

Association between Anthropometric Variables and Patient Outcomes Among Patients with COVID-19 Infection in A Latin-American City

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ABSTRACT

Objective: To determine the relationship between anthropometric variables and patient outcomes among patients hospitalized with COVID-19 at our institution.

Methods: This retrospective cohort study included patients hospitalized with COVID-19 in general wards and critical care unit. Sociodemographic and clinical data were collected.

Results: A total of 130 patients meeting inclusion criteria and hospitalized between April and August 2020 participated in this study. The majority of patients were male (63%), mean age was $59,5 \pm 18.5$ years, and 53,8% were older than 60 years. Mean body mass index (BMI) was 26.7 kg/m^2 (SD 3.69). Patients with diabetes mellitus exhibited a statistically significant increase in mortality (relative risk 4.8; CI95% 1,7 – 13.8). While there was an association between being overweight or having some degree of obesity with greater mortality, this association did not reach statistical significance.

Conclusions: Chronic diseases are associated with complications and increased mortality in patients infected with COVID-19. Thus, efforts should be made towards achieving management of comorbidities and improved lifestyle habits.

Keywords

Obesity, Overweight, COVID-19, Mortality.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a recently described enveloped RNA virus identified as the cause of highly contagious respiratory disease initially reported in late 2019 and now referred to as coronavirus disease 19 (COVID-19), which rapidly spread around the world leading to the current pandemic [1]. Despite that most affected individuals are asymptomatic or exhibit mild symptoms (like cough, fever, loss of taste or smell, aches and pains, headache, sore throat, nasal congestion, red eyes, diarrhea), 14% of patients develop severe disease requiring hospitalization, and around 5% require intensive care secondary to acute respiratory distress syndrome (ARDS), sepsis, septic shock, and multiorgan failure [2].

Retrospective studies in China showed that greater COVID-19 severity and mortality was observed in patients developing pneumonia, and was associated with cytokine release syndrome (CRS) [3]. CRS is an acute inflammatory response characterized by decreased numbers of lymphocytes and natural killer cells, increased secretion of IL-6, continuous fever, deterioration due to a cytokine-mediated immune reaction, and coagulation dysfunction; all of which favor the rapid progression of inflammation, leading to multiorgan failure [4]. Therefore, a state of inflammation may play a role in the development of severe COVID-19.

Obesity is considered a state of chronic inflammation that has been associated with increased production of inflammatory cytokines such as TNF- α , IL-1, IL-6, which in the long term play a role in the development of insulin resistance and cardiovascular disease [7]. Furthermore, patients with obesity tend to have vitamin, mineral, and trace element deficiency, which may lead to alterations in the immune system, and may thus favor development of severe infections [5].

In addition, obesity has been associated with a decrease in expiratory reserve volume, lung capacity, and compliance. In the supine position, lung function in patients with abdominal obesity is mostly compromised due to a decrease in diaphragmatic excursion, thus making ventilation more difficult [6].

Therefore, these immunologic and respiratory conditions make obesity a risk factor for severe COVID-19 disease, since a state of chronic inflammation in addition to the action of an infectious agent that has been shown to cause systemic cytokine release amplifies the immune response, conditioning the presentation of a potentially catastrophic disease [7].

Methods

This was a retrospective cohort study of patients older than 18 years that were hospitalized in the general wards or critical care unit (CCU) of the respiratory isolation pavilion at our institution between April and August 2020 that were diagnosed

with COVID-19 infection according to clinical and/or radiologic findings.

Criteria for SARS-CoV-2 infection were defined following guidelines provided by the Colombian Ministry of Health at the time, and included clinical, paraclinical and radiologic factors considered during this period [8].

A secondary database was used, and medical and nutritional records of the database at our institution were reviewed. Data were manually tabulated using Microsoft Excel, and were subsequently analyzed using IBM SPSS Statistics software, version 25.

In this study, the following variables were individually analyzed: age in completed years, clinically relevant comorbidities, medications, clinical signs and symptoms exhibited and reported in medical records during hospital stay, length of hospital stay -defined as the number of days that elapse before medical discharge or death-, and severity of disease as mild, severe, or critical as defined by the Colombian Ministry of Health guidelines for the clinical management of patients with SARS-CoV-2 infection [9]. Regarding anthropometric variables, weight, height, and body mass index (BMI) were analyzed.

Outcomes were analyzed in relation to length of hospital stay, disease severity, and mortality. BMI was categorized according to the National Heart, Lung, and Blood Institute into low weight (<18,5 kg/m²), normal (18,5 to 24,9 kg/m²), overweight (25 to 29,9 kg/m²), and obese (>30 kg/m²) [9]. The age variable was dichotomized into younger than 60 years and older than or equal to 60 years. The assumption of variable normality was assessed for quantitative variables, and are shown as central tendency measures. Qualitative variables are presented as relative and absolute frequencies.

Bivariate analyses were performed to assess the association of each covariate with patient outcome by comparing surviving and deceased patients using Chi-squared or Fisher's exact test for categorical variables, and Mann-Whitney U test for continuous variables. Clinically relevant covariates were selected for adjusted analysis.

Binary logistic regression was used to predict an association between qualitative and quantitative variables with the dependent variable. Estimates of the association between different risk or protective factors and death caused by SARS-CoV-2 expressed as relative risk (RR) and corresponding 95% confidence intervals (CI95%).

When performing binary logistic regressions, we confirmed that omnibus tests of model coefficients was significant in order to proceed with its use. Similarly, the Hosmer-Lemeshow goodness of fit test for the multivariate analysis was used to assess adequacy of model fit. Initially, univariate estimates were calculated and with the intention of obtaining adjusted estimates, the model was run with all the variables to be studied. For the creation of

the association table, unadjusted values are shown in order to demonstrate their significance, and subsequently adjusted values are shown to describe variations correspondingly.

Due to the retrospective nature of this study, informed consent of the study participants was not required. This study is part of the larger study entitled “Predictive model obesity and COVID-19”, and was approved by the Ethics Committee at Las Americas AUNA Clinic (Minute No. 158) in Medellin, Colombia, as well as by the Research Committee at Hospital Universidad del Norte.

Results

Baseline characteristics of patients treated in the COVID-19 unit at our institution during the period of April – August 2020 are shown in Table 1. While there was a large volume of patients treated during the first months of the pandemic, only 130 met the inclusion criteria during the selected period of time. Of the participating individuals, 63% were male, and the mean age was of 59.5 ± 18.5 years, being 53.8% older than 60 years. Mean BMI was 26.7 kg/m^2 (SD 3.69). Of the 130 study participants, 40 had normal weight, 71

were overweight, and 19 some degree of obesity.

In this study, the most frequent comorbidities were high blood pressure (39.2%), diabetes mellitus (22.3%), and smoking (13.8%). Following the national guidelines for the classification and management of patients with infection by the novel coronavirus SARS-CoV-2 [8], of the 130 patients 8 exhibited mild, 71 severe, and 51 critical disease. A total of 32 patients died (24.6%), with a mean age of 65.6 ± 15.4 years. Length of duration of hospital stay for all patients was 10.8 ± 7.9 days, while for those that died was of 8.9 ± 5.2 days.

Of the deceased patients, 68,7 were male, 37% had normal weight, 46,8% were overweight and 15,6% had some degree of obesity. Almost a third (31,4%) of patients older than 60 years died.

Regarding symptoms, the most frequently observed were fever (85/130), cough (77/130), and dyspnea (73/130). Of the general population, 24,6% died, and almost two thirds (62.7%) of those presenting critical disease passed away.

CHARACTERISTICS	DECEASED PATIENTS	ALL PATIENTS	p-value*
	(n = 32)	(n = 130)	
Sex	n (%)		
Male	22 (26,8)	82	0,444
Female	10 (20,8)	48	
Age			
Mean (SD)	65,6 (15,4)	59,5 (18,5)	0,031
Median (Q1-Q3)	67,5 (56,0 -78,8)	62,0 (45,8 – 75,2)	
By age group			
<60 años	10 (16,7)	60	0,511
≥60 años	22 (31,4)	70	
Body mass index			
<18,5 Kg/m ²	0 (0)	0	0,511
18,5 – 24 Kg/m ²	12 (30,0)	40	
25-29 Kg/m ²	15 (21,1)	71	
≥30 Kg/m ²	5 (24,6)	19	
Duration of hospital stay			
Mean (SD)	8,9 (5,2)	10,8 (7,9)	0,341
Median (Q1-Q3)	8,0 (5,0 – 13,5)	9,0 (6,0 – 13,2)	
Past medical history			
High blood pressure	15 (29,4)	51	0,308
Type 2 Diabetes Mellitus	11 (37,9)	29	0,059
Acute myocardial infact	2 (33,3)	6	0,636
Cerebrovascular disease	3 (37,5)	8	0,406
Smoking	4 (22,2)	18	1,000
COPD - Asthma	3 (37,5)	8	0,406
Medications			
Insulin	3 (23,1)	13	1,000
ARB	10 (26,3)	38	0,772
Calcium channel blockers	2 (15,4)	13	0,518
Beta blockers	4 (33,3)	12	0,488
Aspirin	1 (11,1)	9	0,451
Diuretic	2 (25)	8	1,000
Statins	1 (14,3)	7	1,000
Symptoms			
Fever	20 (23,5)	85	0,693
Cough	21 (27,3)	77	0,397
Dyspnea	23 (31,5)	73	0,039
Joint pain	6 (20,7)	29	0,578
Diarrhea	5 (29,4)	17	0,763
Odynophagia	2 (22,2)	9	1,000
Severity			
Mild	0 (0)	8	<0,001
Severe	0 (0)	71	
Critical	32 (62,7)	51	

ARB: angiotensin II receptor blockers, COPD, Chronic obstructive pulmonary disease, Q: quartile, SD: standard deviation,

*Fisher's exact test was used for variables with counts <5, Mann-Whitney U test was used for continuous variables, and Chi-squared for the remaining variables.

Table 1: Baseline characteristics of patients treated in the COVID-19 unit at Hospital Universidad del Norte during April - August 2020 .

Category		Relative Risk	LL	UL
Sex	Female	Reference		
	Male	17.932	0,73574	4.371
Age	Younger than 60 years	Reference		
	Older than 60 years	18.785	0,76284	4.626
BMI	Normal	Reference		
	Overweight	0,6721	0,26328	1.716
	Obese	11.524	0,3281	4.048
Past medical history	None	Reference		
	High blood pressure	0,9624	0,26777	3.459
	Diabetes	48.009	166.547	13.839
	Smoking	0,4371	0,12321	1.551
	Asthma, COPD	18.902	0,44816	7.972
	Stroke	24.541	0,27577	21.839
	Acute myocardial infarct	0,8989	0,08098	9.979
Used medications	Insulin	0,4077	0,09403	1.768
	ARB	15.187	0,37366	6.173
	Calcium channel blockers	0,6219	0,11698	3.306
	Beta blockers	0,8727	0,15774	4.829
	Aspirin	0,3182	0,02622	3.862
	Diuretic	0,4794	0,07123	3.226
	Statins	0,2328	0,02089	2.595

ARB: Angiotensin II receptor blocker; COPD: Chronic obstructive pulmonary disease; LL: lower limit, UL: Upper limit

Table 2: Relative risk of death by COVID-19 among patients hospitalized during April - August 2020 at Hospital Universidad del Norte.

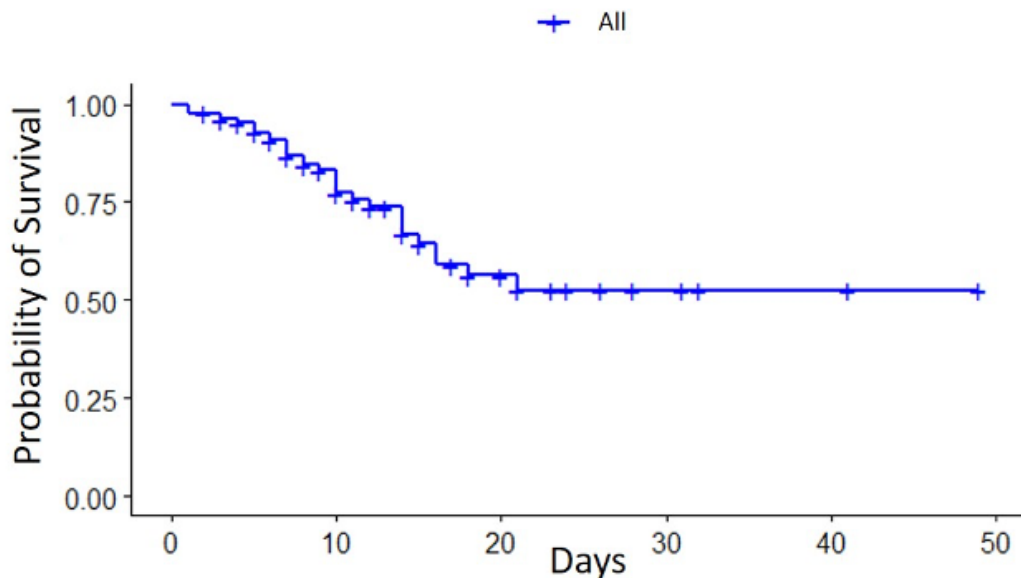


Figure 1: Kaplan-Meier survival curve of patients hospitalized in the COVID-19 unit from April – August 2020 at Hospital Universidad del Norte.

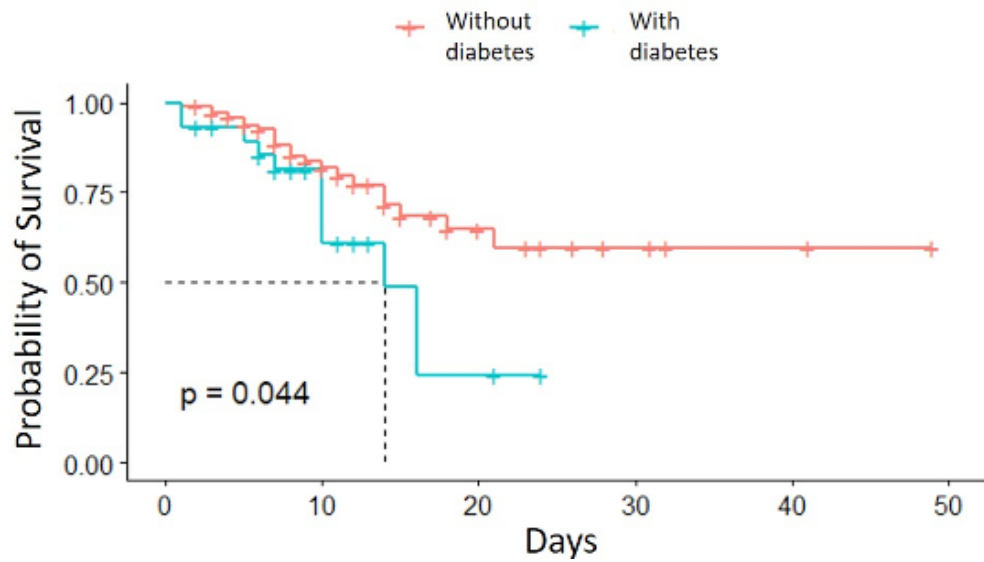


Figure 2: Kaplan-Meier survival curve according to past medical history of type 2 diabetes mellitus of patients hospitalized in the COVID-19 unit from April – August 2020 at Hospital Universidad del Norte.

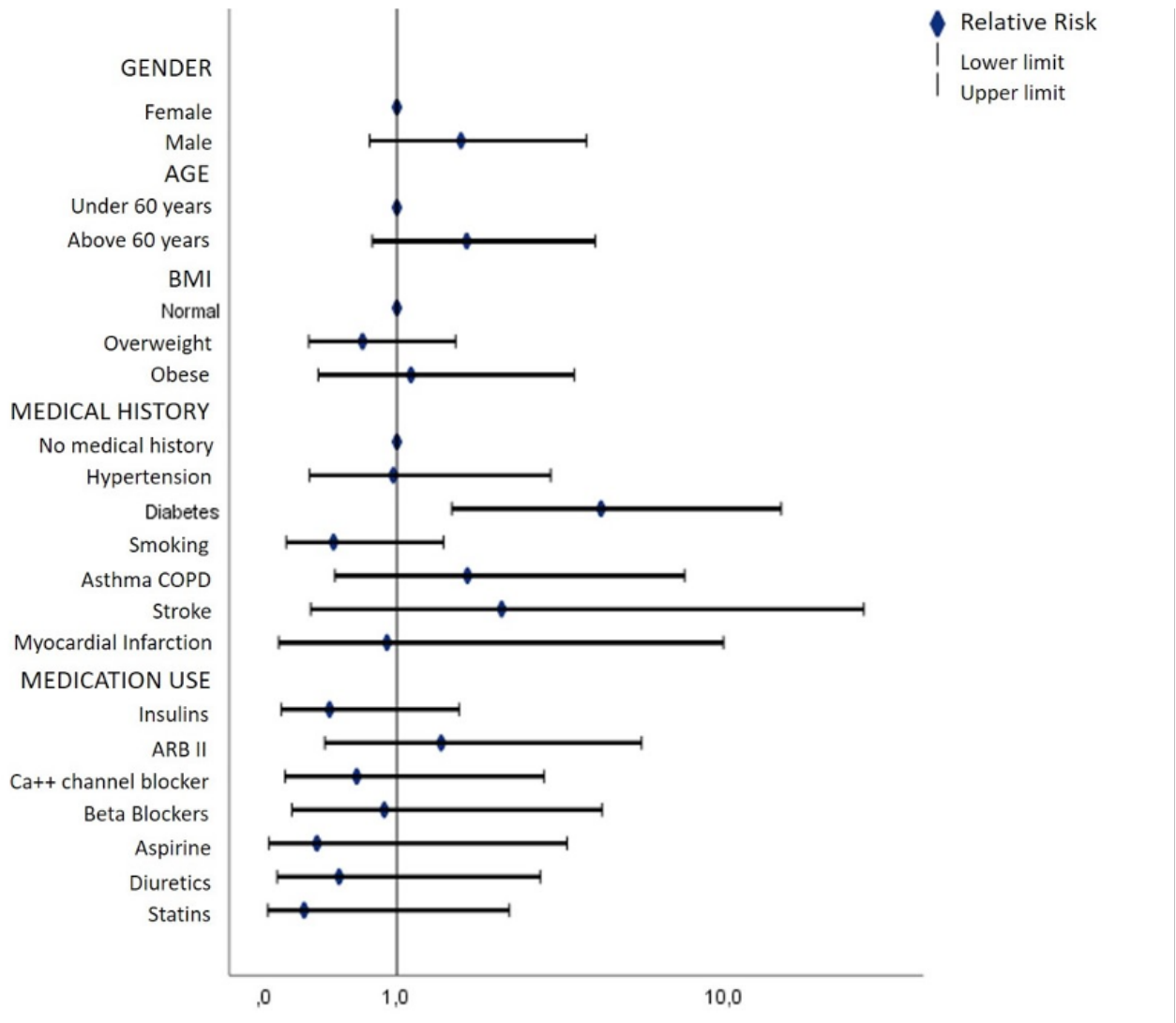


Figure 3: Forest plot of the relative risk of death from COVID-19 according to the indicated variables

With respect to length of hospital stay, survival odds of the general population decreased to approximately 50% after 20 days of hospitalization (Figure 1). Risk of dying from COVID-19 with increasing hospital stay was significantly higher in diabetic patients compared with non-diabetic patients (Figure 2), exhibiting a 4,8-fold increased relative risk (CI95% 1,7 – 13,8) (Table 2, Figure 3). Our data indicated that being male, older than 60 years, or being overweight tended to be associated with having lower odds of survival with increasing length of hospital stay, however this association was not statistically significant. Additionally, a trend was observed for male patients, older than 60 years, with obesity, past medical history of COPD, stroke, or that were taking ARB, to have an increased risk of death from COVID-19, however this association was not statistically significant. A similar pattern of risk of death was observed when variables were subdivided by BMI (Table 2).

Discussion

In this study, we aimed to determine the relationship between anthropometric variables and patient outcomes among patients hospitalized with COVID-19 at our institution. Our results showed a mean patient age of 59.5 years, which is 10 years younger than Spanish patients in the SEMI-COVID study [11], and 10 years older if compared with the Kaiser Permanente study population in Southern California [12].

Despite that only 6 of 130 patients had previous history of acute myocardial infarct, about a third (33,3%) of all patients succumbed to COVID-19.

In our study population, being male, older than 60 years, or individuals with overweight or obesity were variables that tended to increase mortality rates. Meanwhile, Tartof et al. [12], reported that mortality was increased in patients with severe obesity, particularly in those aged 60 years or younger, as well as in those with high blood pressure, dyslipidemia, and acute myocardial infarct. In agreement with that study, our results indicated that history of diabetes mellitus was associated with increased mortality, and that this association was statistically significant. Importantly, of all deceased diabetic patients, 50% were in overweight, and 33,4% in obesity range. In agreement with our findings, the Fadini study [13] showed that while history of diabetes mellitus did not increase the risk of infection with SARS-CoV-2, it did lead to worse patient outcomes.

Although an association between individuals with overweight or some degree of obesity with increased mortality was observed in our study, statistical significance was not reached. This could be partly explained by our small sample size.

Tartof and colleagues [12] reported that patients with BMI greater than 40kg/m² had a 4-fold greater risk of death from COVID-19 than those with lower BMIs. In addition, the Klang et al. study showed that patients aged 50 years or younger that had BMIs greater than 40kg/m² had a 5-fold greater risk of death from this infection [14]. In our study, while a statistically significant

association between patient outcome and a specific BMI category was not identified, we did observe that ranges among overweight or obesity were associated with increased mortality. To our knowledge, there are no studies to date that describe severity of COVID-19 in relation to BMI. Our data showed that of all patients classified as having severe disease, 57.7% were in overweight, and 16.9% had some degree of obesity. Similarly, of the patients presenting critical disease, 50.9% were overweight, and 13.7% had some degree of obesity.

The association between BMI and length of hospital stay has not been currently reported in the literature. In this study, our data suggested that those with mild or severe disease had a longer hospital stay compared with those with critical disease, which may be likely due to the higher mortality of the latter.

One of the main limitations of our study was that diagnosis of COVID-19 was guided by clinical, radiologic, or paraclinical criteria according to the addendum of the Colombian National Health Institute [8], since at the time of the study, there was a significant delay in COVID-19 PCR test results given the context of being in the midst of a pandemic and collapse of our healthcare system.

Importantly, while the majority of patients included in this study were either in overweight or obesity range, they did not have this diagnosis as part of their previous medical history, nor were they undergoing weight management interventions or being guided to improve lifestyle habits. Likewise, it was evidenced that many medical records did not contain all anthropometric variables, nor considered obesity as a condition to be included in their past medical history, which limited the inclusion of a greater number of patients in our study.

Finally, as described by Clement and colleagues [15] in their experience with COVID-19 in France, this pandemic has shown that obesity should be deeply integrated into healthcare and research systems in order to implement interventions in a timely fashion, and to ultimately improve patient care.

Chronic conditions such as obesity, high blood pressure, diabetes mellitus, among others, are associated with complications and increased mortality in patients with COVID-19. In our cohort, the strongest association with mortality was observed for diabetes mellitus. Nonetheless, larger studies are required in order to determine and confirm the impact of comorbidities on mortality. It is important to reinforce in the general population sustainable lifestyle habits aiming not only to maintain a healthy weight, but also to reduce the presence or progression of metabolic and cardiovascular alterations.

Authors contributions

Eder Hernandez, Ricardo Rosero and Kelly Ortiz conceived and carried out experiments. Daniela and Maria Carolina Manzur carried out experiments. Jesus Barrera and Gustavo Vergara

analyzed and interpreted data. All authors were involved in writing the paper and had final approval of the submitted and published versions.

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