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Research Article

Clinical Features and Prognosis of Invasive Ventilation in Hospitalized Patients with COVID-19: A Retrospective Study

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Abstract

Background: World Health Organization (WHO) declared that the outbreak of COVID-19 constituted a public health emergency of global concern.
Objectives: Owing to limited data on critically ill patients admitted to ICU, we aimed to describe the clinical characteristics and prognosis of these patients based on ventilatory variables and clinical features.
Methods: In this retrospective study, 45 critically ill patients with laboratory-confirmed COVID-19 who were admitted to Intensive Care Unit (ICU) wards of the hospital from April 8 to May 9, 2020, were enrolled. Medical files of the patients were reviewed, and demographic and clinical characteristics, laboratory data, lung CT scan findings, causes of intubation, and outcomes of the patients were all collected.
Results: The median age of the patients was 67 years (range 22 to 91), 64% were men, and hypertension was the most common comorbidity. History of close contact with previously confirmed patients was positive in 62.2% of the patients. The mean time from symptom onset to hospital admission was 5.98 $\pm$ 2.93 days. The most common symptoms at the onset of illness were dyspnea (95.6%), and gastrointestinal symptoms (22.2%) were rare. The average length of the intubation was 4.84 $\pm$ 3.28 days. The distribution of intubation causes in the deceased patients was significantly more than the recovered patients (P = 0.031). The mean score of lung CT involvement in deaths (370.26 $\pm$ 207.50) was significantly higher than the recovered patients (235.71 $\pm$ 81.21) (P = 0.042). Length of the intubation had a statistically direct correlation with respiratory rate (P = 0.03).
Conclusions: Most of the critically ill patients admitted to ICU were older men and had poor outcomes with a high mortality rate. Furthermore, the score of chest CT involvement and respiratory rate are important prognostic factors in determining the severity of the illness, requiring ventilatory support, and outcome.

Keywords: COVID-19, SARS-Cov-2, Critically Ill Patients, Ventilation, Mortality

1. Background

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV2) is a new strain of coronavirus, which was first detected in Wuhan, China, in December 2019 (1, 2). Thus far, coronavirus disease 2019 (COVID-19), caused by SARS-CoV2, has rapidly infected millions of people around the world and has become an emerging health threat (3). On February 19, 2020, Iran reported its first cases diagnosed with COVID-19 in Qom; subsequently, the increasing number of cases recorded in Qom, and finally, throughout all 31 provinces of the country (4).

COVID-19 is a novel disease with wide clinical manifestations, encompassing asymptomatic or mild upper respiratory tract illness to severe viral pneumonia with acute respiratory distress syndrome (ARDS) and even death (5). Whereas most infected people develop mild to moderate illness and recover without hospitalization, about 14% present with severe symptoms that require hospital care, and one-third of hospitalized patients need invasive mechanical ventilation (6). Critically ill patients with COVID-19 may develop ARDS, septic shock, sepsis, cardiac injury, acute kidney injury, and multi-organ dysfunction (7). Although risk factors for severe illness remain unclear, comorbidity and older age have been reported as likely important factors for poor prognosis and death (8, 9).

To date, no specific medication or immunomodulatory therapy has yet been approved for the treatment of COVID-19, so the management of critically ill patients is similar to the management of most viral pneumonia, and supportive therapy to control symptoms and to protect multi-organ function is the priority of the management (10). Therefore, due to the increase in the number of hospitalized patients and limited ICU capacity, identifying clinical characteristics and hospital course of severe and ventilated patients with COVID-19 is crucial to guide decision making regarding ICU capacities and allocation of resources to decrease the mortality rate. Most of the previous studies have just reported the general epidemiological, and clinical characteristics of hospital admitted patients with COVID-19, and there are limited data about the clinical course of severe cases of COVID-19 (7, 9, 11-14). Recently, a case series from Italy have reported detailed information on ventilatory parameters, clinical and laboratory characteristics and have determined prognosis and risk factors of ventilated patients with COVID-19 admitted to ICU. Their results showed that older age and pre-admission hypertension are the main mortality risk factors (15).

2. Objectives

Accordingly, we aimed to describe the clinical characteristics and prognosis of critically ill patients with COVID-19 based on ventilatory variables and clinical features.

3. Methods

3.1. Study Population

This retrospective study was done at a teaching hospital, Tehran, Iran, which is one of the referral centers for the COVID-19. The inclusion criteria were all consecutive critically ill patients with laboratory-confirmed COVID-19 who were admitted to intensive care unit (ICU) wards or transferred from wards to ICU of the hospital from April 8 to May 9, 2020. The patients without any imaging documents, either chest X-ray (CXR) or chest CT were excluded. Drug history of all enrolled cases was recorded in detail, but this information was not analyzed. All of the deaths caused by COVID-19 directly or indirectly and also caused by COVID-19 complication were recorded as COVID-19 death. Confirmed infection was defined as positive real-time polymerase chain reaction (RT-PCR) to SARS-CoV-2 in their nasopharyngeal specimens (10). Critically ill patients were defined as intubated patients admitted to ICU who required mechanical ventilation. The respiratory rate of the patients was recorded immediately before intubation, and in case of being higher than the determined limit defined as tachypnea and the relationship between tachypnea with intubation time was then analyzed. The Ethics Commission of Iran University of Medical Sciences approved this study, and written informed consent was waived due to the nature of retrospective chart review.

3.2. Data Collection

Medical files of the patients were reviewed for data collection. We obtained data on demographic, signs and symptoms upon hospital admission, comorbidities, smoking history, contact exposure, history of influenza vaccination, laboratory data, lung CT scan findings, time from symptoms to hospital admission, time from hospital admission to intubation, length of the intubation, causes of intubation, and outcome data. All data were collected by two trained investigators.

Causes of intubation were classified into hypoxia and hypercapnia, hypoxia and tachypnea and hypercapnia, hypoxia and tachypnea, hypoxia, hemodynamic instability, and cardiopulmonary arrest. Hypoxia was defined as SPO_2 under 90% or PaO_2 under 60 mmHg, hypercapnia was defined as $PaCO_2$ above 50 mmHg, and tachypnea was defined as respiratory rate above 30/min.

Lung CT findings were graded on a scale of 1 - 6 based on a classification system which had been previously evaluated in the other diseases: 1 normal; 2 ground-glass; 3 consolidation; 4 ground-glass with traction bronchiolectasis or bronchiectasis; 5 consolidation with traction bronchiolectasis or bronchiectasis, and 6 honeycombing (16, 17). The presence of each of these abnormalities was assessed in three (upper, middle, and lower) zones of each lung. The percentage of involvement in each zone was estimated based on visual criteria by two expert radiologists. The abnormality score for each zone was calculated by multiplying the percentage area by the point value (1-6). The six-zone scores were averaged to determine the total score for each abnormality in each patient. The overall CT score for each patient was obtained by adding the six averaged scores.

3.3. Statistical Analysis

All statistical analyses were performed with the Statistical Package for Social Sciences version 20.0 (SPSS Inc., Chicago, IL, USA). Means $\pm$ standard deviation (SD) and median (with an interquartile range = IQR = Q1-Q3) were used for continuous variables, and frequencies and proportions were used for categorical variables. Variables of both groups (death or survival) were compared using χ^2 tests or Fisher's Exact test for proportions and unpaired *t*-tests for means. Pearson correlation coefficient was used to evaluate the association between characteristics with ventilatory variables. A P-value of less than 0.05 was considered statistically significant.

4. Results

Fifty-four critically ill patients with confirmed COVID-19 were admitted to the ICU of the teaching hospital and

Table 1. Baseline Characteristics of Critically Ill Patients with COVID-19

Characteristics	Total Number of Patients (%)
Age, mean ± SD	65.39 ± 14.60
Gender	
Female	16 (35.6)
Male	29 (64.4)
Asthma	
No	42 (93.3)
Yes	3 (6.7)
Smoking history	
No	37 (82.2)
Yes	8 (17.8)
Diabetes	
No	26 (57.8)
Yes	19 (42.2)
Hypertension	
No	22 (48.9)
Yes	23 (51.1)
Chronic heart failure	
No	39 (86.7)
Yes	6 (13.3)
Received annual influenza vaccine	
No	39 (86.7)
Yes	6 (13.3)
History of close contact with infected patients	
Unknown	17 (37.8)
Yes	28 (62.2)
Outcome	
Recover	7(15.6)
Death	38 (84.6)

Table 2. Signs and Symptoms Upon Hospital Admission of Critically Ill Patients with COVID-19

Signs and Symptoms Upon Hospital Admission	Total Number of Patients (%)
Fever	
No	9 (20)
Yes	36 (80)
Dyspnea	
No	2 (4.4)
Yes	43 (95.6)
SPO_2 < 93%	
No	3 (6.7)
Yes	42 (93.3)
Myalgia or fatigue	
No	25 (55.6)
Yes	20 (44.4)
Cough	
No	10 (22.2)
Yes	35 (77.8)
Nausea and vomiting	
No	41 (91.1)
Yes	4 (8.9)
Diarrhea	
No	39 (86.7)
Yes	6 (13.3)
Sore throat	
No	37 (82.2)
Yes	8 (17.8)

received mechanical ventilation. Overall, 38 (84.4%) cases died, and 7 (15.6%) patients were discharged home. The median age of the patients was 67 years (range 22 to 91), and 29 of the 45 patients (64%) were male. Most of the patients had comorbidity (35 [77.7%]), including hypertension (23 [51.1%]), diabetes (19 [42.2%]), cardiovascular disease (6 [13.3%]), and asthma (3 [6.7%]). In addition, 8 (17.8%) patients have a history of smoking, 6(13.3%) patients had a history of receiving annual influenza vaccine, and 28 (62.2%) patients had a history of close contact with previously confirmed patients. Table 1 represents the baseline characteristics of the patients.

The mean time from symptoms to hospital admission was 5.98 ± 2.93 days, and from illness onset to dyspnea was 2.73 ± 3.07 days. Dyspnea (95.6%), SPO_2 depression (93.3%), and fever (80%) were the most common signs and symptoms upon hospital admission. Gastrointestinal symptoms were rare (diarrhea [13.3%], and nausea and vomiting [8.9%]) (Table 2). The average hospital admission to intubation time was 2.33 ± 2.65 days. The average length of the intubation was 4.84 ± 3.28 days. The causes of intubation were hypoxia and tachypnea 13 (28.88%), hypoxia and hypercapnia 10 (22.22%), hypoxia 8 (17.77%), hypoxia and tachypnea and hypercapnia 7 (15.55%), hemodynamic instability 4 (8.88%), and cardiopulmonary arrest 3 (6.66%). Distribution of intubation causes in the deceased patients was significantly higher in the recovered patients (P = 0.031) (Table 3).

The mean score of lung CT findings in the deceased patients (370.26 ± 207.50) was significantly higher than the

Table 3. Distribution of Intubation Causes Between Deaths and Recovered Patients (P-Value = 0.031)

Causes of Intubation	Total (%)	Recovered Patients (N = 7)	Deaths (N = 38)
Hypoxia and hypercapnia	10 (22.2)	5 (71.4)	5 (13.2)
Hypoxia, tachypnea, and hypercapnia	7 (15.6)	0 (0.0)	7 (18.4)
Hypoxia and tachypnea	13 (28.9)	1 (14.3)	12 (31.5)
Hypoxia	8 (17.8)	1 (14.3)	7 (18.4)
Hemodynamic instability	4 (8.9)	0 (0.0)	4 (10.5)
Cardiopulmonary arrest	3 (6.7)	0 (0.0)	3 (7.9)

recovered patients (235.71 ± 81.21) (P = 0.042). Additionally, we analyzed the association of clinical and laboratory variables with causes of intubation (Table 4). Results show no statistically correlation between LDH, length of the intubation, SPO_2, pH, and cause of intubation (P > 0.05), while respiratory rate, PaO_2, $PaCO_2$, and CT scores had a statistically direct correlation (P < 0.05). The correlation between average hospital admission to intubation time and average length of the intubation was studied with variables LDH, SPO_2, pH, respiratory rate, PaO_2, $PaCO_2$ that results showed a statistically direct correlation between average hospital admission to intubation time and $PaCO_2$ (P = 0.023) and a statistically direct correlation between the average length of the intubation and respiratory rate (P = 0.03). The correlation between other variables was not significant (P > 0.05) (Table 5).

5. Discussion

This retrospective study describes the clinical course and outcomes of 54 critically ill patients with laboratory-confirmed COVID-19 infection who intubated and admitted in ICU wards. As mentioned in previous studies, the population in this study mostly consisted of men (64%) and was generally older (median age, 67 years; range, 22 - 91 years) than previous case series admitted to ICU in China, Italy, and America (11-15). Although previous evidence suggests that older and male patients are the most susceptible individuals to COVID-19, we cannot consider older age and male gender as a risk factor for admission to the ICU or poor prognosis.

In our case series, dyspnea followed by SPO2 depression, fever, and cough were the most prevalent symptoms on admission among critically ill patients with COVID-19, which is in accordance with previous studies (18). It seems that clinical presentations of COVID-19 are relatively similar to other betacoronavirus infections. Furthermore, less than 15% of the patients had gastrointestinal symptoms, and this was consistent with the results from other previous studies. However, the incidence of gastrointestinal symptoms in patients with MERS-CoV or SARS-CoV infection has been reported about 20% - 25% (19, 20).

In accordance with the recent reports, our study reported that 77.7% of the critically ill patients had at least one comorbidity. This is similar to what was reported by Wang et al. (72.2%), and it was 86% in another case series in the USA (13, 21). Hypertension was the most common comorbidity in our study, this is similar to what was reported by other previous studies (18). Moreover, the majority of the patients (62.2%) had a history of close contact with infected patients. This was concordant with the results from Bhatraju et al. (13) reported 54% had recent contact with an infected patient.

Previous studies reported a wide range of mortality rates among critically ill patients admitted to ICU, from 16% to 38%, 62%, 67%, and 80% (12-15, 22-24). In our study, overall outcomes were poor in severe patients who received ICU care, and the mortality rate (84.6%) was considerably higher than other studies. In fact, we reported the final outcomes of the patients, but previous studies just followed the patients for a limited time. Therefore, the majority of the patients were still in the ICU or hospital at the time of gathering data, and there is an underestimation in reporting mortality rate by previous studies. For example, a large Italian case series reported 26% mortality rate at 5 weeks after ICU admission; however, more than 50% of the patients were still in the ICU at the time of submission, and their outcome remains uncertain (14). In addition, we just reported data from intubated patients and those requiring mechanical ventilation. In a case series from Wuhan, the mortality rate among critically ill patients was 62%, and it was 81% among those requiring mechanical ventilation (8).

In agreement with the previous reports, our study confirmed that all patients had abnormal findings in chest CT scan, and bilateral multiple lobular and subsegmental areas of consolidation were the most frequent chest CT findings among ICU patients (8). Additionally, we observed that non-survivors had a significantly higher score of lung CT involvement than survivors. This finding supports the score of chest CT involvement as a prognostic factor in outcomes of severe patients with COVID-19.

Our findings revealed that the majority of patients in this case series intubated and required mechanical ventilation because of hypoxemic, hypercapnic, and tachypneic respiratory failure. This finding supports the results of previous studies that reported respiratory failure and developed ARDS were the main reasons for intubation and

Table 5. The Pearson Correlations Between Average Hospital Admission to Intubation Time and Average Length of the Intubation with LDH, SPO_2, PH, Respiratory Rate, PaO_2, and $PaCO_2$

	Days From Hospital Admission to Need Mechanical Ventilation, d	Duration of Mechanical Ventilation, d	LDH	SPO_2	PH	Respiratory Rate	Pao_2	Pco_2
Days from hospital admission to need mechanical ventilation, d								
Pearson correlation	1	0.030	-0.108	0.109	-0.174	0.167	0.169	0.338[a]
Sig. (2-tailed)		0.847	0.480	0.475	0.253	0.273	0.267	0.023
Number	45	45	45	45	45	45	45	45
Duration of mechanical ventilation, d								
Pearson correlation	0.030	1	-0.146	0.085	0.075	-0.325[a]	-0.220	0.070
Sig. (2-tailed)	0.847		0.338	0.580	0.625	0.030	0.147	0.645
Number	45	45	45	45	45	45	45	45

[a]Correlation is significant at 0.05 level (2-tailed).

ICU admission among critically ill patients with COVID-19 (15, 18). Furthermore, respiratory rate, PaO_2, $PaCO_2$, and CT score had a statistically direct correlation with the distribution causes of intubation.

As new findings, our study demonstrated that the length of the intubation had a direct correlation with respiratory rate. In fact, the length of intubation would be longer in critically ill patients who had higher respiratory rates on admission. Therefore, we can consider the respiratory rate as a prognostic factor for the length of the intubation. This is not investigated in other studies. We can argue that the patients with higher respiratory rate have more lung involvement and greater decline in pulmonary function, so they will require mechanical ventilation and oxygen support longer than other patients.

Our study has some strong points that must be highlighted. First, the data represents certain outcomes of the patients, and the patients were fully recovered or deceased at the time of data collection. Second, we investigated the causes of intubation and scoring lung CT involvement among intubated patients as new aspects of the clinical features of critically ill patients with COVID-19. On the other hand, the small sample size and single-center study were the main limitations of the current study. Finally, we suggest that this study could be performed on a larger sample size and multicenter to clarify risk factors and prognostic factors, especially among intubated patients with COVID-19.

In summary, it was concluded that most of the critically ill patients admitted to ICU were older men and had poor outcomes with a high mortality rate. Furthermore, the score of chest CT involvement and respiratory rate are important prognostic factors in determining the severity of illness, requiring ventilatory support, and outcome. Considering the causes of intubation, especially respiratory distress among critically ill patients, the importance of earlier cardiac monitoring and ventilatory support, must be highlighted.

Footnotes

Authors' Contribution: Study concept and design: RP and FH. Analysis and interpretation of data: HB and FR. Drafting the manuscript: HA and SA. Critical revision of the manuscript for important intellectual contents: HS.

Conflict of Interests: No conflicts of interest were declared by the authors.

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Table 4. Association Between Clinical and Laboratory Variables with Causes of Intubation

Characteristics	Number	Mean ± SD	P-Value
LDH			0.351
Hypoxia and hypercapnia	10	942.30 ± 160.55	
Hypoxia, tachypnea, and hypercapnia	7	951.86 ± 299.61	
Hypoxia, and tachypnea	13	1213.9 ± 399.64	
Hypoxia	8	1093.75 ± 193.63	
Hemodynamic instability	4	1103.75 ± 175.65	
Cardiopulmonary arrest	3	939.00 ± 161.65	
Total	45	1063.31 ± 289.32	
Duration of mechanical ventilation, d			0.073
Hypoxia and hypercapnia	10	7.50 ± 3.56	
Hypoxia, tachypnea, and hypercapnia	7	4.57 ± 3.10	
Hypoxia and tachypnea	13	3.62 ± 2.21	
Hypoxia	8	5.13 ± 3.94	
Hemodynamic instability	4	3.75 ± 2.21	
Cardiopulmonary arrest	3	2.67 ± 2.08	
Total	45	4.84 ± 3.28	
SPO_2			0.574
Hypoxia and hypercapnia	10	69.10 ± 8.34	
Hypoxia, tachypnea, and hypercapnia	7	63.71 ± 10.16	
Hypoxia and tachypnea	13	57.08 ± 16.59	
Hypoxia	8	67.38 ± 2.32	
Hemodynamic instability	4	63.50 ± 14.43	
Cardiopulmonary arrest	3	67.00 ± 19.31	
Total	45	63.84 ± 12.57	
pH			0.175
Hypoxia and hypercapnia	10	7.35 ± 0.0870	
Hypoxia, tachypnea, and hypercapnia	7	7.27 ± 0.1575	
Hypoxia and tachypnea	13	7.35 ± 0.0906	
Hypoxia	8	7.39 ± 0.0261	
Hemodynamic instability	4	7.35 ± 0.0544	
Cardiopulmonary arrest	3	7.29 ± 0.1997	
Total	45	7.34 ± 0.1041	
Respiratory rate			< 0.001
Hypoxia and hypercapnia	10	23.90 ± 2.28	
Hypoxia, tachypnea, and hypercapnia	7	38.43 ± 3.82	
Hypoxia and tachypnea	13	34.92 ± 4.64	
Hypoxia	8	25.13 ± 0.35	
Hemodynamic instability	4	36.00 ± 7.34	
Cardiopulmonary arrest	3	27.67 ± 7.37	

Total	45	30.89 ± 7.01	
PaO_2			0.01
Hypoxia and hypercapnia	10	35.30 ± 10.84	
Hypoxia, tachypnea, and hypercapnia	7	46.42 ± 10.65	
Hypoxia and tachypnea	13	27.23 ± 11.42	
Hypoxia	8	36.50 ± 9.28	
Hemodynamic instability	4	33.87 ± 6.63	
Cardiopulmonary arrest	3	47.333 ± 11.37	
Total	45	35.58 ± 12.12	
$PaCO_2$			< 0.001
Hypoxia and hypercapnia	10	55.60 ± 3.71	
Hypoxia, tachypnea, and hypercapnia	7	73.43 ± 19.57	
Hypoxia and tachypnea	13	38.23 ± 8.41	
Hypoxia	8	34.75 ± 4.83	
Hemodynamic instability	4	38.75 ± 5.79	
Cardiopulmonary arrest	3	81.33 ± 59.53	
Total	45	49.87 ± 22.30	
Lung CT findings score			0.014
Hypoxia and hypercapnia	10	232.00 ± 30.111	
Hypoxia, tachypnea, and hypercapnia	7	304.29 ± 147.858	
Hypoxia and tachypnea	13	463.08 ± 256.950	
Hypoxia	8	337.50 ± 231.686	
Hemodynamic instability	4	457.50 ± 96.047	
Cardiopulmonary arrest	3	240.00 ± 20.000	
Total	45	349.33 ± 198.842	