

Mortality Data in Mechanically Ventilated COVID-19 patients admitted to ICU: A Retrospective Study in Brooklyn

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Abstract

Background: High mortality rates are predominant even in COVID-19 patients requiring minimal supportive therapy, with a short-coming of data on COVID-19 patients requiring mechanical ventilation.

Objectives/Design: We performed a single-center, retrospective, cohort study at a tertiary care, community-based teaching hospital with patient who required invasive mechanical ventilatory support and were COVID-19 positive. All patients were treated according to the ARDSnet protocol. The primary outcome was overall mortality, and secondary outcome was successful extubation.

Results: A total of 72 COVID-19 positive intubated patients were included. Twenty-six (66.6%) patients died within the first 15 days of hospital admission; thirty-eight (52.7%) died within 28 days, and thirty-nine (54.2%) died within 29 days. A total of 22 patients (30.5%) were successfully extubated. 15 patients (20.8%) who required reintubation or could not be extubated further underwent tracheostomy.

Conclusions: Mortality of critically ill COVID-19 patients requiring mechanical ventilatory support is high, our observed mortality rate (54.2%) was significantly lower than currently published reports. We believe our rate to be a consequence of early intubation in conjunction with adherence to ARDSnet protocol. We also observed patients with hyperlipidemia, higher CRP, renal failure, or those requiring vasopressor use had worse outcomes.

Introduction

In early December 2019, a group of acute respiratory illness, now known as Coronavirus Disease 2019 (COVID-19) emerged in Wuhan district of Hubei province in China ¹. Clinical presentation of the viral disease ranges from asymptomatic carriers to severe hypoxemic respiratory failure leading to severe acute respiratory distress syndrome (ARDS) ², labeling the disease as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

Even with ongoing research worldwide, to date there are no specific proven treatments. The main goal is to provide rational and effective respiratory support to achieve appropriate oxygenation ³. Mechanical ventilation is the standard treatment of care for critically ill patients infected with SARS-CoV-2 ⁴. An estimated 2.3% of these patients need tracheal intubation. Despite all adequate support reported mortality rate is still very high ^{3,4}.

The COVID-19 pandemic has spread rapidly across the United States (US) becoming the leading country by number of people infected and associated deaths ^{5,6}. As of April 20th, 2020, the rate of infection in New York (NY) has exceeded every other state becoming more than 30% of all of the US cases ⁷. Those who received mechanical ventilation in NY have a reported mortality rate of 88.1% ⁷.

High mortality rates are predominantly due to severity and rapid spread of the illness associated with the virus ³. Significant differences have been noted in the clinical and demographic features of COVID-19 patients in many regions of the world ⁶. Those particularities, as well as distinct local practices, have been shown to play an major role in determining clinical outcomes ⁸.

There is a lack of data despite increased incidence, in high population density areas³. Detailed data on demographic characteristics, underlying medical conditions, and potential interventions for hospitalized

patients with COVID-19 are needed to conjugate prevention strategies and community specific interventions^{5,9}. In order to improve care and to reduce mortality, we highlight the need for studies to assess mechanisms behind increased disease severity. Thus, we report an analysis of randomized retrospective data on 72 patients who received invasive mechanical ventilation admitted to a large community medical intensive care unit in Borough Park, Brooklyn, New York. We aim to describe possible risk factors and pharmacological interventions associated with positive results; thereby proposing interventions which can potentially improve overall outcomes.

Methods

Study design and Participants

This single-center, retrospective, cohort study was performed at Maimonides Medical Center - a tertiary care, community-based teaching hospital in Brooklyn. All patients admitted to the Medical Intensive Care Unit (MICU) between March 13 and April 30, 2020 who required invasive mechanical ventilatory support were included. Laboratory confirmation of COVID-19 was performed with nasopharyngeal swab reverse transcriptase polymerase chain reaction (RT-PCR). All the participants tested positive.

Exclusion criteria: All patients who tested positive for COVID-19 and not admitted to MICU were excluded. Patients admitted to overflow ICUs and general medical floors were excluded. All patients requiring any form of respiratory support such as: nasal cannula, non-rebreather, high flow nasal cannula, non-invasive ventilation were excluded from the study.

All the patients enrolled in the study were treated according to the ARDSnet protocol, maintaining low tidal volume (4-6ml/kg Ideal body weight). The tidal volume was only increased when any of the patients developed severe respiratory acidosis. Due to limited availability of resources including nursing staff and respiratory therapists, patients were prone when the ratio of partial pressure of arterial oxygen divided by the percentage of inspired oxygen (PaO_2/FiO_2) was less than 100mmHg.

The study was approved by the Institutional Research Board at Maimonides Medical Center, and the requirement for informed consent was waived due to the retrospective nature of the study.

Data Collection

We performed a detailed review of electronic medical records and extracted demographic, clinical and laboratory data. There was no missing information.

The parameters included age (18 to 44, 45-64, 65-74 and 75 years-old); gender (male or female); ethnicity (African American, Asian, Caucasian, and Hispanic or Latino); comorbidities (hypertension, diabetes mellitus, hyperlipidemia, chronic cardiac disease, chronic pulmonary disease, chronic renal disease, malignancy and others which included neurologic, psychiatric and rheumatologic disorders, e.g.); previous use of non-steroidal anti-inflammatory drugs, angiotensin-converting-enzyme inhibitors or angiotensin II receptor blockers; Body mass index (<18.5; 18.5 - 24.9, 25-29.9, 30-34.9; 35-39.9 or 40); highest value of C-reactive protein (CRP), creatinine and blood urea nitrogen (BUN); lowest value of the ratio of partial pressure of arterial oxygen divided by the percentage of inspired oxygen (PaO_2/FiO_2); usage of vasopressors and requirement for dialysis.

Systemic shock and requirement for vasopressors were defined by presence of mean arterial pressure lower than 60mmHg and lack of response to fluid resuscitation. Hemodialysis indication was individualized and based on BUN and creatinine trend and electrolytes abnormalities.

Outcomes

The primary outcome was overall mortality. Secondary outcome was successful extubation (defined by ability to sustain spontaneous breath and no need for reintubation within 72 hours).

Statistical analysis

A descriptive analysis was performed with the aim to correlate all variables to both outcomes in an attempt to determine predictors for successful extubation and death. Therefore, there was no formal hypothesis, and the ideal sample size could not be determined. We included a maximum number of patients based on the expanded capacity of the of the medical intensive care unit.

We assessed the correlation between all parameters and the two outcomes using regression models. Each variable required a different set of univariate logistic regression model.

The variables “age” and “body mass index” were divided into subcategories. In addition to the comparison to outcomes, they were also compared between themselves in order to determine if any significant superiority were present. The last process was performed by using a negative binominal regression model.

A p-value <0.05 was considered statistically significant. All statistical analyses were performed using Statistical Package for Social Sciences (SPSS) statistical software (IBM, NY, USA).

Results

Our final sample included 72 intubated patients. Twenty-six (66.6%) patients died within the first 15 days of hospital admission; thirty-eight (52.7%) died within 28 days, and thirty-nine (54.2%) died within 29 days. All deaths occurred within one month of hospital admission.

Out of 39 patients who expired; 16 (41.1%) were admitted to the medical ICU in March and 23 (58.9%) in April.

A total of 22 patients (30.5%) were successfully extubated. Those who later required reintubation or couldn't be extubated and further underwent a tracheostomy were 15 in total (20.8%).

Demographic and Clinical Parameters

All parameters which were studied are summarized in Table 1. Mean age was 63.9 years and 31.9% were female.

A total of forty-six (63.8%) patients were obese [body mass index (BMI) ≥ 30 kg/m²]. Fifty-seven patients (79.16%) had at least one comorbidity. Those who died had at least one comorbidity and/or were obese.

Laboratory and Treatment Data

All patients developed elevated CRP levels, mean of 28.34mg/dl (11.5mg/dl).

Sixteen (22.2%) patients did not develop an abnormal creatinine result (defined by 1.2mg/dl). Among those who did, the mean creatinine was 4.3mg/dl (2.88mg/dl) and the BUN was 86mg/dl (40.46mg/dl).

A total of 22 (30.5%) participants required hemodialysis and 51 (70.8%) required the use of vasopressors. According to the Berlin Definition Criteria for ARDS¹⁰, thirty-four patients (47.2%) developed a severe form of the disease (PaO₂/FiO₂ ratio < 100mmHg). The mean ratio was 122.65mmHg (60.6mmHg). Due to limited availability of resources during the pandemic, the PaO₂/FiO₂ of <100 and not 150mmHg was followed for patient proning.

The findings are summarized in Table 2.

Discussion

In this study, we investigated 72 critically ill patients with confirmed COVID-19 pneumonia requiring mechanical ventilation. As compared with reported mortality rates of 62% (Wuhan, China), 67% (Washington State, USA)⁸, and 88% (New York, USA)⁷, we hereby present our mortality rate of 54.2% (or our 28-day mortality rate of 52.7%). This study took place in a large community hospital located in a pandemic epicenter area. We attribute our relative low mortality rate to the combination of early intubation and usage of ARDSnet protocol^{11,12}.

Through detailed data analysis of demographic characteristics and underlying medical conditions, significant connections with clinical outcomes were established. We found younger patients who had higher BMI had a worse clinical outcome, reinforcing the already known correlation of obesity and severe disease². Despite this, neither age or BMI significantly correlated with mortality or successful extubation rates. Although the literature recognizes a linear relationship between elderly and obese patients with severity of disease^{5,7}, we found that among those who were already intubated (critically ill) the above risk factors did not predict outcomes. The same findings are also applicable to gender and race.

Chronic conditions such as underlying lung disease, cardiovascular disease, diabetes mellitus, and hypertension also seem to increase the risk for severe COVID-19^{2,4}. Otherwise, we found only hyperlipidemia was strongly associated with risk of death, and not extubation failure.

In regard to laboratory data, we identified statistically significant predictors for worse outcomes. Patients with higher CRP levels, BUN, and creatinine during hospitalization were at increased risk of death and lower successful extubation rates. The same association applies to those who had lower PaO₂/ FiO₂ ratios, reestablishing findings from Wuhan, China⁴.

Emerging therapies along with supportive therapy, is the consensus for treatment worldwide³. In our cohort, 22 (30.5%) participants required hemodialysis. However, this requirement did not correlate with outcomes. Hemodialysis did not predict death, liberation of ventilator, or tracheostomy. The majority (70.8%) received

vasopressors, typically associated with greater mortality, but not with failed extubation. We find these results to be unique, given no available data on dialysis or vasopressors usage for comparison to our knowledge.

Our study has some limitations. First, our sample size of 72 patients is rather small. Yet, we aimed to analyze an exclusive cohort, limited to only intubated patients. This adds reliability to disease severity. We hope the findings presented here will encourage a larger cohort study. Second, this study was performed in a single-center. However, this fact could potentially reduce bias on protocol adherence, increasing the power of our reported mortality rate. Third, this is a retrospective study. Our data permit a preliminary assessment of mortality and successful extubation rates in patients with COVID-19 who are mechanically ventilated. Larger studies are needed to overcome our limitations, and further our knowledge regarding this disease.

In conclusion, although the mortality of critically ill patients is still high, our rate was significantly lower when compared to other studies. We believe this was a consequence of early intubation in conjunction with the usage of the ARDSnet protocol. We also observed patients with hyperlipidemia, higher CRP, renal failure, or those requiring vasopressor use had worse outcomes.

Declarations

Conflicts of Interest

All authors above have no conflicts of interest.

No prior presentations of the data.

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Tables

Table 1

Demographic and Clinical Parameters

Variable		Total Patients (n = 72)	Effect	Primary Outcome		Secondary Outcome	
				r-Value	Odds Ratio (95% CI)	r-Value	Odds Ratio (95% CI)
Age	18 - 44	6 (8.3%)	Age 18-44 vs 45-64	0.4167	0.375 (0.03 – 3.99)	0.2648	3.667 (0.37 – 35.97)
	45 - 64	26 (36.1%)	Age 45-64 vs 18-44	0.4167	0.375 (0.03 – 3.99)	0.2648	3.667 (0.37 – 35.97)
	65 - 74	25 (34.7%)	Age 65-74 vs 18-44	0.7274	0.65 (0.05 – 7.32)	0.7014	1.579 (0.15 – 16.30)
	³ 75	15 (20.8%)	Age ³ 75 vs 18-44	0.472	3 (0.15 – 59.88)	0.6301	1.818 (0.16 – 20.71)
Gender	Male	49 (68.1%)	Male vs Female	0.8487	0.879 (0.23 – 3.31)	0.1071	0.422 (1.47 – 1.20)
	Female	23 (31.9%)					
Race	African Americans	8 (11.1%)	African American vs Asian	0.9432	1.1 (0.08 – 15.15)	0.3691	0.417 (0.06 – 2.81)
	Asians	15 (20.8%)	Asian vs African American	0.9432	1.1 (0.08 – 15.15)	0.3691	0.417 (0.06 – 2.81)
	Caucasian	42 (58.3%)	Caucasian vs African American	0.428	0.4 (0.04 – 3.85)	0.615	0.667 (0.13 – 3.23)
	Hispanic or Latino	7 (9.7%)	Hispanic/Latino vs African American	0.7483	0.6 (0.02 – 13.58)	0.4499	2.222 (0.28 – 17.63)
BMI	<18.5		<18.5 vs 18.5 – 24.9	0.9881	>999.999 (<0.01 - >999)	0.9869	<0.001 (<0.01 - >999)

18.5 – 24.9		18.5 – 24.9 vs < 18.5	0.9881	>999.999 (<0.01 - >999)	0.9869	<0.001 (<0.01 - >999)
25-29.9		25-29.9 vs 18.5 – 24.9	0.6784	1.75 (0.12 – 24.65)	0.5293	0.5 (0.05 – 4.33)
30 – 34.9		30-34.9 vs 18.5 – 24.9	1	1 (0.07 – 13.01)	0.4885	0.474 (0.05 – 3.92)
35 – 39.9		35 – 39.9 vs 18.5 – 24.9	0.8804	1.25 (0.06 – 22.87)	0.4822	0.4 (0.03 – 5.15)
³ 40		³ 40 vs 18.5 – 24.9	0.5771	2.5 (0.1 – 62.60)	0.236	0.222 (0.01 – 2.67)
Comorbidities	57 (79.1%)	Presence vs Absence	0.9674	1.031 (0.23 – 4.54)	0.7931	0.85 (0.25 – 2.86)
Hypertension	42 (58.3%)	Presence vs Absence	0.4782	0.639 (0.18 – 2.20)	0.9312	1.046 (0.37 – 2.89)
Diabetes Mellitus	30 (41.6%)	Presence vs Absence	0.7939	1.174 (0.35 – 3.91)	0.9312	0.956 (0.34 – 2.64)
Hyperlipidemia	21 (29.1%)	Presence vs Absence	0.0455	0.282 (0.08 – 0.97)	0.3748	1.626 (0.55 – 4.76)
Chronic Lung Disease	13 (18%)	Presence vs Absence	0.6295	0.686 (0.14 – 3.17)	0.0514	3.422 (0.99 – 11.80)
Chronic Cardiac disease	13 (18%)	Presence vs Absence	0.8003	0.824 (0.18 – 3.70)	0.4962	1.544 (0.44 – 5.39)
Chronic Renal Disease	3 (4.1%)	Presence vs Absence	0.9798	>999.999 (<0.01 - >999)	0.9787	<0.001 (<0.01 - >999)
Malignancy	5 (6.9%)	Presence vs Absence	0.9766	>999.999 (<0.01 - >999)	0.6001	0.548 (0.05 – 4.33)

							- 5.20)
	Others	16 (22.2%)	Presence vs Absence	0.5954	1.575 (0.29 - 8.42)	0.5856	0.704 (0.19 - 2.48)
	Previous use of NSAID/ ACE-i/ ARBS	24 (33.3%)	Yes vs No	0.5626	0.696 (0.20 - 2.37)	0.7177	1.214 (0.42 - 3.47)

Table 2

Laboratory and Treatment Data

Variable	Primary Outcome		Secondary Outcome	
	r-Value	Odds Ratio (95% CI)	r-Value	Odds Ratio (95% CI)
Highest CRP level	0.0101	1.083 (1.01 - 1.152)	0.0105	0.937 (0.89 - 0.98)
Highest BUN level	0.0269	1.02 (1.00 - 1.03)	0.0024	0.975 (0.95 - 0.99)
Highest Creatinine level	0.1501	1.178 (0.94 - 1.47)	0.0087	0.695 (0.53 - 0.91)
Received Hemodialysis	0.4896	1.586 (0.42 - 5.87)	0.1382	0.395 (0.11 - 1.34)
Required vasopressors	0.0292	4.25 (1.15 - 15.59)	0.1502	0.456 (0.15 - 1.32)
Lowest PaO2/ FiO2	0.0196	0.988 (0.97 - 0.99)	0.0019	1.015 (1.00 - 1.025)