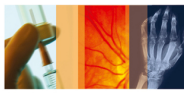
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.



Association Between Hypoxemia and Mortality in Patients With COVID-19

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Abstract

Objective: To identify markers associated with in-hospital death in patients with Coronavirus Disease 2019 (COVID-19) associated pneumonia.

Patients and Methods: Retrospective, cohort study of 140 patients with moderate-to-critical COVID-19 associated pneumonia requiring oxygen supplementation admitted from January 28th, 2020 to February 28th, 2020, and followed up through March, 13th 2020 in Union Hospital, Wuhan, China. Oxygen saturation (SpO_2) and other measures were tested as predictors of in-hospital mortality in survival analysis.

Results: Of 140 patients with COVID-19 associated pneumonia, 51.4% were men, with a median age of 60 years. Patients with SpO_2 ≤90% were older, more likely to be men, to have hypertension and to present with dyspnea than those with SpO_2 >90%. Overall, 36 (25.7%) patients died during hospitalization after a median 14-day follow-up. Higher post-oxygen supplementation SpO_2 levels were associated with reduced mortality independently of age and sex (hazard ratio per 1-unit SpO_2 0.93, 95% confidence interval, 0.91-0.95, $P < .001$). SpO_2 cutoff of 90.5% yielded 84.6% sensitivity and 97.2% specificity for prediction of survival. Dyspnea was also independently associated with death in multivariable analysis (hazard ratio 2.60; 95% confidence interval 1.24-5.43, $P = .01$).

Conclusions: In this cohort of COVID-19 patients, hypoxemia was independently associated with in-hospital mortality. These results may help guide clinical management of severe COVID-19 patients, particularly in settings requiring strategic allocation of limited critical care resources.

Key words: COVID-19; Dyspnea; Hypoxemia

Trial Registration: Chictr.org.cn Identifier: ChiCTR2000030852

http://www.chictr.org.cn/usercenter.aspx

Abbreviations

AUC = area under the curve

CI = confidence interval

COPD = chronic obstructive pulmonary diseases

COVID-19 = coronavirus disease 2019

CRP = C-reactive protein

CT = computed tomography

HR = hazard ratios

IQR = interquartile range

ROC = receiver-operating characteristics

SpO_2 = oxygen saturation

WBC = white blood cell

Introduction

The Coronavirus Disease 2019 (COVID-19) outbreak is now pandemic, straining medical infrastructure, personnel and resources in much of Europe, the Middle East and North America, with significant consequences for clinical management, including rationing of care.[1, 2] Contemporary statistics indicate that 14% of COVID-19 associated pneumonia cases are severe, and 5% of infected patients require intensive care.[3] Mortality rates in severe and critically ill patients are staggering, with the disease being fatal in approximately two-thirds.[4-6] Given the limited availability of critical care resources, it is imperative to identify simple but reliable predictors of survival in COVID-19 patients who present with at least moderate disease severity. We thus sought to identify and compare differential predictive values of demographic, clinical and laboratory measures in moderate-to-critically ill COVID-19 patients from Wuhan, China. Since COVID-19 primarily attacks the respiratory system, measures that reflect respiratory function would more likely relate to outcomes, particularly in a rapidly progressive disease condition. We therefore focused particularly on dyspnea and systemic oxygenation as potential prognostic biomarkers.

PATIENTS AND METHODS

Study Design and Patients

This single-center, retrospective cohort study (ChiCTR2000030852) enrolled patients with moderate-to-critical COVID-19 associated pneumonia hospitalized and treated by the Beijing Medical Team in Union Hospital, Wuhan, from January 28th, 2020 to February 28th, 2020, with follow-up through March, 13th 2020. The Beijing Medical Team consisted of physician volunteers from Beijing (Drs Xie and Gao). The Beijing Anzhen Hospital Institutional Review Board approved this study.

National Health Committee of the People's Republic of China recommendations for diagnosis of COVID-19 associated pneumonia were used.[7] Patients included in this study met the following criteria: confirmed COVID-19 infection based on real-time reverse transcriptase polymerase chain reaction (RT-PCR) testing from throat swab sample; objective evidence of new-onset pneumonia from chest computed tomography (CT) scan; typical symptoms of pneumonia, i.e., fever, cough, dyspnea, etc.; pneumonia severity graded as moderate, severe or critical. Disease severity was defined according to the classification proposed in the Chinese guidelines for COVID-19 associated pneumonia mentioned above (**Supplemental Table**). Moderate cases presented with typical symptoms of pneumonia, i.e. fever, cough, expectoration, dyspnea, with definitive lesions confirmed by CT scan. Severe cases met ≥1 of the following criteria: respiratory rate ≥30bpm, oxygen saturation (SpO_2) ≤93% at rest or pressure of arterial oxygen to fractional inspired oxygen concentration ≤300mmHg, >50% progression of lesion as evident from CT scan over the past 48 hours. Lastly, COVID-19 associated pneumonia cases were regarded as critical if they satisfied ≥1 of the following: intubation needed due to respiratory failure, shock, and multiple organ dysfunction requiring intensive care unit treatment. Patients

with a very high clinical suspicion of COVID-19 associated pneumonia, namely definite epidemiological exposure (such as family breakout) and other aforementioned features were clinically diagnosed by a specialist team, hospitalized in the same quarantine zone, and were included in this study, despite absence of documented confirmation from nucleic acid screening. Importantly, with regard to the appropriate recent concerns of inclusion of the same patients in different reports ,[8] we are aware of only one prior study of patients from Union Hospital which may have included approximately 20 of the 140 patients in our current study.[9] In any event, this paper makes no mention of the key findings in our study, namely the role of dyspnea and hypoxemia as predictors of mortality.

Clinical Management

All patients were treated following the Chinese guidelines. [7] Although antibiotics were not recommended as routine treatment, they were still considered if patients were found to have evidence of definite or suspected bacterial infection, such as abundant purulent sputum, based on clinical assessment by the responsible physician. Depending on disease severity and clinical assessment of patients at hospitalization, oxygen supplementation by nasal cannula was administered to all patients directly at admission. The oxygen flow ranged from low (1-2 L/min) to high flow (10 L/min) and varied as per patient's response, with the goal of maintaining peripheral oxygen saturation (SpO_2) ≥95%. Post-oxygen supplementation SpO_2 was measured from finger oximetry at 2-5 minutes after beginning of oxygen support. If SpO_2 fell below 95%, high flow oxygen supplementation by mask, high nasal flow and mechanical ventilation were considered as needed.

Clinical and Laboratory Data and Outcome Assessment

Demographic and clinical characteristics were collected from patients or patient's relatives, physical examination, and medical records. Blood measures of white blood cell (WBC) count, neutrophils, lymphocytes, platelets, C-reactive protein (CRP), and D-dimer were acquired. Dates of death were obtained from registration and verified by reviewing the medical record. Follow-up duration was computed as time interval (in days) from the date of admission to the date of death or the date of discharge, whichever occurred first. Stable patients who remained hospitalized at the end of the follow-up period were regarded to be alive.

Statistical Analyses

Continuous data are reported as median and interquartile range (IQR), and categorical data are expressed as frequency and percentage. Wilcoxon signed rank-tests and Pearson's chi-squared tests were used to compare continuous and categorical data between patients with post-oxygen supplementation SpO_2 >90 % vs SpO_2 ≤90%, respectively. Survival was calculated by the Kaplan–Meier method and log-rank test, using as exposures SpO_2, dyspnea and other demographic and clinical characteristics. Univariate and multivariable (age-and sex-adjusted) Cox proportional hazards models were run, with associations expressed as hazard ratios (HR) and 95% confidence interval (CI). We used a receiver-operating characteristics (ROC) analysis to determine the optimal cut-off of post-oxygen supplementation SpO_2 for predicting survival based on threshold yielding the best combination of sensitivity and specificity. Statistical analysis was performed using JMP, version 14.1 (SAS Institute, Cary, NC), and a two-sided $P < .05$ was considered significant.

RESULTS

Patients' Characteristics

Generally, 140 patients were considered to have a very high likelihood of COVID-19 associated pneumonia based on exposure and clinical and radiologic criteria; 113 had RT-PCR confirmed COVID-19 infection, RT-PCR data were not available for 20 who were transferred for management of COVID-19 associated pneumonia, and 7 patients were RT-PCR negative, presumably false negatives. Thirty-six (26%) patients (25[34.7%] male and 11[16.2%] female) died in the hospital a median 14 days (6-26) after admission. Among 71 patients of 60 years or older, 33 (46.5%) died, while 9 (69.2%) patients died in the group of ≥80 years. Patients' demographic, clinical and laboratory characteristics and treatment information are presented in **Table 1**. Forty-three (30.7%), 73 (52.1%) and 24 (17.1%) patients met criteria for moderate, severe and critical COVID-19 associated pneumonia, respectively. Patients with SpO_2 ≤90% on oxygen supplementation were older (67 years [61-78] vs 53 years [40-63], $P < .001$), more likely to be men (64.71% vs 43.82%, $P = .02$), and to have hypertension (43.14% vs 20.22%, $P = .004$) than those with SpO_2 >90%. Other comorbidities were similar between groups. Patients with more severe hypoxemia were more likely to present with dyspnea (64.71% vs 40.45%, $P = .006$) and to be classified as critical upon admission (45.10% vs 1.12%, $P < .001$). With regard to treatment, antibiotics (88.2% vs 67.4%, $P = .006$) and high nasal flow (9.80% vs 1.12%, $P = .02$) were more commonly administered in patients with SpO_2 ≤90%. Mechanical ventilation was administered only to these patients group. Analysis of laboratory biomarkers showed that WBC count, neutrophils, CRP, and D-dimer were higher while lymphocytes and platelets were lower in patients with SpO_2 ≤90% vs those with SpO_2 >90%.

Association between Demographic and Clinical Characteristics and In-hospital Mortality

Age >60 years (HR 12.21, 95% CI 3.74-39.84, *P* < .001), male sex (HR 2.30, 95% CI 1.13-4.68, *P* = .02), hypertension (HR 1.97, 95% CI 1.02-3.81, *P* = .04), and presence of any comorbidity (defined as at least one comorbidity among those shown in **Table 1**) (HR 5.26, 95% CI 2.19-12.64, *P* < .001) were associated with mortality in univariate analysis (**Figure 1 A-D** and **Table 2**). Presence of any comorbidity remained a significant risk factor associated with death after adjusting for age and sex (HR 2.65, 95% CI 1.07-6.55, *P* = .04).

Association between Dyspnea and Hypoxemia and In-hospital Mortality

Those reporting dyspnea as initial symptom were more likely to die than those who did not report it (**Figure 2A**) (38% vs 14%, log-rank *P* =0.002; HR, 2.94; 95% CI 1.42-6.11, *P* = .004; **Table 2**). Thirty-five (68.63%) patients with post-oxygen supplementation SpO_2 ≤90% did not survive, while 88 (98.9%) of those >90% did (log-rank *P* < .001; **Figure 2B**). Modeling SpO_2 as a continuous variable in Cox model, we found that for each 1-unit increase in SpO_2, mortality risk decreased by approximately 8% (HR 0.92, 95% CI 0.91-0.94, *P* < .001). Dyspnea and SpO_2 were significantly associated with outcomes in multivariable models (HR 2.60; 95% CI 1.24-5.43, *P* = .01 and HR, 0.93; 95% 0.91-0.95, *P* < .001, respectively; **Table 2**). Notably, sensitivity analysis restricted to patients with confirmed COVID-19 infection based on RT-PCR testing (n=113) showed that the independent association between dyspnea and death persisted in this sample (HR 3.20; 95% CI 1.26-9.79, P = .014), and no patients with SpO_2 >90% died. SpO_2 ≤ 90% was also strongly associated with death, independently of age and sex (multivariable HR 47.41; 95% CI 6.29-357.48, *P* < .001). ROC analysis showed that SpO_2 of 90.5% was the optimal SaO_2 cutoff point for predicting survival, demonstrating 84.6% sensitivity, 97.2%

specificity and 87.9% accuracy. The overall area under the curve [AUC] was 96% (**Figure 3**). In a subgroup analysis of patients ≥80 years (n=13), 9 patients (69.2%) died. All 80 year old patients with SpO_2 >90% (n = 3) on supplemental oxygen survived.

Association between Inflammatory and Hematologic Markers and In-hospital Mortality

Laboratory biomarkers were proved to be associated with mortality by Kaplan-Meier method (**Figure 4 A-D**) and univariate Cox regression analysis (**Table 2**). In adjusted models, WBC count ≥10 $\times 10^9$/L (HR 2.56, 95% CI 1.17-5.63, *P* =0.02), neutrophil count ≥6 $\times 10^9$/L (HR 4.29, 95% CI 1.74-10.58, *P* = .002), and CRP ≥27.8 mg/L (HR 17.02, 95% CI 2.25-128.59, *P* = .006) retained significant associations with death (**Table 2**).

DISCUSSION

These data provide insights into risk factors for mortality in a relatively large sample of moderately to critically ill patients with COVID-19 associated pneumonia. In line with prior reports,[5, 10] our data confirm that age, sex, comorbidities, and inflammatory biomarkers are associated with mortality. We further demonstrate novel and clinically important findings of independent death-associated value of two very simple yet readily assessed characteristics, namely dyspnea and hypoxemia (SpO_2 ≤90% despite oxygen supplementation).

The COVID-19 pandemic is sweeping across Europe and the Middle East and currently threatening North America. Our understanding of clinical presentations and optimal management strategies are evolving rapidly and are primarily based on experiences treating Chinese patients in the epicenter of the disease in Wuhan, China. Experiences initially in Wuhan and subsequently all over the world, suggest that the rapid and life threatening progression of the disease and the need for intense supportive measures have the potential to rapidly overwhelm hospital and other medical resources. The high mortality of the more severely ill patients also suggests that many patients die despite receiving intense care.[4-6] Thus outcome data using readily assessed clinical measures are required to better inform decisions regarding allocation of care resources, especially in those situations requiring triage strategies and care rationing.

We found that dyspnea, an easily assessed symptom, is associated with death in patients with COVID-19 associated pneumonia independently of age and sex. However, a related and also easily acquired clinical measure, oxygen saturation ≤ 90% despite oxygen supplementation, provides a more robust risk factor for fatal outcomes – indeed this measure is the most powerful predictor of the multiple measures we obtained, including the more standard demographic and inflammatory measures reported in earlier studies.[5, 10]

Our findings of important prognostic value of dyspnea and hypoxemia for hospitalized patients with COVID-19 associated pneumonia provide a rationale for applying standard scoring strategies to estimate risk and guide treatment even in this patient population, i.e., CURB-65 Scale, the Pneumonia Severity Index, and Acute Physiology and Chronic Health Evaluation II. [11] *Future studies assessing the prognostic significance of such models in COVID-19 associated pneumonia are needed.*

It is important to note that exploratory subgroup analysis on patients 80 years and older, in whom mortality is known to be especially high (69.2% in our study), revealed that all of patients with oxygen saturation above 90% (n = 3) survived. Although these results must be interpreted with caution given the small sample size and possible confounding effects of age, they may be especially relevant considering the limited access to care in areas overwhelmed by COVID-19 cases, with older age possibly being used as a triage criterion for care prioritization.[2]

As severe hypoxemia was associated with pronounced elevation of inflammatory markers (higher WBC counts, neutrophil counts, D-dimer, and CRP), acute inflammation of the respiratory system, caused by respiratory virus and/or secondary bacterial infection,[12] may be mechanistically responsible for the significant pulmonary injury and thus persistent hypoxemia. Whether attenuating this inflammatory response early in the disease would improve oxygenation and possibly survival remains to be determined.

We acknowledge our study has limitations. A small minority of patients (<6%) had negative RT-PCR testing for infection despite a high clinical probability of COVID-19 associated pneumonia based on clinical and radiographic assessment and epidemiologic exposure. As the proportion of unconfirmed cases is consistent with reported sensitivity data of RT-PCR testing for COVID-19,[13] we presume these were false negatives. Robustness of our findings is further supported by

results of a sensitivity analysis showing that dyspnea and SpO_2 ≤90% remained independently associated with mortality in the sample including only patients with confirmed COVID-19 from RT-PCR testing. Second, these data were acquired under emergency situations operating under crisis conditions, as with many other contemporaneous studies from Wuhan. Therefore completeness of data recording, particularly at time of admission, was less than optimal. For example while oxygen supplementation at admission was administered with the goal of achieving SpO_2 ≥95%, the specific amount of oxygen supplementation administered to each patient upon admission was not recorded. Therefore we cannot incorporate comparisons of administered inspired oxygen concentration into our analyses. Similarly, while recognizing that dyspnea has the inherent limitation of subjectivity, no consistent data relative to dyspnea severity, time to intubation/high flow O_2 and time on mechanical ventilation, and changes in SpO_2 during hospitalization were available. The impact of these variables on outcomes in COVID-19 patients warrants further investigation.

CONCLUSIONS

We report that in moderate-to-critically ill patients with COVID-19, oxygen saturation above 90% with oxygen supplementation indicates a very high likelihood of survival. These patients should thus receive maximal supportive care during the acute illness. We further speculate that patients with oxygen saturation <90% despite oxygen supplementation, in whom there is a particularly high mortality risk, may be more likely to benefit from experimental therapies such as investigational drugs and antibody therapy.

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CONFLICT OF INTEREST: Nothing to disclose.

SUPPORT STATEMENT: None.

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Figure Legends

FIGURE 1. Kaplan-Meier curves for in-hospital mortality by demographic and clinical data.

Panel A. The median follow-up time for patients ≥60 years (n=71) was 12 days (IQR, 5-19) and 17 days (8-33) for those <60 years (n=69). Panel B. The median follow-up time for male (n=72) was 13 days (4-29) and 15 days (8-24) for female (n=68). Panel C. The median follow-up time for patients with at least one comorbidity (n=69) was 14 days (6-32) and 14 days (7-25) for patients without comorbidities (n=71). Panel D. The median follow-up time for hypertension (n=40) was 14 days (7-40) and 14 days (6-22) for non-hypertension (n=100).

IQR = interquartile range

FIGURE 2. Kaplan-Meier curves for in-hospital mortality by hypoxemia indices.

Panel A. The median follow-up time for patients with dyspnea (n=69) was 10 days (IQR, 6-26) and 16 days (8-26) for those without dyspnea (n=71). Panel B. The median follow-up time for the oxygen saturation (SpO_2) ≤ 90% group (n=51) was 8 days (4-20) and 16 days (9-31) for the SpO_2 >90% group (n=89).

IQR = interquartile range; SpO_2 = oxygen saturation,

FIGURE 3. ROC curve of SpO_2 threshold for predicting death in patients with moderate-to-critical COVID-19 associated pneumonia .

AUC = area under the curve; COVID-19 = coronavirus disease 2019; ROC = receiver-operating characteristics.

FIGURE 4. Kaplan-Meier curves for in-hospital mortality by laboratory markers.

Panel A. The median follow-up time for patients with WBC count ≥10 $\times 10^9$/L (n=15) was 6 days (IQR, 4-14) and 15 days (8-29) for those with WBC count <10 $\times 10^9$/L (n=121). Panel B. The median follow-up time for patients with neutrophil count ≥6 $\times 10^9$/L (n=40) was 12 days (5-37)

and 15 days (8-27) for those with neutrophil count <6 $\times 10^9$/L (n=88). Panel C. The median follow-up time for patients with CRP ≥50 mg/L (n=52) was 14 days (4-24) and 14 days (8-32) for patients with CRP <50 mg/L (n=53). Panel D. The median follow-up time for patients with D-dimer ≥0.45 ug/mL (n=42) was 18 days (8-40) and 18 days (9-42) for patients with D-dimer <0.45 ug/mL (n=41).

CRP = C-reactive protein; IQR = interquartile range; WBC = white blood cell.

TABLE 1. Demographic, Clinical, and Laboratory Characteristics of Patients With COVID-19 Associated Pneumonia

	Total (N = 140)	$SpO_2 \leq 90\%$ (n = 51)	$SpO_2 > 90\%$ (n = 89)	*P* Value
Demographics				
Age, years	60 (47-68)	67 (61-78)	53 (40-63)	< .001
Male	72 (51.43)	33 (64.71)	39 (43.82)	.02
Comorbidities				
Any comorbidity[a]	69 (49.29)	39 (76.47)	30 (33.71)	< .001
Hypertension	40 (28.57)	22 (43.14)	18 (20.22)	.004
Diabetes	20 (14.29)	8 (15.69)	12 (13.48)	.72
Cardiovascular disease	8 (5.71)	5 (9.80)	3 (3.37)	.12
COPD/asthma	2 (1.43)	1 (1.96)	1 (1.12)	.69
Renal failure	7 (5.00)	4 (7.84)	3 (3.37)	.24
Cancer	5 (3.57)	2 (3.92)	3 (3.37)	.87
Clinical presentation				
Fever	112 (80.00)	41 (80.39)	71 (79.78)	.93
Cough	79 (56.43)	30 (58.82)	49 (55.06)	.67
Dyspnea	69 (49.29)	33 (64.71)	36 (40.45)	.006
Diarrhea	33 (23.57)	12 (23.53)	21 (23.60)	.99
Disease severity				
Moderate	43 (30.71)	0	43 (48.31)	<.001
Severe	73 (52.14)	28 (54.90)	45 (50.56)	.62
Critical	24 (17.14)	23 (45.10)	1 (1.12)	< .001
Onset of symptom before hospitalization, days	10 (7-14)	10 (7-14)	10 (8-14)	.19
Post-oxygen supplementation SpO_2, %	95 (84-97)	80 (70-85)	97 (95-98)	< .001
Treatment				
Antibiotics	105 (75.00)	45 (88.24)	60 (67.42)	.006
Nasal high flow	6 (4.29)	5 (9.80)	1 (1.12)	.02

Mechanical ventilation	13 (9.28)	13 (25.49)	0	<.001
Invasive mechanical ventilation	6 (4.29)	6 (11.86)	0	< .001
Blood biochemistry				
WBC count, $\times 10^9$/L	5.85 (4.17-8.33)	8.54 (6.61-10.81)	4.75 (3.94-6.78)	< .001
Neutrophil count, $\times 10^9$/L	4.09 (2.65-6.36)	7.46 (5.01-9.60)	3.29 (2.28-4.77)	< .001
Lymphocyte count, $\times 10^9$/L	0.92 (0.68-1.37)	0.70 (0.44-0.98)	1.03 (0.77-1.57)	< .001
Platelets count, $\times 10^9$/L	203 (145-273)	165 (112-240)	215 (162-283)	.003
CRP, mg/L	27.78 (5.64-75.55)	76.51 (41.68-117.09)	12.70 (3.49-32.10)	< .001
D-dimer, µg/mL	0.45 (0.22-1.90)	3.05 (0.45-8.00)	0.30 (0.17-0.81)	< .001
Hospital stay, days	**14 (6-26)**	**8 (4-20)**	**16 (9-31)**	**.004**

Data are presented as median (range) and n (%).
The following variables had missing data: WBC (n=136), neutrophil count (n=128) lymphocyte count (n=135), platelets count (n=127), CRP (n=105), and D-dimer (n=83).
[a] *Presence of any comorbidity was defined as presence of one or more of the following chronic diseases: hypertension, diabetes, cardiovascular disease, chronic obstructive pulmonary diseases, asthma and end-stage renal failure.*

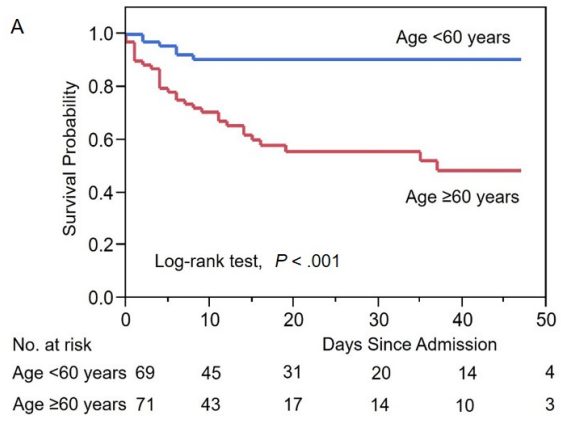
Abbreviation: COPD = chronic obstructive pulmonary diseases; COVID-19 = coronavirus disease 2019; CRP = C-reactive protein; SpO_2 = oxygen saturation; WBC = white blood cell.

TABLE 2. Risk Factors for Mortality in Patients With Moderate to Critical COVID-19 Associated Pneumonia (N = 140)

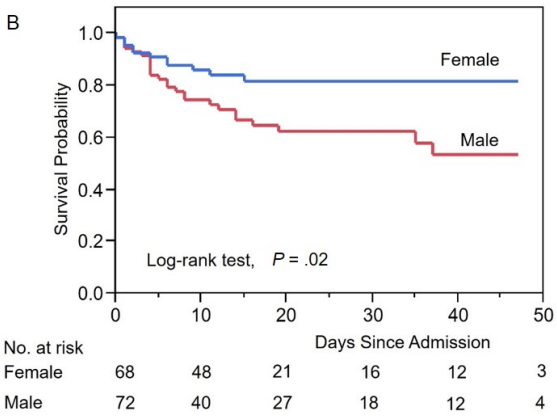
	Unadjusted		Adjusted[a]	
	HR (95%CI)	***P* value**	**HR (95%CI)**	***P* value**
Demographic and clinical characteristics				
Age (≥60 vs <60), y	12.21 (3.74-39.84)	< .001	-	-
Sex (male vs female)	2.30 (1.13-4.68)	.021	-	-
Hypertension (yes vs no)	1.97 (1.02-3.81)	.04	1.19 (0.61-2.33)	.61
Any comorbidity (yes vs no)	5.26 (2.19-12.64)	< .001	2.65 (1.07-6.55)	.04
Hypoxemia indices				
SpO_2, per 1-unit	0.92 (0.91-0.94)	< .001	0.93 (0.91-0.95)	< .001
SpO_2 ≤90% (≤90% vs >90%)	77.06 (10.55-562.76)	< .001	47.41 (6.29-357.48)	< .001
Dyspnea (yes vs no)	2.94 (1.42-6.11)	.004	2.60 (1.24-5.43)	.01
Blood biochemistry[b]				
WBC count (≥10 vs <10), $\times 10^9$/L	6.21 (3.04-12.69)	< .001	2.56 (1.17-5.63)	.02
Neutrophil count (≥6 vs <6), $\times 10^9$/L	7.43 (3.17-17.42)	< .001	4.29 (1.74-10.58)	.002
Lymphocyte count (<1 vs ≥1), $\times 10^9$/L	1.81 (0.84-3.92)	.13	1.10(0.50-2.41)	.81
Platelet count(<150 vs ≥150), $\times 10^9$/L	3.77 (1.79-7.94)	< .001	2.23 (1.01-4.92)	.05
CRP (≥27.8 vs <27.8), mg/L	28.80 (3.91-212.30)	.001	17.02 (2.25-128.59)	.006
D-dimer (≥0.45 vs <0.45), μg/mL	5.41 (1.20-24.42)	.03	3.07 (0.59-15.98)	.18

[a]Adjusted for age and sex.
[b] Laboratory data were dichotomized based conventional clinical cut-offs (WBC count, Neutrophil count, Lymphocyte count and Platelet count) or on median value (CRP and D-dimer).

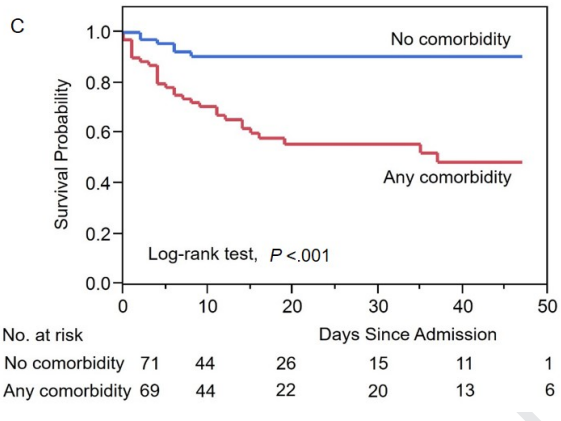
Abbreviations: CI = confidence interval; COVID-19 = coronavirus disease 2019; CRP = C-reactive protein; HR = hazard ratio; SpO_2 = oxygen saturation; WBC = white blood cell count.



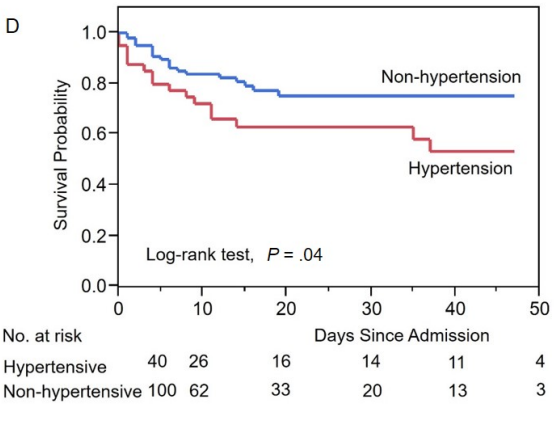
No. at risk						
Age <60 years	69	45	31	20	14	4
Age ≥60 years	71	43	17	14	10	3



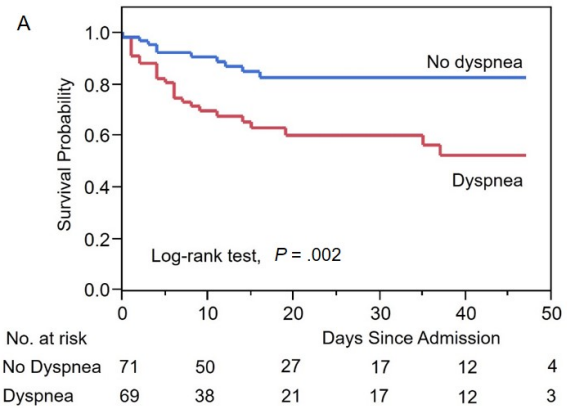
No. at risk						
Female	68	48	21	16	12	3
Male	72	40	27	18	12	4

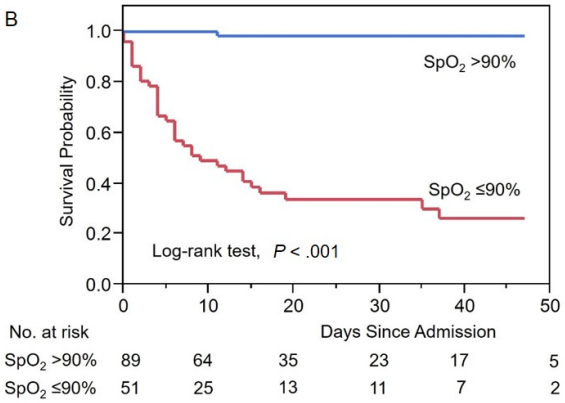


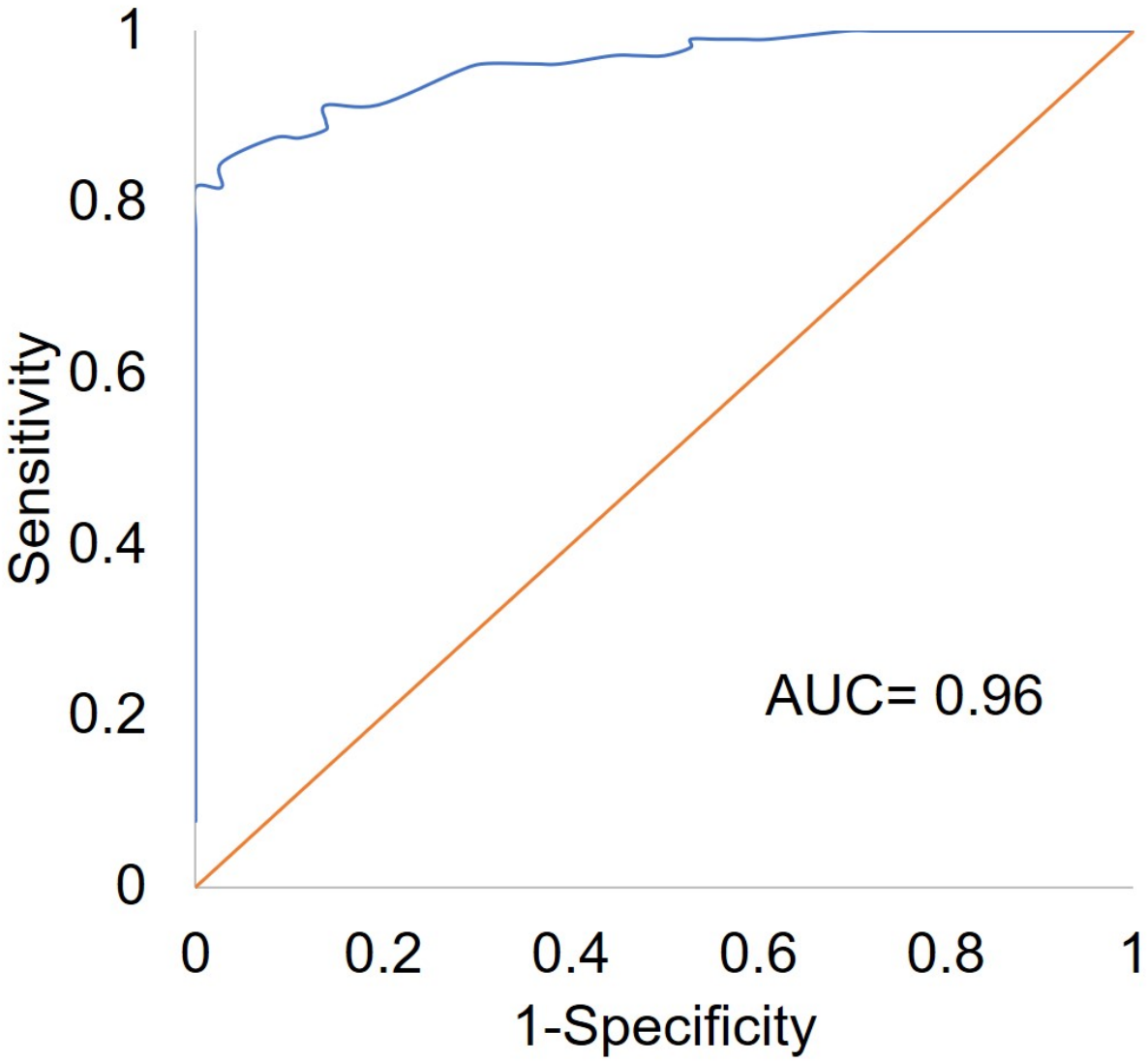
No. at risk						
No comorbidity	71	44	26	15	11	1
Any comorbidity	69	44	22	20	13	6

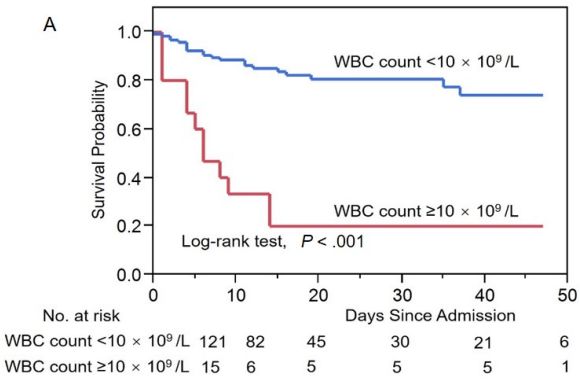


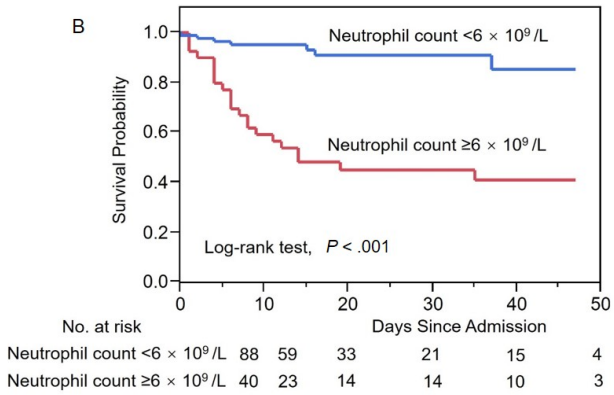
No. at risk						
Hypertensive	40	26	16	14	11	4
Non-hypertensive	100	62	33	20	13	3

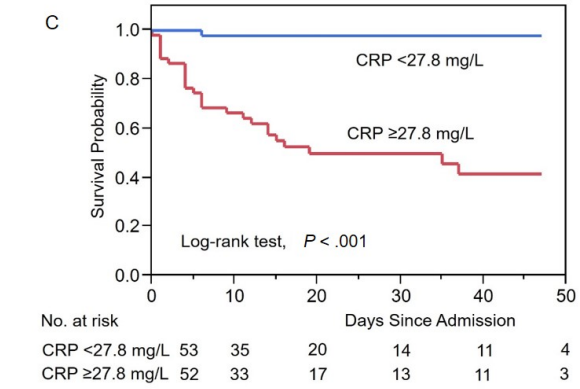


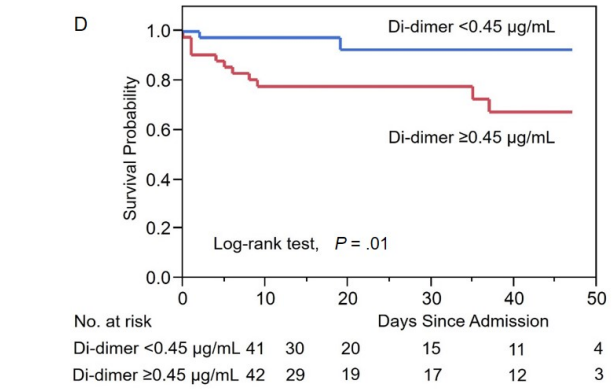



1
0.8
0.6
0.4
0.2
0
Sensitivity
AUC= 0.96
0
0.2
0.4
0.6
0.8
1
1-Specificity


A
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
WBC count <10 × 10⁹/L
WBC count ≥10 × 10⁹/L
Log-rank test, P < .001
0
10
20
30
40
50
Days Since Admission
No. at risk
WBC count <10 × 10⁹/L 121 82 45 30 21 6
WBC count ≥10 × 10⁹/L 15 6 5 5 5 1


B
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
Neutrophil count <6 × 10⁹/L
Neutrophil count ≥6 × 10⁹/L
Log-rank test, P < .001
0
10
20
30
40
50
Days Since Admission
No. at risk
Neutrophil count <6 × 10⁹/L 88 59 33 21 15 4
Neutrophil count ≥6 × 10⁹/L 40 23 14 14 10 3


C
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
CRP <27.8 mg/L
CRP ≥27.8 mg/L
Log-rank test, P < .001
0
10
20
30
40
50
Days Since Admission
No. at risk
CRP <27.8 mg/L 53 35 20 14 11 4
CRP ≥27.8 mg/L 52 33 17 13 11 3


D
Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
Di-dimer <0.45 μg/mL
Di-dimer ≥0.45 μg/mL
Log-rank test, P = .01
0
10
20
30
40
50
Days Since Admission
No. at risk
Di-dimer <0.45 μg/mL 41 30 20 15 11 4
Di-dimer ≥0.45 μg/mL 42 29 19 17 12 3