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Research Article

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 (36.1%) 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 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.

Keywords: Coronavirus; SARS-CoV-2; Acute Respiratory Distress Syndrome; Mortality Rate; Mechanical Ventilation

1. Introduction

In early December 2019, a novel 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 to severe hypoxemic respiratory failure leading to acute respiratory distress syndrome (ARDS) [2], designating 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 constituting 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 a major role in determining clinical outcomes [8]. There is a lack of data despite increased incidence, in high population density areas [3]. 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 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.

2. Materials and Methods

2.1 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 was included. Laboratory confirmation of COVID-19 was performed with reverse transcriptase polymerase chain reaction (RT-PCR) test on nasopharyngeal swab. All the participants tested positive. All patients who tested positive for COVID-19 and not admitted to MICU; admitted to overflow ICUs and general medical floors; placed on ECMO; or requiring any non-invasive form of respiratory support such as: nasal cannula, non-rebreather, high flow nasal cannula, non-invasive mechanical ventilation were excluded from the study. All the patients enrolled in the study were treated according to the ARDSnet protocol, maintaining a 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 proned when the ratio of partial pressure of arterial oxygen divided by the percentage of inspired oxygen (PaO2/FiO2) 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.

2.2 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 (PaO2/FiO2); 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, respectively.

Hemodialysis indication was individualized and based on trend of BUN and creatinine and electrolytes abnormalities.

2.3 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).

2.4 Statistical analysis

An exploratory analysis was performed with the aim of finding the association between all variables to both outcomes in an attempt to determine predictors for successful extubation and death. Asthere was no formal hypothesis as well as COVID-19 being a novel virus with little historical data, the analyses were unpowered, and the sample size was based on the maximum number of patients based on the expanded capacity of the medical ICU.

Univariable logistic regression models were created for each predictor variable and outcome. Age and BMI were categorized. These sub-categories were further analyzed using contrasts to determine pairwise category differences.

Odds ratios with 95% confidence intervals are presented in tables 1 and 2. P-values for the logistic regression models were wald-chi-squares and z-tests for the contrasts. A p-value <0.05 was considered statistically significant, and analyses were not adjusted for multiple comparisons. All statistical analyses were performed SAS Version 9.4, Cary, NC.

3. Results

Our final sample included 72 intubated patients. Twenty-six (36.1%) 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%). Patients with hyperlipidemia (OR 0.282 (0.08 – 0.97)), elevated CRP (OR 1.083 (1.01 – 1.152)), elevated BUN (OR 1.02 (1.00 – 1.03)), requiring vasopressors (OR 4.25 (1.15 – 15.59)), low PaO2/FiO2 ratio (OR 0.988 (0.97 – 0.99)) had a statistically significant higher overall mortality rate.

3.1 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/m^2]. Fifty-seven patients (79.16%) had at least one comorbidity. Those who died had at least one comorbidity and/or were obese.

3.2 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 serum creatinine (defined by ≥ 1.2mg/dl). Among those who did, the mean serum 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 ARDS (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 <100mmHg and not <150mmHg was followed to prone the patients. The findings are summarized in table 2.

				Primary Outcome		**Secondary Outcome**	
Variable		**Total Patients (n = 72)**	**Effect**	**p-Value**	**Odds Ratio (95% CI)**	**p-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)
	≥ 75	15 (20.8%)	Age ≥ 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)

	≥ 40		≥ 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 – 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 1: Demographic and clinical parameters

	Primary Outcome		**Secondary Outcome**	
Variable	**p-Value**	**Odds Ratio (95% CI)**	**p-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)

Table 2: Laboratory and treatment data

4. 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 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 disease [2]. Despite this, neither age nor 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, China [4]. Emerging therapies along with supportive therapy, is the consensus for treatment worldwide [3]. 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 intubate patients. This adds reliability as these patients are suffering from the highest 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. 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 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.

Acknowledgements and conflicts of interest

No funding or contributions other than aforementioned authors were used for this study.

All authors above have no conflicts of interest.

Study protocols were approved by the Maimonides Medical Center Institutional Review Board (IRB),

and informed consent was waived by the IRB. All data collection was completed after IRB approval.

No prior presentations of the data and no patients have been reported in other submissions the authors or anyone else.

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