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Cohort Study

Evaluating characteristics associated with the mortality among invasive ventilation COIVD -19 patients☆

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) is associated acute respiratory distress syndrome that leads to intensive care unit admission and subsequent need of invasive ventilation. The aim of this study is to evaluate mortality rate and associated parameters among COVID 19 patients under invasive ventilation.
Methods: In this retrospective studies, COVID 19 patients referred to our center we evaluated. The data regarding demographic characteristics, comorbidities, biochemical and radiographic findings, need of invasive ventilation and mortality were collected and recorded for all the patients. Statistical analysis was performed to evaluate the risk of mortality in invasive ventilation patients relative to each risk factor or paraclinical or clinical feature.
Results: Among patients included in the study, 63 patients underwent invasive ventilation where 53 (84%) of these died. The mortality rate among invasive ventilation was significantly associated with advanced age, $p = 0.006$ whereas it was not significantly associated with smoking, gender, c-reactive protein, platelet count, hypertension, lymphopenia, leukopenia, creatinine kinase, addiction, blood urea nitrogen to creatinine ratio, malignancy, cough, fever, nausea, chronic obstructive pulmonary disease and erythrocyte sedimentation rate.
Conclusions: The findings of our study indicate that advanced age can increase the risk of mortality in COVID 19 patients under invasive ventilation whereas, mortality among invasive ventilation patients is high, irrespective of their characteristic. Guidelines are therefore, required regarding the use of invasive ventilation among these patients.

1. Introduction

Coronavirus disease 2019 (COVID 19) is caused by extremely contagious new severe acute respiratory coronavirus-2 (SARS-CoV-2) that affected more than 48 million individuals globally and more than 1 million fatalities [1]. Intensive care unit (ICU) admission is reported among these patients presented with acute respiratory distress syndrome (ARDS) and it is significantly associated with increased risk of mortality [2]. Binding of SARS-CoV-2 to angiotensin-converting enzyme receptor and its role in immune system, is likely to be associated with the prognosis of disease and associated complications [3–5]. A number of patient-related features are determined to increase the risk of ICU admission such as heart disease, oxygen saturation, smoking status, lymphocyte count, heart rate, chronic obstructive pulmonary disease (COPD) and age [6]. Depending on patients' conditions, invasive ventilation might be required in ICU patients which adds to the risk of mortality [7] (see Table 1).

Invasive ventilation and intubation leads to cross-infection in these patients [8]. Histopathological findings from deceased COVID 19 patients have questioned if the lung injuries are caused by virus of invasive ventilation High pressure invasive ventilation can also compromise circulation and lead to renal injury [9]. COVID 19 patients undergoing invasive ventilation has increased risk of barotrauma, volutrauma, atelectrauma, biotrauma, and oxytrauma [10–13]. Ventilation-induced lung injury can not only induce lung injury but lead to prolong ventilation requirement. There are no particular guidelines regarding the use of invasive ventilation among COVID 19 patients, however studies like PRactice of VENTilation in Patients with Novel Coronavirus Disease (PRoVENT-COVID) can provide better understanding in this regard [14].

☆ This study was approved by the Research Ethics Board of Qom University of Medical Sciences.

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Table 1
Correlation between mortality and age in patients under invasive ventilation.

			death.status		Total
			.00	1.00	
age (Binned)	<=50	Count	5	6	11
		% within age (Binned)	45.5%	54.5%	100.0%
	>50	Count	4	47	51
		% within age (Binned)	7.8%	92.2%	100.0%
Total		Count	9	53	62
		% within age (Binned)	14.5%	85.5%	100.0%

Despite invasive ventilation is associated with mortality itself, we predict that COVID 19-related risk factors and patients' characteristics can also predict mortality in these cases significantly.

2. Methods

This retrospective study was performed to evaluate the prognosis of invasive ventilation in COVID 19 patients referred at (XXX) March 2020–October 2020.

Data on the rate of invasive ventilation were collected for 317 individuals regarding demographic characteristics, clinical and laboratory signs. The mean and variance indices were used to describe the data and dispersion, relative frequency and frequency indices were used for qualitative variables.

Chi-square and Fisher's exact tests were used to compare the amount of invasive ventilation in qualitative variables. Independent *t*-test was also used to compare quantitative variables according to the state of invasive ventilation. Comparison of clinical symptoms before and after invasive ventilation was performed using paired *t*-test.

Statistical calculations were performed with SPSS 24 software. Significance level was considered to be $p < 0.05$.

This study was approved by the Research Ethics Board of Qom University of Medical Sciences.

Unique identifying number is: researchregistry: 7052.

The work has been reported in line with the STROCSS criteria [15].

3. Results

Of 317 COVID 19 patients included in the study, 173 were male and 144 were female. The frequency of patients over 50 years of age was 217 (68.4%) and for patients under 50 years was 100 (31.5%). The mean age of patients is 59.71 ± 16.46 years. 75% of patients were aged between 48 and 72 years old(Fig. 1).

3.1. The relationship between invasive ventilation and radiographic findings

96.8% patients had unilateral lung involvement and were ventilated whereas 89.6% patients were without invasive ventilation. Chi-square test showed that there was no significant relationship between this radiographic findings and invasive ventilation ($p = 0.073$). Although the chances of unilateral involvement were for patients with invasive ventilation was 3.5 more than patients without invasive ventilation.

Determination of mortality rate in patients with COVID 19 under invasive ventilation according to demographic and clinical characteristics showed that of the 63 patients who underwent invasive ventilation, 53 (84%) died(Fig. 2).

3.2. Correlation between mortality and age in patients under invasive ventilation

The mortality rate was 54.5% in patients under 50 years of age and 92.2% in patients over 50 years. Fisher's exact test showed a significant relationship between age and death status of patients under invasive ventilation, such that the chance of death in patients over 50 years is 9.7 times higher than patients under 50 years ($p = 0.006$).

3.3. Relationship between mortality and gender status in patients under invasive ventilation

The mortality rate was 88.9% in male patients and 76.9% in female patients. Fisher's exact test showed that there was no significant relationship between gender and death status of patients under invasive ventilation. The risk of mortality is the same in men and women under invasive ventilation ($p = 0.297$).

3.4. Relationship between mortality and smoking in patients under invasive ventilation

The mortality rate was 82.1% in smokers and 84.1% in non-smokers. There was no significant relationship between smoking and morality, $p = 0.585$.

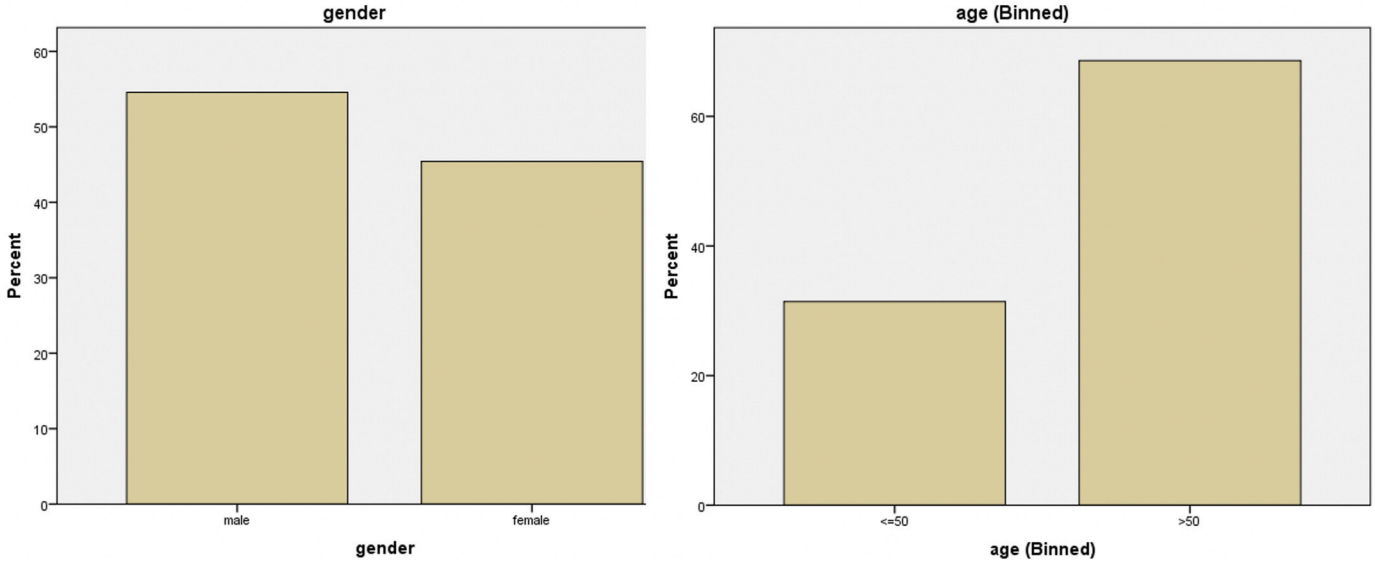

Fig. 1. Diagram of patient information.

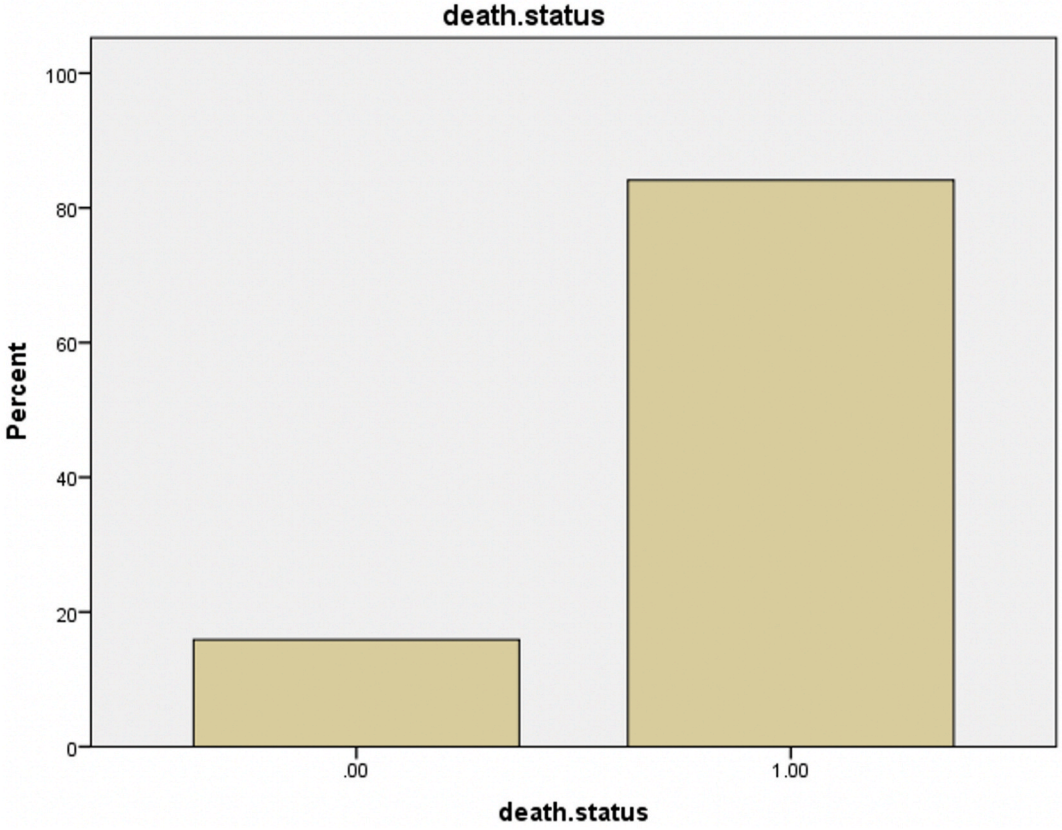

Fig. 2. Determining the mortality rate in patients with Covid-19.

3.5. Correlation between mortality and addiction in patients under invasive ventilation

The mortality rate was 83.1% in non-addicts and 100% in addicts. However, there was no significant relationship between addiction and mortality among patients under invasive ventilation ($p = 1$).

3.6. Relationship between mortality and arthralgia in patients under invasive ventilation

The mortality rate was 81.8% in patients with arthralgia and 89.5% for non-arthralgia patients. There was no significant relationship between arthralgia and mortality among patients under invasive ventilation ($p = 0.709$).

3.7. Correlation between mortality and asthma in patients under invasive ventilation

The mortality rate was 85.2% non-asthmatic patients and 50% among asthmatic patients. Fisher's exact test showed that there was no significant relationship between asthma and mortality among patients under invasive ventilation ($p = 0.294$).

3.8. Correlation between mortality and malignancy in patients with invasive ventilation

The mortality rate was 83.3% among patients without malignancy and 100% in those with malignancy. There was no statistically significant difference in terms of mortality among the two groups ($p = 1$).

3.9. Correlation between mortality and high BUN to Cr ratio in patients under invasive ventilation

The mortality rate was 80.6% in patients with normal BUN to Cr ratio whereas, 88.9% patients with high BUN to Cr died under invasive ventilation. However, the two groups did not have statistically significant difference in terms of mortality ($p = 0.494$).

3.10. Correlation between death status and COPD in patients under invasive ventilation

The mortality rate was 85% in patients without COPD and 66.7% of COPD patients died under invasive ventilation. The two groups showed no significant difference in terms of morality ($p = 0.410$).

3.11. Correlation between mortality and high creatinine kinase in patients under invasive ventilation

The mortality rate in patients with normal creatinine kinase was 83.6% and those with high creatinine kinase was 100%. The two groups were not significantly different in term of mortality ($p = 1$).

3.12. Correlation between mortality and increased CRP in patients under invasive ventilation

The mortality rate among patients with normal CRP was 88.2% and those with high levels of CRP was 79.3%. There was no significant relationship between increased CRP and mortality among patients under invasive ventilation ($p = 0.492$).

3.13. Correlation between mortality and high ESR in patients under invasive ventilation

The mortality rate in patients with normal ESR was 86.7% and among patients with high ESR was 77.8%. There was no significant relationship between ESR and mortality in patients under invasive ventilation ($p = 0.452$).

3.14. Correlation between mortality and hypertension in patients under invasive ventilation

The mortality rate was 84.2% in normotensive patients and 84% in hypertensive patients. There was no significant relationship between hypertension and mortality among patients under invasive ventilation ($p = 1$).

3.15. Correlation between mortality and ischemic heart disease (IHD) in patients under invasive ventilation

The mortality rate among patients without IHD was 86.3% and in patients with IHD was 75%. There was no significant relationship between IHD and mortality among patients under aggressive ventilation, ($p = 0.386$).

3.16. Correlation between mortality and lymphopenia in patients under invasive ventilation

The mortality rate was 77.8% in patients without lymphopenia and 92.6% in patients with lymphopenia. Fisher's exact test showed that there was no significant relationship between lymphopenia and mortality ($p = 0.167$).

3.17. Correlation between mortality and leukopenia in patients with invasive ventilation

The mortality rate in patients without leukopenia was 82.8% and those with leukopenia was 100%. Fisher's exact test showed that there was no significant relationship between leukopenia and mortality ($p = 0.583$).

3.18. Correlation between mortality and organ transplantation in patients under invasive ventilation

The mortality rate in non-transplant patients was 83.6% and in transplant patients was 100%. Fisher's exact test showed no significant relationship the history of organ transplantation and mortality among patients under invasive ventilation, ($p = 1$).

3.19. Correlation between mortality and thrombocytopenia in patients under invasive ventilation

The mortality rate for patients without thrombocytopenia was 83.9% and those with thrombocytopenia was 100%. Fisher's exact test showed no significant relationship between thrombocytopenia and mortality ($p = 1$).

3.20. Correlation between mortality and cough in patients under invasive ventilation

The mortality rate among patients without cough was 84% and in patients presented with cough was 84.2%. Fisher's exact test showed no significant relationship between cough and mortality in patients under invasive ventilation ($p = 1$).

3.21. Correlation between mortality and fever in patients under invasive ventilation

The mortality rate was 88.9% in patients without fever and 82.2% in patients presented with fever. Fisher's exact test showed no significant relationship between fever and mortality in patients under invasive ventilation ($p = 0.710$).

3.22. Correlation between mortality and nausea in patients under invasive ventilation

The mortality rate was 83.6% in patients without nausea and 87.5% in patients presented with nausea. Fisher's exact test showed no significant relationship between nausea and mortality in patients under invasive ventilation ($p = 1$).

3.23. Correlation between mortality and shortness of breath in patients under invasive ventilation

The mortality rate in patients without shortness of breath was 100% and for patients with shortness of breath was 81.8%. The two groups were not significantly different in terms of mortality ($p = 0.335$).

4. Discussion

The results of our study reported that 317 COVID 19 patients who underwent invasive mechanical ventilation at our center, mortality was only associated with advanced age. To our knowledge, this is the first study to evaluate the risk factors associated with mortality in invasive ventilation COVID 19 patients. The overall mortality rate among patients who underwent invasive ventilation was 84%. Hua, Qian [16] reported that among invasive ventilation patient, the rate of mortality was 94%. Furthermore, these patients had greater comorbidities such as kidney injury and these patients were older than other patients in intensive care unit. Biochemical analysis of these patients showed higher levels of white blood cell count, lower lymphocyte count and platelet count, and higher CRP relative to other patients. Nonetheless, the study concluded that invasive ventilation may be reduce mortality in COVID 19 patients. Fang, Li [17] reported that male gender and COPD is associate with increased risk of invasive ventilation, however, this data is not evaluated in terms of mortality. The findings from the study by Asghar, Haider Kazmi [18] concluded that urea, creatinine, sodium, CRP and lactate dehydrogenase are significant markers of invasive ventilation. Among these markers, D-dimer, hypernatremia, procalcitonin, neutrophilia, leukocytosis, and serum urea can predict mortality in these patients. Our study did not find any significant biomarker associated with mortality in invasive ventilation patients.

Failure to be treated with non-invasive ventilation increases the risk of mortality in patients. Patients under invasive ventilation has high rate of mortality [19]. Our study reported that patients' characteristic may not determine the rate of mortality in these patients, in exception to the advanced age. Alone mechanical ventilation is associated with high rate of mortality.

It is recommended that close monitoring of patients' characteristics including demographic features and comorbidities should be performed before intubating them [20]. Furthermore, COVID 19 patient care should be assiduously applied in a stepwise manner, where invasive ventilation should be final step. Nonetheless, timely intubation is also important in reducing risks for patients [21].

5. Conclusion

Our study reported that advanced age can increase the risk of mortality among invasive ventilation COVID 19 patients. Other patients-related characteristics were not significantly associated with the added risk of mortality however, it should be noted that patients who undergo

invasive ventilation are primarily at high risk of mortality, irrespective of their characteristics and comorbidities.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethical approval and consent to participate

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Funding source

No funding was secured for this study.

Authors contributions

Dr. Nina Farzan: Planned the study, wrote the protocol, collected the data and drafted the manuscript and accepted the final draft.

Dr. Sepideh Vahabi and Dr. Shima Sadat Hashemi Madani: Planned and designed the study, collected the data.

Dr. Behrooz Farzan: analyzed the data and critically revised the draft and finally approved the manuscript.

Registration of research studies

Name of the registry: Qom university of medical sciences, Qom, Iran.

Unique Identifying number or registration ID: IR.LUMS.REC.1398.162.

Hyperlink to the registration (must be publicly accessible)

Consent for publication

Not applicable.

Availability of data and material

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Guarantor

Nina Farzan.

Declaration of competing interest

The authors deny any conflict of interest in any terms or by any means during the study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102832.

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