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Predictive performance of emergency department-specific variables on COVID-19 pneumonia

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ABSTRACT

Introduction: The majority of patients with COVID-19 infection do not progress to pneumonia. We report emergency department (ED)-specific variables and evaluate their predictive performance on diagnosis of pneumonia, intensive care unit (ICU) admission and death.

Methods: This was a retrospective, single-centre cohort study of confirmed COVID-19 patients admitted to a Singapore tertiary hospital. Primary outcome was diagnosis of COVID-19 pneumonia. Secondary outcomes were ICU admission and/or death. Multivariate logistic regression was used to analyse the predictive performance of ED-specific variables. Accuracy of continuous variables was measured by area under receiver operating characteristic (ROC) curve.

Results: 294 patients were included. Patients with pneumonia were older (52.0 years, $p < 0.001$) and had higher C-reactive protein (CRP; 33.8 mg/L, $p < 0.001$). Patients with indeterminate chest radiograph (CRX) findings were at risk of pneumonia vs. patients with normal CRX (37.5% vs. 4.3%, $p < 0.001$). Patients admitted to ICU were older (60.0 years, $p < 0.001$) and had higher CRP (40.0 mg/L, $p < 0.001$). Diagnosis of COVID-19 pneumonia was associated with ICU admission and death (30.0% vs 0.39%, $p < 0.001$). Multivariate logistic regression analysis showed that age (aOR 1.07, $p = 0.049$), CRP (aOR 1.05, $p = 0.006$) and CRX findings (aOR 50.00, $p < 0.001$) had increased odds of pneumonia. ROC curve analysis showed that CRP of 23.3 mg/L was the optimal cut-off for predicting pneumonia.

Conclusion: Older age, higher CRP and CRX findings are associated with COVID-19 pneumonia, ICU admission and death. Prospective studies should be undertaken to validate these findings.

Keywords: COVID-19, C-reactive protein, emergency department, pneumonia, SARS-CoV-2 infection

INTRODUCTION

A novel coronavirus was identified in December 2019 as the cause of pneumonia in Wuhan, China. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) subsequently became a global pandemic.[1] Singapore confirmed its first imported case of COVID-19 on 23 January 2020.[2] At the time of writing, more than 18 million confirmed cases of COVID-19 have been reported worldwide.[3] The World Health Organization declared COVID-19 a Public Health Emergency of International Concern on 30 January 2020. An overall case fatality rate of 2.3% was reported in one of the largest studies of COVID-19 pneumonia.[4]

Globally, the large number of COVID-19 infections has resulted in significant morbidity and mortality, overwhelming many healthcare systems.[5] The majority of COVID-19 infections are mild and do not progress to pneumonia.[4] Studies have identified risk factors for disease progression, including male gender, age > 65 years, the presence of underlying comorbidities and certain laboratory features.[6] There is a paucity of published data to assess the predictive performance of emergency department (ED)-specific variables on the progression of COVID-19 infection to pneumonia.

During the initial presentation of COVID-19 infection, radiological abnormalities may not be present despite fever and cough being dominant symptoms of the disease.[7] Given that the median time course for development of pneumonia is three days from the onset of symptoms and only 3.4% of patients progressed to acute respiratory distress syndrome (ARDS),[7] identifying and understanding the predictors of pneumonia and mortality would lead to better siting of care and management following the diagnosis of COVID-19. This is especially important because the spectrum of COVID-19 infection ranges from absent to late pneumonia findings in positive laboratory SARS-CoV-2 infection.[7]

Due to limited hospital beds, some countries have set up sites of care away from traditional brick and mortar hospitals,[8] which may not be equipped to manage acutely deteriorating COVID-19 patients. Understanding patients at risk for deterioration would prevent costly, risky and unnecessary secondary transfers from these facilities to hospitals. This would also enable frontline emergency physicians to streamline the admission criteria, management and disposition status of patients. Early identification of at-risk groups can lead to early treatment options such as dexamethasone and remdesivir therapy, which may alter the disease progression.[9]

In this retrospective cohort study, we aimed to evaluate the predictive performance of ED-specific variables to identify patients at risk of disease progression.

METHODS

This is a retrospective, single-centre, observational cohort study of patients who were diagnosed with COVID-19 infection and admitted to a regional tertiary hospital through its ED. Khoo Teck Puat Hospital (KTPH) is a 761-bed acute care hospital located in the north of Singapore that caters to a population of 550,000. In 2019, the hospital ED saw 133,502 patients, of whom 51,508 (38.6%) were deemed to be high acuity cases. This study was approved by the National Healthcare Group Domain Specific Review Board (DSRB 2020/00448), and informed consent was waived.

All patients with laboratory-confirmed SARS-CoV-2 from 1 February to 15 April 2020 were included in the study. During this period, all diagnosed patients were admitted to the hospital for their entire course of illness. The diagnosis was made based on a nasopharyngeal swab specimen or respiratory sample that was positive for SARS-CoV-2, using a laboratory-based reverse transcription-polymerase chain reaction test.

Data from the electronic medical records was entered and stored in the National Healthcare Group Research Database Platform by a single trained medical data abstractor. Based on literature review, potential predictors were identified *a priori*. The following data was collected by the study team: patient demographics and comorbidities (hypertension, diabetes mellitus, coronary artery disease, lung disease, renal disease); ED triage parameters (body temperature, systolic blood pressure, heart rate, peripheral oxygen saturation measured via pulse oximetry); clinical symptoms (fever, cough, rhinorrhoea, sore throat, dyspnoea, vomiting, diarrhoea); laboratory results (total white cell count [WBC], lymphocytes count, C-reactive protein [CRP], procalcitonin); and imaging findings.

All chest radiographs (CXR) were formally reported by a radiologist. Imaging results were based on the radiologist's formal report. CXR findings were categorised as 'pneumonia', 'indeterminate' and 'normal'. Terminologies used for pneumonia included 'consolidation' and 'ground glass opacities', while those for indeterminate included 'alveolar infiltrates', 'linear opacities', 'pleural thickening', 'prominent bronchovascular markings' and 'faint ill-defined opacities'. CXR that were classified as normal included terminologies such as 'no confluent consolidation' and 'no sizeable pleural effusion'.

Travel history to areas of heightened vigilance within 14 days of symptom onset was factored in based on the date of presentation. High-risk areas and contact history were defined according to the evolving guidelines of the Singapore Ministry of Health, which were regularly updated (Appendix 1). Information on emergency triage category was collected. The Singapore Patient Acuity Category Scale (PACS) is a symptom-based differential diagnosis approach used in all public hospitals in Singapore to triage patients in the ED based on their presenting

complaints, vital signs, Glasgow Coma Scale and objective assessment.[10] PACS classifies patients into four categories, P1, P2, P3 and P4, with P1 being the sickest patients (Appendix 2).

Primary outcome was COVID-19 pneumonia diagnosed at any point during the course of admission. The diagnosis of 'pneumonia' vs. 'non-pneumonia' was independently tabulated by two physicians (MF and MY) through a review of information available in each patient's clinical electronic medical records, namely presence of respiratory symptoms, lung findings on examination and review of CXR images. Any disagreements were resolved through discussion. A third infectious disease physician (STO) was available to adjudicate where disagreements could not be resolved. Secondary outcomes were intensive care unit (ICU) admission and/or death.

Based on pilot data, we set the proportion of pneumonia in patients aged > 50 years and patients aged ≤ 50 years at 30% and 10%, respectively. Based on a power of 90%, an alpha of 0.025 and an enrolment ratio of 4, a sample size of 275 patients was required. Allowing for possible exclusions at 5%, we estimated that a final sample size of 289 would be required.

Continuous study variables were reported as median and interquartile range (IQR). Categorical data was expressed as frequency and percentage. Chi-square and Mann-Whitney U tests were used to analyse categorical and continuous data, respectively. Multivariate logistic regression was performed for significant variables in the univariate analysis. Area under the receiver operating characteristic curve (AUC) was used to measure the accuracy of the variables. For variables with AUC > 0.85, we determined the optimal cut-off based on the threshold probabilities where sensitivity and specificity were maximal.

Analysis was performed for one pre-specified subgroup – patients with 'indeterminate' and 'normal' CXR at initial presentation. Median values were imputed for missing variables only if

the missing values were < 5%. Statistical analysis was performed with IBM SPSS Statistics version 25.0 (IBM Corp, Armonk, NY, USA), and a p-value < 0.05 was considered statistically significant.

RESULTS

A total of 5,690 patients received the SARS-CoV-2 swab from 1 February to 15 April 2020, and of these, 300 patients tested positive. We excluded six patients: three were lost to follow-up, one was transferred to a paediatric hospital, one died in the ED prior to further evaluation and one was a duplicate entry from the dataset (Fig. 1). Of the 294 patients, 40 (13.6%) were diagnosed with COVID-19 pneumonia and 13 (4.4%) were admitted to the ICU and/or died. There was a 98.3% inter-rater agreement between the diagnosis of pneumonia vs. non-pneumonia, with a kappa coefficient of 0.925 ($p \leq 0.01$). All disagreements on the primary outcome were resolved through discussion.

Patient demographics, clinical characteristics, laboratory results and radiological findings are summarised in Table I. Patients with pneumonia were older (52.0 years [IQR 18.8] vs. 34.0 years [IQR 14.0]; $p < 0.001$) and more likely to have comorbidities, particularly hypertension (30.0% vs. 5.1%; $p < 0.001$) and diabetes mellitus (22.5% vs. 3.5%, $p < 0.001$), as compared to patients without pneumonia. 3.4% of the patients were asymptomatic. The median duration of symptom onset to ED presentation for patients with pneumonia vs. those without pneumonia was 3.5 days and 2.0 days, respectively. Patients with pneumonia presented with higher body temperature (38.2˚C [IQR 1.1] vs. 37.6˚C [IQR 1.1]; $p = 0.005$) and were more likely to be triaged as higher acuity – P1 or P2 (10.0% vs. 0.4%, 12.5% vs 1.6%, respectively; $p < 0.001$). 3.4% of the patients were asymptomatic. Patients with pneumonia had lower WBC count (5.4×10^9/L [IQR 2.5] vs. 6.3×10^9/L [IQR 2.7]; $p = 0.025$), lower lymphocytes count (1.2×10^9/L [IQR 0.7] vs. 1.6

× 10^9/L [IQR 0.8]; p < 0.001) and higher CRP (33.8 mg/L [IQR 61.9] vs. 3.9 mg/L [IQR 7.0]; p < 0.001). Patients with indeterminate CXR findings were at a higher risk of having pneumonia when compared to patients with normal CXR (37.5% vs. 4.3%; p < 0.001). 23 out of 277 (8.3%) patients in the indeterminate or normal CXR groups were subsequently re-classified to the pneumonia group. In terms of travel history and exposure risk, patients with pneumonia were more likely to have travelled to areas of heightened vigilance (12.5% vs. 3.5%; p = 0.013).

Patients who were admitted to ICU and/or died were older (60.0 years [IQR 11.0] vs. 35.0 years [IQR 16.0]; p < 0.001), were more likely to have pre-existing hypertension (61.5% vs. 6.0%; p < 0.001) and diabetes mellitus (46.2% vs. 4.3%; p < 0.001), and had lower lymphocytes counts (1.1 ×10^9/L [IQR 0.5] vs. 1.6 × 10^9/L [IQR 0.8]; p = 0.005) and higher CRP (40.0 mg/L [IQR 54.7] vs. 4.2 mg/L [IQR 7.8]; p < 0.001). A diagnosis of COVID-19 pneumonia was associated with ICU admission and/or death (30.0% vs. 0.4%; p < 0.001). All patients, except for two patients who died, were discharged. The median time to discharge was 12 days, while that for transfer to the National Centre for Infectious Disease and community isolation facility was 4.5 days and 7.0 days, respectively.

Multivariate logistic regression analysis of all the admitted COVID-19 patients revealed that age (adjusted odds ratio [aOR] 1.07, 95% confidence interval [CI] 1.0–1.16; p = 0.049), CRP (aOR 1.05, 95% CI 1.02–1.10; p = 0.006) and CXR findings (aOR 50.00, 95% CI 11.90–279.00; p < 0.001) were positive prognostic factors for pneumonia (Table II). Likewise, these same variables were positive prognostic factors for ICU admission and/or death (age: aOR 1.13, 95% CI 1.03–1.27, p = 0.02; CRP: aOR 1.02, 95% CI 1.00–1.04, p = 0.044; CXR findings aOR 11.60, 95% CI 1.33–144.00, p = 0.031).

The highest positive likelihood ratios for a diagnosis of COVID-19 pneumonia were age ≥ 65 (8.5, 95% CI 2.0–36.4) and CXR with pneumonia changes and indeterminate findings (18.5, 95% CI 10.1–33.6). The absence of CXR findings (0.2, 95% CI 0.1–0.4) had the lowest negative likelihood ratio for diagnosis of COVID-19 pneumonia (Table III). The accuracy of the variables in predicting COVID-19 pneumonia was assessed with AUC (Fig. 2). CRP had the largest AUC of 0.87 (95% CI 0.81–0.94), followed by age 0.82 (95% CI 0.74–0.89). Receiver operating characteristic curve analysis showed that a CRP value of 23.3 mg/L was the optimal cut-off for predicting pneumonia, with 65% sensitivity, 96.9% specificity and 92.5% accuracy. Of note, the optimal CRP cut-off for predicting ICU admission and/or death was also 23.3 mg/L, demonstrating 92.3% sensitivity, 92.2% specificity and 92.2% accuracy with an overall AUC of 94.8%.

The subgroup analysis of patients with normal and indeterminate CXR findings (n = 277) showed that age (aOR 1.08, 95% CI 1.00–1.16; p = 0.049), CRP (aOR 1.07, 95% CI 1.03–1.14; p = 0.007) and CXR findings (aOR 112.00, 95% CI 17.70–953.41; p < 0.001) were good predictors of pneumonia (Table IV).

DISCUSSION

The present study showed that age, CRP and CXR findings were strongly associated with the diagnosis of COVID-19 pneumonia, ICU admission and mortality. As expected, patients aged > 50 years had a significantly higher proportion of pneumonia diagnosis as compared to those aged ≤ 50 years. Furthermore, a diagnosis of pneumonia was associated with ICU admission and/or death. These predictors concurred with those reported by other studies on COVID-19 disease progression.[11-13] For patients without obvious pneumonia findings on initial CXR, our subgroup analysis found that CRP and age were robust predictors of pneumonia.

To the best of our knowledge, this is the first study that uses a primary outcome of clinical diagnosis of pneumonia to predict disease progression in COVID-19. Other commonly used outcomes are ARDS, requirement for oxygen supplementation and mechanical ventilation.[11-15] These outcomes may not be ideal in acute care and emergency settings, as they signify severe disease and would exclude the identification of patient populations that may otherwise benefit from treatment to prevent disease progression and morbidity. Moreover, an outcome such as requirement of oxygen supplementation can be subjective.

Pneumonia is an acute infection of the alveolar space and pulmonary parenchyma.[16] A diagnosis of pneumonia is made based on a constellation of symptoms and signs, but individual symptoms and clinical findings lack the accuracy for precise diagnosis.[17] Diagnosis is clinical and based on symptoms and the presence of rales or rhonchi on lung examination with radiographic confirmation.[18] We chose pneumonia as the primary outcome, as the literature revealed that radiological findings correlated with poor disease outcome.[19-20] Furthermore, despite the comparatively high infectivity rates of COVID-19 infection,[21] Singapore has maintained an overall low mortality rate of 0.05%.[22] Possible contributing factors could be a good healthcare system, one of the highest testing rates per million population,[22] and the characteristics of patients who were infected – mainly well and young migrant workers. A more sensitive endpoint was needed to risk stratify patients at risk of deterioration. Our study showed extremely high inter-rater agreement, indicating that this was a reliable diagnosis and primary outcome.

Numerous studies have shown that higher CRP levels were associated with disease progression and disease severity.[23-25] These findings were replicated in our study. When compared to age, CRP was shown to be a better predictor of pneumonia and mortality. Our study found that a higher CRP value, with the optimal cut-off of 23.3 mg/L demonstrating the highest

accuracy, was predictive of pneumonia, ICU admission and death. Our findings confirmed that CRP can be used to diagnose early pneumonia, and is an important marker for diagnosing and assessing severe pulmonary disease.[26]

In line with previous studies,[6,14,27] the present study showed that older age was independently associated with the development of ARDS and disease progression. A similar phenomenon was observed in Italy, where older male patients with multiple comorbidities were found to have higher mortality rates.[28] This could be due to a less heightened immune response and comorbidities that were unaccounted for. Using an age cut-off of ≥ 65 years, our study showed good specificity but poor sensitivity, indicating that an age cut-off should not be used in isolation in the risk stratification of COVID-19 patients.

The American College of Radiology does not recommend the use of chest computed tomography (CT) for screening or diagnosis of COVID-19.[29] In EDs worldwide, including in Singapore, CXR are commonly performed for patients with suspected or diagnosed COVID-19 infection. As CT is not routinely performed in Singapore, it is important for emergency physicians to be able to identify CXR findings that are suggestive of pneumonia in the emergency setting, in order to guide management, predict disease progression and guide disposition.

A study conducted in a New York hospital showed that the presenting symptoms of fever, cough and rhinorrhoea were common but not predictive of pneumonia and mortality in COVID-19 patients.[13] These findings were replicated in our study. We demonstrated that comorbidities, presenting symptoms of dyspnoea and diarrhoea, PAC status, lymphopaenia were significant predictors of pneumonia and mortality. Their combined assessment and incorporation into scoring strategies for ED triage and community facilities transfer criteria allows us to estimate mortality risk, guide treatment and prioritise care for ED patients. These reliable predictors are easily

understood by emergency physicians, widely available, reasonable in cost, safe to administer, and capable of detecting a high proportion of disease in its preclinical state. Finally, our study also has implications for patient disposition, as patients at higher risk of pneumonia may be unsuitable for transfer to low acuity community isolation facilities and are more likely to require closer monitoring when admitted.

Our study has several limitations. Firstly, the retrospective nature of the study and the limited sample size from a single centre limit its generalisability to other settings. Also, our primary outcome measure (i.e. presence or development of pneumonia during the hospital admission) could be perceived as a subjective clinical judgement. However, this was mitigated by a high inter-rater reliability in the outcome. Secondly, we acknowledge the presence of incorporation bias, as the initial CXR findings were part of the outcome. Our study showed that the majority of patients with pneumonia (57.5%) were not diagnosed with pneumonia on initial CXR. Respiratory symptoms, physical examination and repeat CXR aided the eventual diagnosis of clinical pneumonia. Lastly, the external validity of this study may be limited, as COVID-19 affected mainly the younger population and foreign workers in Singapore.

To the best of our knowledge, the present study is one of the first to evaluate ED-specific variables as predictors of COVID-19 pneumonia. Furthermore, in contrast to later datasets, where COVID-19 patients who appeared clinically well were transferred from hospitals to care facilities, the dataset of our study represented patients who had complete follow-up, as they were admitted and followed up for the entire course of their illness.

In conclusion, the present study found that elevated CRP, older age and CXR findings at admission are associated with COVID-19 pneumonia, ICU admission and mortality. Prospective studies should be undertaken to validate these finding.

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FIGURE

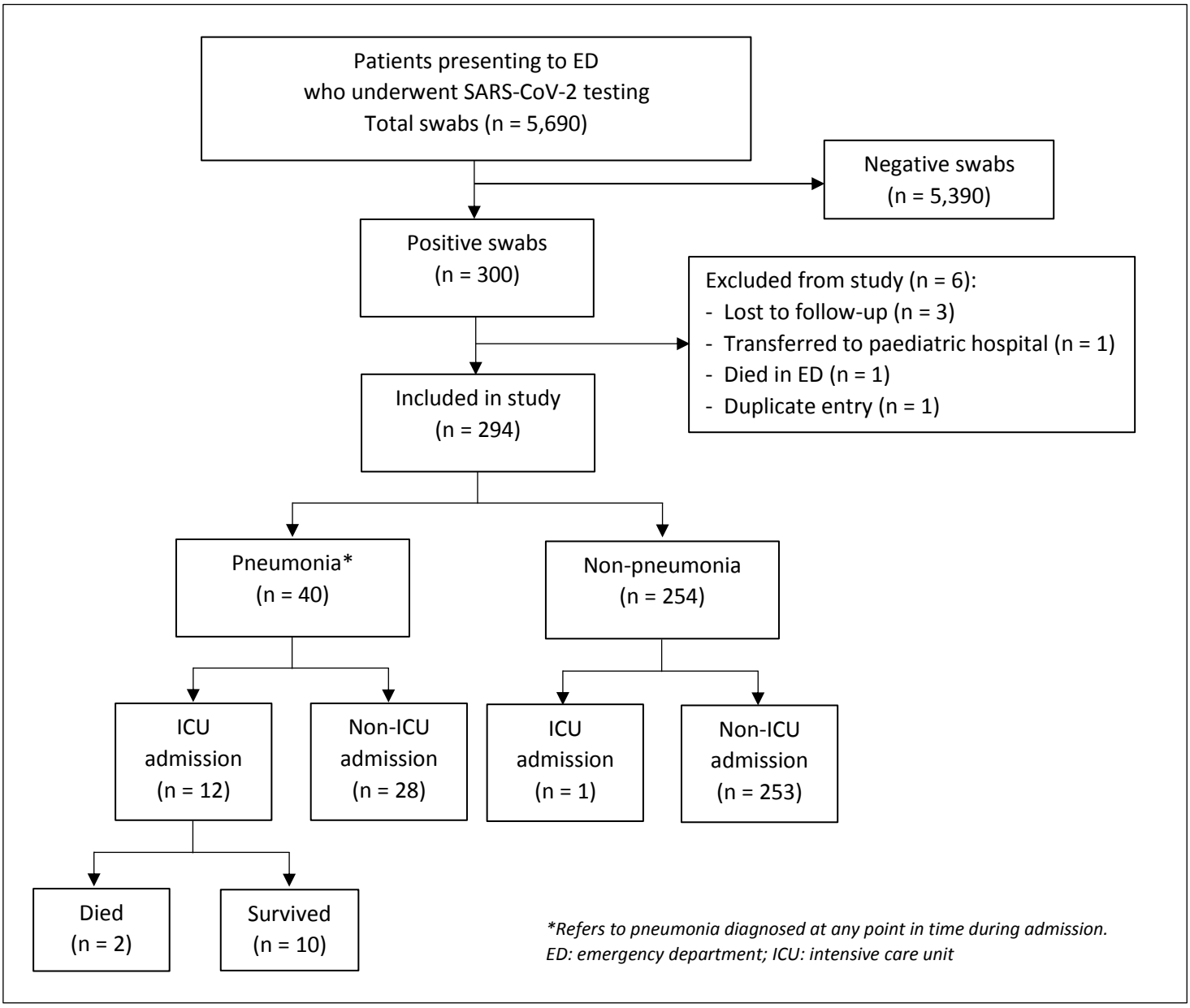

Fig. 1. Flowchart shows the study design.

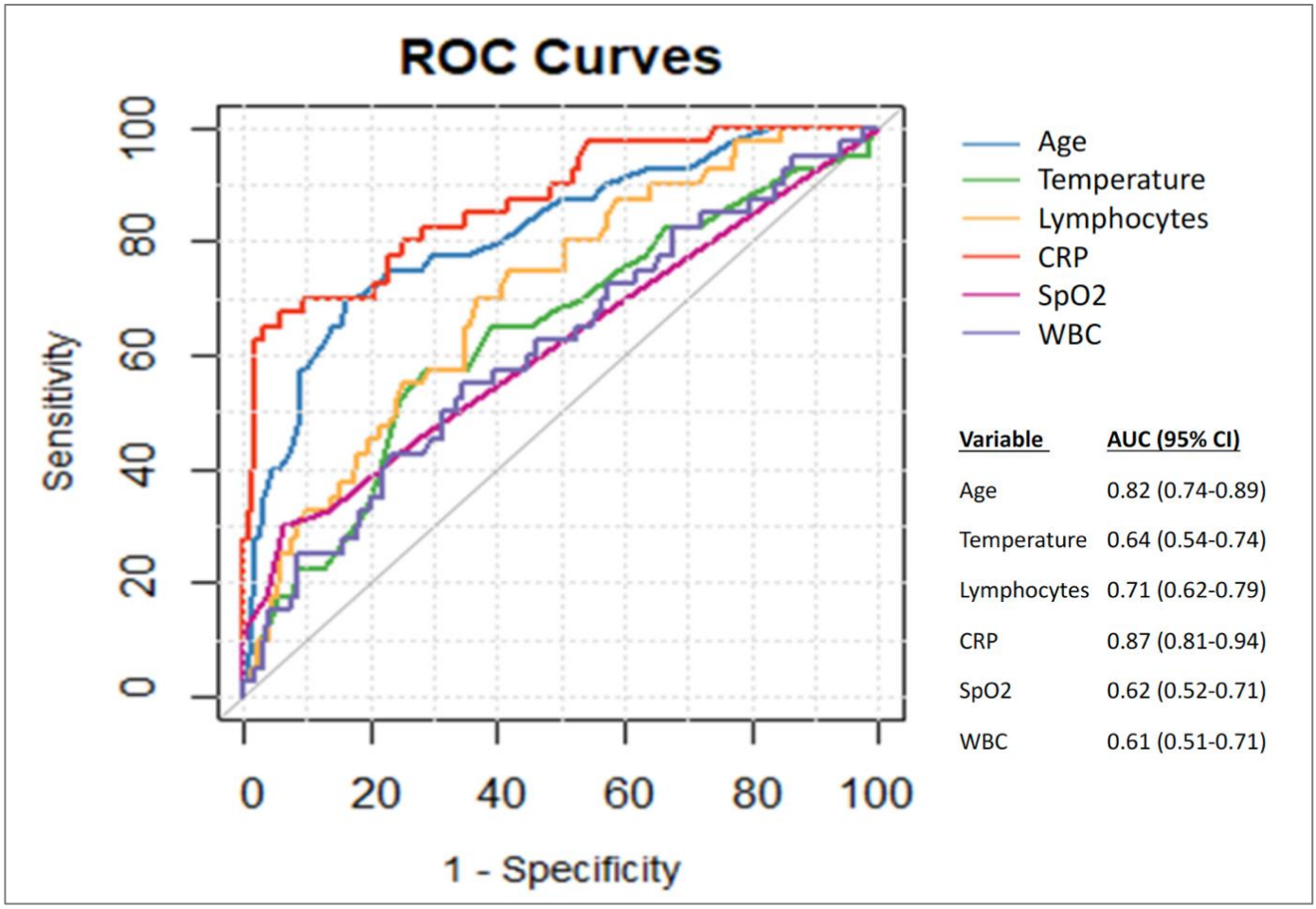

Fig. 2 Graphs shows the receiver operating characteristic (ROC) curve analysis of specific variables. *AUC: area under the ROC curve; CRP: C-reactive protein; SpO2: peripheral oxygen saturation measured via pulse oximetry; WBC: total white cell count*

Table I. Demographics, clinical characteristics, and laboratory and radiological findings of patients based on primary (pneumonia) and secondary (ICU admission and/or death) outcomes.

Parameter	No. (%)					
	Pneumonia (n = 40, 13.6%)	Non-pneumonia (n = 254, 86.4%)	p-value	ICU admission and/or death (n = 13, 4.4%)	Non-ICU admission and/or death (n = 281, 95.6%)	p-value
Median age (yr)†	52.0 (18.8)	34.0 (14.0)	< 0.001	60.0 (11.0)	35.0 (16.0)	< 0.001
Age group						
0–49 yr	16 (40.0)	226 (99.0)	< 0.001	2 (15.4)	240 (85.4)	< 0.001
≥ 50 yr	24 (60.0)	28 (11.0)		11 (84.6)	42 (14.9)	
Male gender	31.0 (77.5)	227.0 (89.4)	0.033	11.0 (84.6)	247.0 (87.9)	0.724
Ethnicity						
Chinese	15.0 (37.5)	29.0 (11.4)	< 0.001	7.0 (53.8)	37.0 (13.2)	< 0.001
Indian	7.0 (17.5)	88.0 (34.6)		2.0 (15.4)	93.0 (33.1)	
Malay	10.0 (25.0)	13.0 (5.1)		3.0 (23.1)	20.0 (7.1)	
Others	8.0 (20.0)	124.0 (48.8)		1.0 (7.7)	131.0 (46.6)	
Comorbidities						
Hypertension	12.0 (30.0)	13.0 (5.1)	< 0.001	8.0 (61.5)	17.0 (6.0)	< 0.001
Diabetes mellitus	9.0 (22.5)	9.0 (3.5)	< 0.001	6.0 (46.2)	12.0 (4.3)	< 0.001
Coronary artery disease	2.0 (5.0)	2.0 (0.8)	0.033	1.0 (7.7)	3.0 (1.1)	0.044
Lung disease	3.0 (7.5)	3.0 (1.2)	0.009	1.0 (7.7)	5.0 (1.8)	0.140
Renal disease	1.0 (2.5)	0 (0.0)	0.012	1.0 (7.7)	0 (0)	< 0.001
Symptoms						
Fever	35.0 (87.5)	195.0 (76.8)	0.126	11.0 (84.6)	219.0 (77.9)	0.568
Cough	27.0 (67.5)	137.0 (53.9)	0.108	11.0 (84.6)	153.0 (54.4)	0.032
Rhinorrhoea	9.0 (22.5)	57.0 (22.4)	0.993	3.0 (23.1)	63.0 (22.4)	0.956
Sore throat	12.0 (30.0)	94.0 (37.0)	0.391	2.0 (15.4)	104.0 (37.0)	0.112
Dyspnoea	10.0 (25.0)	12.0 (4.7)	< 0.001	6.0 (46.2)	16.0 (5.7)	< 0.001
Diarrhoea	5.0 (12.5)	11.0 (4.3)	0.034	4.0 (30.8)	12.0 (4.3)	< 0.001
Vomiting	4.0 (10.0)	7.0 (2.8)	0.025	0 (0)	11.0 (3.9)	0.467
ED triage vitals†						
Body temperature (˚C)	38.2 (1.1)	37.6 (1.1)	0.005	38.2 (1.4)	37.7 (1.1)	0.494
Systolic BP (mmHg)	131.5 (23.0)	131.0 (19.0)	0.592	133.0 (25.0)	131.0 (19.0)	0.704
Heart rate (bpm)	93.5 (17.5)	88.0 (22.0)	0.21	92.0 (14.0)	88.0 (22.0)	0.343
SpO2 (%)	100 (3.0)	100.0 (1.0)	0.004	99.0 (4.0)	100.0 (1.0)	0.002
PACS status						
P1	4.0 (10.0)	1.0 (0.4)	< 0.001	4.0 (30.8)	1.0 (0.4)	< 0.001
P2	5.0 (12.5)	4.0 (1.6)		1.0 (7.7)	8.0 (2.8)	
P3	31.0 (77.5)	249.0 (98.0)		8.0 (61.5)	272.0 (96.8)	

Re-attendance within 72 hours	3.0 (7.5)	55.0 (21.7)	0.037	0 (0)	58.0 (20.6)	0.068
Positive travel history to areas of heightened vigilance within 14 days prior to symptoms onset	5.0 (12.5)	9.0 (3.5)	0.013	2.0 (15.4)	12.0 (4.3)	0.066
Positive contact history based on MOH definition	11.0 (27.5)	147.0 (57.9)	< 0.001	2.0 (15.4)	156.0 (55.5)	0.005
Laboratory finding†						
WBC ($\times 10^9$/L)	5.4 (2.5)	6.3 (2.7)	0.025	5.4 (2.6)	6.1 (2.7)	0.573
Lymphocytes ($\times 10^9$/L)	1.2 (0.7)	1.6 (0.8)	< 0.001	1.1 (0.5)	1.6 (0.8)	0.005
C-reactive protein (mg/L)	33.8 (61.9)	3.9 (7.0)	< 0.001	40.0 (54.7)	4.2 (7.8)	< 0.001
Procalcitonin (ng/mL)	0.1 (0.1)	0.1 (0.1)	0.001	0.2 (0.1)	0.1 (0.1)	0.001
Chest radiograph findings						
Pneumonia changes	17.0 (42.5)	0 (0)	< 0.001	6.0 (46.2)	11.0 (3.9)	< 0.001
Normal	8.0 (20.0)	243.0 (95.7)		2.0 (15.4)	249.0 (88.6)	
Indeterminate	15.0 (37.5)	11.0 (4.3)		5.0 (38.5)	21.0 (7.5)	
Disposition from ED						
General ward	38.0 (95.0)	253.0 (99.6)	0.007			
ICU	2.0 (5.0)	1.0 (0.4)				
Admitted to ICU and/or death	12.0 (30.0)	1.0 (0.4)	< 0.001			

**Refers to pneumonia diagnosed at any point in time during admission. †Data presented as median (interquartile range). BP: blood pressure; ED: emergency department; ICU: intensive care unit; MOH: Ministry of Health; PACS: Patient Acuity Category Scale; SpO2: peripheral oxygen saturation measured via pulse oximetry; WBC: total white cell count*

Table II. Multivariate logistic regression for predictors of pneumonia and ICU admission and/or death in patients admitted for COVID-19.

Variable	Pneumonia*		ICU admission and/or death	
	aOR (95% CI)	p-value	aOR (95% CI)	p-value
Age	1.07 (1.00–1.16)	0.049	1.13 (1.03–1.27)	0.020
C-reactive protein	1.05 (1.02–1.10)	0.006	1.02 (1.00–1.04)	0.044
Total white cell count	0.94 (0.64–1.31)	0.708	1.02 (0.65–1.60)	0.922
Lymphocytes	0.56 (0.18–1.24)	0.246	0.65 (0.09–2.26)	0.620
Temperature	1.61 (0.62–4.35)	0.329	1.32 (0.49–3.45)	0.563
Chest radiograph	50.00 (11.90–279.00)	< 0.001	11.60 (1.33–144.00)	0.031
Hypertension	0.86 (0.06–9.35)	0.907	2.85 (0.43–19.60)	0.273

**Refers to pneumonia diagnosed at any point in time during admission. aOR: adjusted odds ratio; CI: confidence interval; ICU: intensive care unit*

Table III. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR−) of variables.

Variable	Age ≥ 65 yr	WBC > 10 × 10^9/L	Lymphocytes < 1.1 × 10^9/L	CRP > 10 mg/L	CXR (pneumonia changes/indeterminate)
Sensitivity*	10.0 (3.3–24.6)	5.0 (0.9–18.2)	40.0 (25.3–56.6)	70.0 (53.3–82.9)	80.0 (63.4–90.4)
Specificity*	98.8 (96.3–99.7)	93.3 (89.3–95.9)	82.7 (77.3–87.0)	79.9 (74.4–84.6)	95.7 (92.2–97.7)
PPV*	57.1 (20.2–88.2)	10.5 (1.8–34.5)	26.7 (16.5–39.9)	35.4 (25.2–47.1)	74.4 (58.5–86.0)
NPV*	87.5 (82.9–90.9)	86.2 (81.4–89.9)	89.7 (84.9–93.2)	94.4 (90.2–96.9)	96.8 (93.6–98.5)
LR+†	8.5 (2.0–36.4)	0.8 (0.2–3.1)	2.3 (1.5–3.7)	3.5 (2.5–4.8)	18.5 (10.1–33.6)
LR−†	0.9 (0.8–1.0)	1.0 (0.9–1.1)	0.7 (0.6–0.9)	0.4 (0.2–0.6)	0.2 (0.1–0.4)

**Data presented as % (95% confidence interval). †Data presented as ratio (95% confidence interval).*
CRP: C-reactive protein; CXR: chest radiography; WBC: Total white cell count

Table IV. Subgroup analysis of patients that presented without clear-cut pneumonia but subsequently developed pneumonia* (n = 277).

Variable	aOR (95% CI)	p-value
Age	1.08 (1.00–1.16)	0.049
C-reactive protein	1.07 (1.03–1.14)	0.007
Total white cell count	0.94 (0.64–1.33)	0.734
Lymphocytes	0.58 (0.18–1.24)	0.252
Body temperature	1.74 (0.67–4.70)	0.254
Chest radiograph	112.00 (17.70–953.41)	< 0.001
Hypertension	1.08 (0.09–11.43)	0.951

**Refers to pneumonia diagnosed at any point in time during admission.*
aOR: adjusted odds ratio; CI: confidence interval