Original Article

Risk Factors for Mortality in Mechanically Ventilated Patients with COVID-19 in a Mississippi Community Health System

S. Ijlal Babar, MD, *Ashley E. Hawthorne,* PharmD, BCCCP, *and Maggie R. Clarkson,* RN, MSN

Objective: To evaluate differences between survivors versus nonsurvivors undergoing mechanical ventilation for coronavirus disease 2019 (COVID-19)–associated respiratory failure at two community medical centers.

Methods: This was a multicenter, retrospective cohort analysis of all adult patients mechanically ventilated for COVID-19–associated respiratory failure in two community hospital intensive care units in southern Mississippi from March 15, 2020 through October 10, 2020.

Results: Among 56 patients requiring mechanical ventilation, the mortality rate was 75% (42/56). Expired patients were intubated later (2 vs 5 days, 95% confidence interval [CI] 6.314–0.8041, P = 0.0983), had lower PaO_2:FiO_2 ratios (65 vs 77.5 mm Hg, 95% CI 36.08–59.03, P = 0.6305), and tolerated lower levels of positive end-expiratory pressure (7.9 vs 12.6 cm H_2O, 95% CI 0.1373–6.722, P = 0.0415) at the time of intubation.

Conclusions: Our results suggest that earlier intubation may be associated with reduced mortality in patients with COVID-19-associated respiratory failure and should be further evaluated in the form of a randomized controlled trial.

Key Words: COVID-19, critical care, endotracheal intubation, respiration, SARS-CoV-2

Critically ill patients with coronavirus disease 2019 (COVID-19) requiring mechanical ventilation have a mortality rate of approximately 56%.[1] We recently published our experience with hospitalized COVID-19 patients at the community hospital level, which showed that our outcomes were similar to those at larger centers.[2] This retrospective study was designed to evaluate overall differences between survivors and nonsurvivors requiring mechanical ventilation for COVID-19 respiratory failure in two community hospital intensive care units (ICUs). Differences in timing of intubation and ventilator parameters were specifically evaluated.

Methods

This multicenter, retrospective cohort study includes all hospitalized adult patients with COVID-19 requiring mechanical ventilation at both campuses of the Singing River Health System in South Mississippi between March 15 and October 10, 2020. All patients tested positive for COVID-19 by reverse-transcriptase polymerase chain reaction (RT-PCR). This study was approved by the Singing River Health System Institutional Review Board (Registration 00004249).

We compared demographics and ventilator parameters of survivors and non-survivors with evaluate differences in timing of intubation in relation to the date of hospital admission, date of ICU admission, and date of COVID-19 diagnosis and compared the duration of mechanical ventilation before either extubation or death.

Continuous variables were reported as means and standard deviations or medians and interquartile ranges and analyzed with the Student t test or the Mann-Whitney test, respectively. Categorical variables were reported as frequencies and analyzed with the χ^2 or the Fisher exact test, depending on the number of variables per cell. Statistical analyses were performed using GraphPad Prism software (GraphPad Software, San Diego, CA).

Results

A total of 56 patients required mechanical ventilation during the study period, with a mortality rate of 75% (Table 1). Comparisons

Key Points

- Patients intubated for coronavirus disease 2019–associated respiratory failure were separated into two groups (survivors and nonsurvivors) and differences in ventilator parameters and timing of intubation were evaluated.
- Clinically significant differences in PaO_2:FiO_2 ratios were observed on the day of intubation in survivors versus nonsurvivors.
- The timing of intubation was observed to be clinically significant, with survivors being intubated a median of 3 days earlier than nonsurvivors.

From the Singing River Health System, 2809 Denny Ave, Pascagoula, MS 39581, and the William Carey University School of Pharmacy, Biloxi, Mississippi.
Correspondence to Dr Ashley Hawthorne, William Carey University School of Pharmacy, 19640 Hwy 67, Biloxi, MS 39532. E-mail: ahawthorne@wmcarey.edu. To purchase a single copy of this article, visit sma.org/smj. To purchase larger reprint quantities, please contact Reprintsolutions@wolterskluwer.com.
S.I.B. is an advisor to Gen1E Lifesciences and owns shares in the company. The remaining authors did not report any financial relationships or conflicts of interest.
Accepted November 21, 2021.
0038-4348/0–2000/115-349

DOI: 10.14423/SMJ.0000000000001403

Table 1. Demographic characteristics and comorbidities by survival status (N = 56) March 15–October 10, 2020

Characteristic	Total cases, no. (%)	Survivors, no. (%)	Expired, no. (%)	*P*
Total	56 (100)	14 (25)	42 (75)	<0.0001
Sex				
Male	30 (53.6)	4 (29)	26 (62)	0.0305
Female	26 (46.4)	10 (71)	16 (38)	0.0303
Age (mean, SD)	62.8 ± 14.4	59.5 ± 14.1	63.8 ± 14.2	0.3356
Race				
White	31 (55.4)	7 (50)	24 (57)	0.6415
Black	21 (37.5)	6 (43)	15 (36)	0.6326
Other	4 (7.1)	1 (7)	3 (7)	1.00
BMI: median (IQR)	31.8 (27.7–38.3)	34.9 (28.7–38.3)	31.3 (26.6–37.6)	0.2225
Comorbidities				
Hypertension	45 (80.4)	12 (86)	33 (76)	0.7115
Diabetes mellitus	34 (60.7)	10 (71)	24 (57)	0.5287
Cardiovascular disorders	27 (48.2)	4 (29)	23 (55)	0.1255
Pulmonary disorders	18 (32.1)	2 (14)	16 (38)	0.1846
Malignancy	10 (17.9)	1 (7)	9 (21)	0.4266
Autoimmune disorders	4 (7.1)	1 (7)	3 (7)	1.00
Multiple comorbidities: median (IQR)	5 (4–7.7)	6 (4.75–6.25)	5 (3.75–8)	0.8537

BMI, body mass index; IQR, interquartile range; SD, standard deviation.

of demographics and comorbidities did not differ between groups, with the exception of a higher percentage of male patients in the nonsurvivors (29% vs 62%, $P < 0.0001$). The patients in this cohort were severely hypoxemic, with a median PaO_2:FiO_2 ratio of 66.5 on day 1 of intubation (Table 2). Survivors required fewer vasopressors (1.4 vs 2.4, $P = 0.0009$) for shorter durations (6 vs 9 days, $P = 0.2411$) and spent significantly more days on the ventilator (16.5 vs 9 days, $P = 0.0173$). Ventilator parameters differed in regard to positive end-expiratory pressure (PEEP) on days 1 and 3 (PEEP day 1: 12.6 vs 7.9 cm H_2O, 95%

Table 2. Patient parameters by survival status (N = 56), March 15–October 10, 2020

Parameters	Total cases	Survivors	Expired	95% CI	*P*
Ventilator settings					
PEEP cm H_2O, median, IQR					
Day 1	9.2 (5.4–16.6)	12.6 (7.7–20)	7.9 (5.2–12.1)	0.1373– 6.722	0.0415
Day 3	10.2 (6.3–14.1)	8.8 (5–12.5)	10.2 (7.2–14.3)	−4.903 to 1.324	0.2531
FiO_2 median, IQR					
Day 1	100 (80–100)	80.2 (70–100)	100 (85–100)	−19.22 to − 0.7408	0.0348
Day 3	59 (40–80)	48 (40–60)	60 (45–87)	−27.75 to − 1.449	0.0304
PaO_2:FiO_2, mmHg, median, IQR					
Day 1	66.5 (54.5–87.5)	77.5 (56–116)	65 (52–81)	−36.08 to 59.03	0.6305
Day 3	144 (97–212)	144 (127–213)	145 (84–199)	−46.35 to 55.29	0.8601
Vasopressor use, no. (%)	53 (94.6)	13 (93)	40 (95)	0.2481–4.154	1
Duration, d, median (IQR)	8 (3–16)	6 (3–13)	9 (3–18)	−9.679 to 2.490	0.2411
No. agents/case, mean, SD	2 ± 1	1.4 ± 0.6	2.4 ± 0.9	−1.478 to −0.4030	0.0009
Other median (IQR)					
Days proned	2 (0–5)	1.5 (0–4)	2.5 (0–6)	−5.748 to 1.748	0.2895
Total ventilator days	10 (5–21)	16.5 (9–23)	9 (4–17)	1.425–14.11	0.0173
Preintubation hospital days	4 (1–8)	2 (0–3)	5 (1–8)	−6.314 to 0.5523	0.0983
Preintubation ICU days	1 (0–6)	0 (0–2)	2.5 (0–6)	−5.899 to 0.8041	0.1334

CI, confidence interval; ICU, intensive care unit; IQR, interquartile range; PEEP, positive end-expiratory pressure; SD, standard deviation

CI 0.1373–6.722, $P = 0.0415$; PEEP day 3: 8.8 vs 10.2 cm H_2O, 95% CI −4.903 to 1.324, $P = 0.2531$; Table 2).

Discussion

This retrospective cohort study shows a high mortality in patients intubated in the ICUs of a community hospital system. Survivors had higher PaO_2:FiO_2 ratios on the day of intubation (77.5 vs 65 mm Hg, $P = 0.6305$) and were intubated sooner than nonsurvivors (2 vs 5 days, $P = 0.0983$; Table 2). Although not statistically significant, our results represent clinical significance. A recently published study also reported improved outcomes in patients intubated earlier in their course.[3]

Although these survival data are worse than reported in a recent meta-analysis, which showed an adjusted case fatality rate of 56%, the results may be explained by the severity of hypoxia, presence of comorbidities at baseline, and average age (62.8 ± 14.4 years) in our cohort (Table 2).[1] The median PaO_2:FiO_2 ratio in our patient population was 66.5 mm Hg at the time of intubation, as opposed to 105 and 160 mm Hg in similar studies.[4,5] In addition, the mortality rate of 75% was similar to the rate of >70% in patients older than 60 years in the meta-analysis by Lim et al.[1]

Earlier mechanical ventilation in survivors may be reflective of a stage when COVID-19-associated respiratory failure is more responsive to mechanical ventilation. Conversely, patients intubated earlier may be phenotypically different, manifesting more hypoxemia and dyspnea at an earlier stage of the disease. A recent clinical update describes two different phenotypes of respiratory failure in COVID-19. An "L" phenotype, which has higher compliance and more ground glass opacities versus dense consolidation and lower compliance seen in the "H" phenotype.[6] Our cohort of survivors may have been representative of the L phenotype. Unfortunately, we are unable to establish this based on the information available.

Higher PEEP is noted to have been applied initially in survivors compared with nonsurvivors (12.6 vs 7.9 cm H_2O, $P = 0.0415$). Owing to the retrospective design of this study, it is difficult to elucidate which factors led to higher PEEP at the outset in survivors, even though their PaO_2:FiO_2 ratio was higher than that of nonsurvivors (77.5 vs 65 mm Hg, $P = 0.6305$). Because the usual practice in our ICU is to find optimal PEEP using driving pressures, it is plausible that higher PEEP could not be applied in nonsurvivors because of lower lung compliance.[7] In this respect, our surviving patients do not fit the L phenotype because these patients are not described as being PEEP responsive.

The effect of more aggressive PEEP application in survivors can be seen on day 3 postintubation, by which time PEEP had been reduced to 8.8 cm H_2O in survivors versus 10.2 cm H_2O in nonsurvivors ($P = 0.2531$), and FiO_2 had been reduced to 48% vs 60% ($P = 0.0304$). Although the PaO_2:FiO_2 ratio on day 3 postintubation was similar between the two groups (144 vs 145 mm Hg, $P = 0.8601$), survivors maintained this ratio at a lower PEEP.

Survivors spent a significantly longer time on the ventilator than nonsurvivors. In this regard, it is notable that 32 of the 42 nonsurvivors (76%) underwent withdrawal of support as requested by family. This is likely related to the greater comparative severity of illness in these patients, coupled with a perception of poor outcomes that were pervasive during the pandemic.

Conclusions

This small retrospective study shows a high mortality rate in patients intubated for COVID-19–associated acute respiratory failure. We observed improved outcomes with earlier intubation in these patients. Based on the retrospective design of this study, we are unable to state whether the early intubation was coincidental, leading to improved outcomes or necessitated by phenotypic variations in some patients who decline more rapidly in terms of hypoxemia and dyspnea, leading to earlier intubation. This aspect of COVID-19 respiratory failure deserves further study.

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