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

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Letter to the Editor

Comparison of short-term mortality between mechanically ventilated patients with COVID-19 and influenza in a setting of sustainable healthcare system

Dear Editor,

We read with interest the article of *Wang* et al.[1] about a high fatality rate in elderly patients with coronavirus disease 2019 (COVID-19). Furthermore, a very high mortality was reported in mechanically ventilated patients with COVID-19.[2-5] These findings appear to frighten both the general population and clinicians. However, these previous results were derived from an overwhelming outbreak or in nursing home residents, leading to inadequate access to a healthcare system or greater susceptibility to poor outcomes, respectively.

Many experts are concerned about the future seasonal epidemic of COVID-19, like influenza. In available healthcare systems, the mortality of mechanically ventilated patients with community-acquired COVID-19 may be different. Thus, we aimed to investigate the clinical characteristics and short-term outcomes in mechanically ventilated patients with COVID-19 and compared them with those with seasonal influenza to better understand the differences between severe COVID-19 and influenza illness.

Critically ill patients with COVID-19 undergoing mechanical ventilation (MV) at Kyungpook National University Hospital (KNUH), a tertiary referral hospital in Daegu, South Korea, between February 19, 2020 and March 22, 2020, were enrolled. The influenza group included those with seasonal influenza from 2016 to 2019 who received MV. Diagnoses of COVID-19 and influenza were confirmed with real-time reverse-transcriptase polymerase chain reaction from a nasopharyngeal swab. Demographic, clinical, laboratory, and radiologic findings at initial presentation, therapeutic modalities, and 30-day mortality were obtained from electronic medical records of the study population. Statistical analyses were performed using SAS software (SAS Institute; Cary, NC). The study was approved by the Institutional Review Board of the KNUH.

Twenty patients with COVID-19 and nine with influenza receiving MV were included in this study (Table 1). Seven influenza A and two influenza B types were isolated. Only one patient had the H1N1 strain. No bacterial pathogens were detected in these patients on admission.

In patients with COVID-19, the median age was 68 years (interquartile range [IQR], 59–75 years), which was significantly higher than in those with influenza (median [IQR], 57 [44–63] years; P=0.016). About 65% of each group were male and approximately 70% had at least one underlying medical condition with the most common disease being diabetes mellitus. Community-acquired infection accounted for 75% of those with COVID-19 and all patients with influenza. Fever and dyspnea were the most common symptom on admission in both groups. There were no significant differences in sex, body mass index, underlying disease, initial symptoms, or Sequential Organ Failure Assessment (SOFA) score between the two groups. On admission, the median heart rate was significantly lower in the COVID-19 group than in the influenza group (83 vs. 107 bpm; P=0.017).

The median white blood cell count was much lower in the influenza group than in the COVID-19 group (2,680 vs. 7,470 cells/μL; P=0.027). The percentage of lymphocytes and arterial partial pressure of oxygen/fraction of inspired oxygen ratio were abnormally decreased and the levels of lactate dehydrogenase and C-reactive protein were abnormally increased in both groups. There were no relevant differences in those laboratory findings between the groups. Bilateral infiltrates on chest X-rays were noted in most patients in both groups.

The median time from illness onset to admission was 4 (IQR, 3–10) and 5 (IQR, 4–7) days in the COVID-19 and influenza groups, respectively (P=0.766). The median time from illness onset to MV was 7 days in both groups. Acute respiratory distress syndrome (ARDS), based on the Berlin definition,[6] occurred in all patients with COVID-19 and most (89%) patients with influenza. The remaining one patient with influenza received MV due to hypercapnic respiratory failure associated with co-existing bronchiectasis.

General medical managements, including antibiotics, vasoactive drugs, corticosteroids, venous thromboembolism prophylaxis, sedatives, and neuromuscular blocking agents, were directed by the intensivists in charge (Table 1). Corticosteroids were given to most patients of both groups. There were no relevant differences in therapeutic modalities between the groups. The incidences of complications including ventilator associated pneumonia, arrhythmia, and acute kidney injury were similar between the groups.

The overall 30-day mortality was 25% in the COVID-19 group (n=5) and 22% in the influenza group (n=2), showing no significant difference between the groups (Fig. 1, P=0.974). Multi-organ failure (n=5) (COVID-19 [n=4]; influenza [n=1]) was the leading cause of death followed by refractory hypoxemia (n=2) (COVID-19 [n=1]; influenza [n=1]). Among the 5 patients with COVID-19 who died, 3 patients had healthcare-associated infection. On day 30, 12 (60%) patients with COVID-19 and 6 (66%) with influenza achieved successful weaning and their median time of MV use was equally 11 days.

The present study showed low short-term mortality in mechanically ventilated patients with community-acquired COVID-19, compared to previous studies. This mortality was also not significantly different from that of patients with severe influenza, a common seasonal respiratory virus.

Clinical characteristics and laboratory findings, including age, comorbidities, and SOFA score, seemed to not be significantly different between our cohort and previous cohorts.[2-5] Although corticosteroids and antiviral therapy were administered more frequently in our patients, it is unlikely that these differences resulted

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Table 1
Comparison of clinical, laboratory, and radiological characteristics, treatment modalities, and outcomes of mechanically ventilated patients with COVID-19 and influenza.

Variable	COVID-19 (n=20)	Influenza (n=9)	P value
Age, y	68 (59-75)	57 (44-63)	0.016
Male sex	13 (65)	6 (67)	1.0
BMI, kg/m^2	25.9 (21.9-27.1)	25.1 (24.1-30.2)	0.228
Ever-smoker	10 (50)	5 (56)	1.0
Underlying medical disease[a]	14 (70)	6 (67)	1.0
Community acquired	15 (75)	9 (100)	0.153
Initial symptoms			
Fever	20 (100)	8 (89)	0.310
Dyspnea	20 (100)	8 (89)	0.310
Cough	10 (50)	8 (89)	0.096
Sputum	6 (30)	6 (67)	0.106
Myalgia	9 (45)	5 (56)	0.700
Diarrhea	2 (10)	1 (11)	1.0
On admission			
Heart rate, bpm	83 (77-103)	107 (96-113)	0.017
Respiratory rate	25 (20-30)	25 (20-29)	0.923
Mean blood pressure, mmHg	91 (80-109)	93 (68-100)	0.322
SOFA	4 (2-6)	4 (2-5)	0.924
Laboratory findings			
WBC counts, cells/μL	7,470 (5,778-9,948)	2,680 (1,300-14,895)	0.027
Neutrophil, %	86 (81-89)	81 (61-88)	0.109
Lymphocyte, %	9 (6-12)	13 (7-28)	0.104
Albumin, g/dL	3.2 (2.9-3.4)	3.1 (3.0-3.6)	0.553
Lactate dehydrogenase, U/L	539 (414-655)	521 (433-669)	0.883
Aspartate aminotransferase, U/L	49 (37-88)	55 (22-114)	0.706
Alanine aminotransferase, U/L	32 (25-50)	25 (16-52)	0.436
C-reactive protein, mg/dL	11.2 (5.7-17.8)	17.1 (9.9-21.6)	0.258
Lactate, mmol/L	1.7 (1.3-2.7)	1.1 (0.9-5.2)	0.650
Cardiac troponin I, pg/ml	0.03 (0.02-0.44)	0.02 (0.02-0.09)	0.677
Pro-brain natriuretic peptide	651 (245-5,521)	263 (123-852)	0.102
PaO_2/FiO_2	124 (77-215)	186 (122-239)	0.300
Chest X-ray			
Bilateral infiltrate	20 (100)	8 (89)	0.310
Onset of symptom to admission, d	4 (3-10)	5 (4-7)	0.766
Onset of symptom to ICU admission, d	6 (4-12)	7 (6-8)	1.0
Onset of symptom to MV, d	7 (5-12)	7 (6-8)	0.824
ARDS	20 (100)	8 (89)	0.310
Treatment			
High flow oxygen therapy before MV	11 (55)	2 (22)	0.130
Antiviral agents[b]	20 (100)	9 (100)	1.0
Glucocorticoid therapy	16 (80)	9 (100)	0.280
Intravenous immunoglobulin	7 (35)	1 (11)	0.371
Vasoactive drugs	19 (95)	7 (78)	0.220
Neuromuscular blocking agent	4 (20)	5 (56)	0.088
Renal replacement therapy	6 (30)	3 (33)	1.0
ECMO	3 (15)	4 (44)	0.158
Outcome on day 30			
Death	5 (25)	2 (22)	1.0
Successful weaning of MV	12 (60)	6 (66)	1.0
Ventilator d[c]	11 (5-18)	11 (5-20)	0.666

Data are expressed as the median (IQR) or number (%).
Abbreviation: COVID-19, coronavirus disease 2019; BMI, body mass index; SOFA, Sequential Organ Failure Assessment; WBC, white blood cells; PaO_2, arterial partial pressure of oxygen; FiO_2, fraction of inspired oxygen; ICU, intensive care unit; MV, mechanical ventilation; ARDS, acute respiratory distress syndrome; ECMO, extracorporeal membrane oxygenation.
[a] Including diabetes mellitus (n=6), hypertension (n=6), malignancy (n=4), chronic kidney disease (n=2), ischemic heart disease (n=2), and chronic lung disease (n=2) in the COVID-19 group and diabetes mellitus (n=3), hypertension (n=2), chronic liver disease (n=2), chronic lung disease (n=1), and cerebral infarction (n=1) in the influenza group.
[b] Including lopinavir and ritonavir in the COVID-19 group and oseltamivir or peramivir in the influenza group.
[c] Calculated for patients achieving successful weaning of mechanical ventilation.

in mortality differences between patients with invasive MV when considering the uncertain effects of these agents on critically ill patients.[7-9]

Due to less limited medical resources in conjunction with the relatively small outbreak, most critically ill inpatients with COVID-19 were provided with the quality of medical care similar to those with influenza illness. In addition, most of our patients with COVID-19 were not from nursing homes. As mentioned in previous studies,[2-5] these factors may partly explain the different mortality rates between studies of severe COVID-19.

In conclusion, our results suggest that the early mortality of mechanically ventilated patients with community-acquired COVID-19 may not be very high in settings with medical resources to carry out appropriate management, where they would have comparable outcomes to those with seasonal influenza-related respiratory failure.

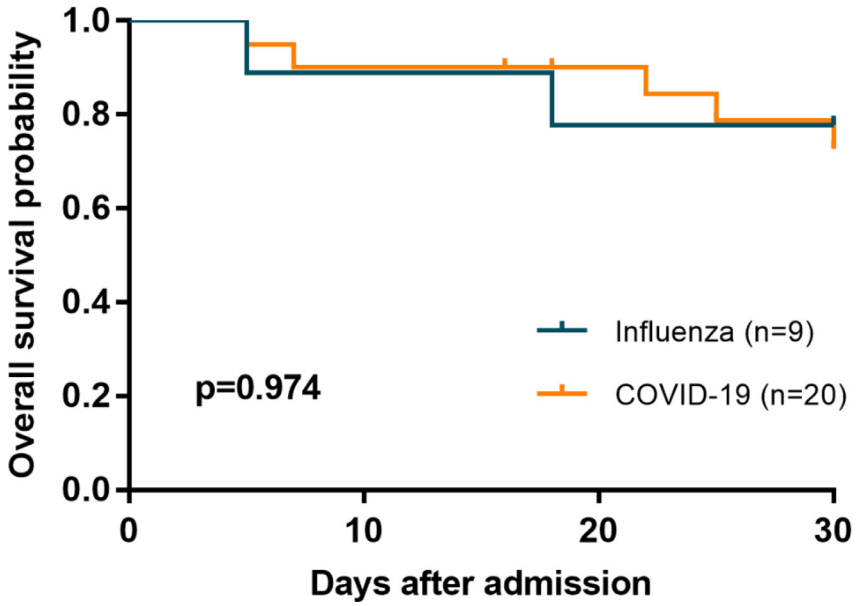

Fig. 1. 30-day mortality of mechanically ventilated patients with COVID-19 and influenza.

Conflict of Interest Disclosures

None of the authors have any conflicts of interest to declare.

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