

COVID-19 Screening for Hospitalized Patients: The Role of Expanded Hospital Surveillance in a Low Prevalence Setting

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Purpose: The COVID-19 pandemic poses a serious threat to healthcare workers and hospitalized patients. Early detection of COVID-19 cases is essential to control the spread in healthcare facilities. However, real-world data on the screening criteria for hospitalized patients remain scarce. We aimed to explore whether patients with negative results of pre-hospital screening for COVID-19 should be rescreened after admission in a low-prevalence (less than 3% of the world average) setting.

Patients and Methods: We retrospectively included patients in central Taiwan who were negative at the first screening but were newly diagnosed with pneumonia or had a body temperature above 38 degrees Celsius during their hospitalization. Each patient might be included as an eligible case several times, and the proportions of cases who were rescreened for COVID-19 and those diagnosed with COVID-19 were calculated. A logistic regression model was constructed to identify factors associated with rescreening. Reverse transcription-polymerase chain reaction tests were used to confirm the diagnosis of COVID-19.

Results: A total of 3549 cases eligible for COVID-19 rescreening were included. There were 242 cases (6.8%) who received rescreening. In the multivariable analysis, cases aged 75 years or older, those with potential exposure to SARS-CoV-2, or patients visiting specific departments, such as the Cardiovascular Center and Department of Neurology, were more likely to be rescreened. None was diagnosed with COVID-19 after rescreening. There was no known cluster infection outbreak in the hospital or in the local community during the study period and in the following two months.

Conclusion: In Taiwan, a country with a low COVID-19 prevalence, it was deemed safe to rescreen only high-risk hospitalized patients. This strategy was effective and reduced unnecessary costs.

Keywords: fever, pneumonia, risk, SARS-CoV-2, screen

Introduction

As of September 20, 2021, the total number of confirmed cases of coronavirus disease 2019 (COVID-19), a disease caused by the Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2), reached 228.4 million, which includes 4.7 million deaths worldwide.¹ In contrast, Taiwan has had relatively few confirmed and fatal cases, at 16,147 and 840, respectively. COVID-19 is highly contagious and is mainly transmitted through respiratory droplets and close contact with an infected individual. In addition to causing community spread, COVID-19 accounts for a high proportion of nosocomial infections, and thus poses a huge threat to healthcare workers and

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hospitalized patients.² The spread of COVID-19 in health-care facilities may lead to shortages of both medical personnel and supplies, and hence preventive actions should be taken as soon as possible.³

The main clinical characteristics of COVID-19 patients vary greatly. The leading clinical symptoms and signs are fever, fatigue, headache, olfactory or gustatory dysfunction, nasal obstruction, rhinorrhea, cough, sore throat, gastrointestinal symptoms, lymphopenia, prolonged prothrombin time, and elevated inflammatory markers, such as C-reactive protein, procalcitonin, erythrocyte sedimentation rate, lactate dehydrogenase, and d-dimer,⁴⁻⁶ while dyspnea, leukocytosis, increased inflammatory markers, and elevation of creatinine and aspartate aminotransferase indicate greater disease severity.^{7,8} The predictors of SARS-CoV-2 infection include contact history with confirmed cases, fever, respiratory symptoms, gustatory dysfunction, gastrointestinal symptoms, and neurological symptoms.⁹⁻¹² The results of laboratory examinations have also been studied to help construct a predictive model using artificial intelligence.¹³ However, patients with early COVID-19 or certain groups of patients, such as pregnant women, may only experience mild symptoms or could even be asymptomatic.^{14,15} Chest computed tomography, which often shows bilateral patchy shadows or ground glass opacity over the peripheral lungs in COVID-19 patients, is a sensitive tool that can be helpful in the diagnosis of COVID-19 when the clinical presentation and molecular test results are conflicting.^{5,6,8,16,17} However, it is not routinely used as a screening tool. Isolation of high-risk patients is not enough to prevent nosocomial infections, and therefore universal screening for COVID-19 using a Reverse Transcription-Polymerase Chain Reaction (RT-PCR) test to detect SARS-CoV-2 remains necessary prior to hospitalization.^{15,18} Nevertheless, it is important to note that negative results from screening at admission may not be used as a basis for estimating the risks of nosocomial transmission.¹⁹

Nosocomial infections due to COVID-19 are not easy to prevent, and it remains difficult to immediately control the spread without proper intervention measures. Several studies have suggested that routine monitoring of COVID-19 transmission should be carried out for high-risk groups, such as patients receiving hemodialysis^{20,21} and patients hospitalized for hemato-oncological diseases.²²⁻²⁴ Other vulnerable patients, such as those in the intensive care units, may also require special attention.²⁵ Universal COVID-19 screening for all hospitalized patients is a resource-intensive task, but it could sometimes still play a key role in limiting the spread from the community,

given the inseparable connection between healthcare institutions and their neighboring communities.²⁶

Although the results of COVID-19 screening prior to hospitalization vary with its prevalence,²⁷⁻³² pre-hospital screening has been widely recommended.^{27,28,30-32} However, real-world data on the screening criteria for hospitalized patients remain scarce. In this study we aimed to explore whether patients with negative results of pre-hospital screening for COVID-19 who develop fever or pneumonia after admission should be rescreened in a low-prevalence setting.

Materials and Methods

Study Population

This study was conducted at Taichung Veterans General Hospital, a medical center with a 1600-bed capacity in central Taiwan. In response to COVID-19 cluster infection outbreaks, the Taiwan government raised the COVID-19 alert to Level 3 on May 19, 2021, restricting both indoor and outdoor gatherings. The alert was then reduced to Level 2 on July 26, 2021. All hospitalized patients at Taichung Veterans General Hospital received their first screening for COVID-19 between May 15, 2021 and May 17, 2021. All patients who were admitted after May 18, 2021 received their first screening for COVID-19 before being hospitalized. We included patients who were negative at the first screening but were newly diagnosed with pneumonia or had a body temperature above 38 degrees Celsius during their hospitalization between May 18, 2021 and August 9, 2021. Those who were positive for screening or rescreening were transferred to a negative-pressure isolation room and were subsequently excluded from the study.

Data Collection

A standardized case record form was used to collect information on gender, age, history of travel, occupation, contacts, and cluster activity, as well as the results of laboratory tests and image studies. Patients were assigned to 1 of 3 different quarantine levels: not quarantined for COVID-19, quarantined due to potential exposure to SARS-CoV-2, and quarantined due to unexplained community-acquired pneumonia. Patients belonged to different departments, including the Department of Internal Medicine, Surgery, Cardiovascular Center, Neurology, Pediatrics, Obstetrics and Gynecology, and others. If a hospitalized patient was newly diagnosed with pneumonia or had experienced a body temperature above 38 degrees

Celsius within the previous 24 hours, the computer system would issue an automated warning reminding the clinician to consider the possibility that the patient was infected with COVID-19. A patient might be included as an eligible case several times if he or she met the inclusion criteria more than once. The decision to rescreen for COVID-19 was made at the discretion of the treating physicians.

Case Definition of COVID-19

To improve the efficiency in clinical practice, all cases were screened or rescreened by detecting SARS-CoV-2 with a nucleic acid amplification test using clinical specimens, such as nasopharyngeal or throat swabs, sputum, or lower respiratory tract aspirate. A COVID-19 case was defined as a patient with a positive SARS-CoV-2 result.

Reverse Transcription-Polymerase Chain Reaction (RT-PCR) Assay

In our study, the nucleic acid amplification test that was used to detect SARS-CoV-2 was the RT-PCR test. All clinical specimens were refrigerated at 4°C and loaded onto a cobas[®] 6800 instrument (Roche Molecular Systems, Rotkreuz, Switzerland) within 24 hours. The cobas[®] SARS-CoV-2 test kits were used. The automated system targeted the SARS-CoV-2 envelope and nucleocapsid gene. The limit of detection was 100 copies per reaction (AccuPlex[™] SARS-CoV-2 reference material kit). All protocols were performed according to the manufacturer's instructions.

Statistical Analysis

The proportions of cases who received rescreening for COVID-19 and those who were diagnosed with COVID-19 were calculated as the total number of occurrences divided by the total number of eligible cases, respectively. As for the associated variables, the median and interquartile range were calculated for quantitative variables, while percentages were calculated for categorical variables. The Kolmogorov–Smirnov test was used to evaluate the normality of variables. The Mann–Whitney *U*-test was used to compare quantitative variables, and the χ^2 or two-tailed Fisher's exact test was used to compare categorical variables. A logistic regression model was constructed to identify any associated factors. Variables with a *P* value ≤ 0.25 in the univariable analysis were added in a stepwise manner, with only significant variables being used in the final, multivariable analysis. Gender and age were included in the final model regardless of the level of significance. All statistical analyses were conducted using Statistical

Analysis System software, version 9.4 (SAS Institute, Cary, NC, USA). A two-sided *P* value ≤ 0.05 was considered statistically significant.

Ethics Statement

This study was approved by the Clinical Ethics Committee of Taichung Veterans General Hospital (no. CE21384B). This study was conducted in accordance with the Declaration of Helsinki. The patients were informed about the objective and the data collection methods of the study, participated benefited potential risk of the study. Informed written consents were received prior to starting the study. The patients understood that they had the right to withdraw anytime if they wanted. All information was kept confidential without identification or name tag on it.

Results

A total of 3549 cases (1628 patients) eligible for COVID-19 rescreening were included, with a median of one case per patient (interquartile range, 1–2). There were 242 rescreened cases (6.8%); most of the patients were rescreened only once, and only 7 patients were rescreened twice. No patients were diagnosed with COVID-19 after rescreening. In addition, there was no known cluster infection outbreak in the hospital or in the local community during the study period and in the following two months.

The clinical characteristics of the rescreened and non-rescreened groups are shown in Table 1. No notable difference in gender proportion existed between the two groups, but the rescreened group had more people aged 75 years or older compared with the non-rescreened group (89/242, 36.8% vs 690/3307, 20.9%) ($P < 0.0001$). The median length of hospital stay was 4 days without a significant difference between the two groups. However, there were significant differences between the two groups regarding the quarantine levels of cases and the departments they belonged to.

Regarding the quarantine levels, 19.4% (47/242) of rescreened cases had been quarantined due to potential exposure to SARS-CoV-2, which was much higher than the 2.1% (68/3307) of non-rescreened cases ($P < 0.0001$). With respect to departments, rescreening was more frequently associated with the Department of Internal Medicine (145/242, 59.9% vs 1877/3307, 56.8%), Cardiovascular Center (12/242, 5.0% vs 56/3307, 1.7%), Neurology (35/242, 14.5% vs 135/3307, 4.1%), and other independent departments (19/242, 7.9% vs 238/3307, 7.2%), but was less frequently associated with the

Table 1 Clinical Characteristics of Rescreened and Non-Rescreened Cases

Variable ^a	Rescreened	Non-Rescreened	
Total Number	N = 242	N = 3307	P value ^b
Demographics			
Male	136 (56.2)	1870 (56.5)	0.9160
Female	106 (43.8)	1437 (43.5)	0.9160
Age (years)	66.7 (51.0–80.3)	61.3 (48.3–72.8)	<0.0001
Age ≥ 75 years	89 (36.8)	690 (20.9)	<0.0001
Hospitalization (days)	4.0 (1.0–10.0)	4.0 (2.0–11.0)	0.0769
Different quarantine levels			<0.0001
Not quarantined for COVID-19	187 (77.3)	3147 (95.2)	
Quarantined due to potential exposure to SARS-CoV-2	47 (19.4)	68 (2.1)	
Quarantined due to unexplained community-acquired pneumonia	8 (3.3)	92 (2.8)	
Departments			<0.0001
Internal Medicine	145 (59.9)	1877 (56.8)	
Surgery	22 (9.1)	616 (18.6)	
Cardiovascular Center	12 (5.0)	56 (1.7)	
Neurology	35 (14.5)	135 (4.1)	
Pediatrics	5 (2.1)	208 (6.3)	
Obstetrics and Gynecology	4 (1.7)	177 (5.4)	
Others	19 (7.9)	238 (7.2)	

Notes: ^aData are presented as median values (interquartile range) for continuous variables and number of cases (percentage) for categorical variables. ^bP value: The Mann-Whitney U-test was used to compare continuous variables, and the χ^2 or two-tailed Fisher's exact test was used to compare categorical variables.

Department of Surgery (22/242, 9.1% vs 616/3307, 18.6%), Pediatrics (5/242, 2.1% vs 208/3307, 6.3%), and Obstetrics and Gynecology (4/242, 1.7% vs 177/3307, 5.4%), when compared with non-rescreening ($P < 0.0001$). Within the Department of Internal Medicine, cases belonging to the Division of Infectious Diseases were more likely to be rescreened (55/145, 37.9% vs 286/1877, 15.2%), while cases belonging to the Division of Hematology and Oncology had a lower prevalence rate of rescreening (14/145, 9.7% vs 711/1877, 37.9%) ($P < 0.0001$) (Table S1).

In the multivariable logistic regression model, the variables associated with rescreening included age, quarantine levels, and departments. Cases with an age of 75 years or older were more likely to be rescreened compared with younger cases (adjusted Odds Ratio [aOR] 1.56, 95% Confidence Interval [CI] 1.16–2.10). Those who had been quarantined due to potential exposure to SARS-CoV-2 were more likely to be rescreened compared with those receiving general care (aOR 11.63, 95% CI 7.80–17.35). Compared with cases in the Department of Internal Medicine, those attending the Cardiovascular Center (aOR 3.97, 95% CI 2.05–7.69) or Department of Neurology

(aOR 4.69, 95% CI 3.05–7.20) were more likely to be rescreened (Table 2).

Discussion

In this real-world experience of COVID-19 rescreening in a low-prevalence setting, we found that the proportion of cases being considered by clinicians to be rescreened because of pneumonia or fever was low, with the results of all rescreened cases coming back negative. Those who were elderly, had potential exposure to SARS-CoV-2, or were treated in a specific department, such as the Cardiovascular Center or Department of Neurology, were more likely to be rescreened. These findings may be of value to frontline medical personnel.

In Taiwan, an outbreak of COVID-19 cluster infections began in mid-May 2021, but the prevalence rate in mid-August 2021 was only 675 cases per million population, which was much lower than the global rate of 26,137 cases per million population.¹ In addition, the dominant SARS-CoV-2 strain in Taiwan was mainly the Alpha variant (B.1.1.7), which is known to be much less contagious than the Delta variant (B.1.617.2), resulting in a relatively slow spread of COVID-19. At the same time, a number of measures have been taken to prevent widespread exposure

Table 2 Univariable and Multivariable Logistic Regression Analysis of Factors Associated with Rescreened Cases

Variable	Univariable Analysis		Multivariable Analysis	
	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Gender				
Male	1.00 (reference)		1.00 (reference)	
Female	1.01 (0.78–1.32)	0.9159	1.17 (0.88–1.55)	0.2839
Age ≥ 75 years	2.21 (1.68–2.90)	<0.0001	1.56 (1.16–2.10)	0.0035
Hospitalization (days)	1.00 (0.99–1.00)	0.5222		
Different quarantine levels				
Not quarantined for COVID-19	1.00 (reference)		1.00 (reference)	
Quarantined due to potential exposure to SARS-CoV-2	11.63 (7.80–17.35)	<0.0001	11.76 (7.64–18.10)	<0.0001
Quarantined due to unexplained community-acquired pneumonia	1.46 (0.70–3.06)	0.3115	1.66 (0.78–3.53)	0.1881
Departments				
Internal Medicine	1.00 (reference)		1.00 (reference)	
Surgery	0.46 (0.29–0.73)	0.0010	0.66 (0.41–1.07)	0.0911
Cardiovascular Center	2.77 (1.45–5.29)	0.0020	3.97 (2.05–7.69)	<0.0001
Neurology	3.36 (2.23–5.05)	<0.0001	4.69 (3.05–7.20)	<0.0001
Pediatrics	0.31 (0.13–0.77)	0.0113	0.48 (0.19–1.21)	0.1221
Obstetrics and Gynecology	0.29 (0.11–0.80)	0.0166	0.44 (0.16–1.23)	0.1180
Other	1.03 (0.63–1.70)	0.8968	1.50 (0.90–2.50)	0.1218

Abbreviations: CI, confidence interval; OR, odds ratio.

to SARS-CoV-2, including following hand hygiene protocols, wearing of protective face masks, disinfection of high-touch surfaces, maintaining strict adherence to social distancing, promoting telecommuting for work, preventing unnecessary activities, instituting enhanced quarantine measures, and enacting rigorous contact tracing.^{33,34} During the three-month period of rising infections, the coverage rate of at least one dose of vaccine being administered increased from 1% to 40%, of which AstraZeneca accounted for 64% and Moderna accounted for 36%. This proactive response also helped to prevent cluster infections.³⁵ In Taiwan, there was no large-scale nosocomial transmission or outbreaks of COVID-19, which was very different from the infection rates of up to 60% that were seen in other countries.³⁶ In this study, in a low-prevalence setting, we found that for patients who were negative at the first screening prior to hospitalization, the subsequent rescreening of hospitalized high-risk individuals was sufficient to avoid nosocomial infections.

In our study, patients older than 75 years and those with potential exposure to SARS-CoV-2 were more likely to be rescreened, while the length of hospital stay was not related to the need for rescreening. Elderly people were determined to be more susceptible to COVID-19 infection, had poorer

viral clearance, and exhibited a higher case fatality rate. Moreover, there were concerns surrounding cluster infections in long-term care facilities and therefore this target group was given additional attention.³⁷ For people diagnosed with COVID-19, SARS-CoV-2 can be detected in the respiratory tract 2–3 days prior to the onset of symptoms, and it can be spread to contacts in as little as 15 minutes through airborne transmission.³⁵ Those who have had potential exposure to SARS-CoV-2 and have not been vaccinated were apparently the highest risk group. The median time for rescreening in our study was 4 days, which is consistent with the possible latent infection period range of 1 to 5 days before the onset of disease.³⁸

Another factor in our study associated with rescreening was the department that the patient attended. Compared with the Department of Internal Medicine where there were more patients with pneumonia or fever, cases in the Department of Neurology and those from the Cardiovascular Center were more likely to be rescreened. Although it has been recommended that emergency neurosurgery patients should be given priority and that elective neurosurgeries should be postponed during the COVID-19 epidemic,^{39,40} it should be borne in mind that any lack or delay of appropriate intervention may lead to deterioration of neurological function.^{40,41}

Therefore, for patients whose neurosurgery should not be delayed, mandatory preoperative screening for COVID-19 was proposed to help minimize the risks, as stipulated in the clinical practice guidelines.⁴² As with neurosurgery, scheduled invasive interventions were reserved for emergent cardiac patients.^{43–46} Additionally, multiple reports have suggested that patients with underlying cardiovascular comorbidities such as heart failure are at higher risk of severe disease and mortality due to COVID-19.^{44,47–50} Collectively, the rescreening of patients with worsening cardiovascular disease was indeed necessary. For patients attending the Department of Internal Medicine, the higher rescreening rate in the Division of Infectious Diseases may be because approximately half of the quarantined patients belonged to that division, while the lower rescreening rate in the Division of Hematology and Oncology could possibly be explained by the fact that around three-quarters of the cases were repeatedly included due to recurrent fever caused by the underlying disease or anticancer therapy.

Our study had several limitations. First, this study was conducted in a medical center with a low prevalence of COVID-19. The results reported herein may not be generalizable to other institutions with a higher prevalence of COVID-19. Hospitals in areas with moderate to high COVID-19 prevalence or a dominant SARS-CoV-2 Delta variant may require more expanded surveillance. More symptoms or signs should be included in the rescreening criteria or hospitalized patients should be extensively rescreened. Second, because this was a retrospective study and most information could only be retrieved from medical records, we were unable to clarify the condition of the disease in patients and the reasons for rescreening or not rescreening patients. Vaccination was an important factor that may affect the decision to rescreen, but complete information could not be obtained in this study because people generally received vaccination outside of hospitals in Taiwan. Nevertheless, we attempted to determine high-risk groups based upon quarantine levels and the departments in which they were being treated. Third, the heterogeneity of patients was large. Some patients who had persistent fever due to another disease would be repeatedly included. Moreover, the rescreening strategies in different departments varied greatly, and thus it was difficult to formulate rules. More research is needed to explore surveillance of COVID-19 in a hospital setting.

Conclusion

The proportion of rescreened cases was low, and the results of all rescreened cases came back negative. There was also no known subsequent cluster infection outbreak. This study determined that in a hospital with a low COVID-19 prevalence, it was safe to rescreen only high-risk cases, such as the elderly, those with potential prior exposure to SARS-CoV-2, and patients belonging to specific departments, which resulted in a rescreening strategy that was both low cost and effective. Further recognition of and adjustments in rescreening criteria remain paramount in different prevalence settings of COVID-19.

Disclosure

The authors report no conflicts of interest in this work.

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