An online tool for predicting the prognosis of cancer patients with SARS-CoV-2 infection: a multi-center study

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Abstract

Purpose: During the coronavirus disease 2019 (COVID-19) pandemic, oncologists face new challenges and they need to adjust their cancer management strategies as soon as possible to reduce the risk of SARS-CoV-2 infection and tumor recurrence. However, data on cancer patients with SARS-CoV-2 infection remains scarce.

Methods: We performed a retrospective study of 223 cancer patients with SARS-CoV-2 from 26 hospitals in Hubei, China. An individualized nomogram was constructed based on multivariable Cox analysis. Considering the convenience of the nomogram application, an online tool was also created by shiny app. C-index, calibration curves and decision curve analysis (DCA) were performed to verify the prediction performance and clinical application of the nomogram.

Results: Among cancer patients with SARS-CoV-2, there were significant differences in clinical characteristics between survivors and non-survivors, and lung cancer patients had similar short-time survival with other cancer patients. Male, dyspnea, elevated PCT, increased heart rate, elevated D-dimers, decreased platelets and so on were risk factors for these patients. Furthermore, good prediction performance of the online tool (dynamic nomogram: <https://covid-19-prediction-tool.shinyapps.io/DynNomapp/>). was also fully demonstrated with the C-index of 0.841 (95% CI: 0.782 - 0.900) in the development cohort and 0.780 (95% CI: 0.678-0.882) in the validation cohort.

Conclusion: Overall, cancer patients with SARS-CoV-2 had unique clinical features, and the established online tool could guide clinicians to predict the prognosis of patients and to develop more rational treatment strategies for cancer patients during the COVID-19 epidemic.

Introduction

Since the outbreak of coronavirus disease 2019 (COVID-19) occurred in December 2019, the number of infected cases has been increasing, which has seriously affected the normal life of human beings. The novel disease is mainly caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, which World Health Organization (WHO) officially named COVID-19 on February 11 (<https://www.who.int/westernpacific/emergencies/covid-19>). On February 28, 2020, WHO raised the risk of global outbreak of COVID-19 to "very high" level, with SARS-CoV-2 infection becoming a severe threat to public health (<https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—28-february-2020>). Up to now, WHO has not lowered this risk level. Recently, increased researches have suggested that cancer patients were more susceptible to SARS-CoV-2 infection.(Dai et al., 2020;Liang et al., 2020) Thus, oncologists face new challenge during the COVID-19 pandemic. They need to adjust their cancer management strategies as soon as possible to reduce the risk of SARS-CoV-2 infection and tumor recurrence without affecting the therapeutic effect. However, to date, data on cancer patients with SARS-CoV-2 infection is still limited and their prognosis is poorly understood. Given this, we performed a retrospective analysis based on the data of 223 cancer patients

with SARS-CoV-2 infection from 26 clinical centers in Hubei province, China. In addition, we constructed an online nomogram to predict the prognosis of these patients, which would help clinicians develop more rational treatment strategies for cancer patients during the COVID-19 epidemic.

Materials And Methods

Study subject and ethical statements

All cancer patients with SARS-CoV-2 infection were hospitalized in 26 hospitals in Hubei province, China between December 27, 2019 and March 19, 2020. A total of 296 patients were enrolled in this study, of whom 62 patients without nucleic acid test were excluded from this study. In addition, a one-year old child was also excluded in this study. Eventually, 223 patients were selected in this study, who met the diagnostic criteria of the WHO interim guidance ([https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-\(nCoV\)-infection-is-suspected](https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(nCoV)-infection-is-suspected)) and were confirmed by nucleic acid test. This study was approved by the ethics committee of the National Cancer Center / Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (Approval No. 20/061-2257).

Data collection and extraction

The clinicopathological characters of 223 patients included in this study were collected from their medical records. General data included age, sex, BMI, smoking history, comorbidities, vital signs, tumor type, dyspnea, fever and other symptoms, survival time, the interval to the negative conversion of SARS-CoV-2 nucleic acid test, etc. Laboratory findings included procalcitonin (PCT), white blood cell counts, neutrophil counts, lymphocyte counts, monocyte counts, eosinophil counts, basophil counts, platelet counts, aspartate aminotransferase (AST), alanine aminotransferase (ALT), C reactive protein (CRP), hypersensitive C reactive protein (hs-CRP), creatinine, serum amyloid A (SAA), creatine kinase isozyme (CKMB), direct bilirubin, total bilirubin, prothrombin time (PT), activation of partial thrombin time (APTT), D-dimer, etc. Besides, treatment included antitumor therapy, antiviral therapy, antibacterial therapy, hormone therapy, and traditional Chinese medicine treatment.

Statistical analysis

Categorical variables were represented by number (percentage). The continuous variables conforming to the normal distribution were represented by mean (standard deviation, SD) otherwise by median (interquartile range, IQR). The unpaired independent sample student-t test was used for the continuous variables with homogeneous variances and normal distribution. Non-parametric tests (Mann-Whitney U and / or Kruskal-Wallis H) were used for those with uneven variances or non-normal distribution. The Chi-square test or Fisher's exact test was used to compare the categorical variables between groups, as appropriate. Nucleic acid test time of diagnosis served as the starting point of survival time, and the Kaplan-Meier method was used for survival analysis. Additionally, propensity score matching (PSM) was applied to minimize the differences in clinical characteristics between the two groups (non-lung cancer

group and lung cancer group). With R software (version 3.6.0), the "MatchIt" package was used to calculate the propensity score. The nearest method was adopted for 1:1 matching analysis, and the caliper was set to 0.05. In this study, all patients were randomly divided into the development cohort and validation cohort according to the ratio of 7:3. Then, the univariate and multivariable Cox analysis were performed in the development cohort. Based on the results of the above analysis, a nomogram was constructed with the "rms" package in R. In addition, we calculated the C-indexes of the development cohort and validation cohort with bootstraps method to evaluate the prediction performance of the nomogram. At the same time, the calibration curves were also used to judge the consistency between the model prediction value and the actual observed value. All statistical analysis was carried out in R software (version 3.6.0). P-value < 0.05 was considered statistically significant.

Results

The clinicopathological features of SARS-Cov-2 infected cancer patients

Of the 223 patients finally included in this study, 186 patients survived, and 37 patients were not survivors. (**Table 1**) 52.1% of patients were male, 52.9% of patients had basic diseases, 59.7% of patients presented dyspnea, and 75.7% of patients had fever. Compared with survivors, non-survivors were older (67 years vs. 62.5 years), more male (70.3% vs. 48.4%), and more likely to have dyspnea (75.7% vs. 66.7%). Moreover, the heart rate of non-survivors was faster than that of survivors (100 bpm vs. 88 bpm). In the vast majority of laboratory findings, non-survivors had higher detection values, such as white blood cell counts, neutrophil counts, PCT, CRP, hs-CRP, direct bilirubin, PT, APTT, creatinine, CK-MB, and D-dimers. While platelet counts and lymphocyte counts were lower in the non-survivors, the differences were statistically significant (all $p < 0.05$). Of these 223 patients, 171 patients turned nucleic acid to be negative before the follow-up deadline, with a median time of 13 days. However, nucleic acid switching negative was not found in 37 non-survivors. In addition, more patients were treated with antibacterial (94.6% vs. 80.1%) and glucocorticoid therapy (75.7% vs. 36.0%) in the non-survivors than in the survivors, with p values of 0.034 and < 0.001 , respectively.

Difference in the short-time survival between lung cancer patients and other cancer patients with SARS-CoV-2 infection

Among the 223 cancer patients, more lung cancer patients (17.5%) contracted SARS-CoV-2. Similarly, lung cancer patients accounted for 21.6% ($n = 8$), which was the highest proportion in 37 non-survivors (**Table 1** and **Figure 1A-B**). PSM was performed to further assess the differences in the short-time survival between lung cancer patients and other cancer patients. After PSM, the differences in clinical features between the two groups were not significant (**Table S1** and **Figure S1**), suggesting that the baseline levels of the two groups were neat. The Kaplan-Meier survival analysis indicated that there were no significant differences in the prognosis between lung cancer patients and other cancer patients before (log-rank test, $p = 0.44$; **Figure 1 C**) and after PSM (log-rank test, $p = 0.16$; **Figure 1 D**).

The univariate and multivariate Cox analysis

To explore the risk factors related to cancer patients with SARS-CoV-2 infection, univariate and multivariate survival analysis were performed based on the Cox proportional hazard model. We randomly divided 223 patients into the development cohort and validation cohort according to a ratio of 7:3. **Table 2** showed the distribution of the clinical features of the two groups. No statistical differences were observed in most of clinical characteristics between the two groups, indicating that the baseline level of the two groups had a uniformity. With the development cohort data, we performed a univariate Cox analysis of 25 clinical variables and found that gender, dyspnea, PCT, heart rate, white blood cell counts, platelet counts, neutrophil counts, AST, direct bilirubin, total bilirubin, and D-dimer affected patient outcomes (**Table 3**). With the mean or median of the continuous variables as the cut-off point, the Kaplan-Meier survival analysis was also performed on the 25 variables. Consistent with the results of univariate Cox analysis, gender, dyspnea, PCT, heart rate, platelet counts, and D-dimer were also considered as prognostic factors (**Figure S2**). Moreover, the multivariate Cox analysis included the variables with $p < 0.05$ in the univariate Cox analysis, where platelet counts (HR = 0.991, $p = 0.007$) and neutrophil counts (HR = 1.047, $p = 0.008$) were considered independent prognostic factors in these patients.

Construction and evaluation of the prognostic nomogram

A nomogram was constructed based on the final multivariate Cox analysis. Five factors closely related to prognosis were included in this model: sex, dyspnea, platelet counts, neutrophil counts, AST. According to the multivariate Cox analysis, each factor (in the nomogram) was assigned a score. We obtained the total nomogram score from the sum of individual scores of all predictors. Based on the total score, patients' survival at 2, 3, and 5 weeks could be calculated by projection downward (**Figure 2**). In this study, the C-indexes were 0.841 (95% CI: 0.782 - 0.900) in the development cohort and 0.780 (95% CI: 0.678-0.882) in the validation cohort, indicating that the constructed model had reliable prediction performance. Both the calibration curves of the development cohort (**Figure 3A-C**) and the validation cohort (**Figure S3A-C**) indicated that the predicted values of the model were in good agreement with the observed values. Moreover, the clinical decision curves of the development (**Figure 3D-F**) and validation (**Figure S3D-F**) cohorts for 2, 3, 5 weeks also suggested that this nomogram had good clinical application significance.

Development of an line tool to facilitate the clinical application of our constructed model

To make it easier for clinicians to use this model, we created a web dynamic version of nomogram (<https://covid-19-prediction-tool.shinyapps.io/DynNomapp/>). The interfaces of this web version were shown in **Figure S4**. On the right side of the interfaces, by inputting the corresponding data of patients, the results would be appeared by clicking on the button above the page. Next, we could obtain the corresponding survival curves, survival probabilities of 2, 3 and 5 weeks and 95% confidence intervals.

Discussion

Although some studies have confirmed that cancer patients were more susceptible to SARS-CoV-2 than the general population,(Dai et al., 2020;Liang et al., 2020) the clinical features and short-term prognosis

of cancer patients infected with SARS-CoV-2 were still unclear. The present study showed that compared to survivors, non-survivors were more male and older, with the vast majority having basic diseases and dyspnea. Moreover, the heart rate of the non-survivors was faster than that of the survivors, and the detection values of non-survivors were higher in most laboratory findings, such as white blood cell counts, neutrophil counts, PCT, CRP, hs-CRP, direct bilirubin, PT, APTT, creatinine, CK-MB, and D-dimer, except for platelet counts and lymphocyte counts. These findings were consistent with previous researches on patients with SARS-CoV-2 infection.(N. Chen et al., 2020;R. Chen et al., 2020;Yang et al., 2020) Although cancer patients infected with SARA-CoV-2 shared common epidemiological characteristics with the general population, they might also have unique clinical features. Thus, this study performed further exploration on cancer patients with SARS-CoV-2 infection to evaluate the potential impact of COVID-19 on cancer patients.

The study of Dai et al. has demonstrated that patients with lung cancer were at the highest risk among patients with solid tumors infected with SARS-CoV-2.(Dai et al., 2020b) They suspected that reduced pulmonary reserve and severe infection were responsible for poor outcomes in these patients. In this study, lung cancer patients had the highest proportion of all cancer patients with SARS-CoV-2 infection. Similarly, lung cancer patients remained the most in 37 non-survivors, which might be associated with the high prevalence of lung cancer. Lung is the leading site of SARS-CoV-2 infection-induced lesions, and it remains unclear whether lung cancer patients have a worse prognosis than other cancer patients during the COVID-19 epidemic. In view of this, we used PSM to balance the differences in clinical characteristics between the lung cancer group and the non-lung cancer group. However, this study did not observe significant difference in short-term outcome between the two groups. Thus, among all cancer patients infected with SARS-CoV-2, we believed that the short-term survival of lung cancer patients was similar to that of other cancer patients.

This study revealed that more patients were treated with antibacterial therapy and glucocorticoid therapy in the non-survivors than in the survivors, suggesting that non-survivors were often associated with bacterial infections, often accompanied by severe symptoms. Higher PCT values and neutrophil counts for non-survivors also appeared to indicate this. PCT, a procalcitonin peptide synthesized from thyroid C cells and released from leukocytes, is a highly specific indicator of bacterial infection and closely related to the prognosis of the disease.(de Jong et al., 2016) In this study, PCT values of non-survivors were significantly higher than that of survivors, and PCT significantly affected the prognosis of patients. This was in line with that of the study by Chen et al..(R. Chen et al., 2020b) Notably, although the participants of this study (cancer patients with SARS-CoV-2 infection) was different from that of Chen et al.(all patients with COVID-19),(R. Chen et al., 2020b) PCT was thought to significantly affect patient outcomes in both studies. In addition, as the first defense barrier against suppurative infection, neutrophils play an essential role in the defense and protection function of the human body and increase significantly in patients with bacterial infections. In this study, the median neutrophil counts of non-survivors was 6.62×10^9 , significantly higher than that of the survivors (3.42×10^9). These findings further suggested that patients with bacterial infections were at a higher risk of death and needed to be paid more attention by clinicians.

Of the 223 patients included in this study, 133 patients had dyspnea and up to 75.7% of the 37 non-survivors had dyspnea. If not correctly managed, dyspnea may aggravate hypoxia and lead to acute respiratory failure and other serious complications. In this study, dyspnea was identified to affect the prognosis of patients in univariate Cox analysis and Kaplan-Meier survival analysis. As with dyspnea, sex, heart rate, platelet counts, D-dimer, and AST were also demonstrated to be important factors affecting patient outcomes. Moreover, platelet counts, as well as neutrophil counts, was considered independent prognostic factors in these patients. These patients with low platelets had a higher risk of death, which was similar with the general patients with COVID-19.(Bi et al., 2020;Lippi et al., 2020) The factors mentioned above could significantly affect the prognosis of patients, so clinicians should focus on the changes in these indicators when managing the patients with SARS-CoV-2 infection. We believed that sufficient identification of prognostic factors in such patients would be helpful for clinicians to determine the prognosis of patients in the early stage and timely adjust treatment strategies.

Nomogram, a graphical prediction tool, can use statistical regression to assess the impact of various clinicopathological parameters on the likelihood of events occurring. Compared with the traditional staging system, nomogram has more accurate risk assessment methods, which is helpful to the proper individual treatment of clinical patients.(Balachandran et al., 2015)According to the results of the multivariate Cox analysis, we also constructed a prognostic nomogram that accurately predicted the overall survival of patients at 2, 3, and 5 weeks based on individual characteristics of patients. Importantly, the predictive performance and clinical utility of this model were also well-validated in an independent validation cohort. Furthermore, for the convenience of clinicians using the model constructed in this study, we created a dynamic nomogram on the web. Clinicians could access the website directly through mobile phone or computer anytime and anywhere, and inputting the corresponding information of patients to predict the survival of patients, which would undoubtedly simplify the application process and facilitate clinical use.

Indeed, this study had the following limitations. First, the nature of retrospective research inevitably led to selection bias. Second, despite our efforts to collect some essential clinical information after feedback, it was inevitable to omit some data that may inform our analysis. In addition, although the study used the patients data from 26 clinical centers in Hubei province, Hubei was only one of the epicenter of the outbreak. It was still less representative than the cohort from the whole country or even several countries. Thus, it was still necessary to strengthen the in-depth cooperation among countries as soon as possible and carry out international large-scale or prospective researches.

In conclusion, this study provided evidence that male, dyspnea, elevated PCT, increased heart rate, elevated D-dimers, decreased platelets and so on were risk factors for cancer patients with SARS-CoV-2 infection. Abnormalities of a series of laboratory findings at admission were more common in non-survivors than survivors. Among cancer patients infected with SARS-CoV-2, lung cancer patients had similar short-time survival with other cancer patients. In addition, the nomogram proposed in this study had good predictive performance, which would assist clinicians to predict the prognosis of patients early and perform more reasonable and effective treatment strategies.

Declarations

Author contributions

Conception and design: Weidong Hu, Xiaoping Liu and Congkuan Song. **Collection and assembly of data:** Data were collected by Weidong Hu in collaboration with the authors. **Data analysis and interpretation:** Weidong Hu, Congkuan Song and Xiaoping Liu. **Manuscript writing:** Congkuan Song, Hongyun Gong and Xiaorong Dong prepared the first draft of the report. Weidong Hu, Qibin Song and Yuan Chen co-supervised the project. **Final approval of manuscript:** Weidong Hu had full access to all the data and had final responsibility to submit for publication.

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Participant consent statement and ethical approval

All participants consented to participate, and editorial support was provided by the ethics committee of the National Cancer Center / Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (Approval No.: 20/061-2257).

Conflict of interest

The authors have no conflict of interest to declare.

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Tables

Table 1: Demographic characteristics of SARS-CoV-2 - infected cancer patients in the entire cohort.

Variables	All patients (n=223)	Survivors (n=186)	Non-survivors (n=37)	P- value
Age (years)	63 (56, 71)	62.5 (56, 70)	67 (54.5, 75)	0.240
Sex				0.015
Female	107 (47.9)	96 (51.6)	11 (29.7)	
Male	116 (52.1)	90 (48.4)	26 (70.3)	
BMI (kg/m^2)				0.183
<18.5	13 (5.8)	12 (6.5)	1 (2.7)	
18.5-24.9	73 (32.8)	65 (34.9)	8 (21.6)	
>=25	30 (13.5)	26 (14.0)	4 (10.8)	
Unknown	107 (47.9)	83 (44.6)	24 (64.9)	
Smoke				0.351
Never	170 (72.6)	144 (77.4)	26 (70.3)	
Previous/present	53 (27.4)	42 (22.6)	11 (29.7)	
Tumor types				0.469
Non-lung cancer	184 (82.5)	115 (61.8)	29 (78.4)	
Lung cancer	39 (17.5)	31 (38.2)	8 (21.6)	
Anti-tumor therapy				0.049
Continuous	126 (56.5)	111 (59.7)	15 (40.5)	
Discontinuous	30 (13.4)	21 (11.3)	9 (24.4)	
Unknown	67 (30.1)	54 (29.0)	13 (35.1)	
Basic diseases *				0.608
Without	105 (47.1)	89 (47.9)	16 (43.2)	
With	118 (52.9)	97 (52.1)	21 (56.8)	
Fever				0.687
Without	54 (24.3)	46 (24.7)	8 (21.6)	
With	169 (75.7)	140 (75.3)	29 (78.4)	
Dyspnea				<0.001
Without	90 (40.3)	62 (33.3)	9 (24.3)	

With	133 (59.7)	124 (66.7)	28 (75.7)	
Other symptoms *				0.643
Without	28 (12.5)	22 (11.8)	6 (16.2)	
With	195 (87.5)	164 (88.2)	31 (83.8)	
PCT (ng/ml)				<0.001
<=0.5	163 (73.0)	144 (77.4)	19 (51.4)	
>0.5	30 (13.5)	17 (9.1)	13 (35.1)	
Not application	30 (13.5)	25 (13.5)	5 (13.5)	
Heart rate (bpm)	88 (78, 100)	86 (77, 97.25)	100 (88.5, 112.5)	<0.001
SBP (mmHg)	130 (120, 140)	130 (120, 140.25)	128 (109, 140.5)	0.314
DBP (mmHg)	78.33 (11.128)	77.8602 (11.132)	80.703 (10.952)	0.156
Respiratory rate (braths/min)	20 (19, 22)	20 (19, 22)	20 (20, 23)	0.152
Temperature (°C)	36.7 (36.5, 37.5)	36.7 (36.5, 37.5)	36.9 (36.4, 38.05)	0.703
WBC count (10E9/L)	5.28 (4.05, 7.18)	5.025 (4.005, 6.423)	7.23 (5.035, 11.785)	<0.001
Neutrophils count (10E9/L)	3.64 (2.59, 5.45)	3.42 (2.563, 4.793)	6.62 (3.25, 10.345)	<0.001
Lymphocyte counts (10E9/L)	0.90 (0.61, 1.42)	0.95 (0.658, 1.433)	0.69 (0.495, 1.125)	0.024
Platelet counts (10E9/L)	188 (117, 249)	196.5 (130.75, 260.25)	142 (51, 203.5)	<0.001
Monocyte counts (10E9/L)	0.43 (0.30, 0.62)	0.42 (0.3, 0.59)	0.64 (0.28, 1.005)	0.041
Eosinophils counts (10E9/L)	0.03 (0, 0.09)	0.05 (0.01, 0.09)	0 (0, 0.02)	<0.001
Basophil counts (10E9/L)	0.01 (0.01, 0.02)	0.01 (0.01, 0.02)	0.01 (0, 0.03)	0.739
ALT (U/L)	22 (13, 36)	23 (14, 37)	18 (10.5, 26.5)	0.068
AST (U/L)	28 (18, 39)	26.5 (18, 38)	35 (20, 51)	0.061
Creatinine (umol/L)	65 (52.7, 85)	63.5 (52.9, 81.025)	94.1 (51.85, 120.5)	0.018
CRP (mg/L)	28.85 (7.7, 77.925) (n=176)	25.4 (5.225, 55.5) (n=144)	94.8 (39.45, 139.525) (n=32)	<0.001

SAA (mg/L)	148.39 (26.8, 300) (n=35)	128.21 (16.25, 300) (n=25)	183.195 (79.483, 300) (n=10)	0.811
hs-CRP (mg/L)	27.4 (5, 71.9) (n=159)	21.965 (5, 59.3) (n=130)	84.1 (55.22, 141.15) (n=29)	<0.001
Total bilirubin (umol/L)	11.1 (8,14.6)	11 (7.8, 14.6)	12.4 (9.35, 15.15)	0.185
Direct bilirubin (umol/L)	3.9 (2.8, 5.5)	3.7 (2.6, 5.3)	5.1 (3.775, 7.8)	<0.001
PT (s)	12.9 (11.9, 14.0) (n=219)	12.8 (11.9, 13.6) (n=182)	14.4 (12.3, 15.75)	<0.001
APTT (s)	34.6 (29.1, 39.7) (n=216)	33.9 (28.8, 38.65) (n=181)	37.8 (30.7, 46.2) (n=35)	0.010
Creatine kinase-MB (U/L)	1.12 (0.525, 4.525) (n=153)	1.03 (0.5, 3.745) (n=133)	3.645 (1.025, 14.738) (n=20)	0.020
D-dimer (mg/L)	0.837 (0.37, 2.14)	0.69 (0.329, 1.9)	1.63 (0.465, 5.865)	0.001
Nucleic acid negative time	13 (9-22)	13 (9-22)		
Antiviral therapy				0.385
No	19 (8.5)	14 (7.5)	5 (13.5)	
Yes	204 (91.5)	172 (92.5)	32 (86.5)	
Antibacterial therapy				0.034
No	39 (17.5)	37 (19.9)	2 (5.4)	
Yes	184 (82.5)	149 (80.1)	35 (94.6)	
Hormone therapy				<0.001
No	128 (57.4)	119 (64.0)	9 (24.3)	
Yes	95 (42.6)	67 (36.0)	28 (75.7)	
Immunoglobulin application				0.052
No	151 (67.7)	131 (70.4)	20 (54.1)	
Yes	72 (32.3)	55 (29.6)	17 (45.9)	
Traditional Chinese medicine treatment				0.129
No	27 (16.6)	34 (18.3)	3 (8.1)	
Yes	186 (83.4)	152 (81.7)	34 (91.9)	

All variables with missing values are marked with a specific number of samples.

Other symptoms include cough, expectoration, fatigue, headache, myalgia, sore throat, diarrhea, nausea, sneezing, nasal congestion, anorexia, night sweats, etc. **Basic diseases** include hypertension, diabetes, cardiovascular and cerebrovascular diseases, chronic obstructive pulmonary disease, chronic bronchitis, emphysema, chronic liver disease, chronic kidney disease, and neuropsychiatric diseases.

Abbreviations: BMI, body mass index; PCT, procalcitonin; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; AST, aspartate aminotransferase; ALT, alanine transaminase; CRP, C-reactive protein; hs-CRP, hypersensitive c-reactive protein; SAA, Serum amyloid A; PT, prothrombin time; APTT, activation of partial thrombin time.

Table 2: Clinical characteristics of SARS-CoV-2 infected cancer patients in the development and validation cohorts.

Variables	Development cohort (n=159)	Validation cohort (n=64)	P-value
Age (years)	62 (55, 70)	64 (57, 73)	0.263
Sex			0.272
Female	80 (50.3)	27 (42.2)	
Male	79 (49.7)	37 (57.8)	
BMI (kg/m^2)			0.323
<18.5	8 (5.0)	5 (7.8)	
18.5-24.9	57 (35.8)	16 (25.0)	
>=25	19 (11.9)	11 (17.2)	
Unknown	75 (47.3)	32 (50.0)	
Smoke			0.143
Never	117 (73.5)	53 (82.8)	
Previous/present	42 (26.5)	11 (17.2)	
Tumor types			0.753
Non-lung cancer	132 (83.0)	52 (81.2)	
Lung cancer	27 (17.0)	12 (18.8)	
Anti-tumor therapy			0.476
Continuous	93 (58.5)	33 (51.6)	
Discontinuous	22 (13.8)	8 (12.5)	
Unknown	44 (27.7)	23 (35.9)	
Basic diseases			0.069
Without	81 (50.9)	24 (37.5)	
With	78 (49.1)	40 (62.5)	
Fever			0.863
Without	39 (24.5)	15 (23.4)	
With	120 (75.5)	49 (76.6)	
Dyspnea			0.724
Without	96 (60.3)	37 (57.8)	
With	63 (39.7)	27 (42.2)	

PCT (ng/ml)			0.114
<=0.5	111 (69.8)	52 (81.2)	
>0.5	22 (13.8)	8 (12.5)	
Not application	26 (16.4)	4 (6.3)	
Heart rate (bpm)	88 (77, 100)	87.5 (78, 100)	0.829
SBP (mmHg)	129.7 (18.58)	131.1 (19.09)	0.622
DBP (mmHg)	78 (70, 85)	80 (71, 85)	0.895
Respiratory rate (braths/min)	20 (19, 22)	20 (20, 22.75)	0.267
Temperature (°C)	36.7 (36.5, 37.5)	36.8 (36.5, 38)	0.798
WBC counts (10E9/L)	5.1 (3.8, 7.08)	5.65 (4.385, 7.215)	0.048
Neutrophils counts (10E9/L)	3.35 (2.48, 5.32)	4.27 (3.01, 5.858)	0.010
Lymphocyte counts (10E9/L)	0.88 (0.62, 1.44)	0.96 (0.553, 1.275)	0.892
Platelet counts (10E9/L)	186.8 (96.71)	200 (89.69)	0.340
ALT (U/L)	21 (12, 35)	25 (15.25, 38.75)	0.120
AST (U/L)	26 (18, 38)	32.5 (22, 44)	0.013
Total bilirubin (umol/L)	11.2 (7.9, 14.8)	10.85 (8.475, 14.15)	0.731
Direct bilirubin (umol/L)	3.9 (2.7, 5.6)	3.95 (2.8, 5.3)	0.914
Creatinine (umol/L)	63 (51, 82)	71.5 (56, 92.75)	0.022
D-dimer (mg/L)	0.86 (0.4, 2.14)	0.74 (0.33, 1.848)	0.544

Abbreviations: BMI, body mass index; PCT, procalcitonin; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; AST, aspartate aminotransferase; ALT, alanine transaminase.

Table 3: Univariate and multivariate COX analysis of prognosis in the development cohort.

Variables	Univariate Cox analysis		Multivariate Cox analysis	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age (years)	1.017 (0.983 - 1.053)	0.332		
Sex (male vs. female)	2.513 (1.042 - 6.059)	0.042	2.996 (0.861-10.43)	0.085
BMI				
18.5-24.9 vs. <18.5	0.965 (0.119 - 7.846)	0.973		
>=25 vs. <18.5	0.777 (0.070-8.578)	0.837		
Unknown vs. <18.5	1.491 (0.671 - 11.34)	0.700		
Smoke (previous/present vs. never)	1.405 (0.601 - 3.283)	0.432		
Tumor types				
Non-lung cancer vs. lung cancer	0.993 (1.007 - 2.905)	0.989		
Anti-tumor therapy				
Discontinuous vs. continuous	2.313 (0.432 - 6.769)	0.126		
Unknown vs. continuous	2.020 (0.495 - 4.972)	0.126		
Basic_diseases				
With vs. without	1.217 (0.821 - 2.718)	0.631		
Fever (with vs. without)	0.933 (1.072 - 2.350)	0.883		
Dyspnea (with vs. without)	5.044 (0.198 - 12.71)	0.001	2.942 (0.934-9.266)	0.065
PCT				
>0.5 vs. <=0.5	6.316 (0.158 - 15.26)	0.000	1.789 (0.598-5.348)	0.298
Not application vs. <=0.5	1.824 (0.548 - 5.816)	0.310	1.619 (0.445-5.887)	0.465
Heart rate	1.051 (1.024 -	0.000	1.018 (0.987-	0.264

	1.079)	1.050)		
SBP	0.993 (0.971 - 1.016)	0.545		
DBP	0.972 (0.936 - 1.008)	0.129		
Respiratory rate	1.034 (0.939 - 1.140)	0.496		
Temperature	0.949 (0.577 - 1.554)	0.828		
WBC count	1.177 (1.063 - 1.305)	0.002	1.115 (0.947-1.312)	0.192
Neutrophils counts	1.035 (1.012 - 1.059)	0.003	1.047 (1.012-1.084)	0.008
Lymphocyte counts	1.571 (0.248 - 1.313)	0.187		
Platelet counts	0.993 (0.988 - 0.998)	0.006	0.991 (0.984-0.997)	0.007
ALT	0.993 (0.973 - 1.013)	0.500		
AST	1.008 (1.001 - 1.014)	0.021	1.010 (0.998-1.020)	0.094
Total bilirubin	1.031 (1.014 - 1.048)	0.000	0.961 (0.872-1.058)	0.413
Direct bilirubin	1.043 (1.022 -1.065)	0.000	1.071 (0.938-1.223)	0.314
Creatinine	1.001 (0.999 - 1.003)	0.146		
D-dimer	1.037 (1.007 - 1.067)	0.014	1.026 (0.985-1.068)	0.225

Figures

Figure 1

(A) Among 223 cancer patients with SARS-CoV-2 infection, the proportion of all types of cancer patients. (B) Distribution of 37 patients with various types of cancer. (C) Kaplan-Meier survival curves of lung cancer patients and other cancer patients infected with SARS-CoV-2 before PSM. (D) Kaplan-Meier survival curves of lung cancer patients and other cancer patients infected with SARS-CoV-2 after PSM.

Figure 2

A prognostic nomogram including significant clinical parameters for 2-week, 3-week, and 5-week OS in cancer patients with SARS-CoV-2 infection.

Figure 3

Construction and evaluation of the prognostic nomogram. Calibration curves for 2-week (A), 3-week (B) and 5-week (C) OS in the development cohort. DCA curves for 2-week (D), 3-week (E) and 5-week (F) OS in the development cohort.

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