Survival and predictors of deaths of patients hospitalized due to COVID-19 from a retrospective and multicenter cohort study in Brazil

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Abstract

The epidemic caused by COVID-19 in Brazil is associated with an unfavorable political scenario, aggravated by intense social inequality and low number of available hospital beds. Therefore, this study aimed to analyze the survival of patients admitted to Brazilian hospitals due to the COVID-19 and estimate prognostic factors. This is a retrospective, multicenter cohort study, based on data from 46285 hospitalizations for COVID-19 in Brazil. Survival functions were calculated using the Kaplan-Meier's method. The Log-rank test compared the survival functions for each variable and from that, hazard ratios were calculated and the proportional hazards model was used in Cox multiple regression. The smallest survival curves were the ones for patients at the age of 68 years or more, black / brown race, illiterate, living in the countryside, dyspnea, respiratory distress, influenza-like outbreak, O_2 saturation <95%, X-ray change, length of stay in the ICU, invasive ventilatory support, previous heart disease, pneumopathy, diabetes, down's syndrome, neurological disease and kidney disease. Better survival was observed in the symptoms and in an asthmatic patient. The multiple model for increased risk of death when they were admitted to the ICU HR 1.28 (95% CI

1.21–1.35), diabetes HR 1.17 (95% CI 1.11–1.24), neurological disease HR 1.34 (95% CI 1.22–1.46), kidney disease HR 1.11 (95% CI 1.02–1.21), heart disease HR 1.14 (95% CI 1.08–1.20), black or brown race of HR 1.50 (95% CI 1.43–1.58), asthma HR 0.71 (95% CI 0.61–0.81) and pneumopathy HR 1.12 (95% CI 1.02–1.23). The overall survival time was low in hospitalizations for COVID-19 and this reinforces the importance of sociodemographic and clinical factors as a prognosis for death. The lack of a protocol for scientific clinical management puts a greater risk of death for about 80 million Brazilians, who are chronically ill or living in poverty. COVID-19 can promote selective mortality that borders the eugenics of specific social segments in Brazil.

Introduction

During the early 20th century, the medical field supported an optimistic discourse on technological advances in the area and the control of infectious diseases, which for many centuries were the main causes of mortality in the world. However, several pathogens that have evolved or increased their ability to infect human beings have shown that curing communicable diseases must be a challenge for scientists for a long time to come. Examples of this are the SARS-CoV, MERS-CoV and now SARS-CoV-2 viruses, initially discovered as zoonoses which managed to change their transmission mechanism and start promoting direct human-to-human infection [1].

The infection caused by SARS-CoV-2 was classified as a differentiated clinical condition, which led to its inclusion as a new one, called Coronavirus Disease 2019 (COVID-19). The first cases were reported in the Wuhan peninsula in China, in December 2019, characterized by the high transmissibility power and cause of a severe acute respiratory dysfunction, with variations between mild, moderate and severe forms, a mortality rate growing according to older ages and to the presence of previous comorbidities, especially those that lead to some degree of cardiovascular impairment [2–3].

As of May 16, 2020, the World Health Organization has appointed 4,530,000 people infected with a total of 307,000 deaths worldwide. In Brazil, there are 220 thousand confirmed cases and 14,962 deaths caused by the disease on the same date. Which places the largest country in Latin America as the second in the world in terms of the rising epidemic curve of active cases and deaths [4].

The great challenge for Brazilian health authorities is to reduce the number of these cases to the minimum, especially the most serious ones, which require hospitalization with the support of invasive mechanical ventilation. The international experiences of countries affected by the COVID-19 epidemic demonstrate that, once the installed capacity of health services is overcome, the disease can raise its lethality rate to worrying levels, possibly leading to the death of millions of people due to the total lack health care, especially in a scenario of economic crisis and intense social inequality, which makes millions of Brazilians living in underprivileged communities more susceptible to death [5].

In Brazil, hospital bed occupancy rates are already at 100% in some states, health professionals are beginning to have to adopt patient admission criteria based on their chances of survival. Complicated decisions like this, which can mean life and death, need maximum scientific support in order to minimize the harm to all patients. Given this scenario, the present study aims to analyze the survival of inpatients and estimate the prognostic factors of patients admitted to Brazilian hospitals due to the COVID-19. Studies with this purpose, with a significant sample and with the level of scientific evidence of this design have not yet been published in the country.

Therefore, its findings may support the creation of scientifically supported clinical management protocols, minimizing conflicting situations and subsidizing decisions made in the hospital setting. In the face of a new disease that has no recognized treatment, a vaccine nor even its pathophysiology fully clarified, survival data and predictive factors are important instruments for the rational control of the epidemic and for scientific purposes, in order to better understand variables not yet discussed about COVID-19.

Methods

Study population and data collection

A retrospective, multicenter cohort study, of the survival analysis type, was carried out in order to estimate the prognostic factors of patients admitted to Brazilian hospitals due to COVID-19. Secondary, public and anonymous data were used from the notification forms of hospitalized patients and notified by SARS-COV-2 in hospitals in Brazil, in the observation period from February 20, 2020 to Jun 02, 2020. All hospitalized subjects and confirmed with COVID-19 through the RT-PCR exam were included in the study.

Participants and variables

80125 hospitalizations due to COVID-19 were registered in the public national epidemiological surveillance system, obtained from the open access database [6], public and anonymous. The counting of the follow-up time starts from the first day of hospitalization until the date of death or discharge. Records of subjects with missing hospitalization dates or inconsistencies in their diagnostic record were excluded from the study. These represent 2.94% (2363/80125) of the records. Censorship occurred in patients who were discharged or transferred, however, all records used in this study had an outcome definition until Jun 02, 2020, excluding from the cohort patients who were still hospitalized, whose representation is of 39,28% of the records (19156/80125) (Figure 1).

The co-variables used to compare survival curves were socioeconomic factors (age, sex, race, education and area of residence), clinical signs and symptoms (fever, cough, sore throat, diarrhea and vomiting), hospital variables (Influenza-like outbreak, hospital-acquired infection, dyspnea, respiratory distress, O2 saturation <95%, ICU admission, ICU length of stay, X-ray result), chronic disease (heart disease, hematology, down syndrome, liver disease, asthma, diabetes mellitus, neurological disease, pneumopathy, immunodepression, kidney disease, BMI), if the patient has had a flu vaccine, use of antiviral against influenza and the type of antiviral. The other variables on the notification form, whose completion was irregular or less than 5% of the cases, were excluded from the analysis (Supplementary form).

Statistical analysis

The data were analyzed from the estimates of survival functions, using the non-parametric Kaplan-Meier method [7]. The Log-rank test and the Wilcoxon test were used to compare the survival functions for each sociodemographic, signs or symptoms, hospital and clinical covariate. The numerical variable age was categorized by tertile and the categorical variables race and education were recategorized according to the similarity of the survival curves of each category, aggregating them by theoretical category. Due to the sample size, a value of p ≤0.01 was considered to accept the significant differences in the survival curves.

To assess the risk factors associated with death, Hazard Ratios (HR) and 95% confidence intervals were calculated, following Cox's proportional hazards model [8]. Covariates with a p-value <0.250 were used to create the multiple model. The modeling was initiated by the most significant variables, both at the level of statistical significance and at the theoretical level, respecting the risk proportionality test and absence of multicollinearity to be able to test the variable in the model. The final model was tested, the device and Cox-Snell residues were

analyzed. The data were analyzed using the STATA 12.0 program and in all analyzes the level of significance was considered equal to 5%.

Results

Survival functions

Between February 20, 2020 and Jun 02, 2020, 46285 hospitalizations due to COVID-19 were followed retrospectively. The median survival time was of 12 days (95% CI 11.82-12.18). At the end of the follow-up, 21408 deaths (46.25%) and 24877 (53.75%) censored patients were recorded (Figure 1).

The overall survival rate estimate was of 79.21% (95% CI 78.82%–79.59%) in 5 days of hospitalization and 59.22% (95% CI 58.69%–59.76%) in 10 days (Figure 2). In Table 1, when comparing the survival curves from the sociodemographic covariates, there is a significantly lower estimate of survival in 10 days in cases of ages above 68 years of 45.4% (95% CI 44.6% –46.2%), black or brown race of 51.3% (95% CI 50.3% –52.2%), living in the countryside 48.8% (95% CI 45.0%–52.5%) and illiterate 37.4% (95% CI 34.0% –40.9%).

Comparing at the same cutoff point in 10 days (Table 1), survival estimates were significantly lower when had dyspnea 57.0% (95% CI 56.4%–57.6%), respiratory distress 55.7% (95% CI 55.0%–56.4%), O_2 saturation <95% 54.4% (95% CI 53.7%–55.0%), mixed X-ray alteration 60.5% (95 % CI 57.8%–63.0%), admitted to the ICU 54.5% (95% CI 53.7%–55.3%), length of permanence in the ICU up to 8 days 15.0% (95% CI 14.0%–16.0%), invasive ventilatory support 41.6% (95% CI 40.7%–42.6%) and influenza-like outbreak 56.4% (95% CI 55.4%-57.5%). Still in Table 1, there was a lower estimate of the 10-day survival rate when the patient had chronic disease, such as heart disease 54.4% (95% CI 53.5%–55.2%), neurological 46.4% (95% CI 44.1%–48.8%), pneumopathy 52.2% (95% CI 49.8%–54.6%), diabetes 52.8% (95% CI 51.8%–53.8%) and kidney disease 48.4% (95% CI 46.2%–50.6%) and down's syndrome 38.5% (95% CI 28.0%–48.8%).

The covariates of clinical signs showed a better estimate of the survival of patients in 10 days when they had fever 61.8% (95% CI 61.2%–62.5%), Cough 61.6% (95% CI 61.0%–62.2%), sore throat 63.3% (95% CI 62.1%–64.5%), diarrhea 64.9% (95% CI 63.4%–66.3%) or vomiting 63.5% (95% CI 61.6%–65.4%). In the same comparison, patients who reported having asthma had a better survival estimate of 69.5% (95% CI 66.3%–72.4%).

Cox's proportional

In Table 2, after assessing the proportional risks, the statistically significant covariates that presented the highest risk of death were the age of 68 years HR 2.77 (95% CI 2.66–2.88), black or brown race of HR 1.54 (95% CI 1.49–1.59), living in the countryside HR 1.26 (95% CI 1.16–1.38) and illiterate HR 3.29 (95% CI 2.95–3.66), dyspnea HR 1.46 (95% CI 1.40–1.53), respiratory distress HR 1.48 (95% CI 1.43–1.54), O_2 saturation <95% HR 1.74 (95% CI 1.67–1.81), mixed X-ray alteration HR 1.42 (95% CI 1.26–1.59), admitted to the ICU HR 1.38 (95% CI 1.34–1.43), length of permanence in the ICU up to 8 days HR 9.15 (95% CI 8.73–9.60), invasive ventilatory support HR 2.94 (95% CI 2.81–3.07), influenza-like outbreak HR 1.18 (95% CI 1.14–1.22), heart disease HR 1.18 (95% CI 1.13–1.22), neurological HR 1.31 (95% CI 1.24–1.39), pneumopathy HR 1.11 (95% CI 1.05–1.18), diabetes HR 1.19 (95% CI 1.14–1.23), kidney disease HR 1.25 (95% CI 1.19–1.32) and down's syndrome HR 1.51 (95% CI 1.20–1.90).

Patients had a better prognosis when they had signs or symptoms such as fever HR 0.79 (95% CI 0.77–0.83), cough HR 0.79 (95% CI 0.76–0.82), sore throat HR 0.88 (95% CI 0.85–0.91), diarrhea HR 0.86 (95% CI 0.82–0.90), vomiting HR 0.93 (95% CI 0.88–0.98) or asthma HR 0.66 (95% CI 0.61–0.73) (Table 2). No significant difference was found in the survival curves of the sex co-variables, hospital-acquired infection, if the patient had previous hematological disease, liver disease, immunodepression, BMI, if they had been vaccinated against influenza, use antiviral or some type of antiviral.

After adjusting for confounding variables, they remained significantly in the multiple model for increased risk of death when they were admitted to the ICU HR 1.28 (95% CI 1.21–1.35), diabetes HR 1.17 (95% CI 1.11–1.24), neurological disease HR 1.34 (95% CI 1.22–1.46), kidney disease HR 1.11 (95% CI 1.02–1.21), heart disease HR 1.14 (95% CI 1.08–1.20), black or brown race of HR 1.50 (95% CI 1.43–1.58), asthma HR 0.71 (95% CI 0.61–0.81) and pneumopathy HR 1.12 (95% CI 1.02–1.23) (Figure 3).

Discussion

This multicenter retrospective cohort study of patients hospitalized with COVID-19 found important differences in survival times, as well as risk factors or protection for the death of patients in Brazilian hospitals. There was a reduced overall survival time, in addition to an association with lower survival estimates and a higher risk of death related to age, race, education, zone, dyspnea, respiratory distress, influenza-like outbreak, O_2 saturation, X-ray changes of chest, ICU stay, length of stay in ICU, use of ventilatory support, presence of heart disease, diabetes, down's syndrome, pneumopathy, kidney disease and neurological

disease. The variables of clinical signs or symptoms, such as fever, cough, sore throat, diarrhea or vomiting, showed greater survival and less risk of death. Finally, the presence of asthma had a better prognosis.

The overall survival of patients hospitalized for treatment of COVID-19 in Brazil was 62.05%. This survival is shown to be lower than other survival studies of hospitalized patients in Brazil. A retrospective cohort study developed by Bonfada at al., whose objective was to analyze the survival of elderly patients admitted to the ICU in a low-development region, found an overall survival of 66.64%, which reinforces the concern about the lethality of COVID-19 in countries with limited resources [9].

The lack of care and clinical management protocols for patients hospitalized by COVID-19 in Brazil, closely linked to internal political disputes in the country, and the consequent delay in training the health team have a direct influence on this context. In addition, there is no strategy for testing the asymptomatic population and even for those with suggestive symptoms there is a delay in the diagnosis of about 10 days for the confirmatory result via RT-PCR, a time interval in which there is already a drop in survival for 62.05%.

In our study when comparing survivals by sociodemographic covariates, a worse prognosis was found for patients over 68 years of age, with 2.77 times the risk of death. Besides that, it was found that people with black or brown skin color had a risk of death 1.54 times bigger and people with illiterate 3.29 times. All consecutive patients diagnosed with COVID-19 admitted to the Renmin Hospital of the Wuhan University, were enrolled in a retrospective cohort study. One third of the patients improved in hospital during follow-up. Twenty-five patients died, a mortality rate of 3.77%. In this study, older patients were prone to have severe COVID-19 symptoms and unimprovement, and were more likely to die in the hospital [10]. Another cohort studies identified several risk factors for death in adults who were hospitalized with COVID-19. Older age was also associated with higher odds of in-hospital death, it revealed age ⬚65 years as a strong predictor for death from COVID-19 pneumonia [11–12].

According to the Brazilian Institute of Geography and Statistics (IBGE), Brazil has a population of about 211 million inhabitants, among which there are 25 million elderly people and 55 million people who are below the poverty line, a group that is mostly composed by black people with low education [13]. Populations that live under vulnerability or social inequity often have less access to information and health services, and may reach hospital services late. In the same way, most of the people working as self-employed or

underemployed, are forced out of social isolation, often without protection, to ensure the livelihood of their families, what makes them subject to potential infection rates even higher.

In this sense, health policies need to have access to the information considered above to promote an adequate confrontation with reality, especially by creating protection mechanisms for these vulnerable groups. Otherwise, the COVID-19 epidemic in Brazil runs the risk of being a catalyst that assumes a higher risk of death of 26% of its entire population, indirectly characterized as a means of eugenics, based on socioeconomic and demographic criteria, worrying and incongruent with the constitutional principles and the guarantee of the principle of equity in health care, one of the pillars of the Brazilian public health system. Underprivileged people are at higher risk of infection and death from COVID-19, and they have less access to care due to systems that treat health as a commodity and not a human right [14–15].

When assessing the context of clinical variables, significance was found for better survival when patients presented signs or symptoms at the time of hospital admission, such as fever, cough, vomiting, sore throat or diarrhea, showing they may still be in the viral replication phase, therefore, the presence of signs or symptoms in this phase could be less severe. In addition, it is likely that patients will have a less severe reaction by the immune system, which would differ from other patients who may progress abruptly to a clinical severity, without having any of these symptoms at the beginning of hospitalization.

COVID-19 pneumonia is a multistate disease with clinically relevant intermediate endpoints like severity onset. Most survival data analyses set the onset as the primary endpoint, and censor recovery or hospital discharge. However, when competing risks of severity onset are present, this analytical method induces bias. The risk of severe progression assessed without considering the competition would be overestimated because the patients who would never progress (those who discharged from hospital without progression) were treated as if they could progress [16].

It has been shown that the ICU length of stay of up to three days has the worst prognosis, which reinforces our hypothesis that patients worsen their clinical condition abruptly during hospitalization, whose admission to the ICU would have little therapeutic capacity in these more severe cases of COVID-19. However, it would be necessary to develop prospective cohort studies to monitor, mainly, the changes in the clinical signs of patients with COVID-19 and their impact on the survival of hospitalized patients and how this interferes with the length of stay in the ICU.

The level and duration of infectious virus replication are important factors in assessing the risk of transmission and guiding decisions regarding isolation of patients. Because the coronavirus RNA detection is more sensitive than the virus isolation, most studies have used qualitative or quantitative viral RNA tests as a potential marker for infectious coronavirus. The detectable SARS-CoV-2 RNA persisted for a median of 20 days in survivors and it was sustained until death in no survivors [11].

In addition to clinical symptoms, an important result found in this study was asthma as a protective factor against death. Interestingly, the prevalence of asthma in patients with COVID-19 was 0.9% in ambispective cohort study of consecutive hospitalized patient. Thus, it was speculated that TH2 immune response in patients with asthma may counter the inflammation process induced by SARS-CoV-2 infection. Further studies are required to characterize the immune response and inflammation features of COVID-19 [17].

Hospitalized patients in the No. 7 Hospital of Wuhan, clinically diagnosed as "viral pneumonia" based on their clinical symptoms (fever or respiratory symptoms) with typical changes in chest radiology, were preliminarily involved in a study. No asthmatic patient was identified in this report, and only a few patients had self□reported drug hypersensitivity and urticaria. Taken together, virus infections have been associated with acute exacerbation of asthma, and allergy may not be a risk factor for virus infection. It is plausible that this concept may also apply to SARS□CoV□2; however, having no asthma patients and no respiratory allergies does not support this concept at least in this series of 140 patients [18].

Regardless of the sociodemographic variables and signs and symptoms, when analyzing the risks in the multivariate model, patients who were admitted to the ICU or who had heart, kidney, diabetes and neurological disease as comorbidities had the worst prognosis.

Most severe patients with COVID-19 admitted to the Tongji Hospital that were retrospectively enrolled and followed-up showed rapid progression and multiple organ dysfunction. During hospitalization, a substantial proportion of patients presented cardiac injury, liver and kidney dysfunction, and hyperglycemia. This present study also revealed that hyperglycemia was related with increased mortality in patients with COVID-19. The prevalence of hyperglycemia may be associated with underlying diabetes and corticosteroid therapy [17].

Led by the National Health Commission of the People's Republic of China, a retrospective cohort, to study COVID-19 admitted cases from 575 hospitals throughout China, was established [19]. Nonsurvivors present with a higher proportion of various coexisting chronic illness in univariate analysis. Coronary heart disease and cerebrovascular disease are

confirmed to be independent risk factors for death. Another study in Wuhan Pulmonary Hospital revealed that underlying cardiovascular or cerebrovascular diseases contributed to high mortality from COVID-19 pneumonia [12].

220 patients with confirmed COVID-19 were recruited from the Union Hospital of Huazhong University of Science and Technology. The present study showed that 161 COVID-19 patients (80.5 %) were with at least one of the comorbidities, including diabetes, hypertension, hepatic disease, cardiac disease, chronic pulmonary disease and others. Interestingly, COVID-19 patients with chronic pulmonary disease, mainly Chronic obstructive pulmonary disease (COPD), obviously presented elevated risk of death. It was found that there was a trend for hypertension and diabetes to elevate the risk of death from COVID-19 pneumonia [20].

In this aspect, it is necessary to develop strategies that aim to make a consistent clinical assessment on the organic impacts of patients with SARS-VOC-2 infection and comorbidities. Because of these, of course, there is already a higher risk of death on hospitalization due to factors such as a greater inflammatory response, propensity to chronic endothelial lesions and intravascular coagulation, acid/basic blood imbalance and impaired immune response.

Although the work with secondary data notification forms has its limitations, this problem is partially solved, mainly due to the country's urgency to maintain more accurate data in the monitoring of COVID-19, so that health institutions are able to plan actions to control the epidemic. In some cases, there was incomplete documentation of the history and symptoms in the electronic database, even after making efforts regarding feedback and recollection. Some diagnoses of co-existing illnesses were originated in self-reports from patients at their admission, which might lead to recall bias.

However, this study has a robust methodology, with appropriate data analysis and the first research in the country with all hospitalization in this gap of time. Furthermore, this research confirmed the importance of age and the presence of chronic diseases not only in the incidence of more serious cases of COVID-19, but also its effects on the drop in the survival curve of patients in hospital in Brazil. Nowadays this country is considered one of the worldwide epicenters to COVID-19.

In conclusion, it is considered important that scientifically supported protocols are developed for the management of appropriate clinical care for patients in hospital due to the COVID-19, especially in the face of a scenario where there is no consensus on pharmacological treatment or even therapeutic management. It is worth mentioning the

importance in the development of new studies, such as controlled and randomized clinical trials, in order to reaffirm the results of the present study, especially regarding the variable asthma as a protective factor against death.

Conflicts of interest. The authors have no conflicts of interest in this work.

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Table 1. Comparison of survival estimates for patients hospitalized due to SARS-COV-2 at 5 and 10 days

	Deths	%	5 Days	95% CI	10 Days	95% CI	Value of p
Age							
Up to 50 years old	3119	14.6%	89.7%	89.2%-90.3%	77.0%	76.0%-77.9%	<0.001
51 to 67 years old	6763	31.6%	81.1%	80.5%-81.8%	62.5%	61.5%-63.4%	
68 years old or more	11526	53.8%	69.2%	68.5%-69.9%	45.4%	44.6%-46.2%	
Sex							
Male	12667	59.2%	79.5%	79.0%-80.0%	59.2%	58.5%-59.9%	0.6595
Female	8738	40.8%	78.8%	78.2%-79.4%	59.2%	58.4%-60.1%	
Race							
White or Yellow	5930	42.9%	83.8%	83.2%-84.4%	65.8%	64.9%-66.7%	<0.001
Black or brown	7893	57.1%	72.8%	72.0%-73.5%	51.3%	50.3%-52.2%	
Level of education							
Illiterate	633	10.0%	62.9%	59.6%-66.0%	37.4%	34.0%-40.9%	<0.001
Low education	3201	50.7%	74.4%	73.2%-75.5%	53.7%	52.3%-55.2%	
Itermediate /Ellementary education	1775	28.1%	85.4%	84.3%-86.4%	68.0%	66.4%-69.6%	
Higher education	704	11.2%	90.9%	89.6%-91.9%	77.7%	75.6%-79.7%	
Zone							
Urban	18315	97.3%	79.3%	78.8%-79.7%	59.5%	58.9%-60.0%	<0.001
Rural	503	2.7%	70.2%	67.1%-73.2%	48.8%	45.0%-52.5%	
Influenza-like outbreak							
Yes	5961	39.7%	76.8%	76.0%-77.6%	56.4%	55.4%-57.5%	<0.001
No	9047	60.3%	80.8%	80.2%-81.3%	61.9%	61.1%-62.7%	
Hospital-acquired infection							
Yes	815	5.6%	77.5%	75.0%-79.8%	56.9%	53.9%-59.8%	0.0387
No	13714	94.4%	80.2%	79.8%-80.7%	60.7%	60.1%-61.4%	
Fever							
Yes	15199	80.1%	80.9%	80.5%-81.4%	61.8%	61.2%-62.5%	<0.001
No	3781	19.9%	75.7%	74.6%-76.7%	53.9%	52.5%-55.2%	
Cough							
Yes	15691	82.7%	80.9%	80.5%-81.3%	61.6%	61.0%-62.2%	<0.001
No	3283	17.3%	74.4%	73.2%-75.5%	53.7%	52.3%-55.2%	
Throat							
Yes	3768	25.4%	82.0%	81.2%-82.8%	63.3%	62.1%-64.5%	<0.001
No	11088	74.6%	79.7%	79.1%-80.2%	60.3%	59.6%-61.0%	
Dyspnea (Shortness of Breath)							

Yes	16847	87.1%	77.4%	76.9%-77.9%	57.0%	56.4%-57.6%	<0.001
No	2503	12.9%	86.6%	85.8%-87.4%	69.7%	68.4%-71.0%	

Respiratory distress

Yes	14495	80.2%	76.4%	75.9%-76.9%	55.7%	55.0%-56.4%	<0.001
No	3577	19.8%	85.9%	85.2%-86.6%	68.5%	67.3%-69.6%	

O$_2$ <95% saturation

Yes	15209	83.2%	75.3%	74.8%-75.8%	54.4%	53.7%-55.0%	<0.001
No	3063	16.8%	88.5%	87.8%-89.1%	72.6%	71.5%-73.7%	

Diarrhea

Yes	2406	16.6%	83.5%	82.5%-84.4%	64.9%	63.4%-66.3%	<0.001
No	12106	83.4%	79.6%	79.1%-80.1%	60.1%	59.4%-60.8%	

Vomit

Yes	1440	10.2%	81.3%	80.0%-82.6%	63.5%	61.6%-65.4%	0.0057
No	12728	89.8%	80.1%	79.6%-80.6%	60.5%	59.8%-61.2%	

Cardiopathy

Yes	9032	70.9%	76.4%	75.7%-77.1%	54.4%	53.5%-55.2%	<0.001
No	3705	29.1%	78.8%	77.9%-79.7%	60.2%	58.9%-61.5%	

Hematological

Yes	290	3.4%	76.3%	72.1%-79.9%	55.4%	50.4%-60.2%	0.619
No	8335	96.6%	77.4%	76.7%-78.0%	56.8%	56.0%-57.7%	

Down's syndrome

Yes	73	0.9%	70.9%	61.3%-78.5%	38.5%	28.0%-48.8%	<0.001
No	8512	99.1%	77.2%	76.5%-77.9%	56.7%	55.8%-57.5%	

Hepatic

Yes	298	3.5%	72.5%	68.2%-76.4%	51.1%	46.0%-55.9%	0.0364
No	8262	96.5%	77.5%	76.8%-78.2%	57.0%	56.1%-57.9%	

Asthma

Yes	488	5.7%	85.6%	83.5%-87.4%	69.5%	66.3%-72.4%	<0.001
No	8149	94.3%	76.9%	76.2%-77.5%	56.2%	55.3%-57.0%	

Diabetes

Yes	6899	59.1%	75.3%	74.4%-76.0%	52.8%	51.8%-53.8%	<0.001
No	4772	40.9%	78.7%	77.9%-79.6%	59.2%	58.1%-60.3%	

Neurological

Yes	1409	15.6%	70.5%	68.4%-72.5%	46.4%	44.1%-48.8%	<0.001
No	7643	84.4%	77.9%	77.2%-78.5%	57.8%	56.8%-58.7%	

Pneumopathy

Yes	1266	14.1%	75.4%	73.4%-77.3%	52.2%	49.8%-54.6%	0.0003
No	7694	85.9%	77.6%	76.9%-78.3%	57.4%	56.5%-58.3%	

Immunodepression

Yes	865	9.9%	77.8%	75.6%-79.9%	59.7%	56.9%-62.4%	0.0558
No	7883	90.1%	77.2%	76.5%-77.9%	56.7%	55.8%-57.6%	

Kidney disease

Yes	1556	17.2%	73.1%	71.1%-74.9%	48.4%	46.2%-50.6%	<0.001
No	7512	82.8%	77.6%	76.9%-78.3%	57.6%	56.7%-58.5%	

BMI

Normal	7	0.9%	91.7%	53.9%-98.8%	46.9%	17.6%-71.8%	0.117

Overweight	52	6.7%	81.5%	71.8%-88.1%	50.0%	37.8%-61.1%	
Obesity I	373	47.9%	82.0%	79.1%-84.7%	62.6%	58.6%-66.3%	
Obesity II	192	24.6%	82.1%	77.7%-85.7%	60.0%	54.1%-65.5%	
Obesity III	155	19.9%	76.7%	71.2%-81.2%	52.9%	46.0%-59.4%	
Vaccine							
Yes	2371	32.1%	80.9%	79.8%-82.0%	62.2%	60.7%-63.8%	0.5214
No	5012	67.9%	81.1%	80.3%-81.8%	62.4%	61.4%-63.5%	
Anti-viral							
Yes	8324	51.3%	81.3%	80.7%-81.8%	61.1%	60.3%-62.0%	0.0682
No	7889	48.7%	80.1%	79.5%-80.7%	61.3%	60.4%-62.1%	
Antiviral Type							
Oseltamivir	7675	97.3%	81.5%	80.9%-82.1%	61.4%	60.6%-62.3%	0.591
Zanamivir	35	0.4%	76.2%	64.0%-84.7%	50.0%	35.4%-63.0%	
Other	178	2.3%	82.7%	78.5%-86.1%	64.5%	58.7%-69.8%	
ICU							
Yes	11070	58.5%	77.1%	76.5%-77.8%	54.5%	53.7%-55.3%	<0.001
No	7869	41.5%	82.5%	82.0%-83.0%	66.2%	65.4%-66.9%	
Ventilatory Support							
Yes, invasive	2439	13.4%	66.1%	65.2%-67.0%	41.6%	40.7%-42.6%	<0.001
Yes, not invasive	6525	35.9%	82.7%	82.1%-83.3%	65.4%	64.6%-66.3%	
No	9202	50.7%	90.3%	89.7%-90.8%	77.6%	76.5%-78.6%	
X-ray							
Normal	406	6.0%	87.1%	85.0%-88.9%	71.5%	68.3%-74.5%	<0.001
Infiltrate Interstitial	4732	70.2%	80.3%	79.5%-81.1%	60.9%	59.8%-62.0%	
Consolidated	735	10.9%	80.5%	78.3%-82.5%	60.5%	57.6%-63.3%	
Mixed	866	12.9%	79.8%	77.8%-81.7%	60.5%	57.8%-63.0%	
ICU length of stay							
Up to 8 days	6418	58.9%	57.0%	55.9%-58.0%	15.0%	14.0%-16.0%	<0.001
>8 days	4486	41.1%	95.2%	94.7%-95.6%	89.5%	88.8%-90.2%	

Table 2. Comparison of Cox proportional Hazards (HR) in relation to the risk of death

	n	HR	95% CI	p
Age				
Up to 50 years old	27932	1.00		
51 to 67 years old	25747	1.74	1.67-1.82	<0.001
68 years old or more	26444	2.77	2.66-2.88	<0.001
Sex				
Male	45926	1.01	0.98-1.03	0.668
Female	34176	1.00		
Race				
White or Yellow	24091	1.00		
Black or brown	26614	1.54	1.49-1.59	<0.001
Level of education				
Higher education	5223	1.00		
Itermediate/Ellementary education	8954	1.49	1.36-1.62	<0.001
Low education	10391	2.23	2.06-2.42	<0.001
Illiterate	1630	3.29	2.95-3.66	<0.001
Zone				
Urban	68418	1.00		
Rural	1864	1.26	1.16-1.38	<0.001
Influenza-like outbreak				
Yes	19609	1.18	1.14-1.22	<0.001
No	35911	1.00		
Hospital-acquired infection				
Yes	2143	1.07	1.00-1.15	0.044
No	52180	1.00		
Fever				
Yes	58977	0.79	0.77-0.83	<0.001
No	13132	1.00		
Cough				
Yes	61368	0.79	0.76-0.82	<0.001
No	10817	1.00		
Throat				
Yes	17084	0.88	0.85-0.91	<0.001
No	40740	1.00		
Dyspnea (Shortness of Breath)				
Yes	55650	1.46	1.40-1.53	<0.001
No	15218	1.00		
Respiratory distress				
Yes	46460	1.48	1.43-1.54	<0.001

No	19326	1.00		
O$_2$ <95% saturation				
Yes	44351	1.74	1.67-1.81	<0.001
No	21198	1.00		
Diarrhea				
Yes	10881	0.86	0.82-0.90	<0.001
No	45191	1.00		
Vomit				
Yes	6128	0.93	0.88-0.98	0.007
No	48436	1.00		
Cardiopathy				
Yes	25160	1.18	1.13-1.22	<0.001
No	12619	1.00		
Hematological				
Yes	759	1.03	0.91-1.16	0.629
No	25487	1.00		
Down's syndrome				
Yes	200	1.51	1.20-1.90	<0.001
No	25911	1.00		
Hepatic				
Yes	680	1.13	1.01-1.26	0.042
No	25372	1.00		
Asthma				
Yes	2238	0.66	0.61-0.73	<0.001
No	24492	1.00		
Diabetes				
Yes	18872	1.19	1.14-1.23	<0.001
No	15655	1.00		
Neurological				
Yes	3007	1.31	1.24-1.39	<0.001
No	24212	1.00		
Pneumopathy				
Yes	2935	1.11	1.05-1.18	<0.001
No	24148	1.00		
Immunodepression				
Yes	2405	0.93	0.87-1.00	0.063
No	24237	1.00		
Kidney disease				
Yes	3258	1.25	1.19-1.32	<0.001
No	23729	1.00		
BMI				
Normal	17	1.00		
Overweight	139	1.18	0.53-2.61	0.675
Obesity I	1227	1.00	0.47-2.12	0.990
Obesity II	616	1.16	0.54-2.45	0.706
Obesity III	475	1.27	0.59-2.70	0.539

Vaccine				
Yes	9914	1.01	0.97-1.07	0.532
No	21723	1.00		
Anti-viral				
Yes	26461	0.97	0.94-1.00	0.076
No	34881	1.00		
Antiviral Type				
Oseltamivir	23906	1.00		
Zanamivir	114	1.13	0.81-1.57	0.473
Other	910	0.95	0.82-1.10	0.491
ICU				
Yes	24284	1.38	1.34-1.43	<0.001
No	40834	1.00		
Ventilatory Support				
Yes, invasive	23638	2.94	2.81-3.07	<0.001
Yes, not invasive	27900	1.59	1.52-1.66	<0.001
No	14806	1.00		
X-ray				
Normal	2173	1.00		
Infiltrate Interstitial	16003	1.42	1.28-1.57	<0.001
Consolidated	2277	1.42	1.26-1.61	<0.001
Mixed	2723	1.42	1.26-1.59	<0.001
ICU length of stay				
Up to 8 days	9452	9.15	8.73-9.60	<0.001
>8 days	7588	1.00		

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┌─────────────────────────────┐
│ 80125  hospitalizations due to │
│          COVID-19            │
│ 3103  Health Units           │
│ 1238  municipalities         │
└─────────────────────────────┘
              │
┌──────────────────────────┐   │
│ 2363  inconsistencies     │◄──┤
│ 19156  still hospitalized  │   │
└──────────────────────────┘   │
              │
              ▼
┌─────────────────────────────┐
│ 46285  hospitalizations due to │
│          COVID-19            │
└─────────────────────────────┘
              │
              ▼
┌─────────────────────────────┐
│ 21408  deaths                │
│ 24877  censored patients      │
└─────────────────────────────┘
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		HR Aj
ICU		
Yes		1.28
No		1.00
Diabetes		
Yes		1.17
No		1.00
Neurological		
Yes		1.34
No		1.00
Kidney disease		
Yes		1.11
No		1.00
Cardiopathy		
Yes		1.14
No		1.00
Race		
Black or brown		1.50
White or Yellow		1.00
Asthma		
Yes		0.71
No		1.00
Pneumopathy		
Yes		1.12
No		1.00

0.00   0.50   1.00   1.50   2.00

← Protetion   Risk →