ABSTRACT

Background: A coronavirus disease 2019 (COVID-19) outbreak started in February 2020 and was controlled at the end of March 2020 in Daegu, the epicenter of the coronavirus outbreak in Korea. The aim of this study was to describe the clinical course and outcomes of patients with COVID-19 in Daegu.

Methods: In collaboration with Daegu Metropolitan City and Korean Center for Diseases Control, we conducted a retrospective, multicenter cohort study. Demographic, clinical, treatment, and laboratory data, including viral RNA detection, were obtained from the electronic medical records and cohort database and compared between survivors and non-survivors. We used univariate and multi-variable logistic regression methods and Cox regression model and performed Kaplan–Meier analysis to determine the risk factors associated with the 28-day mortality and release from isolation among the patients.

Results: In this study, 7,057 laboratory-confirmed patients with COVID-19 (total cohort) who had been diagnosed from February 18 to July 10, 2020 were included. Of the total cohort, 5,467 were asymptomatic to mild patients (77.4%) (asymptomatic: 30.6% and mild: 46.8%), 985 moderate (14.0%), 380 severe (5.4%), and 225 critical (3.2%). The mortality of the patients was 2.5% (179/7,057). The Cox regression hazard model for the patients with available clinical information (core cohort) (n = 2,254) showed the risk factors for 28-day mortality: age > 70 (hazard ratio [HR], 4.219, \( P = 0.002 \)), need for O2 supply at admission (HR, 2.995; \( P = 0.001 \)), fever (> 37.5°C) (HR, 2.808; \( P = 0.001 \)), diabetes (HR, 2.119; \( P = 0.008 \)), cancer (HR, 3.043; \( P = 0.011 \)), dementia (HR, 5.252; \( P = 0.008 \)), neurological disease (HR, 2.084; \( P = 0.039 \)), heart failure (HR, 3.234; \( P = 0.012 \)), and hypertension (HR, 2.160; \( P = 0.017 \)). The median duration for release from isolation was 33 days (interquartile range, 24.0–46.0) in survivors. The Cox proportional hazard model for the long duration of isolation included severity, age > 70, and dementia.

Conclusion: Overall, asymptomatic to mild patients were approximately 77% of the total cohort (asymptomatic, 30.6%). The case fatality rate was 2.5%. Risk factors, including older age, need for O2 supply, dementia, and neurological disorder at admission, could help clinicians to identify COVID-19 patients with poor prognosis at an early stage.
INTRODUCTION

The coronavirus disease 2019 (COVID-19) outbreak which was caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a global pandemic infectious disease. Daegu City, Korea, had the first large outbreak of COVID-19 outside China. 

In Daegu, the outbreak crisis started on February 18, 2020, and peaked on February 29, 2020, with 741 new cases confirmed in a day. This crisis was caused by Shincheonji Daegu Church worship events. The outbreak was controlled by the active management of patients with isolation in hospitals and 15 therapeutic living centers, treatment of patients and prevention with civic participation in the use of mask, hand hygiene, and social distancing. Despite immense pressures on its health-care system, Daegu was able to avoid the destruction of the health-care system with these interventions that relieved hospital shortages and protected health-care workers. After the outbreak, the detection rate of confirmed patients was lower than other areas.

A report about the clinical course and outcomes of COVID-19 in Korea with 3,060 patients, gave us a lot of information for the COVID-19 patients. A report that focused on the test, tracing and treatment of COVID-19 patients in Seoul was also published. However, whole picture of Daegu COVID-19 outbreak, which is the first outbreak crisis in Korea, was not reported until now. Therefore, the aim of this study is to evaluate and describe the clinical characteristics, risk factors for the case fatality rate, and duration of isolation in patients with COVID-19 in Daegu Metropolitan City (February to June 2020) after making and clearing of Daegu COVID-19 cohort data.

In this study, the details of all patients registered in Daegu Metropolitan City with polymerase chain reaction (PCR)-confirmed COVID-19 are presented. Only a few city-wide large-scale cohort studies on patients with COVID-19 were conducted.

METHODS

Study design, participants, and data collection

Korea Centers for Diseases Control and Prevention (KCDC) requested that all hospitals in Daegu submit clinical records for the standardized data collection to make web-based electronic database (iCReat). Thus, nine hospitals in Daegu submitted clinical data to the KCDC database. One additional hospital data and data of Daegu patients with COVID-19 chest were merged for the analysis (total cohort) (Daegu MediCity database). Fig. 1 shows the flowchart of cohort establishment. Data on the initial and worst severity clinical characteristics, worst illness severity, outcomes, radiological assessments (e.g., chest radiographs or computed tomography [CT]), and the time to symptom onset to release from isolation were obtained from 10 hospitals (5 tertiary hospitals and 5 secondary hospitals) (Table 1, A-J hospitals) to establish the core cohort (Fig. 1). Patients in the core cohort were admitted patients in 10 hospitals in Daegu with available clinical information. Most asymptomatic and approximately 80% of mild patients were not included due to isolated in the therapeutic living center (facility isolation). On the initial phase (from February 18, 2020, to early March 2020) of the outbreak, all of the patients were admitted to the hospitals. On March 2, 2020, facility (therapeutic living centers) isolation was done for asymptomatic
Characteristics of COVID-19 Cohort Patients in Daegu

Fig. 1. Patient flow diagram of 2,254 confirmed patients with coronavirus disease 2019 from the core cohort for the analysis of the clinical course and outcome.

KCDC = Korea Centers for Diseases Control and Prevention, PCR = polymerase chain reaction.

Table 1. Clinical characteristics and outcomes of patients hospitalized for the treatment of COVID-19 in 10 hospitals (core cohort) in Daegu

| Characteristics                                | Alive (n = 2,075) | Dead (n = 179) | Total (n = 2,254) | P value |
|------------------------------------------------|------------------|----------------|-------------------|---------|
| **Hospitals in Daegu**                          |                  |                |                   | < 0.001 |
| A                                              | 642 (30.9)       | 22 (12.3)      | 664 (29.5)        |         |
| B                                              | 531 (25.6)       | 42 (23.5)      | 573 (25.4)        |         |
| C                                              | 358 (17.3)       | 0 (0.0)        | 358 (15.9)        |         |
| D                                              | 180 (8.7)        | 3 (1.7)        | 183 (8.1)         |         |
| E                                              | 106 (5.1)        | 19 (10.6)      | 125 (5.5)         |         |
| F                                              | 104 (5.0)        | 16 (8.9)       | 120 (5.3)         |         |
| G                                              | 67 (3.2)         | 23 (12.8)      | 90 (4.0)          |         |
| H                                              | 50 (2.4)         | 25 (14.0)      | 75 (3.3)          |         |
| I                                              | 21 (1.0)         | 20 (11.2)      | 41 (1.8)          |         |
| J                                              | 16 (0.8)         | 9 (5.0)        | 25 (1.1)          |         |
| **Intensive care unit**                        |                  |                |                   | < 0.001 |
| No                                             | 1,989 (95.9)     | 106 (59.2)     | 2,095 (92.9)      |         |
| Yes                                            | 86 (4.1)         | 73 (40.8)      | 159 (7.1)         |         |
| **Symptom onset or the first diagnosis to isolation release** |                  |                |                   | < 0.001 |
| Mild                                           | 656 (32.0)       | 0 (0.0)        | 664 (29.5)        |         |
| Moderate                                       | 985 (47.5)       | 0 (0.0)        | 985 (43.7)        |         |
| Severe                                         | 380 (18.3)       | 0 (0.0)        | 380 (16.9)        |         |
| Critical                                       | 46 (2.2)         | 179 (100.0)    | 225 (10.0)        |         |
| **Severity (worst severity during the clinical course)** |                  |                |                   | < 0.001 |
| Mild                                           | 713 (34.4)       | 95 (53.1)      | 808 (35.8)        |         |
| Moderate                                       | 1,362 (65.6)     | 84 (46.9)      | 1,446 (64.2)      |         |
| Severe                                         | 16 (0.8)         | 9 (5.0)        | 25 (1.1)          |         |
| Critical                                       | 16 (0.8)         | 9 (5.0)        | 25 (1.1)          |         |
| **Sex**                                        |                  |                |                   | < 0.001 |
| Male                                           | 713 (34.4)       | 95 (53.1)      | 808 (35.8)        |         |
| Female                                         | 1,362 (65.6)     | 84 (46.9)      | 1,446 (64.2)      |         |
| **Age**                                        |                  |                |                   | < 0.001 |
| No Age                                         | 1,622 (78.2)     | 39 (21.8)      | 1,661 (73.7)      |         |
| Yes Age                                        | 433 (21.8)       | 140 (78.2)     | 573 (26.3)        |         |
| **Pregnancy**                                  |                  |                |                   | 0.584   |
| No                                             | 2,062 (99.4)     | 179 (100.0)    | 2,241 (99.4)      |         |
| Yes                                            | 13 (0.6)         | 0 (0.0)        | 13 (0.6)          |         |
| **Body mass index**                            |                  |                |                   | 0.224   |
| No                                             | 23.2 (20.9–25.4) | 23.5 (21.3–26.4) | 23.2 (20.9–25.6) |         |
| Yes                                            | 23.2 (20.9–25.4) | 23.5 (21.3–26.4) | 23.2 (20.9–25.6) |         |
| **Body mass index, > 25**                      |                  |                |                   | 0.027   |
| No                                             | 1,016 (72.2)     | 52 (60.5)      | 1,068 (71.5)      |         |
| Yes                                            | 392 (27.8)       | 34 (39.5)      | 426 (28.5)        |         |
| **Initial systolic blood pressure**             |                  |                |                   | 0.995   |
| No                                             | 133.0 (120.0–148.0) | 133.5 (118.0–152.0) | 133.0 (120.0–149.0) |         |
| Yes                                            | 133.0 (120.0–148.0) | 133.5 (118.0–152.0) | 133.0 (120.0–149.0) |         |
| **Shock**                                      |                  |                |                   | < 0.001 |
| No                                             | 2,008 (99.9)     | 158 (92.9)     | 2,166 (99.3)      |         |
| Yes                                            | 9 (0.1)          | 12 (7.1)       | 15 (0.7)          |         |

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Table 1. (Continued) Clinical characteristics and outcomes of patients hospitalized for the treatment of COVID-19 in 10 hospitals (core cohort) in Daegu

| Characteristics                                           | Alive (n = 2,075) | Dead (n = 179) | Total (n = 2,254) | P value |
|-----------------------------------------------------------|-------------------|---------------|-------------------|---------|
| Need for O2 supply at admission                           |                   |               |                   | < 0.001 |
| No                                                        | 1,849 (89.1)      | 65 (36.3)     | 1,914 (84.9)      |         |
| Yes                                                       | 226 (10.9)        | 114 (63.7)    | 340 (15.1)        |         |
| Fever, > 37.5°C                                           |                   |               |                   | < 0.001 |
| No                                                        | 1,724 (83.1)      | 112 (62.6)    | 1,836 (81.5)      |         |
| Yes                                                       | 351 (16.9)        | 67 (37.4)     | 418 (18.5)        |         |
| Diabetes                                                  |                   |               |                   | < 0.001 |
| No                                                        | 1,777 (85.6)      | 102 (57.0)    | 1,879 (83.4)      |         |
| Yes                                                       | 298 (14.4)        | 77 (43.0)     | 375 (16.6)        |         |
| Heart failure                                             |                   |               |                   | < 0.001 |
| No                                                        | 2,046 (98.6)      | 165 (92.2)    | 2,211 (98.3)      |         |
| Yes                                                       | 29 (1.4)          | 14 (7.8)      | 43 (1.9)          |         |
| Hypertension                                              |                   |               |                   | < 0.001 |
| No                                                        | 1,541 (74.3)      | 67 (37.4)     | 1,608 (71.3)      |         |
| Yes                                                       | 534 (25.7)        | 112 (62.6)    | 646 (28.7)        |         |
| Chronic heart disease except heart failure or hypertension|                   |               |                   | < 0.001 |
| No                                                        | 1,986 (95.7)      | 158 (88.3)    | 2,144 (95.1)      |         |
| Yes                                                       | 89 (4.3)          | 21 (11.7)     | 110 (4.9)         |         |
| Asthma                                                    |                   |               |                   | 0.132   |
| No                                                        | 2,018 (97.3)      | 170 (95.0)    | 2,188 (97.1)      |         |
| Yes                                                       | 57 (2.7)          | 9 (5.0)       | 66 (2.9)          |         |
| COPD                                                      |                   |               |                   | 0.773   |
| No                                                        | 2,049 (98.7)      | 174 (97.2)    | 2,223 (98.6)      |         |
| Yes                                                       | 26 (1.3)          | 5 (2.8)       | 31 (1.4)          |         |
| Chronic renal disease                                     |                   |               |                   | < 0.001 |
| No                                                        | 2,054 (99.0)      | 165 (92.2)    | 2,219 (98.4)      |         |
| Yes                                                       | 21 (1.0)          | 14 (7.8)      | 35 (1.6)          |         |
| Cancer                                                    |                   |               |                   | < 0.001 |
| No                                                        | 2,010 (96.9)      | 159 (88.8)    | 2,169 (96.2)      |         |
| Yes                                                       | 65 (3.1)          | 20 (11.2)     | 85 (3.8)          |         |
| Chronic liver disease                                     |                   |               |                   | 0.770   |
| No                                                        | 2,041 (98.4)      | 175 (97.8)    | 2,216 (98.3)      |         |
| Yes                                                       | 34 (1.6)          | 4 (2.2)       | 38 (1.7)          |         |
| Neurological disease                                      |                   |               |                   | < 0.001 |
| No                                                        | 2,067 (99.6)      | 172 (96.1)    | 2,239 (99.3)      |         |
| Yes                                                       | 8 (0.4)           | 7 (3.9)       | 15 (0.7)          |         |
| Hematological disease                                     |                   |               |                   | 0.090   |
| No                                                        | 2,060 (99.3)      | 175 (97.8)    | 2,235 (99.2)      |         |
| Yes                                                       | 15 (0.7)          | 4 (2.2)       | 19 (0.8)          |         |
| HIV                                                       |                   |               |                   | 0.972   |
| No                                                        | 2,070 (99.8)      | 178 (99.4)    | 2,248 (99.7)      |         |
| Yes                                                       | 5 (0.2)           | 1 (0.6)       | 6 (0.3)           |         |
| Autoimmune disease                                        |                   |               |                   | 0.210   |
| No                                                        | 2,063 (99.4)      | 176 (98.3)    | 2,239 (99.3)      |         |
| Yes                                                       | 12 (0.6)          | 3 (1.7)       | 15 (0.7)          |         |
| Dementia                                                  |                   |               |                   | < 0.001 |
| No                                                        | 1,950 (94.0)      | 123 (68.7)    | 2,073 (92.0)      |         |
| Yes                                                       | 125 (6.0)         | 56 (31.3)     | 181 (8.0)         |         |
| Psychiatric disease                                       |                   |               |                   | 0.006   |
| No                                                        | 1,957 (94.3)      | 159 (88.8)    | 2,116 (93.9)      |         |
| Yes                                                       | 118 (5.7)         | 20 (11.2)     | 138 (6.1)         |         |
| Smoking and ex-smoking                                    |                   |               |                   | 0.110   |
| No                                                        | 1,938 (93.4)      | 161 (89.9)    | 2,099 (93.1)      |         |
| Yes                                                       | 137 (6.6)         | 18 (10.1)     | 155 (6.9)         |         |
| Mental status, worst during admission                     |                   |               |                   | < 0.001 |
| Alert                                                     | 1,955 (94.2)      | 6 (3.4)       | 1,961 (87.0)      |         |
| Drowsy                                                    | 78 (3.8)          | 26 (14.5)     | 104 (4.6)         |         |
| Pain response                                             | 10 (0.5)          | 4 (2.2)       | 14 (0.6)          |         |
| Unresponsive                                              | 5 (0.2)           | 92 (51.4)     | 97 (4.3)          |         |
| Sedation                                                  | 27 (1.3)          | 51 (26.5)     | 78 (3.5)          |         |

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Table 1. (Continued) Clinical characteristics and outcomes of patients hospitalized for the treatment of COVID-19 in 10 hospitals (core cohort) in Daegu

| Characteristics                      | Alive (n = 2,075) | Dead (n = 179) | Total (n = 2,254) | P value |
|--------------------------------------|------------------|---------------|------------------|---------|
| CRRT                                 |                  |               |                  | 1.000   |
| No                                   | 2,070 (99.8)     | 179 (100.0)   | 2,249 (99.8)     |         |
| Yes                                  | 5 (0.2)          | 0 (0.0)       | 5 (0.2)          |         |
| Vasopressor                          |                  | < 0.001       |                  |         |
| No                                   | 2,067 (99.6)     | 151 (84.4)    | 2,218 (98.4)     |         |
| Yes                                  | 8 (0.4)          | 28 (15.6)     | 36 (1.6)         |         |
| Lopinavir/ritonavir                  |                  | 0.700         |                  |         |
| No                                   | 1,300 (62.7)     | 109 (60.9)    | 1,409 (62.5)     |         |
| Yes                                  | 775 (37.3)       | 70 (39.1)     | 845 (37.5)       |         |
| Interferon-beta                      |                  | < 0.001       |                  |         |
| No                                   | 2,074 (100.0)    | 174 (97.2)    | 2,248 (99.7)     |         |
| Yes                                  | 1 (0.0)          | 5 (2.8)       | 6 (0.3)          |         |
| Ribavirn                             |                  | 0.372         |                  |         |
| No                                   | 2,074 (100.0)    | 178 (99.4)    | 2,252 (99.9)     |         |
| Yes                                  | 1 (0.0)          | 1 (0.6)       | 2 (0.1)          |         |
| Hydroxychloroquine                   |                  | 0.001         |                  |         |
| No                                   | 1,554 (74.9)     | 113 (63.1)    | 1,667 (74.0)     |         |
| Yes                                  | 521 (25.1)       | 66 (36.9)     | 587 (26.0)       |         |
| Steroid                              |                  | < 0.001       |                  |         |
| No                                   | 2,057 (99.1)     | 164 (91.6)    | 2,221 (98.5)     |         |
| Yes                                  | 18 (0.9)         | 15 (8.4)      | 33 (1.5)         |         |
| Remdesivir                           |                  | 1.000         |                  |         |
| No                                   | 2,074 (100.0)    | 179 (100.0)   | 2,253 (100.0)    |         |
| Yes                                  | 1 (0.0)          | 0 (0.0)       | 1 (0.0)          |         |
| Antibiotic                           |                  | < 0.001       |                  |         |
| No                                   | 1,231 (59.3)     | 46 (25.7)     | 1,277 (56.7)     |         |
| Yes                                  | 844 (40.7)       | 133 (74.3)    | 977 (43.3)       |         |
| Worst hemoglobin                     |                  | 0.001         |                  |         |
| No                                   | 11.7 (10.6–12.8) | 9.1 (7.4–11.3)| 11.6 (10.5–12.7) |         |
| Yes                                  | 190.6 (170.0–243.0) | 111.0 (57.0–159.0) | 193.0 (146.5–239.0) |         |
| Worst platelet                       |                  | < 0.001       |                  |         |
| No                                   | 7.0 (5.6–8.7)    | 15.4 (10.6–21.6)| 7.2 (5.7–9.2)     |         |
| Yes                                  | 1.1 (1.1–1.3)    | 1.4 (1.2–1.9) | 1.2 (1.1–1.4)    |         |
| Worst AST                            |                  | < 0.001       |                  |         |
| No                                   | 34.0 (21.0–57.0) | 52.0 (27.0–136.0)| 35.0 (22.0–60.0)  |         |
| Yes                                  | 34.0 (24.0–51.0) | 90.0 (51.0–274.0)| 35.0 (25.0–57.0)  |         |
| Worst creatinine                     |                  | < 0.001       |                  |         |
| No                                   | 0.8 (0.7–1.0)    | 1.6 (1.0–3.3) | 0.8 (0.7–1.1)    |         |
| Yes                                  | 460.0 (364.0–596.0) | 763.0 (562.0–1,432.5) | 474.0 (373.5–637.0) |         |
| Worst lactate dehydrogenase          |                  | < 0.001       |                  |         |
| No                                   | 0.8 (0.5–1.2)    | 1.4 (0.8–2.7) | 0.8 (0.5–1.2)    |         |
| Yes                                  | 117 (84.8)       | 27 (51.9)     | 144 (75.8)       |         |
| Worst total bilirubin                |                  | < 0.001       |                  |         |
| No                                   | 21 (15.2)        | 25 (48.3)     | 46 (24.2)        |         |
| Yes                                  | 177 (84.8)       | 77 (51.9)     | 252 (75.8)       |         |
| Worst troponin I, > 0.045            |                  | < 0.001       |                  |         |
| No                                   | 98 (70.0)        | 17 (32.7)     | 115 (59.9)       |         |
| Yes                                  | 42 (30.0)        | 35 (67.3)     | 77 (40.1)        |         |
| Infiltration on the chest X-ray at initial diagnosis | | < 0.001 | | |
| No                                   | 1,226 (59.1)     | 41 (22.9)     | 1,267 (56.2)     |         |
| Yes                                  | 849 (40.9)       | 138 (77.1)    | 987 (43.8)       |         |
| Infiltration on the chest X-ray during admission | | 0.888 | | |
| No                                   | 1,845 (88.9)     | 158 (88.3)    | 2,003 (88.9)     |         |
| Yes                                  | 230 (11.1)       | 21 (11.7)     | 251 (11.1)       |         |
| Chest CT initial                     |                  | < 0.001       |                  |         |
| Bilateral                            | 423 (56.8)       | 41 (87.2)     | 464 (58.6)       |         |
| None                                 | 172 (23.1)       | 4 (8.5)       | 176 (22.2)       |         |
| Unilateral                           | 150 (20.1)       | 2 (4.3)       | 152 (19.2)       |         |
| Chest CT last                        |                  | 0.512         |                  |         |
| Bilateral                            | 147 (62.8)       | 5 (83.3)      | 152 (63.3)       |         |
| None                                 | 54 (23.1)        | 1 (16.7)      | 55 (22.9)        |         |
| Unilateral                           | 33 (14.1)        | 0 (0.0)       | 33 (13.8)        |         |

Data are presented as number (%) or median (interquartile range).
COVID-19 = coronavirus disease 2019, COPD = chronic obstructive lung disease, HIV = human immunodeficiency virus, PT = prothrombin time, INR = international normalized ratio, AST = aspartate aminotransferase, ALT = alanine aminotransferase, CK-MB = creatine kinase-MB, CRRT = continuous renal replacement therapy.
to mild cases of COVID-19 due to hospital-bed shortage.\textsuperscript{3} Moderate severity patients were considered suitable for the community hospital. Moreover, severe and critical patients were to be admitted to a tertiary care hospital in Daegu.\textsuperscript{3}

**Definition**

Fever was defined as a body temperature of at least 37.5°C. The illness severity scores used for collecting data were as follows: 1) no limitation of daily activities; 2) limitation of daily activities but no need for supplemental oxygen; 3) supplemental oxygen via nasal cannula; 4) supplemental oxygen via facial mask; 5) noninvasive mechanical ventilation; 6) invasive mechanical ventilation; 7) multi-organ failure or extracorporeal membrane oxygenation therapy; and 8) death. The illness severity scores were re-classified with clinical information on the whole duration of the clinical course as follows: 1) Asymptomatic: no symptoms or discomfort throughout the whole disease period with a body temperature below 37.5°C, 2) Mild: presence of any symptoms with or without fever (≥ 37.5°C), but no demonstrated pneumonia, 3) Moderate: pneumonia diagnosis by clinician but no need for oxygenation with room air, 4) Severe: pneumonia diagnosis by clinician and need for oxygenation therapy (nasal prong or facial mask or high flow oxygen therapy), and 5) Critical: pneumonia diagnosis by clinician and need for mechanical ventilation therapy or ECMO (extracorporeal membrane oxygenation) or death.

Death in this study is a COVID-19 death, which is defined as a death resulting from a clinically compatible illness in a confirmed COVID-19 case, unless a clear alternative cause of death that cannot be associated with COVID-19 can be proven. The case fatality rate is an estimate of the number of deaths and a proportion of the total number of cases, including those who are mild and asymptomatic.

**Clinical management**

All hospitals cared for patients with the help of COVID-19 clinicians in accordance with the COVID-19 management guidelines released from KCDC.

**Statistical analysis**

Continuous variables were expressed as the mean ± standard deviation or median (interquartile range [IQR]) as appropriate. The categorical variables were summarized as counts and percentages in each category. Descriptive statistics were used to characterize the cohort. The categorical variables were compared using Fisher’s exact test, whereas the non-categorical variables were tested using the Mann-Whitney U test.

We used univariate and multi-variable logistic regression methods to explore the risk factors associated with 28-day mortality. We considered Cox proportional hazard model and Kaplan–Meier analysis for the analysis of 28-day mortality and the release time from isolation. Variables from the univariate analysis were excluded if their between-group differences were not significant and if the number of events was too small to calculate odds ratios. Moreover, the multi-collinearity of the variables was considered for the modeling regression. We used the COVID-19 symptom onset or diagnosis date as the time of entry and follow-up were censored on the death date for the survival analysis. All tests were considered statistically significant at a P value of less than 0.05. The statistical analyses were performed using R statistics, version 4.0. (The R Foundation, https://www.r-project.org, Vienna, Austria).
Ethics statement
The study was approved by the Institutional Review Board of Kyungpook National University Hospital (KNUH 2020-03-044), which waived informed consent.

RESULTS

Patients’ flow and baseline characteristics
In this study, 7,057 laboratory-confirmed patients with COVID-19 who had been diagnosed from February 18 to July 10, 2020 were included, with 2,254 patients (core cohort) having available clinical information (Fig. 1). Cases were confirmed through reverse-transcriptase–polymerase-chain-reaction assays performed on nasopharyngeal swab specimens.

The main isolation methods were hospitalization (57.8%, 4,079/7,057) and facility isolation (isolation in the therapeutic living center) (39.5%, 2,784/7,057). A minor portion of the patients were isolated at home (2.9%, 202/7,057). The distribution of districts in Daegu City for the Daegu COVID-19 patients was summarized in Supplementary Table 1. Dalseo-gu (442, 18.7%) was the largest district in the COVID-19 patient population.

The median age of the total cohort was 57 years (IQR, 42.0–70.0; ranging from 0 to 98 years), whereas the median age of the core cohort was 58 years (IQR, 42.0–70.0; ranging from 1 to 98 years) (Table 1). In the core cohort, 808 (35.8%) patients were male and 593 (26.3%) had an age of > 70 (Table 1).

Of the total cohort, 5,467 were asymptomatic to mild patients (77.4%) (asymptomatic 30.6% and mild 46.8%), 985 moderate (14.0%), 380 severe (5.4%), and 225 critical (3.2%) (Fig. 1A). Of the core cohort, 664 were mild patients (29.5%), 985 moderate (43.7%), 380 severe (16.9%), and 225 critical (10.2%) (Fig. 1B). In the core cohort, 159 patients were admitted to the intensive care unit (7.1%) (Table 1). Types of 10 hospitals in Daegu City and distribution of maximum disease severity during the whole disease course COVID-19 patients (core

Fig. 2. A pie graph of the distribution of severity (five categories) of patients with coronavirus disease 2019 from the (A) total cohort (n = 7,057) and (B) core cohort (n = 2,254).
cohort) are summarized in Supplementary Table 2. Five tertiary hospitals took care of critical patients and referred the improving patients to the secondary hospitals or discharged patients. Shock was documented in 0.7% of the total cohort (15/2,254) (Table 1 and Fig. 2). The mortality of the patients was 2.5% (152/7,057).

In the core cohort, the most common presenting symptoms were cough (38.0%), sputum production (29.6%), fever (18.5%), myalgia (17.1%), headache (16.8%), diarrhea (11.1%), and sore throat (10.4%) (Supplementary Table 3 and Fig. 3).

Comorbidities were present: hypertension (25.4%), diabetes (14.4%), and dementia (6.0%) (Table 1).

Furthermore, abnormal manifestations in chest radiographs and CT were present in 11.1% (251/2,254) and 77.8% (176/617) of the patients, respectively (Table 1).

Table 1 summarizes the initial and worst laboratory findings and therapeutic trials in the clinical situations.

**Mortality and risk factors for mortality**

The case fatality rate of the patients was 2.5% (179/7,057) (Table 1). Supplementary Fig. 1 shows the case fatality rate according to age distribution in the Daegu outbreak. Case fatality rates in age < 20, 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and > 80 were 0.0%, 0.0%, 0.7%, 0.4%, 1.8%, 6.4%, 16.5%, and 32.8%, respectively (Supplementary Fig. 1).

Figure 3. Distribution of symptoms and signs of patients with coronavirus disease 2019.
In 32 patients, extracorporeal membrane oxygenation was used, wherein 16 (50%) of whom survived (Table 1), whereas in 36 patients, vasopressor was used for shock treatment.

Multi-variable logistic regression was performed using clinically important variables and variables with $P < 0.05$ in the univariate analysis. Age > 70, body mass index > 25, need for O$_2$ supply at admission, fever (> 37.5°C), diabetes, heart failure, hypertension, cancer, chronic liver diseases, dementia, neurological disease, and infiltration on chest X-ray at initial diagnosis were significant risk factors for mortality (Table 2).

The Cox proportional hazard model of the patients with available clinical information ($n$ = 2,254) showed risk factors for 28-day mortality: age > 70 (HR, 4.219; $P = 0.002$), need for O$_2$ supply at admission (HR, 2.995; $P = 0.001$), fever (> 37.5°C) (HR, 2.808; $P = 0.001$), diabetes (HR, 2.119; $P = 0.008$), cancer (HR, 3.043; $P = 0.011$), dementia (HR, 5.252; $P = 0.008$), neurological disease (HR, 2.084; $P = 0.039$), heart failure (HR, 3.234; $P = 0.012$), and hypertension (HR, 2.160; $P = 0.017$) (Table 2).

The Kaplan–Meier analyses with some important variables in the Cox proportional hazard model were performed and presented in Fig. 4 (age ≥ 70, diabetes, need for O$_2$ supply at admission, and infiltration on chest X-ray at initial diagnosis) and Supplementary Fig. 2 (heart failure, chronic heart disease, cancer, and dementia).

### The duration of isolation in the early outbreak in Daegu, Korea
The median time from symptom onset or the first diagnosis to isolation release of the total cohort was 30 days (IQR, 22.0–40.0; ranging from 0 years to 98 years), and the mean age of the 2,254 patients was 33 years (IQR, 24.0–46.0; ranging from 1 years to 98 years) (Table 1).

The median duration for release from isolation was 33 days (IQR, 24.0–46.0) in survivors. The Cox proportional hazard model for the long duration of isolation included severity (from mild to critical), age > 70, and dementia (Table 3).

### DISCUSSION

This retrospective cohort study showed the clinical manifestations in the Daegu City COVID-19 outbreak and identified the distributions of the severity of patients with COVID-19.
in the epidemic of a metropolitan city. The isolation methods in the outbreak were also shown. Moreover, this study found several risk factors for death in adults hospitalized with COVID-19. The risk factors for sustained viral detection in the respiratory tract included severe disease and old age.

Facility isolation (therapeutic living center) was first introduced in Korea during the Daegu COVID-19 outbreak. This isolation method was effective for resolving hospital-bed shortage. Facility isolation for asymptomatic and mild cases were crucial to helping overcome COVID-19 outbreaks in Daegu, Korea because > 80% of cases did not require special therapies, such as oxygen supplementation or parenteral fluid infusion or antiviral therapy. This study revealed that approximately 40% of patients were isolated using this method.

The clinical spectrum of COVID-19 infection is wide, encompassing asymptomatic infection, mild upper respiratory tract illness, and severe viral pneumonia with respiratory failure and
even death in the previous reports.\textsuperscript{7} Previous studies reported that COVID-19 is characterized by various clinical manifestations.\textsuperscript{8} In a typical case, a high fever appears after dry cough; in some cases, viral pneumonia develops and progresses, resulting in shortness of breath.\textsuperscript{5,9} Common symptoms among patients with COVID-19 include fever, dry cough, shortness of breath (dyspnea), muscle ache (myalgia), confusion, headache, sore throat, rhinorrhea, chest pain, diarrhea, nausea/vomiting, conjunctival congestion, nasal congestion, sputum production, fatigue (malaise), hemoptysis, and chills.\textsuperscript{8,10-13} Some published articles and a study from Daegu also reported the significance of anosmia or ageusia (loss of taste) as symptoms of COVID-19.\textsuperscript{14-17} However, only 1.2\% of the patients in the present study presented with anosmia, indicating that clinicians did not actively obtain the presence of anosmia in the early period of the outbreak. The clinical manifestations of the present study are similar to the previous reports characterized primarily by fever, cough, dyspnea, and bilateral infiltrates on chest imaging.\textsuperscript{18}

In the present study, asymptomatic patient proportion is approximately 30\%. In some studies of asymptomatic individuals who were hospitalized and monitored, approximately 77\% to 89\% remained asymptomatic over time.\textsuperscript{19} The definition of “asymptomatic” varies across studies, depending on which specific symptoms were assessed. A review paper estimated that it is as 40\%–45\% based on data from three large cohorts that identified cases through population-based testing.\textsuperscript{20} However, in most studies, longitudinal follow-up to assess for symptom development was not performed.\textsuperscript{19} Therefore, an overestimation of the number of asymptomatic COVID-19 patients might be possible. In the present study, “asymptomatic” means no symptom described or observed during the whole duration of infection, which can explain the lesser proportion of asymptomatic infection.

The case fatality rate of patients with COVID-19 varies among countries related to demographics, patient comorbidities, surge capacity of healthcare systems, and quality of medical care.\textsuperscript{4} The case fatality rate of COVID-19 in the Daegu City outbreak was 2.5\%, which is higher than the recently reported estimation of case fatality (0.68\%) in a meta-analysis report.\textsuperscript{21} Also, a paper reported that the infection fatality rate for Spain as a whole was 1.15\% (range, 0.13\% to 3.25\%) and is not fixed.\textsuperscript{22} The Spanish regions with more rapid and extensive spread of SARS-CoV-2 had higher case fatality rate.\textsuperscript{22} In the outbreak in China, it was reported that the case fatality rate was 2.3\% (1,023 of 44,672 confirmed cases), which is similar to that of the present study.\textsuperscript{23}

A study with 3,060 Korean COVID-19 patients reported that the mortality was 1.1\% (27/2,524).\textsuperscript{4} The differences in mortality among study populations may be explained by the differences that include age distribution, the prevalence of comorbid conditions of the patients, and public health crisis preparedness and response of health-care systems. The median age of our study population was 58 years, which is older than the median (43 years) of the study population with 3,060 Korean COVID-19 patients.\textsuperscript{4} Higher mortality in our study may be related to this different age distribution.

The Daegu City outbreak was the first one in Korea. Unpreparedness to the explosive COVID-19 outbreak at spring in 2020 might have contributed to the higher mortality rate in Daegu. Moreover, hospital shortage in the early period of the outbreak was the most prominent obstacle in overcoming the outbreak.\textsuperscript{3} A telephone severity scoring system and therapeutic living centers solved acute hospital-bed shortage during the COVID-19 outbreak in Daegu, Korea.\textsuperscript{3}
Previously, older age has been reported as an important independent predictor of mortality in COVID-19. This study also found that increased age (age > 70) was associated with death in patients with COVID-19.

Cardiovascular disease, diabetes, respiratory disease (including severe asthma), obesity, a history of hematological malignancy or recent other cancers, kidney, liver and neurological diseases, and autoimmune conditions were reported to be risk factors for mortality. A meta-analysis with 44,672 patients with COVID-19 reported that cardiovascular disease, hypertension, diabetes, respiratory disease, and cancers were the risk factors for fatality. We found that age > 70, fever (> 37.5°C), need for O2 supply at admission, diabetes, dementia, cancer, heart failure, hypertension, and neurological disease were independent risk factors for 28-day mortality. This finding is similar to that of previous reports on the most important risk factors. The present study emphasizes the significance of dementia and neurological disease as risk factors of mortality. Dementia as a predictor of mortality of COVID-19 patients is also reported in some studies.

A study with COVID-19 with Daegu population was published and reported that mortality as 2.6% (18/694) and significant risk factors for severe disease were lymphopenia, lactate dehydrogenase, C-reactive protein, and low albumin in the study. However, the study was conducted with univariate analysis. A study with COVID-19 with 352 Korean patients (hospitalized in Dongguk University Gyeongju Hospital and the Andong Medical Center) with multi-variable regression analysis reported age (≥ 70 years), a history of malignancy, fever (≥ 37.5°C), and diabetes were significant risk factors of mortality. We found that the risk factors for 28-day case fatality rate with multi-variable logistic analysis and Cox hazard model with a relatively large population (2,254 patients).

Comparison between COVID-19 studies had limitations because the collected variables and definition of severity category are largely different.

The duration of virus detection determined the isolation period during the study period. Two consecutive negative COVID-19 PCR tests with a 24-hour interval were required for the release from isolation in Daegu, Korea. Median (33 days) of isolation duration was over a month; this long isolation occupied the beds or isolation facilities and made medical resource shortage. This criteria for the release from isolation were used among the patients in this study population. Recently, Korea Disease Control and Prevention Agency revised the criteria of stopping isolation to avoid medical resource shortage. The modified criteria for discharge include no 3-day symptoms and passing 10 days after the first symptom onset. This modification was based on scientific evidence of a very low possibility of virus transmission after 10 days from the onset of infection.

The present study has some limitations. First, due to the retrospective study design, not all information is available. Therefore, we focused on the initial and worst data for clinical information. Moreover, the laboratory values were not included such as C-reactive protein and procalcitonin and D-dimer for the analysis of risk for mortality due to inconsistent values in the multicenter study. Instead, initial clinical manifestations were mainly used for predicting outcomes. Second, the retrospective study design also has difficulty in the assessment of the efficacy of treatment such as steroids, hydroxychlorquine, and anti-retroviral agents such as lopinavir/ritonavir.
In conclusion, this study described the clinical manifestations in the city-wide outbreak cohort of COVID-19 patients in Daegu City, Korea. The case fatality rate was 2.5% in the first outbreak in Korea in 2020. Asymptomatic to mild patients were approximately 77% of the total cohort (asymptomatic: 30.6%). Risk factors, including older age, need for O2 supply, dementia, and neurological disorder at admission could help clinicians identify patients with poor prognosis at an early stage.

**SUPPLEMENTARY MATERIALS**

**Supplementary Table 1**
The distribution of districts in Daegu City for the Daegu coronavirus disease 2019 patients

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**Supplementary Table 2**
Types of 10 hospitals in Daegu City and distribution of maximum disease severity during the whole disease course coronavirus disease 2019 patients (core cohort)

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**Supplementary Table 3**
Distribution of symptoms and signs of patients with coronavirus disease 2019

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**Supplementary Fig. 1**
The case fatality rate of patients with coronavirus disease 2019 according to age distribution in the Daegu outbreak.

Click here to view

**Supplementary Fig. 2**
Kaplan–Meier plots with log-rank tests for the risk factors of the 28-day mortality in coronavirus disease 2019 patients: heart failure, chronic heart disease, cancer, and dementia.

Click here to view

**REFERENCES**

1. Kim JH, An AR, Min PK, Bitton A, Gawande AA. How South Korea responded to the COVID-19 outbreak in Daegu. NEJM Catal Innov Care Deliv 2020;1(4):1-14.
2. Lee Y, Min P, Lee S, Kim SW. Prevalence and duration of acute loss of smell or taste in COVID-19 patients. J Korean Med Sci 2020;35(18):e174.
3. Kim SW, Lee KS, Kim K, Lee JJ, Kim JY; Daegu Medical Association. A brief telephone severity scoring system and therapeutic living centers solved acute hospital-bed shortage during the COVID-19 outbreak in Daegu, Korea. J Korean Med Sci 2020;35(15):e152.
4. Sung HK, Kim JY, Heo J, Seo H, Jang YS, Kim H, et al. Clinical course and outcomes of 3,060 patients with coronavirus disease 2019 in Korea, January–May 2020. J Korean Med Sci 2020;35(30):e280.

5. Park Y, Huh IS, Lee J, Kang CR, Cho SI, Ham HJ, et al. Application of testing-tracing-treatment strategy in response to the COVID-19 outbreak in Seoul, Korea. J Korean Med Sci 2020;35(45):e996.

6. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382(18):1708–20.

7. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395(10229):1054–62.

8. Zhu FC, Guan XH, Li YH, Huang JY, Jiang T, Hou LH, et al. Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial. Lancet 2020;396(10249):479–88.

9. Epidemiology Working Group for NCIP Epidemic Response, Chinese Center for Disease Control and Prevention. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. Zhonghua Liu Xing Bing Xue Za Zhi 2020;41(2):145–51.

10. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395(10223):507–13.

11. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382(18):1708–20.

12. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395(10223):497–506.

13. Kim ES, Chin BS, Kang CK, Kim NJ, Kang YM, Choi JP, et al. Clinical course and outcomes of patients with severe acute respiratory syndrome coronavirus 2 infection: a preliminary report of the first 28 patients from the Korean Cohort Study on COVID-19. J Korean Med Sci 2020;35(13):e142.

14. Lechien JR, Chiesa-Estomba CM, De Siati DR, Horoi M, Le Bon SD, Rodriguez A, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. Eur Arch Otorhinolaryngol 2020;277(8):2251–61.

15. Giacomelli A, Pezzati L, Conti F, Bernacchia D, Siano M, Oreni L, et al. Self-reported olfactory and taste disorders in SARS-CoV-2 patients: a cross-sectional study. Clin Infect Dis 2020;

16. Eliezer M, Hautefort C, Hamel AI, Verillaud B, Herman P, Houdart E, et al. Sudden and complete olfactory loss function as a possible symptom of COVID-19. JAMA Otolaryngol Head Neck Surg 2020;146(7):674–5.

17. Jang Y, Son HJ, Lee S, Lee EJ, Kim TH, Park SY. Olfactory and taste disorder: The first and only sign in a patient with SARS-CoV-2 pneumonia. Influenza and Other Respiratory Viruses 2020;14(9):1103.

18. Stokes EK, Zambrano LD, Anderson KN, Marder EP, Raz KM, El Burai Felix S, et al. Coronavirus Disease 2019 Case Surveillance — United States, January 22–May 30, 2020. MMWR Morb Mortal Wkly Rep 2020;69(24):759–65.

19. Ooi EE, Low JG. Asymptomatic SARS-CoV-2 infection. Lancet Infect Dis 2020;20(9):996–8.

20. Oran DP, Topol EJ. Prevalence of asymptomatic SARS-CoV-2 infection: a narrative review. Ann Intern Med 2020;173(5):362–7.

21. Meyerowitz-Katz G, Merone L. A systematic review and meta-analysis of published research data on COVID-19 infection fatality rates. Int J Infect Dis 2020;101:138–48.
22. Kenyon C. COVID-19 Infection fatality rate associated with incidence-a population-level analysis of 19 Spanish autonomous communities. *Biology (Basel)* 2020;9(6):128.
PUBMED | CROSSREF
23. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72,314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020;323(13):1239-42.
PUBMED | CROSSREF
24. Williamson EL, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 2020;584(7821):430-6.
PUBMED | CROSSREF
25. Deng G, Yin M, Chen X, Zeng F. Clinical determinants for fatality of 44,672 patients with COVID-19. *Crit Care* 2020;24(1):179.
PUBMED | CROSSREF
26. Hariyanto TI, Putri C, Situmeang RF, Kurniawan A. Dementia is a predictor for mortality outcome from coronavirus disease 2019 (COVID-19) infection. *Eur Arch Psychiatry Clin Neurosci*. Forthcoming 2020. DOI: 10.1007/s00406-020-01205-z.
PUBMED | CROSSREF
27. Moon SS, Lee K, Park J, Yun S, Lee YS, Lee DS. Clinical characteristics and mortality predictors of COVID-19 patients hospitalized at nationally-designated treatment hospitals. *J Korean Med Sci* 2020;35(36):e328.
PUBMED | CROSSREF
28. Lee JY, Hong SW, Hyun M, Park JS, Lee JH, Suh YS, et al. Epidemiological and clinical characteristics of coronavirus disease 2019 in Daegu, South Korea. *Int J Infect Dis* 2020;98:462-6.
PUBMED | CROSSREF
29. Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature* 2020;581(7809):465-9.
PUBMED | CROSSREF