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Mortality Rates in a Diverse Cohort of Mechanically Ventilated Patients With Novel Coronavirus in the Urban Midwest

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Objectives: Differences in mortality rates previously reported in critically ill patients with coronavirus disease 2019 have increased the need for additional data on mortality and risk factors for death. We conducted this study to describe length of stay, mortality, and risk factors associated with in-hospital mortality in mechanically ventilated patients with coronavirus disease 2019.

Design: Observational study.

Setting: Two urban, academic referral hospitals in Indianapolis, Indiana.

Patients or Subjects: Participants were critically ill patients 18 years old and older, admitted with coronavirus disease 2019 between March 1, 2020, and April 27, 2020.

Interventions: None.

Measurements and Main Results: Outcomes included in-hospital mortality, duration of mechanical ventilation, and length of stay. A total of 242 patients were included with mean age of 59.6 years (SD, 15.5 yr), 41.7% female and 45% African American. Mortality in the overall cohort was 19.8% and 20.5% in the mechanically ventilated subset. Patients who died were older compared with those that survived (deceased: mean age, 72.8 yr [SD, 10.6 yr] vs patients discharged alive: 54.3 yr [SD, 14.8 yr]; $p < 0.001$ vs still hospitalized: 59.5 yr [SD, 14.4 yr]; $p < 0.001$) and had more comorbidities compared with those that survived (deceased: 2 [0.5–3] vs survived: 1 [interquartile range, 0–1]; $p = 0.001$ vs still hospitalized: 1 [interquartile range, 0–2]; $p = 0.015$). Older age and end-stage renal disease were associated with increased hazard of in-hospital mortality: age 65–74 years (hazard ratio, 3.1 yr; 95% CI, 1.2–7.9 yr), age 75+ (hazard ratio, 4.1 yr; 95% CI, 1.6–10.5 yr), and end-stage renal disease (hazard ratio, 5.9 yr; 95% CI, 1.3–26.9 yr). The overall median duration of mechanical ventilation was 9.3 days (interquartile range, 5.7–13.7 d), and median ICU length of stay in those that died was 8.7 days (interquartile range, 4.0–14.9 d), compared with 9.2 days (interquartile range, 4.0–14.0 d) in those discharged alive, and 12.7 days (interquartile range, 7.2–20.3 d) in those still remaining hospitalized.

Conclusions: We found mortality rates in mechanically ventilated patients with coronavirus disease 2019 to be lower than some previously reported with longer lengths of stay.

Key Words: coronavirus disease 2019; critical illness; respiratory failure

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The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), also known as coronavirus disease 2019 (COVID-19), has created a global public health emergency (1) due to its rapid spread and significant morbidity and mortality. More than 11 million cases of COVID-19 have been identified worldwide (1), and as of July 10, 2020, there have been 3.1 million confirmed cases and over 130,000 deaths in the United States (2). Older individuals and patients with cardiovascular disease, chronic lung disease, hypertension, and diabetes are at particular risk for death from COVID-19, often due to the development of severe acute respiratory distress syndrome (ARDS) (3–5).

The mortality of critically ill mechanically ventilated patients with COVID-19 was reported as high as 88–97% (3, 5–8). A recent study reported mortality rates of 30.9%, but whether these low rates are seen at other centers is not known (9).

Further data on mortality and length of stay are needed to advance the global understanding of outcomes in critically ill COVID-19 patients. We carried out this analysis with the primary aim to describe the length of stay, mortality, and risk factors associated with death in ICU patients with COVID-19 infection.

MATERIALS AND METHODS

This observational study was conducted at two large urban academic centers affiliated with Indiana University School of Medicine: Indiana University Health Methodist Hospital, an 802-bed quaternary care referral center, and Eskenazi Health, a 336-bed safety net hospital. All consecutive patients admitted to the ICUs with a positive result by SARS-CoV-2 nasopharyngeal swab polymerase chain reaction test from March 1, 2020, to April 27, 2020, were included. Patients under the age of 18 were excluded. Clinical outcomes were collected until April 29, 2020. The primary outcomes were in-hospital mortality, duration of mechanical ventilation, and length of ICU and hospital stay. The study received approval from the local Institutional Review Board.

Data Collection

Data were extracted from hospital electronic medical systems (Cerner PowerChart, Epic Health Systems) and entered directly into a REDCap database. Records were randomly audited to reduce the risk of measurement error or bias. Data included patient demographics, comorbidities, Acute Physiology and Chronic Health Evaluation (APACHE) II score (10), vital signs and laboratory results (from first 24 hr of ICU admission), including SARS-CoV-2 test results, and dates of admission, discharge, and death. APACHE II was calculated using values from the first 24 hours of admission to the ICU. If the patient was readmitted during the study follow-up period, laboratory data from the initial ICU admission was used. For patients transferred to the two hospitals, data collection began at time of ICU admission to our system.

Statistical Analysis

Demographic and clinical characteristics were compared between patients who were discharged alive, those still admitted at the end of the follow-up period, and those who died in the hospital using analysis of variance (normal data) and Wilcoxon rank-sum tests (skewed data) for continuous outcomes or Fisher exact test for categorical variables. For significant variables, we explored pairwise comparisons and adjusted for multiple comparisons using the stepdown Bonferroni method. Summary statistics were provided for mechanically ventilated patients and those who were not ventilated. Variables with significant group differences in univariate analysis (with the exception of insurance as it was collinear with age) were included in a cause-specific Cox's proportional hazards model to identify risk factors associated with in-hospital mortality. For this model, the event of interest was time from ICU admission to death with a competing event as time to discharge. Patients still in the hospital were censored.

RESULTS

Six-hundred forty-four consecutive patients with COVID-19 were admitted from March 1, 2020, to April 29, 2020. Two-hundred forty-two were ICU admissions (including 2% [5/242] transferred from other hospitals) and comprised the study cohort (**Figure E1** in the Supplemental Digital Content http://links.lww.com/CCX/A283). Demographics and clinical characteristics for the cohort are presented in **Table 1**. The mean age of the cohort was 59.6 years (SD, 15.5 yr), 41.7% were female and 45% African American. Hypertension (61.6%), obesity (56.4%), diabetes mellitus (43%), and tobacco use (26.9%) were the most frequent comorbid conditions. The median APACHE II score calculated using values from the first 24 hours of ICU admission was 19 (interquartile range [IQR], 13–26), and median Charlson Comorbidity Index (11) was 1 (IQR, 0–2). The mean Pao_2:FIO_2 ratio for the cohort was 116.6 (SD, 77.6). **Table 2** provides additional laboratory and hemodynamic characteristics of the cohort by mechanical ventilation status.

Differences in Characteristics Between Patients That Died, Survived, or Remained Admitted

Table 1 compares clinical characteristics and comorbidities of patients who died, discharged alive, or were still admitted at the end of the study period, including pairwise *p* values adjusted for multiple comparisons. Patients who died were older compared with those that survived (deceased: mean age, 72.8 yr [SD, 10.6 yr] vs patients discharged alive: 54.3 yr [SD, 14.8 yr]; $p < 0.001$ and vs still hospitalized: 59.5 yr [SD, 14.4 yr]; $p < 0.001$). Patients that died also had more comorbidities as assessed by the Charlson Comorbidity Index compared with patients who were alive (deceased: 2 [0.5–3] vs survived: 1 [IQR, 0–1]; $p = 0.001$ vs still hospitalized: 1 [IQR, 0–2]; $p = 0.015$). Median APACHE II scores were higher in patients that died (24 [IQR, 16–31]) versus those discharged alive (16 [IQR, 11–23]; $p < 0.001$) or those still in the hospital (20 [IQR, 12–27]; $p = 0.015$).

Mortality and Length of Stay Outcomes

Mechanical ventilation occurred in 76.4% of patients (185/242) in the overall cohort (**Table 3**). Mortality in the overall cohort was 19.8% (48/242) and 20.5% (38/185) among mechanically ventilated patients. There were no differences in mortality rates between the two health centers. The median duration of mechanical ventilation in the overall cohort was 9.3 days (IQR, –5.7 to 13.7 d). In patients that died, median ICU length of stay was 8.7 days (IQR, 4.0–14.9 d), compared with 9.2 days (IQR, 4.0–14.0 d) in those discharged alive, and 12.7 days (IQR, 7.2–20.3 d) in those still admitted at the end of the follow-up period (Table 3).

Risk Factors Associated With Mortality

Older age and end-stage renal disease (ESRD) were associated with increased hazard of in-hospital mortality: age 65–74 years (hazard ratio [HR], 3.1 yr; 95% CI, 1.2–7.9 yr; $p = 0.021$), age 75+ (HR, 4.1 yr; 95% CI, 1.6–10.5 yr; $p = 0.003$) compared with those

TABLE 1. Characteristics of ICU Patients With Coronavirus Disease 2019 (*n* = 242)

Variable	All Patients (*n* = 242)	Patients That Discharged Alive (*n* = 116)	Patient Still Admitted in Hospital (*n* = 78)	Patients That Died (*n* = 48)	*p*
Age, yr, mean (SD)	59.6 (15.5)	54.3 (14.8)	59.5 (14.4)	72.8 (10.6)	< 0.001 ([a]< 0.001, [b]< 0.001, [c]0.0099)
Female, *n* (%)	101 (41.7)	48 (41.4)	32 (41.0)	21 (43.8)	0.955
Race, *n* (%)[d]					0.003 ([a]0.091, [b]0.001, [c]0.123)
Caucasian	75 (31.3)	35 (30.7)	22 (28.2)	18 (37.5)	
African American	108 (45.0)	54 (47.4)	27 (34.6)	27 (56.3)	
Hispanic/Latino	43 (17.9)	19 (16.7)	23 (29.5)	1 (2.1)	
Other	14 (5.8)	6 (5.3)	6 (7.7)	2 (4.2)	
Insurance, *n* (%)					< 0.001 ([a]< 0.001, [b]0.026, [c]0.026)
Medicare	65 (27.0)	16 (13.8)	21 (27.3)	28 (58.3)	
Medicaid	36 (14.9)	16 (13.8)	15 (19.5)	5 (10.4)	
Medicare and Medicaid	26 (10.8)	9 (7.8)	11 (14.3)	6 (12.5)	
Commercial	66 (27.4)	45 (38.8)	15 (19.5)	6 (12.5)	
Self-pay	27 (11.2)	16 (13.8)	10 (13.0)	1 (2.1)	
Other	21 (8.7)	14 (12.1)	5 (6.5)	2 (4.2)	
Comorbidities[e], *n* (%)					
Hypertension	149 (61.6)	66 (56.9)	46 (59.0)	37 (77.1)	0.045 ([a]0.061, [b]0.105, [c]0.882)
Diabetes mellitus	104 (43.0)	46 (39.7)	38 (48.7)	20 (41.7)	0.461
Tobacco use	65 (26.9)	29 (25.0)	16 (20.5)	20 (41.7)	0.033 ([a]0.080, [b]0.044, [c]0.499)
Asthma	34 (14.0)	18 (15.5)	8 (10.3)	8 (16.7)	0.495
Chronic kidney disease	35 (14.5)	10 (8.6)	10 (12.8)	15 (31.3)	0.002 ([a]0.002, [b]0.040, [c]0.349)
End-stage renal disease	8 (3.3)	0 (0.0)	4 (5.1)	4 (8.3)	0.003 ([a]0.020, [b]0.050, [c]0.479)
Coronary artery disease	28 (11.6)	12 (10.3)	7 (9.0)	9 (18.8)	0.240
Congestive heart failure	31 (12.8)	14 (12.1)	10 (12.8)	7 (14.6)	0.907
Obstructive sleep apnea	35 (14.5)	13 (11.2)	12 (15.4)	10 (20.8)	0.256
Chronic obstructive pulmonary disease	22 (9.1)	9 (7.8)	3 (3.8)	10 (20.8)	0.008 ([a]0.058, [b]0.013, [c]0.365)
Obesity[f]					0.052
Body mass index < 30	96 (43.6)	41 (39.0)	28 (40.0)	27 (60.0)	
Body mass index ≥ 30	124 (56.4)	64 (61.0)	42 (60.0)	18 (40.0)	
Charlson Comorbidity Index[g], median (IQR)	1 (0–2)	1 (0–1)	1 (0–2)	2 (0.5–3)	0.001 ([a]0.001, [b]0.012, [c]0.301)
Severity of illness					
Acute Physiology and Chronic Health Evaluation II[h] at ICU admission, median (IQR)	19 (13–26)	16 (11–23)	20 (12–27)	24 (16–31)	< 0.001 ([a]< 0.001, [b]0.015, [c]0.062)
Pao_2:FIO_2, mean (SD)	116.6 (77.6)	136.8 (92.2)	99.2 (54.5)	102.0 (65.5)	0.007 ([a]0.044, [b]0.022, [c]0.986)

IQR = interquartile range.

Pairwise *p* values adjusted for multiple comparisons are as follows:

[a]Deceased vs discharged alive.

[b]Deceased vs still hospitalized.

[c]Discharged alive vs still admitted.

[d]Race was available for 163 subjects.

[e]Comorbidities assessed using diagnoses recorded in the medical record.

[f]Body mass index was available for 150 subjects.

[g]Charlson Comorbidity Index predicts mortality over 10 yr.

[h]Acute Physiology and Chronic Health Evaluation calculated using clinical data from first 24 hr of ICU admission.

TABLE 2. Laboratory Values, Oxygenation, and Hemodynamic Characteristics of Patients Admitted with Novel Coronavirus on Day of ICU Admission[a]

Variable	Total (*n* = 242)	Mechanical Ventilation (*n* = 185)	No Mechanical Ventilation (*n* = 57)
All ICU patients			
Sodium, mmol/L, median (IQR)	137.0 (135.0–140.0)	137.0 (135.0–140.0)	137.0 (136.0–140.0)
WBC count × 10^9/L, median (IQR)	8.7 (6.6–12.7)	8.9 (6.7–13.0)	7.8 (6.5–10.1)
Hematocrit %, median (IQR)	37.0 (32.0–41.3)	37.0 (31.4–40.8)	38.2 (34.5–41.7)
Platelet count × 10^3, median (IQR)	208.0 (151.0–255.5)	207.5 (149.0–251.0)	225.0 (175.0–266.0)
Creatinine, mg/dL, median (IQR)	1.1 (0.8–1.9)	1.2 (0.8–1.9)	1.1 (0.8–1.9)
pH, median (IQR)	7.4 (7.3–7.4)	7.4 (7.3–7.4)	7.4 (7.3–7.4)
Pao_2, mm Hg, median (IQR)	71.0 (58.0–95.0)	71.0 (58.0–97.5)	65.0 (43.0–81.0)
Mean arterial pressure, mm Hg, median (IQR)	101.0 (90.0–115.0)	102.5 (90.0–117.0)	96.0 (88.0–111.0)
Pao_2/Fio_2 ratio, median (IQR)	93.8 (69.0–135.0)	90.0 (68.0–128.9)	145.5 (91.7–185.7)
Presence of shock, *n* (%)	46 (19.0)	41 (22.2)	5 (8.8)

IQR = interquartile range.

[a]Data presented is from laboratory values, arterial blood gas results, vitals, and other components of the electronic medical record (first 24 hr of ICU admission).

TABLE 3. Mortality Outcomes and Length of Stay for ICU Patients With Coronavirus Disease 2019 (*n* = 242)

Variable	Total (*n* = 242)	Mechanically Ventilated (*n* = 185)	Not Mechanically Ventilated (*n* = 57)
All patients in cohort (*n* = 242)			
Mechanically ventilated, *n* (%)	185 (76.4)	185 (100.0)	0 (0.0)
Time from ICU admission to mechanical ventilation, hr, median (IQR)	0.5 (0–7.4)	0.4 (0–7.4)	–
Duration of mechanical ventilation, d, median (IQR)	9.3 (5.7–13.7)	9.3 (5.7–13.7)	0 (0–0)
Disposition status, *n* (%)			
Died (total)	48 (19.8)	38 (20.5)	10 (17.5)
Remain admitted in hospital or ICU	78 (32.2)	66 (35.7)	12 (21.0)
Discharged alive	116 (47.9)	81 (43.8)	35 (61.4)
Patients who died	(*n* = 48)	(*n* = 38)	(*n* = 10)
Died in ICU, *n* (%)	42 (87.5)	38 (100.0)	4 (40.0)
Died in hospital, *n* (%)	6 (12.5)	0 (0.0)	6 (60.0)
ICU LOS[a], d, median (IQR)	8.7 (4.0–14.9)	10.5 (7.0–15.8)	3.3 (2.0–6.3)
Time from hospital admission to death, d[a], median (IQR)	29.5 (22.5–33)	31 (23–34)	28 (20–30)
Duration of mechanical ventilation, d, median (IQR)	8.8 (5.4–15.1)	8.8 (5.4–15.1)	0 (0–0)
Patients discharged alive, median (IQR)	(*n* = 116)	(*n* = 81)	(*n* = 35)
ICU LOS, d	9.2 (4.0–14.1)	10.8 (7.5–15.2)	2.8 (1.7–5.0)
Hospital LOS	30 (23–34)	31 (26–34)	27 (18–32)
Duration of mechanical ventilation, d	8.7 (4.9–11.4)	8.7 (4.9–11.4)	0 (0–0)
Patients still in hospital or ICU, median (IQR)	(*n* = 78)	(*n* = 66)	(*n* = 12)
ICU LOS, d	12.7 (7.2–20.3)	16.1 (9.3–21.3)	2.6 (2.1–3.3)
Hospital LOS	15.5 (7–24)	18.5 (10–27)	5 (3–6)
Duration of mechanical ventilation, d	10.9 (7.2–14.9)	10.9 (7.2–14.9)	0 (0–0)

IQR = interquartile range, LOS = length of stay.

Dash indicates data cannot be calculated because these are nonventilated subjects.

[a]LOS and time to death were calculated from time of admission to hospital and/or ICU until time of discharge or death.

TABLE 4. Cause-Specific Cox's Proportional Hazards Model for Death With Discharge As a Competing Risk (*n* = 242)

Variable	Hazard Ratio (95% CI)	*p*
Age, yr	0.012	
< 65 (reference)	1.0	
65–74	3.1 (1.2–7.9)	0.021
75+	4.1 (1.6–10.5)	0.003
Race	0.334	
Caucasian	1.0	
African American	0.6 (0.3–1.3)	0.214
Hispanic/Latino	0.2 (0.03–1.7)	0.148
Other	0.5 (0.1–2.7)	0.405
Severity of illness (Acute Physiology and Chronic Health Evaluation II)[a]	1.01 (0.97–1.06)	0.553
Pao_2:Fio_2 ratio	0.996 (0.991–1.000)	0.077
Charlson Comorbidity Index[b]	1.1 (0.9–1.3)	0.389
Other comorbidities[c]		
Hypertension	1.9 (0.7–5.2)	0.189
Chronic obstructive pulmonary disease	1.5 (0.6–3.7)	0.391
Chronic kidney disease	1.0 (0.5–2.3)	0.942
End-stage renal disease	5.9 (1.3–26.9)	0.021
Tobacco use	0.9 (0.4–1.8)	0.700

[a]Acute Physiology and Chronic Health Evaluation and Pao_2:Fio_2 ratios calculated using clinical data from first 24 hr of ICU admission.

[b]Charlson Comorbidity Index predicts mortality over 10 yr.

[c]Comorbidities assessed using diagnoses recorded in the medical record.

younger than age 65, and ESRD (HR, 5.9; 95% CI, 1.3–26.9; p = 0.021). In our cause-specific Cox's proportional hazard model, race, Charlson Comorbidity Index, and severity of illness by APACHE II were not significantly associated with increased odds of hospital mortality (**Table 4**).

DISCUSSION

In this study, we report a mortality rate of approximately 20% in mechanically ventilated COVID-19 patients, lower than recently published reports (3, 5–9). Furthermore, the mortality in our cohort is even lower than reported 28-day mortality of 35–46% for mild to severe ARDS (12).

Our mortality results are likely due to the surge in COVID-19 patients occurring later in Indiana than in other places, providing us the opportunity to learn from experiences at other centers. In addition, our medical system was not highly stressed. Due to a lack of strain on ventilator resources, clinicians at our hospitals elected to intubate patients early, as evidenced by 76% of the COVID-19-related ICU admissions receiving invasive ventilation. In contrast to other centers, we saw a relatively rapid but brief increase in COVID-19 ICU cases beginning in mid-March, peaking in early April (**Figure E2** in the Supplemental Digital Content http://links.lww.com/CCX/A283), and subsequently declining. Near the peak, only 58% of ICU beds and 27% of ventilators in the state were being used. This flattening of the curve can be attributed to a lower population density and early implementation of social distancing restrictions, allowing the medical system to effectively deal with the COVID-19 surge. This relationship between medical system capacity, the number of patients, and outcomes have been well described in the context of pandemic influenza (13, 14).

Our study is smaller compared with other cohorts limiting our ability to draw conclusions about mortality risk factors, although, like others, we found older age to be a significant risk factor, while patients identified as African American or Hispanic did not have increased risk of in-hospital mortality. We did not identify specific treatments, which led to a decreased mortality in our ventilated COVID-19 patients. Such work will require more granular analysis. However, we believe that sites able to prepare resources without getting overwhelmed with disease surges will show similar experiences. Our cumulative experience at Indiana University counterbalances prior published reports leading to the public perception that ventilatory support in COVID-19 patients frequently results in death, causing some to question the utility of mechanical ventilation in these patients.

CONCLUSIONS

In conclusion, we found lower mortality among mechanically ventilated COVID-19 patients than recently reported by others. This highlights that clinical experience with COVID-19 will vary widely across the country, which may be due to differences in public health practices, local medical practices, or resource availability. Ascertainment of comprehensive and accurate statistics will be important when developing policies and guidelines regarding the COVID-19 pandemic (15).

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