Comparative analysis of the effects of COVID-19 infection on nutritional status of hospitalized cardiac patients

Análise comparativa dos efeitos da infecção de COVID-19 no estado nutricional de pacientes cardíacos hospitalizados

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ABSTRACT

Introduction: The effect of impaired nutritional status on the evolution of COVID-19 infection is not yet clear, but research already suggests that nutritional status can influence the individual risk of SARS-CoV-2 progression. In patients with COVID-19 and underlying cardiovascular disease, the respiratory symptoms of the infection are more severe and inflammatory levels may be markedly higher. The aim was to evaluate the effects of COVID-19 infection on the nutritional status of hospitalized cardiac patients. **Methods:** Cross sectional study on hospitalized cardiac patients with suspected or confirmed COVID-19 infection. The patients with confirmed COVID-19 constituted the case group, while the suspected patients with negative testing for COVID-19 constituted the comparison group. In both groups, we assessed the Body Mass Index (BMI), arm circumference (AC), calf circumference (CC), tricipital skinfold (TSF), arm muscle circumference (AMC), total lymphocyte count (TLC) and nutritional prognostic index (NPI). **Results:** A total of 32 patients were evaluated, with 18 cases. Malnutrition in patients with COVID-19 ranged from 30.8% (according to BMI) to 55.6% (according to AMC). At admission, mean BMI, AC, and TLC were lower in the case group ($p<0.05$). Comparing admission and discharge data, only the case group showed a significant reduction in AC and TSF ($p<0.05$). Nutritional variables did not correlate with length of stay in the two groups evaluated. **Conclusion:** Malnutrition was high in patients with COVID-19, with marked muscle reserve impairment. Infected patients had lower mean BMI, AC, and TLC at hospital admission and had reduced anthropometric measurements (AC and TSF) at the end of hospitalization.

RESUMO

Introdução: O efeito do estado nutricional comprometido na evolução da infecção de COVID-19 ainda não é claro, mas há indícios de que o estado nutricional pode influenciar o risco individual da progressão do SARS-CoV-2. Em pacientes com COVID-19 afetados por uma doença cardiovascular, os sintomas respiratórios da doença são mais graves e os níveis de inflamação podem ser marcadamente maiores. O objetivo foi avaliar os efeitos da infecção de COVID-19 no estado nutricional de pacientes cardíacos hospitalizados. **Método:** Estudo transversal em pacientes cardíacos hospitalizados com suspeita ou confirmação de infecção por COVID-19. Os pacientes confirmados com COVID-19 constituíram o grupo de caso, enquanto os pacientes suspeitos com teste negativo para COVID-19 constituíram o grupo de comparação. Nesses dois grupos, nós investigamos o Índice de Massa Corporal (IMC), circunferência do braço (CB), circunferência da panturrilha (CP), dobra cutânea tricipital (DCT), circunferência muscular do braço (CMB), contagem total de linfócitos (CTL) e índice de prognóstico nutricional (IPN). **Resultados:** Um total de 32 pacientes foram avaliados, com 18 casos. Desnutrição em pacientes com COVID-19 variou de 30,8% (de acordo com o IMC) a 55,6% (de acordo com a CMB). À admissão, IMC, CB e CTL médios foram mais baixos no grupo de caso ($p<0,05$). Comparando dados de admissão e alta, somente o grupo de caso demonstrou redução significante na CB e DCT. Variáveis nutricionais não foram correlacionadas com o tempo de estadia no hospital nos dois grupos avaliados. **Conclusão:** Desnutrição foi alta em pacientes com COVID-19, com marcado comprometimento da reserva muscular. Pacientes infectados tinham menor IMC, CB e CTL médios à admissão e menores medições antropométricas (CB e DCT) no fim da hospitalização.

Unitermos:
COVID-19. Estado nutricional. Avaliação nutricional. Cardiopatias.

Keywords:
COVID-19. Nutritional status. Nutritional assessment. Heart diseases.

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INTRODUCTION

COVID-19 infection is characterized by very diverse clinical manifestations[1]. In addition to the remarkable respiratory involvement, the virus causes a disproportionate immune response in many individuals, with a major inflammatory reaction[2]. It can also attack the mucous epithelium, causing adverse gastrointestinal symptoms, which negatively influence food intake and can compromise the nutritional status of affected patients[3,4]. It is noteworthy that some drugs used in the treatment can exacerbate these symptoms[2].

The effect of impaired nutritional status on the evolution of COVID-19 infection has not yet been fully understood[5,6]. Nonetheless, some authors have already pointed out that nutritional status can influence the individual risk of SARS-CoV-2 progression, and that adequate food intake may be essential to protect against an excessive inflammatory response to infection[7], to improve resistance to infections, and to mitigate the disease burden[2,8].

To date, few investigations have described the nutritional status of patients infected with COVID-19. A study carried out in Wuhan, China, addressed 182 infected elderly patients. The authors reported a 27.5% prevalence of nutritional risk and a 52.7% prevalence of malnutrition[9]. Some authors suggest that early identification and correction of malnutrition have the potential to improve patient outcome[6,10].

In patients with COVID-19 and underlying cardiovascular disease, the respiratory symptoms of the infection are more severe, and these manifestations are independent of nutritional status[11,12]. Data from the United States Centers for Disease Control and Prevention (CDC) demonstrate the high risk of mortality in individuals with pre-existing hypertension[13] due to the increased risk of thrombotic complications[11]. These patients may also have a cytokine storm syndrome with markedly higher levels[14].

There are still no studies on the nutritional status of cardiac patients infected with the new coronavirus. In this context, this study evaluates the effects of COVID-19 infection on the nutritional status of hospitalized cardiac patients in comparison to a control group.

METHODS

Study Design and Sampling

This is a cross sectional study carried out in a reference hospital in cardiology in Recife, Pernambuco, Brazil. The sample consisted of all patients with suspected or confirmed COVID-19 infection hospitalized from June to August 2020, admitted to the ward, and aged ≥18 years.

The sample was obtained by convenience. Patients with confirmed COVID-19 constituted the case group, and those with negative testing for COVID-19 constituted the comparison group. COVID-19 infection was considered positive when confirmed by a RT-PCR test using a naso-oropharyngeal swab.

Nutritional Assessment

We assessed the nutritional status of patients at admission and discharge considering the following parameters: body mass index (BMI), arm circumference (AC), tricipital skinfold (TSF), and arm muscle circumference (AMC).

Weight measurements followed standardized techniques[15]. For that, we used an electronic scale (Welmy®, Santa Bárbara d'Oeste, São Paulo, Brazil) with capacity of 150 kg and accuracy of 100 g. The patients were weighed barefoot, with light clothes, standing upright, with their feet together and their arms extended along the body. We estimated height from the predictive equation[16], with the individual with the left leg flexed at 90°. With an inextensible tape graduated in millimeters, we measured the distance between the left foot heel and the upper edge of the knee patella.

We determined BMI by the weight/height squared ratio (in meters). Classification followed the standards of the World Health Organization (WHO) for adults[17], and of Lipshitz (1994) for the elderly[18].

AC and TSF measurements followed standard techniques[19]. We measured AC with an inextensible millimeter tape, on the nondominant arm relaxed in flexion until it formed a 90° angle with the forearm, where we marked the midpoint between the scapula acromion and the ulna olecranon. Then, the patient extended the arm along the body, and in this same anatomical site of AC measurement, we measured TSF. This measurement took place in the posterior region of the arm using a scientific adipometer (Lange Skinfold Caliper) with a constant pressure of 10 g/mm^3 on the contact surface. We made three consecutive measurements and considered the average of the readings.

Using the established equation and the measurements of AC and TSF, we obtained the AMC[19]. These three measurements - AC, TSF, and AMC - were classified according to the reference standard[20].

We measured calf circumference (CC) with the patient standing upright, with feet 20 cm apart and distributing the weight equally on both feet. For that measurement, we positioned a millimeter tape around the calf (maximum circumference in the plane perpendicular to the longitudinal line of the calf)[21].

We also evaluated the following biochemical parameters: albumin, C-reactive protein (CRP), and leukocytes and lymphocyte percentage to calculate the total lymphocyte count (TLC). These data were obtained from the first examination of the patient in the hospital.

We calculated the nutritional prognostic index (NPI) using the formula: 10 x serum albumin value (g/dl) + 0.005 x total lymphocyte count (TLC) in peripheral blood (per mm^3)[22].

Ethical Aspects

This study followed the ethical precepts established in resolution No. 466/12 of the National Health Council, being approved by the Human Research Ethics Committee of the Hospital Complex HUOC/PROCAPE (Hospital Universitário Oswaldo Cruz and Pronto Socorro Cardiológico de Pernambuco) under protocol number 4.075.096/2020. All patients were informed of the objectives and procedures of the study and signed a Free and Informed Consent Form - FICF.

Statistical Analysis

We analyzed the data using the SPSS program, version 13.0 (SPSS Inc., Chicago, IL, USA). We described quantitative variables as mean and standard deviation since they showed normal distribution using the Kolmogorov-Smirnov test.

We compared the means of age and anthropometric variables between cases and comparison group by the Student t-test for independent samples. To compare continuous variables at admission and discharge, we used the paired t test. We compared the proportions using the Pearson chi-square test or the Fisher exact test. Statistical significance was considered when $p<0.05$.

RESULTS

Thirty-two patients with a mean age of 60.7 ± 13.5 years were evaluated, 18 of which were confirmed cases of COVID-19. The mean age was similar between cases (61.8 ± 13.3) and comparison group (59.8 ± 14.0) ($p=0.887$).

The groups were homogeneous in terms of demographic, clinical, and anthropometric characteristics ($p>0.05$). Malnutrition ranged from 30.8% (according to BMI) to 55.6% (according to AMC). The TSF measurement showed excess weight in 38.9% of patients. Both malnutrition and excess weight were similar in the case and comparison groups (Table 1).

Table 1 – Comparison among demographic, clinical, and anthropometric characteristics with confirmed (case group) and negative testing (comparison group) for COVID-19, of hospitalized cardiac patients.

Variable	N=32	COVID Negative (n=14)		COVID Positive (n=18)		p-value*
	n (%)	n	%	n	%	
Gender						0.292
Male	20 (62.5)	10	71.4	10	55.6	
Female	12 (37.5)	4	28.6	8	44.4	
Age Range						0.292
Adult	12 (37.5)	4	28.6	8	44.4	
Elderly	20 (62.5)	10	71.4	10	55.6	
Coronary disease	12 (37.5)	4	28.6	8	44.4	0.292
Heart Failure	15 (46.9)	7	50.0	8	44.4	0.755
Systemic Arterial Hyperfension	12 (37.5)	3	21.4	9	50.0	0.098
Diabetes mellitus	8 (25.0)	3	21.4	5	27.7	0.504
Outcome						0.349
Discharged	32 (100.0)	14	100.0	18	100.0	
Died	–	–	–	–	–	
BMI						0.349
Underweight	7 (28.0)	3	25.0	4	30.8	
Normal	9 (36.0)	3	25.0	6	46.1	
Overweight	9 (36.0)	6	50.0	3	23.1	
AC						0.501
Underweight	17 (31.3)	8	57.2	9	50.0	
Normal	10 (53.1)	3	21.4	7	38.9	
Overweight	5 (15.6)	3	21.4	2	11.1	
TSF						0.260
Underweight	12 (37.5)	4	28.6	8	44.4	
Normal	9 (28.1)	6	42.8	3	16.7	
Overweight	11 (34.4)	4	28.6	7	38.9	
AMC						0.051
Underweight	13 (40.6)	3	21.4	10	55.6	
Normal	19 (59.4)	11	78.6	8	44.4	

*Chi-square test of Pearson. BMI: Body Mass Index; AC: Arm Circumference; TSF: Tricipital Skinfold; AMC: Arm Muscle Circumference.

Nevertheless, at hospital admission, mean body mass index (BMI) and arm circumference (AC) were lower in the group of patients with COVID-19 ($p<0.05$). Tricipital skinfold (TSF) was also lower in the case group ($p<0.01$). The average length of hospital stay for all patients was 14.3 ± 7.2 days, being similar between groups ($p>0.05$) (Table 2).

The comparison between admission and discharge showed that patients infected with COVID-19 had a significant reduction in AC (about 3.5%; $p=0.048$) and in TSF (about 15%; $p=0.002$), while the patients in the comparison group showed no reduction in anthropometric parameters between admission and discharge ($p>0.05$).

The nutritional variables did not correlate with length of stay in the two groups evaluated (Table 4).

Table 2 – The association among age, nutritional variables, length of stay and patients with positive and negative testing for COVID-19.

Variable	n	Total Mean (SD)	COVID Negative (n=14)		COVID Positive (n=18)		p-value*
			Mean	SD	Mean	SD	
Age (years)	32	60.7 (13.5)	61.8	13.3	59.8	14.0	0.887
AC (cm)	32	31.6 (7.1)	31.9	12.8	31.5	4.2	0.016
TSF (mm)	32	16.4 (6.6)	16.9	7.8	15.9	5.7	0.104
AMC	32	24.8 (4.0)	26.2	4.3	23.7	3.4	0.076
BMI (kg/m²)	25	26.4 (6.8)	28.5	8.2	24.4	4.7	0.020
CC (cm)	31	33.6 (5.4)	34.4	6.7	33.0	4.5	0.097
NPI	26	42.9 (7.3)	45.1	9.2	41.3	5.3	0.138
TLC	32	1413.5 (861.8)	1763.3	1165.2	1141.4	370.1	<0.001
Albumin (mg/dL)	26	3.6 (0.6)	3.6	0.7	3.6	0.5	0.143
CRP (mg/dL)	29	54.0 (59.7)	50.7	52.8	57.1	67.3	0.782
LS (days)	32	14.3 (7.2)	11.5	5.8	16.6	7.6	0.520

*Student T test for independent samples. SD: Standard Deviation; AC: Arm Circumference; TSF: Tricipital Skinfold; AMC: Arm Muscle Circumference; BMI: Body Mass Index; CC: Calf Circumference; NPI: Nutritional Prognostic Index; TLC: Total Lymphocyte Count; CRP: C-Reactive Protein; LS: Length of Stay.

Table 3 – Comparison of nutritional parameters of patients with positive and negative testing for COVID-19 at admission and discharge of hospitalized cardiac patients in a reference hospital in cardiology.

Variable	n	COVID Negative (n=14)		p-value*	n	COVID Positive (n=18)		p-value*
		Admission M(SD)	Discharge M(SD)			Admission M(SD)	Discharge M(SD)	
Weight (kg)	11	83.4 (24.7)	81.8 (24.2)	0.150	13	67.4 (11.7)	67.0 (12.3)	0.339
BMI (kg/m²)	11	25.5 (7.7)	29.5 (8.6)	0.944	13	24.5 (4.7)	24.3 (4.9)	0.390
AC (cm)	14	31.8 (6.2)	31.2 (5.4)	0.166	18	29.0 (4.6)	28.0 (3.9)	0.048
TSF (mm)	14	16.9 (7.8)	15.7 (7.9)	0.150	18	15.9 (5.7)	13.6 (6.1)	0.002
AMC	14	26.2 (4.3)	26.3 (3.6)	0.812	18	23.7 (3.4)	23.7 (2.4)	0.909
CC (cm)	12	34.4 (7.0)	33.9 (5.2)	0.498	18	33.0 (4.5)	32.5 (4.5)	0.234

* Paired T test. M: Mean; SD: Standard Deviation; AC: Arm Circumference; TSF: Tricipital Skinfold; AMC: Arm Muscle Circumference; BMI: Body Mass Index; CC: Calf Circumference.

Table 4 – Correlation of nutritional variables at admission and lengths of stay in patients admitted to a reference hospital in Cardiology in northeastern Brazil, with positive and negative testing for COVID-19.

Variable	COVID Negative (n=14)		COVID Positive (n=18)	
	r	p-value	r	p-value
Weight (kg)	0.270	0.397	0.114	0.711
BMI (kg/m²)	0.492	0.104	-0.278	0.357
AC (cm)	0.251	0.387	-0.047	0.854
TSF (mm)	0.285	0.324	-0.301	0.224
AMC	0.226	0.438	0.194	0.440
CC (cm)	0.365	0.221	0.272	0.276
TLC	0.219	0.451	0.146	0.563
NPI	0.017	0.961	0.153	0.585
Albumin	-0.232	0.493	0.095	0.737

*Paired T test. M: Mean; SD: Standard Deviation; BMI: Body Mass Index; AC: Arm Circumference; TSF: Tricipital Skinfold; AMC: Arm Muscle Circumference; CC: Calf Circumference; TLC: Total Lymphocyte Count; NPI: Nutritional Prognostic Index.

DISCUSSION

Considering that the COVID-19 infection is quite recent, few studies have been undertaken on the nutritional status of these patients. Initial evidence links the new coronavirus infection with nutritional status. Malnutrition seems to be a risk factor for COVID-19 infection and once the infection is established, both malnutrition and obesity are important predictors of unfavorable evolution[23].

Our findings revealed a high percentage of malnutrition in infected patients, reaching 55.6% of them when considering the parameter AMC, which correlates with muscle reserve. By using the Mini Nutritional Assessment method, the authors of the study in Wuhan, China, described a similar prevalence (52.7%) in hospitalized elderly (≥65 years)[9]. This muscle reserve impairment can be attributed to the acute inflammatory response of the new coronavirus infection, which leads to muscle proteolysis and consumption of albumin for synthesis of acute phase proteins[9,24]. A high rate of comorbidities can also contribute to the significant percentage observed.

The lower mean BMI and AC at hospital admission of COVID-positive patients in comparison to the other group has two interpretations. First, there is a greater risk of contamination in patients with more compromised nutritional status. Malnutrition impairs immune function, especially cell-mediated immunity, making malnourished individuals a group at higher risk for viral infections[25]. The preservation of nutritional status can help prevent infection, and its treatment is very important since it has the potential to reduce complications and negative results in patients who may have COVID-19 in the future[10].

Another plausible explanation would be the possibility that these patients were already experiencing symptoms and complications of the evolution of the disease, such as reduced food intake (caused by anosmia, ageusia, and anorexia) and increased catabolism and inflammation[26]. Previous research reports a significant reduction of food intake in infected patients in the days prior to hospitalization[27]. In Lausanne, Switzerland, Berger[28] studied a cohort of COVID-19 patients comprising 117 critically ill patients. In that study, the median of the Nutritional Risk Score (NRS) was 5 points, and the average score for the variable food intake was 2 (out of a maximum of 3), contributing strongly to NRS. According to that same author, data from another cohort in Wuhan demonstrated that about 60% of patients were unable to eat normally in the days prior to hospital admission[29]. This acute malnutrition compromised immune defenses and contributed to the rapid loss of lean mass, which correlates with immunity and adverse outcomes[28].

Therefore, when associating our results with this previous evidence that demonstrates acute malnutrition in COVID-19 patients, it can be thought that this infection has a short-term impact on nutritional status, and this impact is stronger in comparison to other conditions.

Patients infected with the new coronavirus also showed lower TLC, corroborating previous research that pointed to low lymphocyte levels in COVID-19 patients[30]. Regarding this infection, some authors have associated lower TLC with higher mortality, reinforcing the prognostic predictive role of this parameter[31].

Data on nutritional evolution during hospitalization show that COVID-positive patients had a reduction in AC and TSF, and maintained AMC, differently from their counterparts. This evidence points to a compromise in the global nutritional status (AC) and in the adipose reserve (TSF), without altering the muscle reserve (AMC). In addition to the remarkable respiratory involvement, the virus causes a disproportionate immune response in many individuals, with a major inflammatory reaction and brief repercussions on nutritional status[2].

The acute malnutrition common in COVID-19 infection mobilizes adipose tissue through lipolysis induced by increased adiponectin secretion and reduced leptin[27,28,32]. The inflammatory state induces the release of cortisol and adrenergic hormones, which can also increase fat oxidation and decrease adipose tissue[33].

The preservation of AMC is a finding that does not corroborate the expected results for hospitalized patients infected with COVID-19 since hypermetabolism and excessive nitrogen loss are factors known to be associated with infectious states[34]. Furthermore, the angiotensin-converting enzyme 2 is the receptor for coronavirus-2 and occurs in skeletal muscle; thus, COVID-19 infected subjects have myalgia and muscle loss, which can be enhanced by rest[35].

Despite the reduction in measures, patients in both groups had no significant weight loss. Previous research has shown an unavoidable trend of weight loss in individuals affected by COVID-19 due to inflammatory storm and acute decrease in appetite, in addition to the presence of underlying diseases, which can also contribute to nutritional impairment[36].

The lack of correlation between nutritional variables and length of stay in both groups does not agree with previous findings since nutritional impairment delays healing time and increases length of stay[10,37]. Thus, despite the lower averages of anthropometric parameters and lower TLC in the presence of COVID-19 infection, the length of stay and the outcome were similar between the case and comparison groups, showing that these aspects were not predictors of unfavorable outcomes or increased length of stay.

Some limitations must be considered when interpreting our results. The small sample size and the single-center design limit the generalization of the results, as well as the absence of analysis of variables such as length of illness prior to hospitalization and the symptoms present. In addition, the risk of false negative tests cannot be ignored.

Despite this, it is noteworthy that few studies assess nutritional aspects during the hospitalization of COVID-19 patients. We proposed assessment of nutritional status of cardiac patients affected by this infection and considered different assessment methods, addressing body compartments (muscle and fat reserve). These factors have rarely been investigated previously. Furthermore, few studies have carried out a direct anthropometric evaluation due to the adaptations necessary in the clinical-nutritional management to minimize the risk of contamination and spread of the virus. The presence of a comparative group, consisting of patients with a similar clinical picture and with characteristics homogeneous to the cases - but lacking COVID-19 infection - reinforces the causal inferences about the impact of this disease on the nutritional status of affected patients.

CONCLUSION

Malnutrition was high in patients with COVID-19, with marked muscle reserve impairment. Patients infected with the new coronavirus had lower mean BMI, AC, and TLC at hospital admission. At the end of hospitalization, only patients with COVID-19 had a reduction in anthropometric measurements (AC and TSF). Despite this, nutritional variables were not predictive of a longer hospital stay.

Despite the difficult emergency context, it is important that the nutritional status of all infected patients be assessed on admission and during hospitalization to provide early prevention and intervention measures. This will mitigate the effects of the disease on the nutritional condition, minimizing the impact of acute malnutrition in an unfavorable evolution. Contamination prevention and safety measures must be strictly adopted during the evaluations.

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