



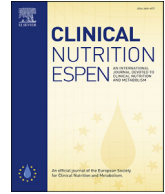
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Short Communication

Obesity contributes to mortality and displays alterations in calcium, urea and hemoglobin levels in SARS-CoV-2 infected individuals

Giovanna Uliana Rodrigues^a, Paula Renata Bueno Campos Canella^b,
Raquel de Cássia dos Santos^c, Daniela Soares Razolli^{b,*}^a São Francisco University, Bragança Paulista, São Paulo, 12916-900, Brazil^b Postgraduate Program in Health Sciences, São Francisco University, Bragança Paulista, São Paulo, 12916-900, Brazil^c Laboratory of Pharmacology and Molecular Biology, Post Graduate Program in Health Sciences, Medical School, São Francisco University, Bragança Paulista, São Paulo 12916-900, Brazil

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SUMMARY

Background & aims: Obesity courses with metabolic and inflammatory changes that include, among others, higher expression of the renin-angiotensin-aldosterone system. The pathophysiology of the new coronavirus suggests an affinity for angiotensin-2 converting enzyme receptors, cytokine storm, and systemic hypercoagulability. Thus, obesity could contribute to the worse evolution of individuals with COVID-19. Here we evaluated the clinical outcome and age of SARS-CoV-2 infection in patients with higher BMI compared with normal BMI at the São Francisco de Assis University Hospital (HUSF), in Bragança Paulista, SP.

Methods: Retrospective observational study with a review of medical records from June of 2020 to May of 2021 of patients positive for SARS-CoV-2 from HUSF. Demographic, anthropometric, and metabolic data were collected for correlation analysis. The study was approved by the Ethical Committee under CAAE: 34121820.3.0000.5514.

Results: 360 medical records were analyzed, of which 125 were included. The mean age of patients with obesity was significantly lower than overweight and normal weight, both in the overall mean (p -value 0.002–66 versus 56 and 56) and in the mean age of mortality (p -value 0.003–59 versus 61 and 76). The mean plasma calcium in the last sample collected during hospitalization of patients with obesity was significantly higher than that of overweight and normal weight (p -value < 0.001–7.8 versus 8.1 and 8.6). The mean hemoglobin in the first admission sample was also significantly higher in patients with obesity compared to the other groups (p -value 0.041–12.5 versus 12.9 and 13.6). On the other hand, the plasma concentration of urea in the first sample of hospitalization of patients with normal weight was higher than in patients with overweight and obesity (p -value 0.036–90.4 versus 64.8 and 57.1).

Conclusion: Our findings suggest that age is not a determining factor for the death outcome in patients with obesity. However, obesity contributes to metabolic changes and mortality in SARS-CoV-2 infected patients.

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1. Introduction

Overweight and obesity affect 1.9 billion and 650 million individuals, which correspond to 39% and 13% of the worldwide population, respectively. Obesity is a consequence of disruption of energy homeostasis, which leads to abnormal adipose tissue

accumulation impacting lifespan and elevating costs to the public health systems. Once established obesity predisposes to the development of comorbidities such as diabetes, cardiovascular diseases, and certain types of cancer [1].

COVID-19 is an emerging disease caused by SARS-CoV-2 identified in 2019 at Wuhan, China. In March 11 the World Health Organization declared a pandemic of COVID-19 and, since, the infection is progressively spreading, mostly because of its transmission characteristics [2]. Although the pathophysiology of the

* Corresponding author.

E-mail address: danirazolli@yahoo.com.br (D.S. Razolli).

virus it's not completely understood, studies have shown a cytokine storm, hypercoagulability, and most prominent, pulmonary injury in infected individuals [3].

Among the obesity-related comorbidities, cardiovascular disease, diabetes, and hypertension had higher prevalence and fatality rates in hospitalized patients positive for COVID-19. Also, preexisting chronic diseases and unhealthy lifestyle habits like smoking, sedentarism, and obesity were significantly correlated with the severity of the disease and increased admittance in Intensive Care Unit (ICU), moreover, the infection risk is dose-dependent with less favorable lifestyle records [4,5]. Lastly, a recent meta-analysis study concluded that those with severe COVID-19 may have a higher BMI, and patients with obesity were more likely to develop severe conditions, indicating that obesity may exacerbate COVID-19 infection [6].

Here, we evaluated the clinical outcomes and age in SARS-CoV-2-infected patients with obesity compared to overweight and normal weight, admitted to the São Francisco de Assis University Hospital (HUSF), located in the city of Bragança Paulista, state of São Paulo, Brazil.

2. Material and Methods

The data were obtained by reviewing the medical records of all SARS-CoV-2 positive patients at the HUSF admitted from June of 2020 to May of 2021 after Ethical Committee approval under CAAE: 34121820.3.0000.5514. Among the 360 medical records of hospitalized patients with suspected COVID-19, were excluded negative PCR for SARS-CoV-2, patients under 18 years old, and lack of data for calculating BMI, resulting in 125 medical records.

Age, sex, comorbidities, mortality, days of hospitalization, lungs computerized tomography (CT), dialysis, orotracheal intubation (OTI), and need of intensive care unit (ICU) were collected. Also, a biochemical screening was analyzed for the first biological sample collected immediately after hospitalization (initial) and the last sample collected before the clinical outcome (final) for the following parameters: creatinine, calcium, potassium, lactate, magnesium, sodium, urea, protein C reactive, hemoglobin, hematocrit, leukocytes, lymphocytes, platelets, international normalized ratio, partial thromboplastin time.

The statistical analyses were performed for categorical variables by a Chi-squared test or two-way mixed ANOVA followed by Sidak's post hoc, with a significant level of <0.05 using Statistical Package for Social Sciences SPSS TM version 26.0 for Windows TM (SPSS Inc./IBM Group, Chicago, IL, USA). For the continuous variables, the one-way ANOVA followed by the Tukey post hoc test was applied using GraphPad Prism V.8, with a significance of $p < 0.05$.

3. Results

For the analyses, the patients were distributed according to BMI, among which 28 (22.4%) were normal weight, 47 (37.6%) overweight, and 50 (40%) obese (Table 1). The mean age of patients with overweight and obesity was significantly lower than patients with normal weight, followed by a lower age of mortality (Fig. 1a, b). In Table 1 the number of patients with normal weight that needed ICU and dialysis was 21 (75%) and 8 (28.5%) respectively, followed by 33 (70.2%) and 11 (21.2%) of the patients with overweight and 35 (70%) and 11 (22%) of the ones with obesity. In Table 2, it is possible to verify that obesity is a risk factor for death in SARS-CoV-2 infected patients, independent of age.

The number of patients that needed OTI was 13 (50%) for normal weight, 24 (51%) for overweight and 28 (56%) for patients with obesity. There were 32 (68%) patients with overweight who presented any comorbidity, as well as 36 (72%) of the patients with

Table 1
Demographic distribution of patients according to Body Mass Index (BMI).

Total	Normal Weight N (%) 28 (22)	Overweight N (%) 47 (37)	Obese N (%) 50 (40)	p-value
Death	13 (46)	13 (27)	16 (32)	0.239
ICU	21 (75)	33 (70)	35 (70)	0.880
OTI	14 (50)	24 (51)	28 (56)	0.818
CT > 50%	9 (32)	25 (53)	25 (50)	0.280
Dialysis	8 (28)	10 (21)	11 (22)	0.941
<50 years	4 (14)	17 (36)	18 (36)	0.090
Any comorbidity	19 (67)	32 (68)	36 (72)	0.893

A Chi-squared test for categorical variables with a significant level of 5% was performed using Statistical Package for Social Sciences SPSS TM version 26.0 for Windows TM (SPSS Inc./IBM Group, Chicago, IL, USA), with no statistical significance. ICU: intensive care unit; OTI: orotracheal intubation; CT: computerized tomography.

obesity. The computerized tomography revealed a >50% lungs impairment in 9 (32%) of patients with normal weight compared to 25 (53%) with overweight and 25 (50%) of the patients with obesity. Among the patients under 50 years, 3 (14%) were from normal weight group compared to 7 and 21 patients with overweight and obesity (36%), respectively. Finally, the mortality rate for the normal weight group was 13 (46%) followed by 13 (27%) patients with overweight and 16 (32%) patients with obesity.

The biochemical analysis revealed that the initial sample of plasmatic urea concentration of normal weight patients was significantly higher compared to overweight and obese (Fig. 1c), and the initial mean hemoglobin in patients with obesity was significantly higher than overweight and obese (Fig. 1d). At the clinical outcome, the final plasmatic calcium levels of patients with obesity were significantly increased compared to overweight and normal weight patients (Fig. 1e, Tables 2–4). For the other biochemical parameters analyzed there were no significant differences between normal weight, overweight and patients with obesity (data not shown).

4. Discussion

The literature reveals that laboratory analysis of obese patients with COVID-19 embrace variations such as higher C-reactive protein count, lower lymphocyte count, lower platelet count, higher levels of hemoglobin, CK, creatinine and, LDH [7,8]. Similar to our data, some studies have already demonstrated that obesity is an important risk factor among young people, suggesting a positive correlation between higher BMI, the severity of the disease, and mortality risk [9,10].

Our main interest was to investigate the differences regarding BMI during SARS-CoV-2 infection in order to provide insights for personalized medicine to treat those patients. We showed death in patients with overweight and obesity compared to normal weight, confirming that overnutrition is a risk factor for coronavirus disease. These data corroborate a recent retrospective study confirming obesity as an independent risk factor for COVID-19 severity [10]. We hypothesized that the differences related to plasmatic urea concentrations may be due to the increased age in normal weight patients, once in our population the patients with obesity were significantly younger. However, studies are necessary to confirm it. Here we corroborate the alterations observed for hemoglobin in the literature and provide the first evidence for alterations in calcium levels in patients with obesity during hospitalization compared to patients with normal weight. However, more studies are necessary to evaluate the causality link and pathophysiology mechanisms involved in the calcium and hemoglobin alterations during

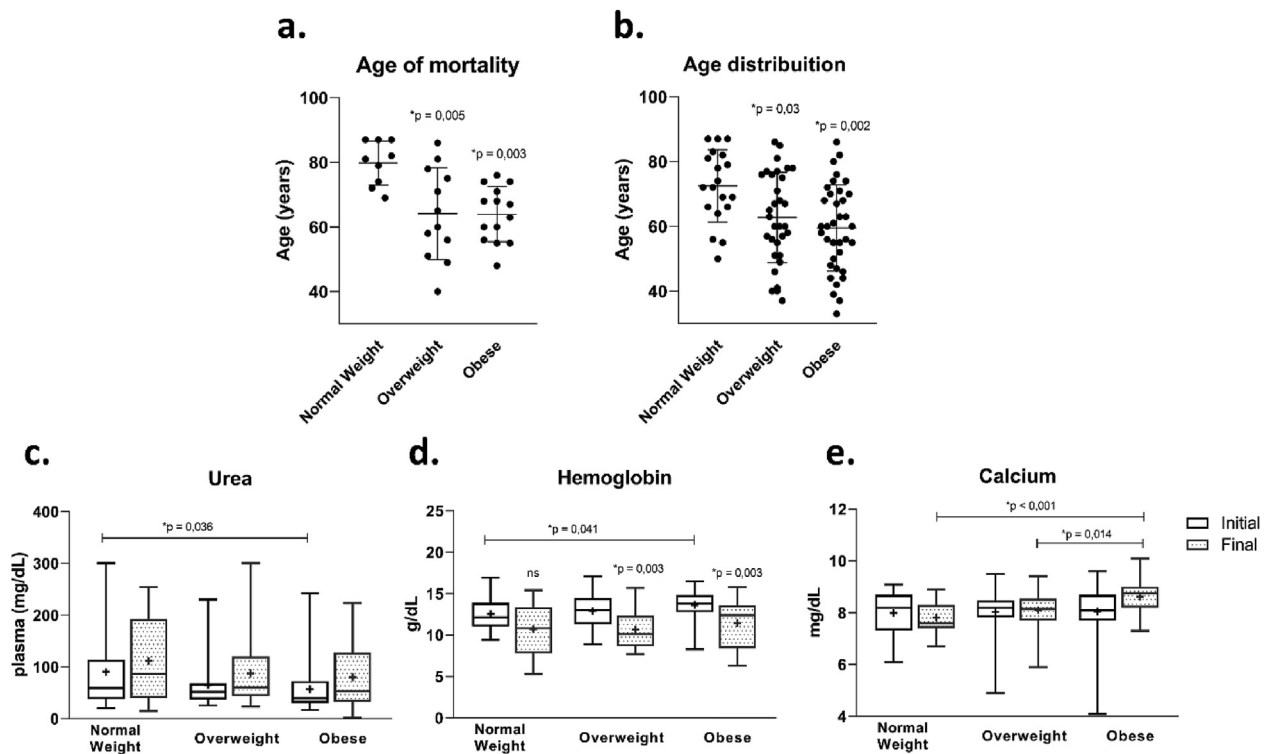


Fig. 1. Analyses of medical records of the patients with normal weight, overweight, and obesity, positive for SARS-CoV-2. In a: Age of patients per group; b: Age of mortality per group; c: Plasmatic concentrations of urea; d: Plasmatic concentrations of hemoglobin; e: Plasmatic concentrations of calcium. From e–g: “Initial” represents the results of the first sample collected on the hospitalization and “final” represents the last sample collected before the clinical outcome. For the numerical variables the **p*-value represents the difference measured by ANOVA followed by the Tukey post hoc test. ns = non-significant.

Table 2

Comparative analysis between death, Body Mass Index (BMI), and age.

Variable	BMI	Age ^b	Age ^b	<i>p</i> -value ^a
Death	Normal weight	Adult	Elderly ^c	0.006
	Overweight	Adult	Elderly	0.558
	Obese	Adult	Elderly	0.097

^a Univariate Test. This test is based on the linearly independent pairwise comparisons among the estimated marginal means it was performed using Statistical Package for Social Sciences SPSS TM version 26.0 for Windows TM (SPSS Inc./IBM Group, Chicago, IL, USA. Comparison between BMI groups and age of participants, using mortality between different groups as a measure.

^b Adjustment for multiple comparisons: Sidak.

^c *p* < 0.05 Age data were stratified for 20–59 years old (adult), and over 60 years (elderly).

Table 3

Pairwise comparison between calcium, hemoglobin, and urea with Body Mass Index (BMI).

Measure	BMI	BMI	<i>p</i> -value
Calcium	Normal Weight	Overweight	0.474
		Obese	0.026
Hemoglobin	Normal Weight	Overweight	0.869
		Obese	0.467
Urea	Normal Weight	Overweight	0.009
		Obese	0.017

Pairwise comparisons for categorical variables was performed using Statistical Package for Social Sciences SPSS TM version 26.0 for Windows TM (SPSS Inc./IBM Group, Chicago, IL, USA. Based on estimated marginal means. *Adjustment for multiple comparisons: Sidak). The *p* < 0.05 indicates that the group of individuals with obesity presented an alteration in the level of calcium when compared to the normal weight group and the difference was repeated when analyzing the urea of patients with overweight and obesity compared to the same group, indicating that BMI is related to these changes.

Table 4

Pairwise comparison between Body Mass Index (BMI) and initial and final levels of calcium, hemoglobin, and urea.

Measure	BMI	BMI	<i>p</i> -value
Calcium	Normal Weight (I)	Overweight	0.990
		Obese	0.909
	Normal Weight (F)	Overweight	0.113
		Obese	<0.01
Hemoglobin	Normal Weight (I)	Overweight	0.869
		Obese	0.467
	Normal Weight (F)	Overweight	0.932
		Obese	0.786
Urea	Normal Weight (I)	Overweight	0.268
		Obese	0.252
	Normal Weight (F)	Overweight	0.05
		Obese	0.012

Pairwise comparisons for categorical variables was performed using Statistical Package for Social Sciences SPSS TM version 26.0 for Windows TM (SPSS Inc./IBM Group, Chicago, IL, USA. Based on estimated marginal means. *Adjustment for multiple comparisons: Sidak). I - initial, F - final, relative to the admission and clinical outcome, respectively. Changes in calcium and urea levels were significant in the group with obesity when compared to the normal weight group at the time indicated as F (clinical outcome).

coronavirus infection in obesity. In conclusion, results suggest that COVID-19 contributes to metabolic changes and death in patients with obesity, independent of the age.

Statement of authorship

GUR, DSR designed the study; GUR collected data; GUR, RCS, and DSR interpreted and analyzed the results; GUR, PRBCC, DSR wrote

and critically revised the manuscript; DSR coordinate the study and funding acquisition. DSR takes responsibility for the data analysis and content of the manuscript.

Declaration of competing interest

The authors declare they have no conflict of interest.

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