A Universal Screening Strategy for SARS-CoV-2 Infection in Intensive Care Units: Korean Experience in a Single Hospital

Euijin Chang 1,2,*, Jae-Sung Choi 3,4,*, Tae Yun Park 3, Seung Bin Kim 4, Suhui Ko 5, Yang Sun Kwon 2, Eun Jin Kim 2, Hyunju Song 5, Hwa Kyung Noh 2, and Sang-Won Park 1,2,5

1Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea
2Infection Control Office, Seoul National University, Boramae Medical Center, Seoul, Korea
3Intensive Care Units, Seoul National University, Boramae Medical Center, Seoul, Korea
4Department of Thoracic and Cardiovascular Surgery, Seoul National University, Boramae Medical Center, Seoul, Korea
5Department of Internal Medicine, Seoul National University, Boramae Medical Center, Seoul, Korea

ABSTRACT

Background: Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection is not differentiated clinically from other respiratory infections, and intensive care units (ICUs) are vulnerable to in-hospital transmission due to interventions inducing respiratory aerosols. This study evaluated the effectiveness of universal SARS-CoV-2 screening in ICUs in terms of screened-out cases and reduction in anxiety of healthcare personnel (HCP).

Materials and Methods: This prospective single-armed observational study was conducted in 2 ICUs of a single hospital. The number of patients diagnosed with SARS-CoV-2 infection by the screening program and healthcare workers in ICUs that visited the SARS-CoV-2 screening clinic or infection clinic were investigated.

Results: During the 7-week study period, no positive screening case was reported among a total of 142 patients. Among 86 HCP in the ICUs, only 2 HCP sought medical consultation for SARS-CoV-2 infection during the initial 2 weeks.

Conclusion: A universal screening program for SARS-CoV-2 infection in ICUs with the coordination of other countermeasures in the hospital was reasonably effective in preventing in-hospital transmission in a pandemic situation and making clinical practices and HCP stable.

Keywords: SARS-CoV-2; COVID; Screening; Intensive care unit; Nosocomial infection

INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection is a worldwide pandemic causing extensive damage and overwhelming health care systems in many countries since it was first identified in December 2019 [1]. The spectrum of SARS-CoV-2 infection varies widely from asymptomatic disease to severe pneumonia [2-4]. The community-based spread is estimated to continue at least over 1 year worldwide [5]. At the current stage of community spread, the risk of nosocomial spread is high, and the result would be devastating, with partial or wide shut down of facilities, which are already
overburdened. During local SARS-CoV1 outbreaks in 2003 - 2004, the number of nosocomial transmissions also increased dramatically [6]. Moreover, asymptomatic or mild cases of SARS-CoV-2 infection are difficult to screen out by usual criteria [7]. SARS-CoV-2 infection is known to have overlapping clinical features with other respiratory infections; therefore, it is difficult to differentiate it reliably based only on clinical information [3].

SARS-CoV-2 is transmitted mainly through respiratory droplets. However, the procedures likely to generate high concentrations of respiratory secretions or aerosols which cause a much higher risk for transmission are commonly performed in intensive care units (ICUs), which makes ICUs vulnerable to the nosocomial spread of highly transmissible respiratory infections, such as SARS-CoV-2 infection [8]. The best preventative approach against the nosocomial transmission of SARS-CoV-2 infection in ICUs is not known, and therefore, we need a new reasonable systemic strategy to prevent infection.

Here, we tried to set up an active screening program for SARS-CoV-2 infection in ICUs to prevent the infection in line with multiple hospital-wide measures to counteract coronavirus disease 2019 (COVID-19). A universal screening program could be a financial burden with waste of resources and pose additional tasks to medical staffs. However, it could effectively control the initial influx of COVID-19 and provide stepwise countermeasures to relieve the risk of transmission in the hospital resulting the real prevention of COVID-19 and the decrease of healthcare workers’ anxiety. We evaluated the effectiveness of this program in terms of screened-out cases and the anxiety of healthcare personnel (HCP) in ICUs.

**MATERIALS AND METHODS**

1. **Study design and subjects**

To prevent unnoticed introduction and minimize exposure to SARS-CoV-2, we implemented a prospective single-armed observational screening program for SARS-CoV-2 in 2 ICUs at Boramae Medical Center beginning on 28 February 2020, which is a university-affiliated hospital with 761 beds and approximately 3,500 daily outpatient visits. The two ICUs consist of one medical ICU (17 beds) and one surgical ICU (18 beds). Target subjects were all patients who were in the ICUs or newly admitted to the ICUs since 28 February. The exception was patients who were expected to stay in ICUs for less than 24 hours due to acute transit care after invasive interventions or surgical operations under the expected turn-around time of 12 - 24 hours of the SARS-CoV-2 tests and those who had already been tested for SARS-CoV-2 infection in the emergency room (ER) or SARS-CoV-2 screening clinic within 24 hours before ICU admission. Chief medical and surgical intensivists at each ICU were in charge of the screening program details. Hospital policy required that any patient who development new fever or respiratory manifestation within 14 days of hospital admission should be subjected to another COVID-19 testing regardless of initial result.

The primary goal of this study was to estimate the number of patients diagnosed with SARS-CoV-2 infection by the screening program and patients diagnosed later that were undiagnosed initially in this program. The secondary endpoint was to determine the number of healthcare workers in the ICUs who visited the COVID-19 screening clinic or infection clinic in the hospital for a SARS-CoV-2 test as an index of HCP anxiety about SARS-CoV-2 infection in ICUs.
2. Clinical characteristics of the subjects
Clinical characteristics of the subjects on ICU admission were analyzed to assess whether the clinical features of subjects were similar to manifestations of SARS-CoV-2 infection except the epidemiologic linkage to COVID-19. Age, sex, underlying comorbidities, active problems, indication of ICU admission, status of endotracheal intubation, the presence of initial chest X-ray abnormalities, and the presence of leukocytosis, thrombocytopenia and elevation of C-reactive protein (CRP) level on ICU admission were reviewed. Leukocytosis was defined as a white blood cell count more than 10,000/mm³, thrombocytopenia as a platelet count less than 130 × 10³/mm³, and elevation of CRP level as more than 0.5 mg/dL.

3. The screening protocol
Test for SARS-CoV-2: Both nasopharyngeal and throat swabs were obtained for upper respiratory specimens, and sputum or transtracheal aspirates were gathered for lower respiratory specimens. Upper respiratory specimens were obtained from patients whose chest X-rays were normal or when lower respiratory specimens were difficult to collect. Lower respiratory specimens were used in patients who were intubated or had pneumonia. Respiratory specimens were tested with a PowerChek™ 2019-nCoV Real-time PCR Kit v.1.1 (Kogene Biotechnology, Seoul, Korea). This test kit used E gene detection for Betacoronaviruses and RdRP gene detection specific for SARS-CoV-2. The usual turn-around time of results was about 6 to 10 hours according to the timing of sample collection.

Personal protective equipment (PPE): Healthcare personnel were educated to wear a 4-piece PPE set (N95 respirator, disposable gown, glove, and facial shield) during a procedure likely to generate high concentrations of respiratory secretions or aerosols, including respiratory specimen collection. Until the SARS-CoV-2 test results came out, HCP wore the appropriate PPE as recommended according to case-by-case considerations [9].

Isolation of the examinee: Each ICU had two negative pressure isolation rooms, and subject patients were isolated until the screening results were obtained. In case of competition for the isolation room, the intensivists made a triage in view of the severity and aerosol/secretion-generating potential. The rest of the patients with lower risk were positioned in the arbitrary cohort area of each ICU.

Active surveillance for HCP: Fever or respiratory symptoms were monitored daily for HCP in charge, and the presence of such symptoms was reported to the Infection Control Office, which considers immediate SARS-CoV-2 testing and temporary exclusion from work until the notification of the test result if needed. In addition, HCP who wanted to seek medical examination for SARS-CoV-2 infection due to any other medical discomfort could also visit an infection clinic for a SARS-CoV-2 test free of charge.

4. Hospital-wide strategies to prevent the influx of unnoticed COVID-19 patients
The hospital had several systematic measures, as follows, to prevent the unnoticed influx of SARS-CoV-2-infected patients and to diagnose the infection in a timely manner, and the ICU screening program was one of them (Fig. 1). Respiratory clinics were positioned outside the hospital and had the role of screening all patients with fever or respiratory symptoms to allow the patients within-the-hospital services. A dedicated COVID-19 screening clinic was run to address patients suspected of having SARS-CoV-2 infection and to collect respiratory specimens for the SARS-CoV-2 test [10]. Respiratory isolation rooms with a negative pressure
facility were operated for patients with respiratory infections of undetermined etiology until the confirmation of the SARS-CoV-2 test. For the laboratory test of SARS-CoV-2, an in-hospital laboratory facility and outsourcing to a commercial laboratory to accommodate a potentially large volume of tests were prepared and operated. Regular newsletters regarding COVID-19-related matters were issued to communicate internally with the hospital workforce.

5. Ethics approval and consent to participate
This study was approved by the institutional review board at Boramae Medical Center (20–2020-36). Collection of informed consent was waived because this study was conducted as an institutional policy to improve infection control and was retrospective in the final data collection. All personal identifiers were anonymized for confidentiality before data processing. This research was performed in compliance with the Helsinki Declaration.

RESULTS
For 7 weeks following 28 February 2020, 177 patients were admitted to the medical ICU (MICU) and surgical ICU (SICU) in total, with 77 patients in the MICU and 100 patients in the SICU. Among them, 35 patients (19.7%) did not go through the screening test for SARS-CoV-2 infection due to their short stay of less than 24 hours in the ICU (4 patients) or the confirmation of negativity for SARS-CoV-2 in the ER or SARS-CoV-2 screening clinic within one day before ICU admission (31 patients). There was no initial positive test result among the 142 patients and none of them got repetitive tests for COVID-19. Also, none of the 142 patients had epidemiologic risk factors for SARS-CoV-2 infection within recent 2 weeks. Upper respiratory specimens (both nasopharynx and throat swabs) were obtained from 63 (44.4%) patients, lower respiratory specimens were obtained from 78 (54.9%) patients, and both upper and lower respiratory specimens were obtained from 1 (0.7%) patient (Table 1). Meanwhile, 157 patients confirmed with COVID-19 were isolated and treated in the study.
hospital during the same period. The number of COVID-19 tests performed in the respiratory/fever clinic were 854 cases with a positivity of 2 cases (0.2%). During the study period of 7 weeks, there were 86 HCP working in the ICUs on a regular basis, excluding HCP from other departments working in the ICUs irregularly, and only 2 (2.3%) HCP sought medical consultation for SARS-CoV-2 infection only within the initial 2 weeks of the program. There was a total of 58 HCP who sought medical consultation for SARS-CoV-2 infection in the hospital during the study period, and the majority of them were working in COVID-19 wards.

Table 1. Clinical characteristics of screened patients on intensive care unit admission (n = 142)

| Characteristics                                                      | N (%), if not otherwise specified |
|---------------------------------------------------------------------|----------------------------------|
| Age, years (mean ± SD)                                               | 65.9 ± 16.2                      |
| Age range                                                           |                                  |
| <60 years                                                           | 39 (27.5)                        |
| 60 - 79 years                                                       | 73 (51.4)                        |
| ≥80 years                                                           | 30 (21.1)                        |
| Sex                                                                 | 49 (34.5) : 93 (65.5)            |
| Presence of comorbidities                                           |                                  |
| Diabetes mellitus                                                   | 46 (32.4)                        |
| Chronic heart disease                                               | 28 (19.7)                        |
| Malignancy                                                          | 25 (17.6)                        |
| Chronic kidney disease                                              | 22 (15.5)                        |
| Cerebrovascular disease                                             | 20 (14.1)                        |
| Chronic liver disease                                               | 12 (8.5)                         |
| COPD/bronchial asthma                                               | 11 (7.7)                         |
| None                                                                | 46 (32.4)                        |
| Diagnosis on ICU admission                                          |                                  |
| Seizure/stroke/other neurologic problems                            | 38 (26.8)                        |
| Pneumonia                                                           | 26 (18.3)                        |
| Malignancy                                                          | 16 (11.3)                        |
| Vascular problems                                                   | 15 (10.6)                        |
| Sepsis/diabetic ketoacidosis                                        | 12 (8.5)                         |
| Gastrointestinal bleeding, obstruction or perforation               | 11 (7.7)                         |
| Heart failure                                                       | 6 (4.2)                          |
| Fracture                                                            | 6 (4.2)                          |
| Renal transplantation/acute kidney injury                          | 5 (3.5)                          |
| Acute exacerbation of COPD or asthma/other airway problems          | 4 (2.8)                          |
| Cardiac arrest                                                      | 3 (2.1)                          |
| Indication for ICU admission                                        |                                  |
| Postoperative care                                                  | 74 (52.1)                        |
| Mechanical ventilation                                              | 28 (19.7)                        |
| Close monitoring                                                    | 24 (16.9)                        |
| Conventional renal replacement therapy                              | 9 (6.3)                          |
| Post-CPR care                                                       | 7 (4.9)                          |
| Intubated state at SARS-CoV-2 screening                             | 81 (57.0)                        |
| Chest abnormality on ICU admission                                  |                                  |
| No active lung lesion                                               | 72 (50.7)                        |
| Patchy or reticular opacities                                       | 31 (21.8)                        |
| Pulmonary edema                                                     | 16 (11.3)                        |
| Granulomas/nodules/atelectasis                                      | 12 (8.5)                         |
| Pleural effusion                                                     | 11 (7.7)                         |
| Laboratory abnormalities                                            |                                  |
| Leukocytosis                                                        | 87 (61.3)                        |
| Thrombocytopenia                                                    | 24 (16.9)                        |
| Elevation of C-reactive protein level                               | 93 (65.5)                        |

Data are presented as n (%), if not otherwise specified.
SD, standard deviation; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; CPR, cardiopulmonary resuscitation; SARS-CoV-2, severe acute respiratory syndrome-coronavirus-2.
Among the 142 subjects going through screening for SARS-CoV-2 infection, 93 (65.5%) patients were male, and 103 (72.5%) patients were over 60 years old, with a mean age of 65.9 years (standard deviation, ± 16.2 years). Chronic comorbidities were present in 96 (67.6%) patients; 46 (32.4%) patients had diabetes mellitus, 28 (19.7%) patients had a chronic heart disease, and 25 (17.6%) patients had a malignancy. The active problems on ICU admission were neurologic problems such as stroke and seizure in 38 (26.8%) patients, pneumonia in 26 (18.3%) patients and vascular diseases such as coronary heart disease or peripheral vascular disease in 15 (10.6%) patients. The indications for ICU admission were the need for mechanical ventilation in 28 (19.7%) patients, continuous renal replacement therapy in 9 (6.3%) patients, post-cardiopulmonary resuscitation (CPR) care in 7 (4.9%) patients and postoperative care in 74 (52.1%) patients. Endotracheal intubation was already performed at the point of SARS-CoV-2 screening in the ICUs in 81 (57.0%) patients, and the major causes of intubation were type I or II respiratory failure, post-CPR care, and postoperative care. Abnormal findings on chest X-ray or computed tomography were present in 70 (49.3%) patients, and 31 of them showed patchy or reticular lung opacities indicating pneumonia. Leukocytosis, thrombocytopenia and an elevated CRP level were observed in 87 (61.3%), 24 (16.9%) and 93 (65.5%) patients, respectively (Table 1). Among the 142 patients, 64 (45.1%) patients without epidemiologic risk factors for COVID-19, new onset of fever or respiratory symptoms, and evidence of pneumonia were admitted to the ICUs directly from the ER on the same day as the initial ER visit, and 78 patients were transferred from general wards. The median time from initial hospital admission to ICU admission for the 78 patients transferred from general wards was 3.5 days (range, 1 - 64 days).

**DISCUSSION**

This study is the first prospective study to investigate the efficacy of a screening system for SARS-CoV-2 infection in ICUs under a pandemic situation. The urgent reasons to implement this program were, first, to cope with the real threat of the SARS-CoV-2 pandemic and, second, to ease the extreme anxiety of healthcare workers in the ICUs. Before the start of this program, we had already considered this screening program, but a consensus was not reached between ICU members due to the burden of logistics and the uncertainty of effectiveness without prior positive studies or governmental guidelines. However, there was a case of CPR and an uncoordinated order for the SARS-CoV-2 test in the SICU, which was preliminarily positive. At the early stage of the SARS-CoV-2 pandemic, we had two stages of screening and confirmation tests. With the preliminary positive result, a wide range of healthcare workers inside and outside the ICU were self-quarantined, and the ICU was temporarily shut down. The final confirmatory result was negative, and all the precautionous actions were normalized. However, the overall process was so confusing, complicated and stressful that a full consensus to introduce a systematic screening program and counterstrategy scenario was reached to minimize the potential damage that could happen in ICUs in this SARS-CoV-2 pandemic period. If there were a truly infected patient, the damage would be to a much greater extent.

As this was not a comparative study, we could not prove the effectiveness of this program in terms of preventing the influx of SARS-CoV-2-infected patients. In addition, no positive screening results for SARS-CoV-2 were found. There are several possible explanations for this result. As of April 17, 2020, there were 624 confirmed cases of SARS-CoV-2 infection among approximately 9,776,000 citizens in Seoul, where this hospital is located. This means that
the pandemic density in this area was not very high. A relatively low level of infections in the community might contribute to a low chance of SARS-CoV-2 influx to the hospital. Another point to be addressed is that there were multiple barriers against SARS-CoV-2-infected patients entering the ICUs from the community. As described in the Methods section, we have multiple measures at each point of patient entry to screen out SARS-CoV-2 infection. However, the basic characteristics of patients in this study showed that the study subjects represented common ICU patients, and the majority of the patients still had the risk of SARS-CoV-2 infection, considering the high proportion (45.1%) of direct ICU admission from the ER without SARS-CoV-2 screening and the short hospital stay (median 3.5 days) before ICU admission in the patients transferred from general wards. This means that the patients could be in the incubation period at first and show signs of SARS-CoV-2 infection after ICU admission.

This program seems to be a reasonable measure to prevent SARS-CoV-2 infection in the absence of scientifically solid guidelines. Several other small studies supported that universal screening could be helpful for preventing in-hospital transmission of SARS-CoV-2. Sutton et al reported a universal screening in women who were admitted for delivery at a hospital in New York under the intensive pandemic; 15.4% of subjects were positive for SARS-CoV-2, and 13.5% were asymptomatic on admission [11]. Also, Al-Shamsi et al conducted a universal screening for COVID-19 infection in all asymptomatic patients with cancer before admission at the hospital in Dubai under the pandemic situation; 7 patients were diagnosed as COVID-19 infection among 85 patients [12]. Additionally, the optimal specimen for screening is unknown, but upper respiratory specimens are a reasonable option in view of the high SARS-CoV-2 viral load of the nasopharynx or oropharynx in the early phase of illness and lower respiratory specimens in the presence of lung lesions [13].

This program also seems to be effective from the view of HCP working in the ICUs. SARS-CoV-2 infection in HCP is an important problem in this pandemic situation [7, 14]. Our hospital has a systematic protocol to assess and diagnose HCP infection free of charge according to the degree of infection risk. Since the implementation of the screening program, there was no major feedback regarding the safety of HCP, and the absolute number of HCP seeking medical consultation for SARS-CoV-2 infection was small.

There are several limitations and points to be improved in our study. First, we did not experience a high influx burden of SARS-CoV-2 infection into the ICUs and are not sure if this program would still work well in such circumstances. Second, the ICU screening program is coordinated with other hospital-wide countermeasures, and all these measures may also be negatively affected by the overwhelming burden of SARS-CoV-2 infection, disrupting the integrity of effectiveness. Third, there is further room for improvement. The subjects for the screening program may be further detailed according to their degree of risk. The facility of the ICU needs to be improved. Most ICUs in Korea have a common spatial layout, and only a minority of hospitals have individual rooms for each ICU patient.

In conclusion, the universal screening program for SARS-CoV-2 infection in ICUs was reasonably effective in coping with the infection and made the clinical practices stable and HCP not anxious. This program, in line with other coordinated countermeasures to prevent and diagnose SARS-CoV-2 infection early in ICUs, may be useful in other hospitals or countries under a pandemic situation. Further experience with this program may guide finer revision of practice details.
REFERENCES

1. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KSM, Lau EHY, Wong JY, Xing X, Xiang N, Wu Y, Li C, Chen Q, Li D, Liu T, Zhao J, Liu M, Tu W, Chen C, Jin L, Yang R, Wang Q, Zhou S, Wang R, Liu H, Yao Y, Liu Y, Shao G, Li H, Tao Z, Yang Y, Peng J, Liu B, Ma Z, Zhang Y, Shi G, Lam TTY, Wu JT, Gao GF, Cowling BJ, Yang B, Leung GM, Feng Z. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med 2020;382:1199-207.

2. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, Zimmer T, Thiel V, Janke C, Guggemos W, Seilmaier M, Drosten C, Vollmar P, Zangho S, Wölfel R, Hoelscher M. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. N Engl J Med 2020;382:970-1.

3. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Li J, Zeng G, Yuen KY, Chen RC, Tang CL, Wang T, Chen PY, Xiang J, Li SY, Wang JL, Liang ZJ, Peng YX, Wei L, Liu Y, Hu YH, Peng P, Wang JM, Liu JY, Chen Z, Li G, Zheng ZJ, Qiu SQ, Luo J, Ye CJ, Zhu SY, Zhong NS; China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382:1708-20.

4. Weiss P, Murdoch DR. Clinical course and mortality risk of severe COVID-19. Lancet 2020;395:1014-5.

5. Puui T. How long will the coronavirus pandemic last? Available at: https://www.zmescience.com/medicine/how-long-will-the-coronavirus-pandemic-last/. Accessed 28 April 2020.

6. Svoboda T, Henry B, Shulman L, Kennedy E, Rea E, Ng W, Wallington T, Yaffe B, Gournis E, Vicencio E, Basrur S, Glazier RH. Public health measures to control the spread of the severe acute respiratory syndrome during the outbreak in Toronto. N Engl J Med 2004;350:2352-61.

7. Hunter E, Price DA, Murphy E, van der Loeff IS, Baker KF, Lendrem D, Schmid ML, Pareja-Cebrian L, Welch A, Payne BA, Duncan CJA. First experience of COVID-19 screening of healthcare workers in England. Lancet 2020;395:e77-8.

8. Wu D, Wu T, Liu Q, Yang Z. The SARS-CoV-2 outbreak: what we know. Int J Infect Dis 2020;94:44-8.

9. Centers for Disease Control and Prevention (CDC). Interim U.S. guidance for risk assessment and public health management of healthcare personnel with potential exposure in a healthcare setting to patients with 2019 novel coronavirus (2019-nCoV). Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assesment-hcp.html. Accessed 28 April 2020.

10. Koo BK, Bang JH, Kim SY, Kim EJ, Park SW. Glove-Wall system for respiratory specimen collection and COVID-19 mass screening. Infect Chemother 2020;52:219-21.

11. Sutton D, Fuchs K, D’Alton M, Goffman D. Universal screening for SARS-CoV-2 in women admitted for delivery. N Engl J Med 2020;382:2163-4.

12. Al-Shamsi HO, Coomes EA, Alrawi S. Screening for COVID-19 in asymptomatic patients with cancer in a hospital in the United Arab Emirates. JAMA Oncol 2020. [Epub ahead of print].

13. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, Yu J, Kang M, Song Y, Xia J, Guo Q, Song T, He J, Yen HL, Peiris M, Wu J. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. N Engl J Med 2020;382:1177-9.

14. Zhan M, Qin Y, Yue X, Zhu S. Death from Covid-19 of 23 health care workers in China. N Engl J Med 2020;382:2267-8.