132) in Cancer COVID-19 Cohort, significantly higher than that in COVID-19 Cohort (0.4%, 2/456,  $P < .001$ ) and showing no statistical difference from Cancer Cohort (15%, 72/490,  $P = .084$ ).

### 3.6 | Outcomes of primary tumor subtype

For 1-year all-cause post-admission mortality, comparing to COVID-19 Cohort (9%, 44/498), COVID-19 patients

TABLE 2 Primary tumor subtype among Cancer COVID-19 Cohort

Primary tumor subtype	Patients, no. (%)				
	Total (n = 166)	Hospital mortality		1-year mortality	
		Dead (n = 34)	Alive (n = 132)	Dead (n = 49)	Alive (n = 117)
Total	166 (100)	34 (20)	132 (80)	49 (30)	117 (70)
Solid tumors	149 (90)	26 (17)	124 (83)	38 (26)	111 (74)
Thyroid and breast	33 (20)	2 (6)	33 (84)	2 (6)	33 (84)
Thyroid	14 (8)	0	14 (100)	0	14 (100)
Breast	19 (11)	2 (11)	17 (89)	2 (11)	17 (89)
Female genital	16 (9)	1 (6)	15 (94)	2 (13)	14 (87)
Cervical	9 (5)	1 (11)	8 (89)	1 (11)	8 (89)
Ovary	4 (2)	0	4 (100)	1 (25)	3 (75)
Endometrial	3 (2)	0	3 (100)	0	3 (100)
Genitourinary	22 (13)	3 (14)	19 (86)	3 (14)	19 (86)
Prostatic	7 (4)	2 (29)	5 (71)	2 (29)	5 (71)
Bladder	7 (4)	0	7 (100)	0	7 (100)
Renal	5 (3)	1 (20)	4 (80)	1 (20)	4 (80)
Penile	2 (1)	0	2 (100)	0	2 (100)
Testicular	1 (1)	0	1 (100)	0	1 (100)
Lung	25 (15)	4 (16)	21 (84)	8 (32)	17 (68)
Digestive system	42 (25)	12 (29)	30 (71)	18 (43)	24 (57)
Colon	18 (11)	3 (17)	15 (83)	7 (39)	11 (61)
Gastric	10 (6)	5 (50)	5 (50)	5 (50)	5 (50)
Liver	6 (4)	1 (17)	5 (83)	2 (33)	4 (67)
Rectal	5 (3)	2 (40)	3 (60)	2 (40)	3 (60)
Pancreas	3 (2)	1 (33)	2 (67)	2 (67)	1 (33)
Other solid	11 (7)	4 (36)	7 (64)	5 (45)	6 (55)
Bone	4 (2)	0	4 (100)	1 (25)	3 (75)
Nasopharyngeal	4 (2)	2 (50)	2 (50)	2 (50)	2 (50)
Brain	2 (1)	1 (50)	1 (50)	1 (50)	1 (50)
Skin	1 (1)	1 (100)	0	1 (100)	0
Hematologic malignancies	17 (10)	8 (47)	9 (53)	11 (65)	6 (35)
Lymphoid malignancy	14 (8)	7 (50)	7 (50)	9 (64)	5 (36)
Multiple myeloma	6 (4)	4 (67)	2 (33)	5 (83)	1 (17)
Non-Hodgkin lymphoma	4 (2)	1 (25)	3 (75)	2 (50)	2 (50)
Chronic lymphoblastic leukemia	2 (1)	0	2 (100)	0	2 (100)
Acute lymphoblastic leukemia	2 (1)	2 (100)	0	2 (100)	0
Myeloid malignancy	3 (2)	1 (33)	2 (67)	2 (67)	1 (33)
Acute myelogenous leukemia	2 (1)	1 (50)	1 (50)	2 (100)	0
Myelodysplastic syndrome	1 (1)	0	1 (100)	0	1 (100)

with hematologic malignancies (65%, 11/17,  $P < .001$ ) had the highest rate, followed by some solid tumors such as brain/nasopharyngeal/bone and skin tumors (45%,

5/11,  $P < .001$ ), digestive system tumors (43%, 18/42,  $P < .001$ ), and lung cancers (32%, 8/25,  $P < .001$ ). COVID-19 patients with breast and thyroid tumors were

TABLE 3 Outcomes of Cancer COVID-19 Cohort, COVID-19 Cohort, and Cancer Cohort

	Patients, no. (%)				
	Cancer COVID-19 cohort (n = 166)	COVID-19 cohort (n = 498)	P value <sup>a</sup>	Cancer cohort (n = 498)	P value <sup>b</sup>
COVID-19 severity					
Non-severe	106 (64)	399 (80)	<.001	NA	NA
Severe	60 (36)	99 (20)		NA	NA
Oxygenation and ventilation					
Not requiring supplement oxygen	47 (29)	170 (34)	<.001	NA	NA
Requiring supplement oxygen	93 (56)	279 (56)		NA	NA
HFNC	2 (1)	23 (5)		NA	NA
NIV	11 (7)	8 (2)		NA	NA
IMV or ECMO	12 (7)	18 (4)		NA	NA
Length of hospital stay, median (IQR), d	25 (15–33)	21 (11–28)	.005	NA	NA
Time from symptom onset to admission, median (IQR), d	10 (7–16)	10 (5–15)	.047	NA	NA
Time from admission to follow-up, median (IQR), m	12.2 (12.1–12.6)	12.2 (12.1–12.6)	.36	12.1 (11.7–12.4)	.063
Time from discharge to follow-up, median (IQR), m	11.2 (10.8–11.6)	11.4 (11.2–11.8)	.051	11.2 (10.7–11.7)	.82
Mortality					
1-year all-cause mortality	49 (30)	44 (9)	<.001	80 (16)	<.001
12-month post-discharge mortality	15 (11)	2 (0.4)	<.001	72 (15)	.084
Hospital mortality	34 (20)	42 (8)	<.001	8 (2) <sup>c</sup>	<.001
Consequences at 1-year followed up					
Number of patients	114	432		NA	NA
Any one of symptoms	26 (23)	130 (30)	0.13	NA	NA
Fatigue	5 (4)	53 (12)	0.016	NA	NA
Chest congestion	3 (3)	38 (9)	0.027	NA	NA
Cough	10 (9)	25 (6)	0.24	NA	NA
Expectoration	4 (4)	7 (2)	0.20	NA	NA
Dyspnea	9 (8)	27 (6)	0.51	NA	NA
Palpitations	2 (2)	9 (2)	0.83	NA	NA
Waist pain	7 (6)	20 (5)	0.50	NA	NA
Anxiety	0	23 (5)	0.021	NA	NA
Sleep difficulties	1 (1)	5 (1)	0.65	NA	NA

Abbreviations: ECMO, Extracorporeal membrane oxygenation; HFNC, high-flow nasal canula for oxygen therapy; IMV, Invasive mechanical ventilation; NIV, Noninvasive mechanical ventilation.

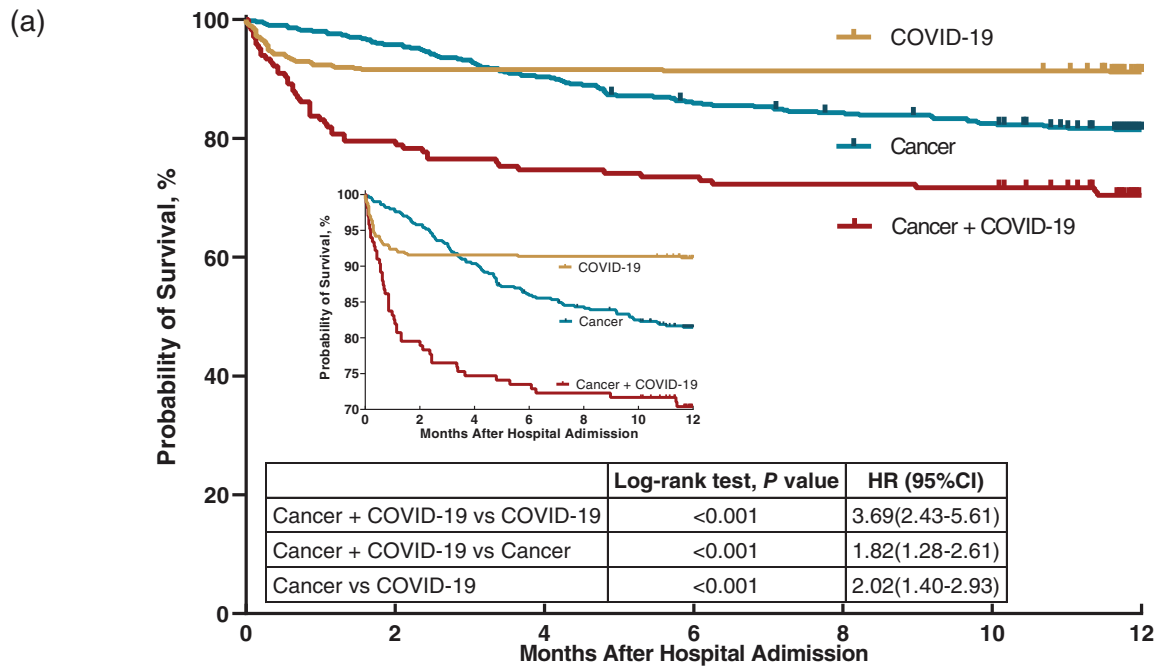
<sup>a</sup>Cancer COVID-19 cohort vs COVID-19 cohort.

<sup>b</sup>Cancer COVID-19 cohort vs cancer cohort.

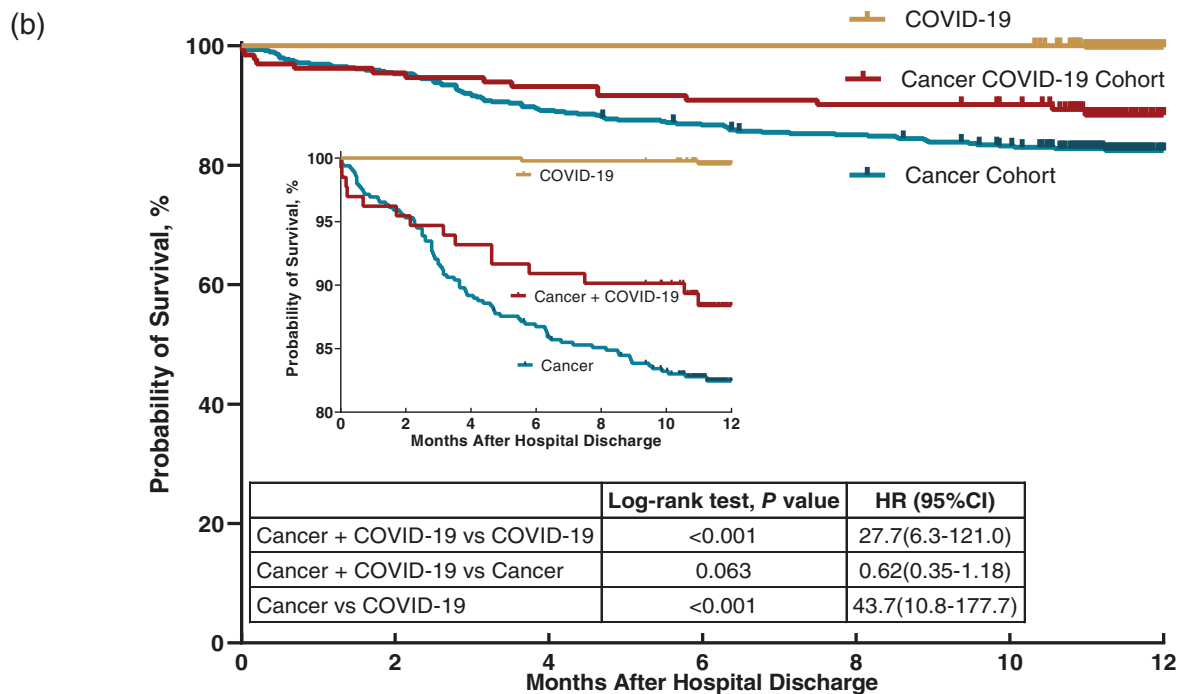
<sup>c</sup>As these patients were not necessarily hospitalized, their hospital mortality rate was calculated as when one deceased within the hospitalization time duration of their cancer COVID-19 cohort match patient.

associated with relatively low mortality (6%, 2/33,  $P = .57$ ), while patients with female genital tumors (13%, 2/16,  $P = .43$ ) and genitourinary (14%, 3/22,  $P = .61$ ) had moderate high mortality rate (Table 2 and Figure 2). Compared with 1-year all-cause post-admission mortality

in the COVID-19 Cohort (9%, 44/498), patients with hematologic, brain, nasopharyngeal, digestive system, and lung malignancies, combined as the high-risk group (43%, 42/95,  $P < .001$ ), showed a significantly higher risk of 1-year post-admission mortality [5.4 (3.5–8.3),



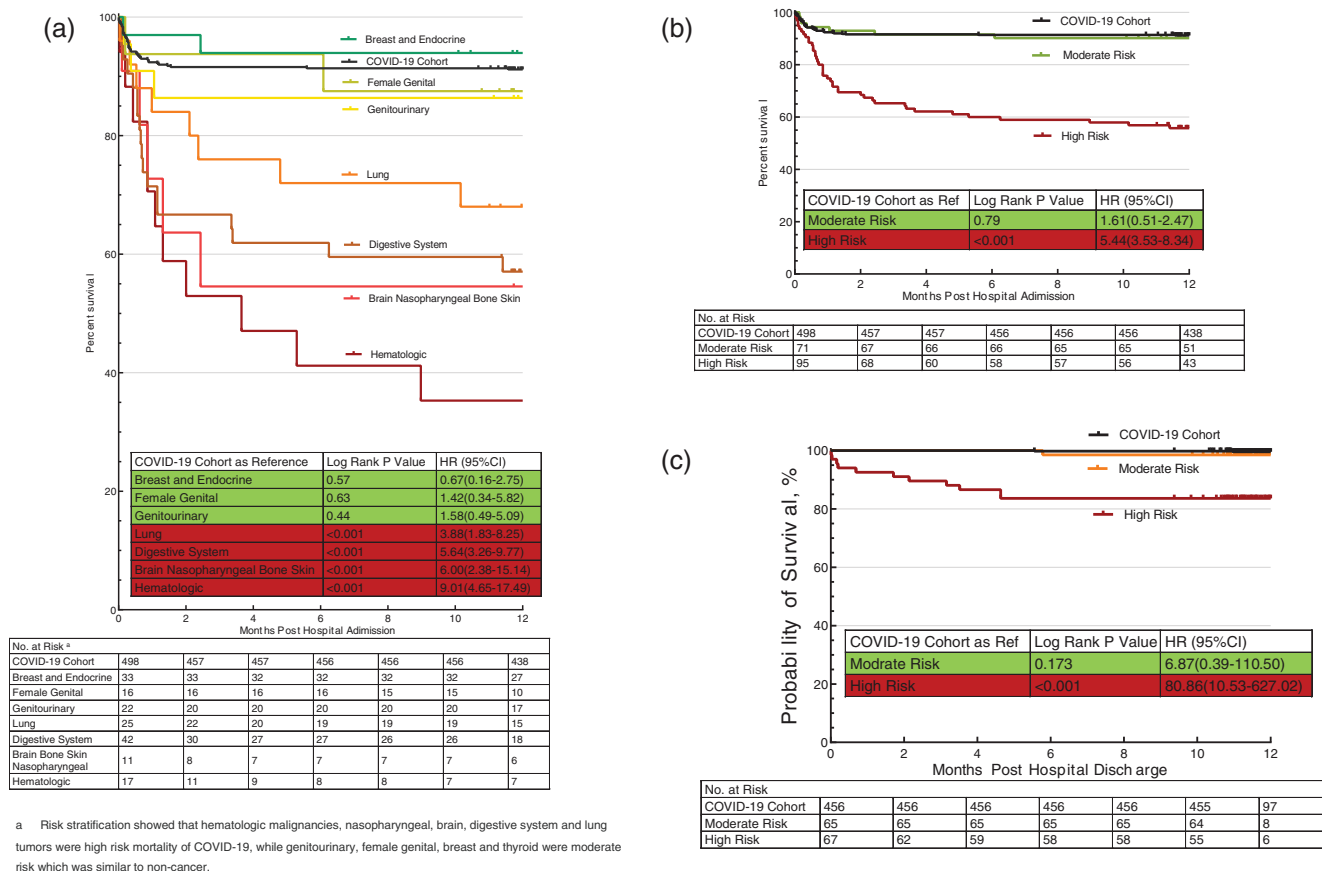
No. at Risk		0	2	4	6	8	10	12
COVID-19	498	457	457	456	456	456	456	438
Cancer + COVID-19	166	134	125	123	121	120	120	93
Cancer	498	478	451	427	417	407	407	325



No. at Risk		0	2	4	6	8	10	12
COVID-19	456	456	456	456	456	455	455	97
Cancer + COVID-19	132	127	124	121	120	117	117	13
Cancer	490	468	438	424	414	397	397	76

**FIGURE 1** Kaplan-Meier analysis mortality of Cancer COVID-19 Cohort, COVID-19 Cohort, and Cancer Cohort. (a) Kaplan-Meier analysis of Cancer COVID-19 Cohort, COVID-19 Cohort and Cancer Cohort in 1-year all-cause post-admission mortality; (b) Kaplan-Meier analysis of Cancer COVID-19 Cohort, COVID-19 Cohort and Cancer Cohort in 12-month all-cause post-discharge mortality





**FIGURE 2** Kaplan-Meier analysis of mortality in primary tumor subtype among Cancer COVID-19 Cohort. (a) Kaplan-Meier analysis of primary tumor subtype among Cancer COVID-19 Cohort. Compared with the COVID-19 Cohort, COVID-19 patients with hematologic, brain, nasopharyngeal, digestive system, and lung malignancies showed a significantly high risk of 1-year all-cause post-admission mortality, defined as the high-risk group; while patients with breast and endocrine, genitourinary, and female genital tumors showed a moderate risk of 1-year post-admission mortality with no statistical difference from the COVID-19 Cohort, defined as the moderate-risk group. (b) Kaplan-Meier analysis of high and moderate risk stratification of primary tumor subtype among cancer COVID-19 Cohort in 1-year all-cause post-admission mortality; (c) Kaplan-Meier analysis of high and moderate risk stratification of primary tumor subtype among cancer COVID-19 Cohort in 12-month all-cause post-discharge mortality

$P < .001$ ] and 12-month post-discharge mortality [80.9 (10.5–627.0),  $P < .001$ ]; patients with breast and endocrine, genitourinary, and female genital tumors, combined as the moderate-risk group (10%, 7/71,  $P = .71$ ), showed a moderate risk of 1-year post-admission mortality [1.6 (0.5–2.5),  $P = .79$ ] and 12-month post-discharge mortality [6.9 (0.4–110.5),  $P = .17$ ] (Figure 2).

### 3.7 | Risk factors for outcomes of Cancer COVID-19 cohort

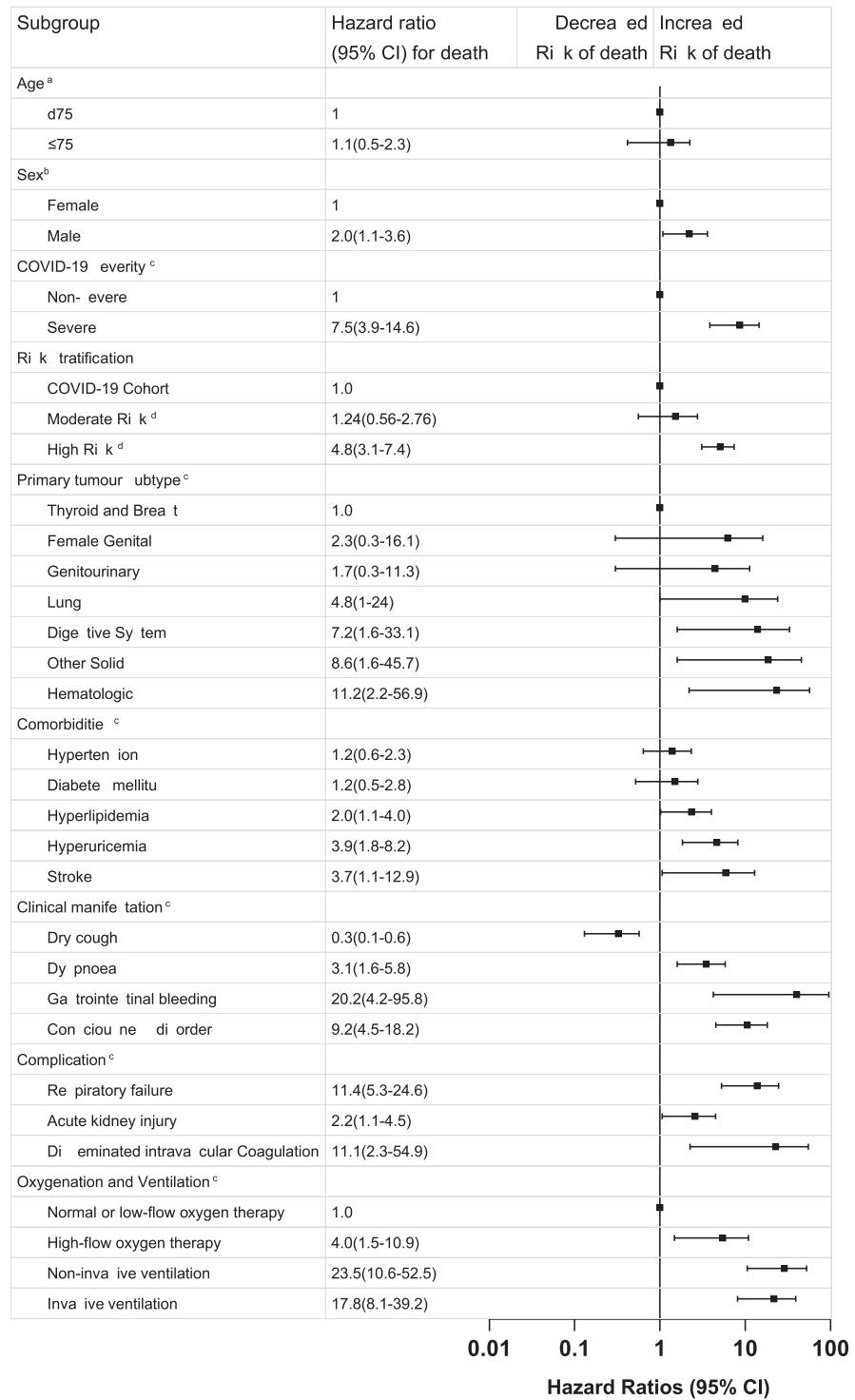
In the multivariate cox regression model (Figure 3), we observed that male [HR 2.0, 95% CI 1.1–3.6], severe COVID-19 disease [non-severe; HR 7.5, 95%CI 3.9–14.6], hyperuricemia [HR 3.9, 95% CI 1.8–8.2], stroke [HR 3.7, 95% CI, 1.1–12.9], dyspnea [HR 3.1, 95% CI 1.6–5.8],

consciousness disorder [HR 9.2, 95% CI, 4.5–18.2], respiratory failure [HR 11.4, 95% CI 5.3–24.6], and acute kidney injury [HR 2.2, 95% CI 1.1–4.5] were significantly associated with increased mortality. Characteristic analysis of Cancer COVID-19 Cohort on the 1-year all-cause mortality did not show any age bias.

## 4 | DISCUSSION

The current COVID-19 pandemic, a novel coronavirus first detected in Wuhan, China, has created a global crisis. The cancer center of Union Hospital of Huazhong University of Science and Technology was enlisted as a designated hospital to fight against COVID-19. The Asian National Cancer Centers have also implemented pragmatic strategies, distancing strategies, and telemedicine

**FIGURE 3** Multivariable cox regression model among Cancer COVID-19 Cohort for 1-year all-cause post-admission mortality



a: Adjusted for sex; b: Adjusted for age; c: Adjusted for age and sex; d: Low risk tumor: thyroid, breast, female genital, genitourinary; e: High risk malignancies: hematologic, nasopharyngeal, brain, digestive system and lung tumor and colon

in challenges and countermeasures against COVID-19.<sup>14</sup> Judging from recent studies, patients with active malignancies might be more likely to contract SARS-CoV-2 and have an increased risk of short-term mortality. However, the 1-year mortality and health consequences of COVID-19 in cancer patients have remained elusive.

To our knowledge, this study represents the longest follow-up on the mortality and health consequences of hospitalized cancer patients with COVID-19. One-year mortality (30%) of Cancer COVID-19 Cohort was nearly two times higher than that of Cancer Cohort (16%,  $P < .001$ ) and more than three times higher than that of COVID-19 Cohort (9%,  $P < .001$ ). As it was difficult to determine whether COVID-19 was the direct cause of death or an inevitably terminal event of cancer caused the death, we are reporting the all-cause case fatality rate. All COVID-19 patients in our cohort had finished their clinical treatment. The hospital mortality of the Cancer COVID-19 Cohort was 20%, 2.5 times higher than that of the COVID-19 Cohort (8%,  $P < .001$ ) and 10 times higher than that of the Cancer Cohort (2%,  $P < .001$ ). The difference in the hospital mortality among the three cohorts shows the strong adverse effect of COVID-19 on both cancer and non-cancer patients. A cohort study reported a death rate of 20% (40/205) in cancer patients with COVID-19 in Hubei, China.<sup>3</sup> A series of 218 cancer patients with COVID-19 from a New York Hospital System reported a case fatality rate of 28% because of a bias towards more severe cases.<sup>5</sup> The 12-month all-cause post-discharge mortality rate in survival discharged Cancer COVID-19 Cohort (8%) was higher than that in COVID-19 Cohort (0.4%,  $P < .001$ ) but similar to that in Cancer Cohort (15%,  $P = .084$ ). Therefore, if cancer patients manage to survive their COVID-19 infections, then long-term sequelae appear to be similar to other cancer patients. The patients served as uninfected controls were based on age, gender, and cancer subtype from cancer patients admitted to the same four hospitals. The risk factors of age, gender, and cancer subtype had been excluded.

We found that at 1 year after hospital admission, 23% of cancer COVID-19 patients endorsed at least one symptom, a similar risk to that of COVID-19 Cohort (30%,  $P = .13$ ). Cough (9%) or dyspnea (8%) were common among Cancer COVID-19 Cohort, while fatigue (12%) or chest congestion (9%) were common in COVID-19 Cohort. Huang and colleagues found that fatigue or muscle weakness (63%) were the most common symptoms in a 6-month follow-up survey of 1733 COVID-19 patients.<sup>15</sup> A 3-month follow-up survey of 538 COVID-19 patients reported that fatigue (28%) was the most common symptom.<sup>16</sup>

Our results showed that different tumor subtypes among Cancer COVID-19 Cohort had different outcomes.

Compared with the COVID-19 Cohort, COVID-19 patients with hematologic, brain, nasopharyngeal, digestive system, and lung malignancies showed a significantly high risk of mortality (44% vs 9%,  $P < .001$ ), while patients with breast and endocrine, genitourinary, and female genital tumors showed a moderate mortality risk just similar to the COVID-19 Cohort (10% vs 9%,  $P = .85$ ). This is consistent with a few other studies. Studies showed that COVID-19 patients with hematologic malignancies were reported to have high mortality rate in China (41%-62%),<sup>3,17</sup> USA (37%, 20/54),<sup>5</sup> UK (36%, 81/224),<sup>8</sup> and Spain (33%, 230/697).<sup>18</sup> Thoracic cancer patients with COVID were reported with high mortality rate in The Thoracic Cancers International COVID-19 Collaboration (TERAVOLT) registry (33%, 66/200),<sup>19</sup> China (25%, 6/24),<sup>3</sup> USA (55%, 6/11),<sup>5</sup> UK (39%, 43/111),<sup>8</sup> and Turkey [11%, 18/157 (vs total cancers 4%, 50/1122)].<sup>15</sup> Digestive system tumors were associated with high mortality rate in China (23%, 9/40),<sup>3</sup> USA (38%, 15/39),<sup>5</sup> UK (30%, 63/219).<sup>8</sup> COVID-19 patients with breast, thyroid or endocrine tumors had lower mortality rate in China (7%, 4/56),<sup>3</sup> USA (13%, 4/31),<sup>5</sup> UK (18%, 26/143),<sup>8</sup> and Turkey (1%, 4/442).<sup>15</sup> However, COVID-19 patients with genitourinary or gynecologic tumors in our study, showing a generally low mortality rate with small sample size, had different outcomes in other studies (genitourinary: low in the USA, 15%, 7/46; high in the UK, 38%, 72/191; gynecologic, high in USA 38%, 5/13; low in UK 13%, 7/56).<sup>5,8</sup> The UK study might be more representative as it had a bigger sample size.

Many of the predictive risk factors for mortality in the Cancer COVID-19 Cohort were similar to data reported in COVID-19 patients.<sup>20</sup> In the adjusted Cox proportional hazards model, we observed significant associations of death with chronic diseases including hypertension, diabetes, hyperuricemia, COPD, cardiovascular disease, and cerebrovascular disease in COVID-19 patients.<sup>21,22</sup> Serologic predictors for mortality in our dataset included anemia, and elevated LDH, D-dimer, and lactic acid, which correlated with available data from all COVID-19 patients.<sup>23</sup>

## 5 | LIMITATION

This study has several limitations. First of all, this study population only included hospitalized COVID-19 patients within Hubei Province, China. Therefore, the cohort might not exactly represent all cancer patient populations, such as the patients who were on end-of-life care and/or residing in nursing homes, which may potentially bias our study to more severe cases of COVID-19. Secondly, our Cancer Cohort was admitted into hospital

for active cancer during a different time frame (1 January 2019 to 17 March 2020) from the COVID-19 Cohorts (1 January 2020 to 17 March 2020), the hospitals might be under different stress levels and operation modes during these two time frames, although it should not affect the patient care significantly. Nonetheless, it would be desired to use contemporaneous control groups when these data become available. Lastly, it would be ideal to have cancer stages identified and matched between cohorts in addition to the cancer subtypes. However, the cancer staging information required extensive manual review and verifications, eventually becoming prohibitively time-consuming and technically difficult for the involved COVID-19 clinicians to collect and confirm on, especially on the deceased patients. Also, the sample size of stratified populations would be too limited to be meaningful. Hopefully, our larger sample size of controls compensates for some of the potential skews.

## 6 | CONCLUSION

If cancer patients with COVID-19 manage to survive their COVID-19 infections and immediate sequelae, then long-term mortality appears to be similar to the cancer patients without COVID-19, and their long-term clinical sequelae were similar to the COVID-19 patients without cancer. Different tumor subtypes had different effects on COVID-19. Comparing to the COVID-19 Cohort, risk stratification showed that hematologic, nasopharyngeal, brain, digestive system, and lung tumors were high risk (44% vs 9%,  $P < .001$ ), while genitourinary, female genital, breast, and thyroid tumors had moderate risk (10% vs 9%,  $P = .85$ ) in the COVID-19 Cancer Cohort.

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## CONFLICT OF INTEREST

The authors declare no conflict of interests.

## AUTHOR CONTRIBUTIONS

Zehai Tang, Yuxiong Weng, Jinnong Zhang, Chen Chai conceived the project; Zehai Tang, Xiaojun Feng, Meixia Lu, Shoupeng Li, Kui Chen, Hongxiang Wang, Wendan Wang, Zhaoming Tang, Gang Cheng, Xiaoxiong Wu, Yunfeng Li, Yuying Wen, Banghong Da, Hong Fan, Lei Wang, Fen Ai, Wei Li, Cao Peng, Hongrong Zhang, and Shuang Wen analyzed the data; Zehai Tang, Chen Chai, Xiaojun Feng, Meixia Lu, Shoupeng Li, Kui Chen,

Hongxiang Wang, and Wendan Wang extracted data and generated figures; Zehai Tang, Chen Chai, Xiaojun Feng, Meixia Lu, Shoupeng Li, Kui Chen, Hongxiang Wang, and Wendan Wang wrote the manuscript which was reviewed and edited by the other co-authors.

## ETHICS STATEMENT

The study was approved by the Institutional Ethics Committee of Union Hospital (2021-0005-01) and Institutional Ethics Committee of the Central Hospital of Wuhan (2020-7), Tongji Medical College, Huazhong University of Science and Technology. The data used were de-identified. No reference has been made at any point to individually identifiable data. All of the data used in this study come from Wuhan Union Hospital and its affiliated hospitals or the Central Hospital of Wuhan.

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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## SUPPORTING INFORMATION

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