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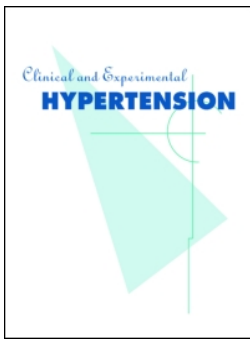
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To cite this article: Amir Emami , Fatemeh Javanmardi , Ali Akbari , Javad Kojuri , Hamid Bakhtiari , Tahereh Rezaei , Abdolkhalegh Keshavarzi & Farshad Falahati (2020): Survival rate in hypertensive patients with COVID-19, Clinical and Experimental Hypertension, DOI: [10.1080/10641963.2020.1812624](https://doi.org/10.1080/10641963.2020.1812624)

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Published online: 24 Aug 2020.



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## Survival rate in hypertensive patients with COVID-19

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### ABSTRACT

**Introduction:** A life-threatening respiratory disease, coronavirus 2019 (COVID-19), has spread across the globe since December 2019. Many prognostic factors have already been put forward to predict the risk of death and other outcomes. The current study is evaluating the survival rate between hypertensive and non-hypertensive infected patients.

**Methods:** Patients who were included in this study were admitted between 20 February to 1 March 2020 in Fars (southwest of Iran) province hospitals. Data were collected from the electronic base registry which contained demographic information, medical symptoms, and signs, underlying diseases, CT scan results, and final outcome.

**Results:** Of all 1239 positive cases, 159 (12.83%) had known with hypertension and this group was significantly older than non-hypertensive patients (66.1 years Vs 48.95 years,  $p < .001$ ). According to Kaplan–Meier survival curve and log-rank test, it was seen hypertensive patients deteriorated more rapidly than non-hypertensive group ( $p = .032$ ). Moreover, HIV, cardiovascular, and kidney disease were diagnosed as factors that increase the risk of death in hypertensive patients.

**Conclusion:** The current study about the survival rate of COVID-19 patients had shown hypertensive patients are in danger of disease severity, although it may be related to their age. Moreover, the probability of other complications like diabetes, smoking, asthma, kidney, and cardiovascular diseases, and either some other infections such as HIV can make the condition complicated and need more consideration to prevent noxious outcomes.

### ARTICLE HISTORY

Received 19 July 2020  
Revised 1 August 2020  
Accepted 4 August 2020

### KEYWORDS

CoVID-19; hypertension; survival

### Introduction

A life-threatening respiratory disease, coronavirus 2019 (COVID-19), has spread across the globe, since December 2019 and become a major public health concern (1). Despite 7 months passing the incidence of disease around the world and infection of more than 7 million cases spanning 213 countries and territories, many different disease presentations have been reported and different patterns of underlying risks have been introduced for this infection crisis (2). Although there are no certain documents so far about mortality rate before the pandemic is over, but current estimations have been shown that fatality rate is about 4.1% in China, 12.8% in Italy, 10.2% in Spain, 3.9% in the USA and 2.3% in Germany (3,4). Recently, multiple prognostic factors for COVID-19 severity have been identified. In this regard, many prognostic factors have already been put forward to predict the risk of death and other outcomes. There are various studies that show a strong relation between underlying diseases and severity of disease and death related to COVID-19 (5). Although most of the patients with COVID-19 were in mild phase and had influenza-like illness, but a minority of patients

were severe and developed to multi-organ failure (MOF), severe pneumonia, acute respiratory distress syndrome (ARDS) and finally death. Frequent reports have shown that specific comorbidities in patients with COVID-19, increase the risk of infection and have an important role in worse outcomes. According to a study, it was reported that 25.2% of people with COVID-19 had at least one underlying disease (6). Although it is not a certain order about the importance of underlying diseases in patients with COVID-19, but it has been revealed that hypertension, cardiovascular disease, and diabetes are the most common comorbidities in this group of patients (7). The prevalence of hypertension varies from 4.5% to >30%, this is while the prevalence of cardiovascular diseases and diabetes ranged between 1% to 18% and 7.2% to 15.7%, respectively (4). Various studies suggested that angiotensin-converting enzyme (ACE-2) receptor has a critical role in SARS-CoV-2 infection. There are different hypotheses about the interaction between SARS-COV-2 and ACE-2 and the importance of this receptor in pathogenicity of COVID-19 in individuals with hypertension. Based on the first descriptive study in China it has been regarded that hypertension is the

most risk factor in the COVID-19 infection but there are some major gaps are remaining in the impact of hypertension on the survival of patients with CoVID-19 (8). To find these gaps, current study is evaluating the survival rate between hypertensive patients and other patients.

## Methods

Patients who were included in this study were admitted between 20 February and 1 March 2020 in Fars province hospitals (Fars is the fourth largest and fourth-most populous province in south of Iran). All patients were hospitalized based on the presentation of ARDS and molecular positive results for SARS-CoV-2 infection. Data were collected from the electronic base registry which contained demographic information, medical symptoms and signs, underlying diseases, High-resolution computed tomography (HRCT) scan results, and final outcome. Quantitative variables were expressed as mean  $\pm$  standard deviation. Qualitative information was described by frequency and percentage. Mann-Whitney test was used to compare the quantitative variables between groups with and without hypertension; moreover, the Chi-Square test was used to evaluate the categorical data. Kaplan-Meier curve and log-rank test were used to evaluate the survival over time in these two groups, also Cox-regression was used to estimate the relative hazards of other comorbidities than hypertension. The study was carried out in accordance with the Declaration of Helsinki and was approved by the Shiraz

University of Medical Sciences ethics committee (Ethical code: IR.SUMS.REC.1399.022)

## Results

Among the 43056 molecular tests which were performed during the study period, 1239 patients were diagnosed with COVID-19. Of all positive patients, 159 (12.83%) had known with hypertension. As shown in Table 1, hypertensive group was significantly older than non-hypertensive patients (66.1 years Vs 48.95 years,  $p < .001$ ). Among the most common symptoms and signs for COVID-19 at the onset of disease, cough, headache, respiratory distress, pO<sub>2</sub>, and abnormal HR-CT were remarkably different between studies groups. Based on the clinical outcomes in hypertensive patients, it was found that 16 (10.06%) and 19 (11.94%) individuals needed intensive care and intubation, respectively. Co-existing of other comorbidities like diabetic mellitus, cardiovascular disease, chronic kidney disease, smoking, and asthma was different between these two groups.

According to Kaplan-Meier survival curve and log-rank test, it was seen hypertensive patients deteriorated more rapidly than non-hypertensive groups ( $p = .032$ ) (Figure 1). However, it is a clear evidence that mortality in patients with hypertension steeply increases. Table 2 also shows Cox proportional hazard regression model results and reveals hypertensive patients with HIV, cardiovascular, and kidney disease are at higher risk of death related to COVID-19.

**Table 1.** Clinical characteristics of patients with and without hypertension.

Variables	Total (1239)	Hypertension (159)	Non-hypertension (1080)	P-value
Age, years	51.48 $\pm$ 19.54	66.18 $\pm$ 12.70	48.95 $\pm$ 19.40	$P < .001$
Sex				
Male	692 (55.9%)	72(45.30%)	620 (57.4%)	0.003
Female	547 (44.1)	87(54.7%)	460 (42.6%)	
Symptoms				
Fever	459 (37%)	52 (32.7%)	407 (37.7%)	0.13
Cough	614 (49.6%)	90 (56.6%)	524 (48.5%)	0.03
Muscle ache	257 (20.7%)	31 (19.5%)	226 (20.9%)	0.38
Diarrhea	6 (0.5%)	-	6(0.5%)	0.43
Headache	11 (0.9%)	4 (2.5%)	7 (0.6%)	0.04
Chest Pain	8 (0.6%)	2 (1.3%)	6 (0.6%)	0.27
Dizziness	7 (0.6%)	1 (14.3%)	6 (85.7%)	0.61
Respiratory Distress	576 (46.5%)	94 (59.1%)	482 (44.6%)	$P < .001$
PO <sub>2</sub> < 93%	481 (38.8%)	86 (54.1%)	395 (36.6%)	$P < .001$
Abnormal Chest CT	421 (34%)	79 (18.8%)	342 (81.2%)	$P < .001$
Comorbidities				
Diabetes mellitus	176 (14.2%)	68(42.76%)	108 (10.0%)	$P < .001$
Cardiovascular disease	132 (10.7%)	45 (28.3%)	87 (8.1%)	$P < .001$
Chronic liver disease	22 (1.8%)	4 (2.5%)	18 (1.7%)	0.309
Chronic kidney disease	44 (3.6%)	15 (34.1%)	29 (65.9%)	$P < .001$
Cancer	22 (1.8%)	2 (1.3%)	20 (1.9%)	0.44
HIV	5 (0.4%)	0 (0%)	5 (0.5%)	0.503
Smoking	27 (2.5%)	8 (5.2%)	19 (2.0%)	0.02
Addict	23 (2.1%)	4 (2.6%)	19 (2.0%)	0.41
Asthma	25 (2.0%)	8 (5.0%)	17 (1.6%)	0.01
Immunodeficiency Disease	10 (0.8%)	1(0.6%)	9 (0.8%)	0.62
Clinical prognosis				
ICU admission	98 (7.9%)	16 (10.06%)	82 (83.7%)	0.09
Intubation	106 (8.55%)	19 (11.94%)	87	0.24
Death	98	16	82	0.09
Length of hospital stay	5.44 $\pm$ 6.89	6.60 $\pm$ 6.61	5.27 $\pm$ 6.92	0.02
Onset of symptom to hospital admission	5.62 $\pm$ 5.1	4.82 $\pm$ 2.28	5.00 $\pm$ 3.25	0.41

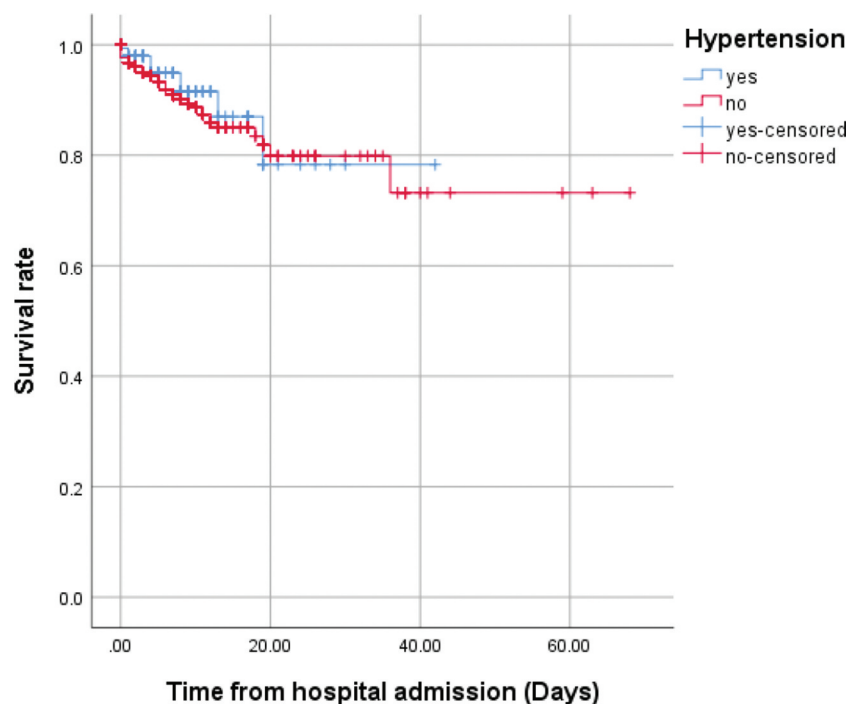


Figure 1. Kaplan-Meier survival curve in COVID-19 patients with and without hypertension.

Table 2. Multivariate cox regression for prognostic factors.

Variables	HR (95%CI)	p-value
Age	1.41 (1.23–2.5)	0.02**
Diabetes mellitus	1.25 (0.36–4.36)	0.72
Cardiovascular disease	3.52 (1.23–11.15)	0.02**
Chronic liver disease	0.807 (0.35–1.15)	0.807
Chronic kidney disease	1.15 (0.35–3.74)	0.012**
Cancer	0.58 (0.08–4.24)	0.59
HIV	10.46 (3.27–33.45)	P < .001**
Smoking	0.61 (0.15–2.52)	0.5
Asthma	1.04 (0.53–2.02)	0.89
Immunodeficiency Disease	1.65 (0.98–1.42)	0.97

## Discussion

Nowadays, the world is suffering from a crisis that caused a pandemic by new coronavirus, SARS-CoV-2, and the disease COVID-19. From the beginning of the outbreak, various clinical and epidemiological features of this disease have been repeated in different reports (2). According to the investigations, it was revealed that mortality in COVID-19 patients with underlying diseases and comorbidities tend to be higher and chronic illness increases the risk of infection. Since the appearance of COVID-19 in hypertensive patients seems to have poor outcome, the current study compares the survival rate of patients with and without hypertension. Based on the national survey conducted in Fars in recent years (South province in IRAN), the total prevalence of hypertension was estimated at 26.9% (9). During the current crisis in Fars, a total of 159 hypertensive patients were diagnosed with COVID-19 with a prevalence of 12.83 (159/1239). This is while the estimation is about 30% in other studies around the world.

Although there is no certain treatment for COVID-19 until now, the curation rate is identical in hypertension and non-hypertension groups. This is while clearly the mortality

rate is significantly different between groups and this result was the same as other studies. According to that most cases with hypertension are older than non-hypertension, this makes the condition more complicated and increase the mortality rate. Similar results were seen in other literature reports (10,11).

According to the recent study and along with other articles, it was found hypertensive patients with COVID-19 deteriorated faster than patients without hypertension (11). Similar results were seen in previous coronavirus epidemics such as Severe Acute Respiratory Syndrome (SARS) and Middle East respiratory syndrome (MERS) which was shown that hypertension is a risk factor for increased mortality in infected patients (12). Although the relationship between the pathogenesis of hypertension and the severity of coronaviruses infection needs more evaluation and clinical studies, a controversial issue is declared about antihypertensive drugs and the progress of the disease. Based on the different studies, it has been showed that Angiotensin-converting enzyme 2 (ACE-2) is the main receptor for SARS-COV-2 which mediates the invasion of the virus infection (13). This enzyme is widely expressed in different organs which may make them susceptible to this virus. Due to some documents using ACE-Inhibitors and Angiotensin receptor blockers (ARBs) can increase the expression of ACE-2 which may increase the field of binding virus and makes the host susceptible (14). Based on these, in fact, ACE-2 acts by catalyzing AngII to Ang1-7 and increases its anti-inflammatory effect (15). Experimental observation about this function was seen in 1128 hypertensive patients of COVID-19 and revealed a significant reduction in the fatality rate of patients who received ACEI/ARBs (16). Although in other studies by Xian Zhou *et al*, no statistical significant difference was seen in clinical outcomes of hypertensive patients whether receiving ACEI or ARB for treatment (17).

Our results suggested that hypertensive patients with co-existing other comorbidities like HIV, kidney, and cardiovascular disease should be more cautious in this crisis, and the hazard rate is more than other comorbidities. One reason which may justify this event is decreasing the lymphocyte count in HIV and HTN groups. It is mentioned that there is a relation between lymphopenia and decreasing ACE-2 and so increasing the AngII and Des-Arg and results in lung injury. Uncertainties in these issues require further clinical research (18).

The current study has several limitations: We did not record the history of medicine treatment and used drug in hypertensive patients. Also diagnose of hypertension was based on the medical history and patient's expression. There may be some unknown hypertensive patients who are unaware of their disease.

## Conclusion

Overall, our comparative study about the survival rate of COVID-19 patients had shown hypertensive patents are in danger of disease severity, although it may be related to their age. Moreover, the probability of other complications like diabetes, smoking, asthma, kidney, and cardiovascular diseases, and either some other infections such as HIV can make the condition complicated and need more consideration to prevent noxious outcomes.

## Competing interest

The authors declare that they have no competing interests.

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