

Original Article

Hospital Length of Stay among COVID-19 Patients: An Application of Competing Risk AnalysisYousef Alimohamadi¹, Mojtaba Sepandi^{1*}, Aniseh Dadgar², Homeira Sedighi Nezhad³, Reza Mosaed⁴, Sanaz Zargar Balaye Jame⁵¹Exercise Physiology Research Center, Life Style Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran.²Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran.³AJA University of Medical Science, Tehran, Iran.⁴Faculty of Medicine, Aja University of Medical Sciences, Tehran, Iran.⁵Department of Health Management and Economics, School of Medicine, AJA University of Medical Sciences, Tehran, Iran.

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ABSTRACT

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Key words:Hospital Length of Stay;
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Competing risk analysis**Introduction:** In the present study, the goal was to estimate the hospital length of stay among patients admitted with COVID-19 in a hospital in Tehran.**Methods:** We used retrospective data on 446 hospitalized patients with COVID-19 who admitted from 7 March to 8 Oct 2020 in a referral hospital in Tehran, Iran. The prognostic effects of variables, including age, gender, comorbidity status, and symptoms were analyzed by using Kaplan-Meier methods and a competing risk analysis. Length of stay in hospital was calculated using time of last status minus time of admission. All analyses performed using SPSS version 22.0 and STATA version 15.**Results:** The mean age of cases was 57.09±16.85 years old. The median (IQR) of hospital length of stay among all patients was 7 (11-5) days. The length of Hospital stay, for >80 years' patients (9days (15-5)) and females (7days (11-5)) was the longest. The most of cases (94 (21.1%)) were in 60–69 age group. In overall 267 (59.9%) of all cases were males and 179 (40.1%) were females. The most common symptom among patients was Respiratory distress 249 (55.8), Cough 233 (52.2) and fever 209 (46.9) respectively. Regarding having any comorbidities, 106 (23.8%) of COVID-19 cases had Cardiovascular disease, 114 (25.6%) had diabetes and 100 (22.4%) had hypertension. Most of deaths (21 (32.3%)) occurred in 70-79 years' age group. The overall Case Fatality Rate (CFR) in under-studied cases was 14.6%.**Conclusion:** Although the result of the present study showed that hospital length of stay in Iran is not higher than in other countries, but by applying some measures including the early detection of suspected cases and timely treatment and necessary funding on preparing required facilities, medicine and equipment, it could be shortened or at least prevented from increasing.**Introduction**

The COVID- 19 (stand for coronavirus disease

2019) as an highly contagious disease in a way that each infected person could infect at least 3 other people on average, has been seen for

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the first time in December 2019 in China.¹ As of, November 20, 2020, 828, 377 patients with COVID-19 have been identified in Iran, of which 43,896 deaths have been occurred by the virus.² Severe cases can develop harmful consequences; recent reports have shown that mortality rates are rising around the world.³ So that, the case fatality rate (CFR) among the hospitalized patients in Iran was reported to be 8.06%.⁴ Given the continuing spread of the COVID-19 pandemic, healthcare systems and healthcare workers in many countries including Iran are facing a great challenge.⁵ To date, epidemiological and clinical features of COVID-19 in Iran and other countries,⁶⁻¹⁰ have been previously reported and fewer studies have considered the duration of COVID-19 patients' hospital length of stay.^{11, 12}

Serious concerns are raised over developing countries, such as Iran, when the well-equipped health care systems of developed countries such as Italy are disrupted by a sharp increase in COVID-19 patients need to be hospitalized.¹³ Predicting the required number of hospital beds and medical equipment provides essential evidences for decision-making by health authorities during an epidemic.¹³ In order to predicting demand for hospital care one need to know the number of patients requiring hospitalization, and an estimate of how long each person will stay at hospital. So the Knowledge on hospital length of stay in COVID-19 hospitalized patients and its affecting factors is informative for planning of distribution of medical resources to those most in need and consequently help to make appropriate decisions and better manage the epidemic.

The present study was aimed to estimate the hospital length of stay among patients admitted

with COVID-19 in Iran as well as the relationship between Demographic, epidemiological, and basic clinical characteristics of confirmed cases of COVID-19 and length of stay in hospital assessed through a multivariate Cox regression analysis, in relation to hospital length of stay in Tehran.

Materials and Methods

The used dataset includes information about the 446 confirmed cases of COVID-19 who admitted in a referral hospital in Tehran province, Iran between 7 March to 8 Oct 2020. The study variables include Age, Gender, Comorbidity status, symptoms, level of blood Spo₂, time of admission and time of discharge status. In the current study, the length of stay in hospital was calculated using time of discharge status minus time of admission. Patients were confirmed by RT-PCR (Reverse transcription-polymerase chain reaction) using throat and nose swab specimens from the upper respiratory tract.

Statistical analysis

Descriptive analyses of data were expressed as mean (\pm Standard Deviation=SD), median (Inter Quartile Range=IQR: Q₃-Q₁), or number (%). For hospitalized people, we face one of the following situations:

- Death
- Recovery and discharge
- Lack of information about the patient's final condition at the end of the study (censor)

We should look at the first two events as two competing events and the third as censorship. We gave the above three cases codes 0, 1 and 2, respectively.

The Kaplan-Meier method was used to show survival function for a certain time after hospital admission of COVID-19 patients. To investigate the effect of the explanatory variables such as age, gender, symptoms, level of blood Spo₂, and comorbidity status, we introduce the competing risk model and regulate the competitive regression such that the competing risks are death from disease versus recovery and discharge and survival time is the duration of Hospitalization and the other factor like age, gender, spo₂, diabetes are used as explanatory variables in the model.

In the first step, we construct a competing risk regression model with each of the explanatory variables separately and obtain the Hazard Ratio. Then we select the items which $P < 0.20$. In the next step, from the variables of the above table, we select the items whose significance is a maximum of 0.2. We form a multivariate competing risk regression model with all of them in the model, so this time we get the Adjusted Hazard Ratio for each variable with the presence of other variables. Finally, from the above model, we remove the not significant variable by the backward method in order to fit a suitable model. All analyses performed using SPSS version 22.0 and STATA version 15, considering $\alpha:0.05$ as a statistically significant level.

Results

In the current study 446 cases of COVID-19 who admitted in a hospital in Tehran were entered to study. The mean age of cases was 57.09 ± 16.85 years. The most of cases (94 (21.1%)) were in 60–69 age group and the lowest (22 (4.9%)) were in less than 30-year age group. In overall 267 (59.9%) of all cases

were male and 179 (40.1%) were female. In overall, 104 (23.3%) of patients had positive history for contact with other COVID-19 patients. The most common symptom among patients was respiratory distress 249 (55.8%), Cough 233 (52.2%) and fever 209 (46.9%) respectively. The prevalence of other symptoms are shown in table 1. In terms of having comorbidity, 106 (23.8%) of COVID-19 cases had Cardiovascular diseases, 114 (25.6%) had diabetes and 100 (22.4%) had hypertension. Most of deaths (21 (32.3%)) occurred in 70–79-year age group. About the gender, most of the COVID-19 related deaths were seen among males (38 (58.5%)). The overall CFR in under-studied cases was 14.6%. The most CFR was seen in >80-year age group (40.8%), females (15.1%) and patients who didn't had comorbidity (16.2%). More information is shown in Table 2.

The median (IQR) of hospital length of stay among all patients was 7 (11-5) days (figure 1). The length of Hospital stay, for >80 years' patients was the longest (9 (15-5)) days. Female patients had longer hospital stay time with (7 (11-5)) days than male patients. The hospital length of stay among COVID-19 Patients, who does not have any comorbidity was 7 (11-5) days. Other important information is showed in Table 2 and Figure 2. The effect of explanatory factors (separately) on hospitalization time of COVID-19 patients in a competing risk regression model for death versus discharge was showed in Table 3.

According to our results, the effective variables on the Hospital length of stay were age, respiratory distress, cancer, and SPO₂. The effective variables on the survival time of patients were respiratory distress, cancer, and SPO₂. The adjusted Hazard Ratio is shown in

Table 4. According to this table that Adjusted HR in Patients with SPo2, $\geq 93\%$ for discharge event was 2.05 times more comparing reference group with SPo2 $<93\%$. (P <0.001), and for the occurrence of death, Adjusted HR

was 0.19 times comparing the reference group (P=0.001).

Table 1. prevalence of different symptoms among hospitalized COVID-19 patients

Symptoms	N (%)	Symptoms	N (%)
Fever	209 (46.9)	Organ lesion	123 (27.6)
Cough	233 (52.2)	Chest pain	18 (4)
Muscular pain	127 (28.5)	Skin lesion	1 (0.2)
Respiratory distress	249 (55.8)	Stomach pain	40 (9)
Loss of consciousness	10 (2.2)	Nausea	61 (13.7)
Loss of smell	19 (4.3)	Vomiting	18 (4)
Loss of taste	11 (2.5)	Diarrhea	36 (8.1)
Headache	53 (11.9)	Anorexia	115 (25.8)
Dizziness	19 (4.3)		

Table 2. The descriptive characteristics of COVID-19 hospitalized patients.

	All Cases N (%)	Died N (%)	Median estimate of length of stay (IQR)	Range of length of stay	Case Fatality Rate (%)
Overall	446	65 (14.6)	7 (5-11)	0 - 67	14.6
Age					
<30	22 (4.9)	2 (3.1)	5 (3-8)	1 - 14	9.1
30-39	47 (10.5)	3 (4.6)	6 (5-8)	1 - 20	6.4
40-49	74 (16.6)	3 (4.6)	6 (5-8)	1 - 43	4.1
50-59	89 (20.0)	3 (4.6)	8 (5-10)	1 - 34	3.4
60-69	94 (21.1)	13 (20.0)	7 (5-11)	2 - 33	13.8
70-79	71 (15.9)	21 (32.3)	7 (5-11)	2 - 67	29.6
≥ 80	49 (11.0)	20 (30.8)	9 (5-11)	0 - 47	40.8
Gender					
Female	179 (40.1)	27 (41.5)	7 (5-11)	1 - 67	15.1
Male	267 (59.9)	38 (58.5)	7 (5-10)	0 - 59	14.2
Comorbidity					
No	241 (54)	39 (60.0)	7 (5-11)	0 - 47	16.2
Yes	205 (46)	26 (40.0)	6 (5-9)	1 - 67	12.7

Hospital Length of Stay among COVID-19 Patients ...

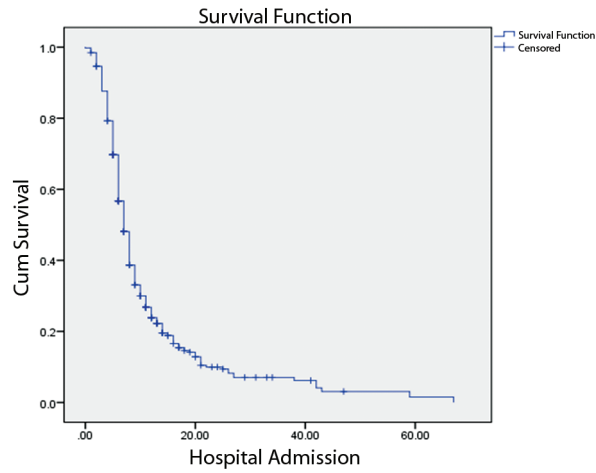


Figure 1. The Kaplan-Meier curve for Hospital Length of stay among all COVID-19 patients.

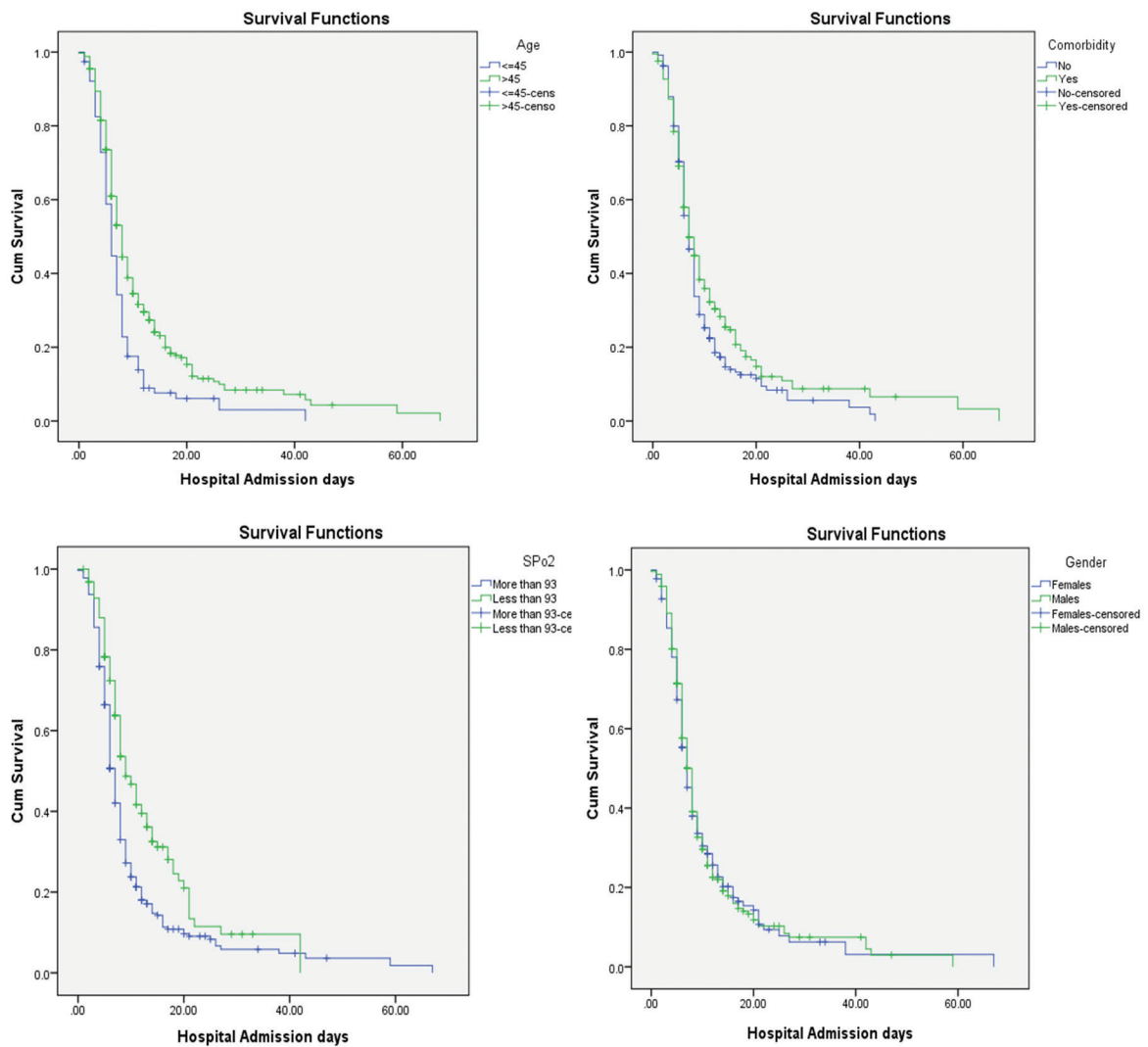


Figure 2. The Kaplan-Meier curve for Hospital Length of stay among COVID-19 patients.

Table 3. The effect of explanatory factors (separately) on hospitalization time of COVID-19 patients in a competing risk regression model for death versus discharge

	Discharge				Death			
	HR	95% CI		P	HR	95% CI		P
		LCL	UCL			LCL	Uper	
Age								
<45	Ref				Ref			
≥45	0.66	0.51	0.85	0.001	2.09	0.9	4.86	0.08
Sex								
Female	Ref	-	-	-	Ref	-	-	-
Male	0.96	0.78	1.17	0.67	1.26	0.73	2.2	0.4
Fever								
Negative	Ref	-	-	-	Ref	-	-	-
Positive	1.09	0.89	1.34	0.38	0.64	0.36	1.15	0.13
Cough								
Negative	Ref	-	-	-	Ref	-	-	-
Positive	1	0.82	1.22	0.97	0.83	0.48	1.41	0.48
Respiratory Distress								
Negative	Ref	-	-	-	Ref	-	-	-
Positive	0.64	0.52	0.8	<0.001	2.5	1.39	4.52	0.002
Muscular Pain								
Negative	Ref	-	-	-	-	-	-	-
Positive	1.12	0.89	1.4	0.32	0.51	0.22	1.19	0.12
Cancer								
Negative	Ref	-	-	-	-	-	-	-
Positive	0.51	0.26	1	0.05	3.29	1.12	9.63	0.003
loss of Consciousness								
Negative	Ref	-	-	-	-	-	-	-
Positive	0.59	0.27	1.27	0.18	3.66	1.37	6.39	0.01
SPo2								
<93	Ref	-	-	-	-	-	-	-
≥93	2.22	1.67	2.94	<0.001	0.2	0.12	0.34	<0.001
Diabetes								
Negative	Ref	-	-	-	-	-	-	-
Positive	1.05	0.84	1.3	0.68	0.85	0.45	1.59	0.6

Table 4. The effective explanatory factors on hospitalization time in a competing risk regression model for death versus (discharge (backward fitted model)

	Discharge				Death			
	HR	95% CI		P	HR	95% CI		P
		LCL	UCL			LCL	Uper	
Age								
<45	Ref							
≥45	0.76	0.59	0.98	0.032	-	-	-	-
Respiratory Distress								
Negative	Ref				Ref			
Positive	0.7	0.57	0.86	0.001	2.39	1.31	4.35	0.004
Cancer								
Negative	Ref				Ref			
Positive	0.5	0.28	0.92	0.020	5.43	2	14.7	0.001
SPo2								
<93	Ref				Ref			
≥93	2.05	1.54	2.72	<0.001	0.19	0.11	0.33	<0.001

Adjusted Hazard ratio*

Discussion

On December 31, 2019, China had first reported unexplained pneumonia in Wuhan to the World Health Organization (WHO). On January 30, 2020, the spread of COVID-19 was considered as an emergency and international public health concern. On March 11, 2020, the WHO declared COVID-19 as a pandemic.^{1, 14}The COVID-19 outbreak in Iran is a component of the pandemic of coronavirus disease 2019 caused by SARS-CoV-2. On 19 February 2020, Iran reported its first confirmed cases of infection.¹⁵ To our knowledge, the current study is the first study about the hospital length of stay among the Iranian community. According to results of the current study, the most common symptoms among patients were Respiratory distress,

Cough and fever respectively. According to results of a systematic review and meta-analysis the most common symptoms in COVID-19 patients include: Fever, Cough, Fatigue, Dyspnea, and the Sputum.¹⁶ So it seems the cough, fever and Respiratory distresses are most common symptoms among COVID-19 patients. In the current study, most of deaths occurred in older ages (70-79 years' age group), males and patients who didn't had comorbidity. Other studies showed that the age, male gender and comorbidities are related to the risk of death in COVID-19 patients.^{17, 18} The overall CFR in our study was 14.6%. The overall CFR in other studies were reported 10.8%,¹⁹ 8.06 %⁴ and 13 %²⁰ in COVID-19 patients. This controversy between different studies may be due to use different denominator in calculation of CFR

by different studies. For example, some discharged cases may not consider in some studies.

Based on the results of the present study, the median (IQR) of length of stay at hospital among all patients was 7 (11-5) days. which is shorter than that reported in Vietnam (14 (19-10)),¹² China (19(3-14)).¹¹ Also, in western countries the average duration of stay for COVID-19 patients has been reported to be 4-8 days.²¹⁻²⁴ This variation may be explained by a difference in strategies and policies for the prevention and control of COVID-19 between countries. In western countries as well as Iran, health care professionals encourage patients with mild symptoms to stay at home instead of going to hospital.¹² Nevertheless, Hospital length of stay may depend on factors, such as the time space between the exposure to the onset of symptoms, the time space between the onset of symptoms and hospital admission and the percentage of older patients and the percentage of patients who suffer from comorbidities.

The length of stay, for >80 years old patients was longer than other age groups. Female patients had longer hospital stay time. The findings consistent to another study in China¹¹ which showed that patients with underlying diseases had longer duration of hospitalization. It seems that areas with elderly populations need to allocate more medical resources to deal with longer hospital stays. However, due to limited information sources in this study, there was no data on the time interval between the onset of symptoms and the patient's visit, but past studies suggest that the patient's timely referral to a physician appears to have no significant effect on hospitalization.²⁵

According to our results, the effective variables on the Hospital length of stay were

age, respiratory distress, cancer, and SPO₂. The effective variables on the survival time of patients were respiratory distress, cancer, and SPO₂. The adjusted Hazard Ratio is shown in Table 4. According to this table that Adjusted HR in Patients with SPO₂, $\geq 93\%$ for discharge event was 2.05 times more comparing reference group with SPO₂<93%. (P<0.001), and for the occurrence of death, Adjusted HR was 0.19 times comparing the reference group (P=0.001). A study showed that older age and immune system status were associated with the length of stay at hospital.²⁶ Other studies showed that the having comorbidities such as diabetes are associated with the length of stay at hospital.^{27,28} It seems having risk factors such as SPO₂ less than 93 % and comorbidities can increase the risk of deaths of COVID-19 and may decrease the hospital length of stay.

The current study had some limitations, the medical records or laboratory results were incomplete for some patients. Diagnosis of comorbidities were based on patients' self-reports, which could result in recall bias. Our patients were all from a single center; factors associated with poor outcomes may differ elsewhere.

Conclusion

A longer stay at hospital is associated with a greater medical burden, specifically when the transmission of COVID-19 might rapidly increase number of patients. Although the result of the present study showed that hospital length of stay in Iranian hospital; was not higher than in other countries, but by applying some measures including the early detection of suspected cases and timely treatment and necessary funding on preparing required

facilities, medicine and equipment, it could be shortened or at least prevented from increasing.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

Authors' contributions

All the authors contributed to the study, YA, AD and MS: Idea, data analysis, manuscript preparation. HSN, RM: data collection, data analysis, manuscript preparation. SZBJ Manuscript edition. All activities were supervised by MS.

Ethics Statement

This study was approved by ethical committee of AJA University of medical sciences (IR. AJAUMS.REC.1399.065)

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