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NUTRITIONAL STATUS AND BIOMARKERS OF SARS-CoV-2 INFECTED CARDIOPATH PATIENTS

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ABSTRACT

Objective: To assess the nutritional status of heart disease patients infected with SARS-CoV-2, comparing the results with data from a comparison group. **Methods:** Cross-sectional study conducted with heart disease patients infected with SARS-CoV-2 The parameters were considered: arm circumference (AC), triceps skinfold thickness (TSF), arm muscle circumference (AMC), calf circumference (CC); and the biomarkers: total lymphocyte count (TLC), serum albumin, and prognostic nutritional index (PNI). **Results:** The study included 112 patients, of which 43.8% tested positive for the infection. The prevalence of malnutrition in patients with COVID-19 was 48.8% according to AC, and 43.9% according to AMC. For the same mean age, patients with COVID-19 who progressed to death (30.6%) had lower mean AMC ($p=0.012$), PNI ($p<0.001$), TLC ($p=0.010$), and albumin ($p=0.006$). **Conclusions:** Heart disease patients with COVID had a high frequency of malnutrition and low levels of TLC and serum albumin. Lower mean AM, TLC, albumin, and lower PNI scores were markers of poor prognosis, regardless of age, in COVID patients.

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INTRODUCTION

In late 2019, a new coronavirus called SARS-CoV-2 appeared in Wuhan, China, and was responsible for the emergence of a new acute respiratory infection, now known as "COVID-19" (Sohrabi *et al*., 2020). The high infectivity of COVID-19 has led to a rapid and exponential increase in new cases worldwide (Zou *et al*., 2020 and Zhu *et al*., 2019). In this scenario, the World Health Organization (WHO) declared the disease a pandemic on March 11, 2020, (Haraj, 2021). COVID-19 manifests as systemic disorders with a broad clinical spectrum, ranging from asymptomatic to severe pneumonia, resulting in acute respiratory distress syndrome (ARDS) (Fedele, 2021). The virus mainly affects the lungs; however, it can affect other organs such as the heart, brain, kidneys, and liver (Cummings *et al*., 2019). The main symptoms of COVID-19 are fever, headache, vomiting, diarrhea, loss of appetite, dry cough, anosmia, and ageusia. It is more severe in individuals with comorbidities such as systemic arterial hypertension (SAH), diabetes mellitus (DM), cardiovascular disease (CVD), cancer, chronic lung disease, and obesity (Haraj *et al*., 2019 and Morley *et al*., 2021). Patients with previous or underlying cardiovascular diseases are at higher risk of developing severe symptoms if infected with SARS-CoV-2, and have a higher mortality rate (Hulot, 2020). Cardiovascular disease can potentially exacerbate the severity of COVID-19 by an intense storm of inflammatory cytokines, which can play a role in coronary plaque instability. Moreover, subjects with CVD have an increased risk of thrombotic complications (Hulot, 2020; Siddiqi and Mehra, 2020). Although studies have poorly addressed nutritional status in patients with COVID-19, preliminary evidence shows that nutritional disorders lead to a worse course and outcome of the disease. Due to both its inflammatory state and metabolic factors, obesity is an important predictor of complications from the new coronavirus, making obese individuals more susceptible to worse prognosis and clinical outcomes of COVID-19. Acute respiratory distress syndrome (ARDS), the main clinical manifestation related to mortality in infected patients, is more prevalent in obese patients. This highlights the direct relationship between nutritional status and COVID-19 (Popkin *et al*., 2020). Malnutrition, in turn, is mainly present in elderly people infected with COVID-19. It is considered a poor prognostic factor in this population, as it has a direct correlation with longer hospital stays, clinical complications, and mortality (Henriques, 2020). Thus, an adequate nutritional status plays a key role in the individual's immune response and may influence immunomodulatory aspects and the risk and management of diseases (Venter, 2020). As this is a new disease, with studies still in progress, data on the nutritional status of patients infected with the new coronavirus are scarce in the literature, especially in specific subgroups such as patients with pre-existing heart disease. In this context, the present study assessed the nutritional status of heart disease patients infected with SARS-CoV-2 and compared the results with data from a comparison group.

METHODS

This is a cross-sectional study coupled with a hospital-based prospective analysis (length of stay and outcome), conducted in a unit of reference in cardiology in XXXXXXXXXXX, from May to August 2020. The study included heart disease patients of both genders, aged 18 years or more, infected with SARS-CoV-2, and admitted to a clinical ward or Intensive Care Unit. The study had a comparison group comprising hospitalized cardiac patients with a similar clinical picture and under suspicion for COVID-19 infection, but who tested negative for the disease. The sample was a convenience sample, and all patients under suspicion of infection were assessed at hospital admission. The assessment considered the RT-PCR molecular test, applied through a naso-oropharyngeal swab. Those who tested positive for COVID-19 were considered the cases, and those with a negative test result constituted the comparison group. The authors analyzed the following anthropometric parameters: arm circumference (AC), triceps skinfold thickness (TSF), arm muscle circumference (AMC), and calf circumference (CC). Arm circumference (AC) and triceps skinfold thickness (TSF) measurements followed standard techniques (Chumlea, 1985). Arm circumference was measured with an inextensible millimeter tape on the nondominant arm, which should be relaxed, flexed, and forming a 90º angle with the forearm. The measurement considered the midpoint between the acromion process of the scapula and the olecranon process of the ulna. Then, with the arm relaxed and extended along the body, in the same anatomical site of AC measurement, triceps skinfold thickness (TSF) was measured with a scientific adipometer Lange Skinfold Caliper. The authors performed three consecutive measurements and considered the mean value of the readings. From AC and TSF measurements, the authors calculated arm muscle circumference (AMC) using an established equation. Arm circumference (AC), triceps skinfold thickness (TSF), and arm muscle circumference (AMC) measures were compared with the reference standard (50^{th} percentile for age) for their classification. For calf circumference (CC) measurement, the patient laid in supine position, with knees flexed at 90° and heels resting on the bed; the evaluator then positioned a millimeter tape around the calf (maximum circumference in the plane perpendicular to the longitudinal line of the calf) (Frisancho, 1981).

The authors also analyzed the following biochemical parameters: albumin, C-reactive protein (CRP), and leukocytes and lymphocyte percentage to calculate total lymphocyte count (TLC), whose data were obtained through the first examination of the patient in the hospital. Moreover, the authors calculated the prognostic nutritional index (PNI) using the formula: *10 x serum albumin (g/dl) + 0.005 x total lymphocyte count (TLC) in peripheral blood (per* mm^3*)* (Çınar *et al*., 2021). This study followed the ethical guidelines of the Brazilian National Health Council (Resolution No. 466/12), and was approved by the Committee of Ethics and Research in Human Beings of XXXXXXXXXXX under Protocol No. 32282020.3.0000.5192. All patients gave their express consent. Data were analyzed using the Statistical Package for Social Sciences – SPSS version 13.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were tested for normal distribution using the Kolmogorov Smirnov test. These variables were expressed as mean and standard deviation when presenting a Gaussian distribution, and as medians and interquartile ranges when not presenting a normal distribution. The Student t test for independent samples or the Mann Whitney U test were used to compare anthropometric and biochemical measurements between groups (case and comparison). Proportions between groups were compared using the Chi-square test. Statistical significance was established when $p < 0.05$.

RESULTS

During the study period, 120 patients were admitted under suspicion of SARS-CoV-2 infection, of which 112 met the eligibility criteria and were included in the analysis. Of these, 49 (43.8%) had confirmed infection (cases) and 63 (56.2%) had a negative result, constituting the comparison group. Mean age was similar between groups, being 64.0 ± 13.5 in the COVID-19 group and 68.0 ± 11.9 in the comparison group (p = 0.424). Case and comparison groups were homogeneous in terms of sociodemographic and clinical characteristics. Noteworthy, 30.6% of patients with COVID-19 died, and 44.9% were admitted to the ICU (Table 1). The prevalence of malnutrition in patients with COVID-19 was 48.8% according to AC, and 43.9% according to AMC. Excess weight affected 48.8% of the patients infected with SARS-CoV-2 according to TSF, a value higher than that of the comparison group (20.8%; p = 0.015). Hypoalbuminemia was similar between the groups of COVID-19 cases and comparison, but patients with COVID had a high percentage of low levels of TLC (95.9%), which was higher than that of the comparison group (74.2%; p = 0.002) (Table 2). When comparing the means (or medians) of nutritional and biochemical parameters and length of stay between groups, for the same mean age, patients with COVID-19 tended to have a longer hospital stay than patients of the comparison group, with p value at the threshold of statistical significance (15.0 vs 9.0 years; p = 0.053) (Table 3). Regarding the death of patients with COVID-19 (30.6%), patients who progressed to death had lower mean AMC (p = 0.012), PNI (p < 0.001), TLC (p = 0.010), and albumin (p = 0.006) than infected patients who did not have this adverse outcome (Table 4).

Table 1. Sociodemographic and clinical variables of hospitalized cardiac patients infected with the SARS-COV-2 virus and the comparison group. Recife-PE, Brazil (n=112)

Variable	Total	Comparison group (n=63)		COVID positive (n=49)		p-value*
	N (%)	n	%	n	%	
Gender						0.828
Mascle	65 (58.0)	36	57.1	29	59.2	
Female	47 (42.0)	27	42.9	20	40.8	
Coronary disease Coronariopatia	41 (36.6)	24	38.1	17	34.7	0.711
Cardiac insufficion	40 (35.7)	25	39.7	15	40.0	0.320
Hypertension	38 (33.9)	18	28.6	20	40.8	0.175
Diabetes mellitus	41 (36.6)	24	38.1	17	34.7	0.711
Internment sector						0.198
Clinical ward	54 (48.2)	27	42.9	27	55.1	
ICU	58 (51.8)	36	57.1	22	44.9	
Outcome						0.420
Discharged	82 (73.2)	48	76.2	34	69.4	
Died	30 (26.8)	15	23.8	15	30.6	

Comparison group: patients admitted with suspected SARS-COV-2 infection who tested negative by the RT-PCR test. *Qui Quadrado; ICU: Intensive Care Unit.

Table 2. Comparative analysis of nutritional and biochemical parameters of hospitalized cardiac patients infected with SARS-COV-2 virus and the comparison group. Recife PE, Brazil (n=112)

Variable	Total	Comparison Group (n=63)		COVID positive (n=49)		p-value*
	n (%)	n	%	n	%	
AC						0.505
Underweight	49 (51.0)	29	52.7	20	48.8	
Normal	37 (38.5)	22	40.0	15	36.6	
Overweight	10 (10.4)	4	7.3	6	14.6	
TSF						0.015
Underweight	23 (24.5)	16	30.2	7	17.1	
Normal	40 (42.6)	26	49.5	14	34.1	
Overweight	31 (33.0)	11	20.8	20	48.8	
AMC						0.239
Underweight	35 (37.2)	17	32.1	18	43.9	
Normal	59 (62.8)	36	67.9	23	56.1	
PNI						0.282
Bad	25 (26.9)	16	31.4	3	8.3	
Good	68 (73.1)	35	68.6	33	91.7	
CTL						0.002
>2000 cel/m^3	18 16.2)	16	25.8	2	4.1	
≤2000 cel/m^3	93 (83.8)	46	74.2	47	95.9	
Albumin						0.853
<3,5mg/dL	58 (62.4)	32	61.5	26	63.4	
≥3,5mg/dL	35 (37.6)	20	38.5	15	36.6	

Comparison group: patients admitted with suspected SARS-COV-2 infection who tested negative by the RT-PCR test. *Qui Quadrado. AC: Arm Circumference; TSF: Tricipital Skinfold; AMC: Arm Muscle Circumference; PNI: Prognostic Nutritional Index; TLC:Total Lymphocyte Count.

Table 3. Mean (or median) of nutritional and biochemical parameters of hospitalized cardiac patients infected with SARS-COV-2 virus and the comparison group. Recife-PE, Brazil (n=112)

Variable	Comparison Group (n=63)		COVID positive (n=49)		p-value*
	M ou Med	SD ou QI	M ou Med	SD ou QI	
Age (year)	68.0	11.9	64.0	13.5	0.424
AC (cm)	28.9	4.5	29.2	4.4	0.829
TSF (mm)	13.9	5.7	16.7	6.2	0.644
AMC	24.4	3.5	24.3	3.3	0.512
PNI	39.5	8.5	38.2	6.5	0.095
TLC	1096.5	704.7-2076.5	993.3	768.9-1370.2	0.254
Albumin (mg/dl)	3.3	0.7	3.3	0.6	0.433
HT (days)	9.0	6.0-15.0	15.0	7.5-20.0	0.053
Time of ICU (days)	7.0	5.2-13.0	15.0	6.2-21.0	0.116

*Student's T for comparing means and Mann Whitney U for comparing medians. M: Average; Med: Median; SD: Standard Deviation; QI: Interquartile Interval; AC: Arm Circumference; TSF: Tricipital Skinfold; AMC: Arm Muscle Circumference; PNI: Prognostic Nutritional Index; TLC: Total Lymphocyte Count; HT: Hospitalization Time; ICU: Intensive Care Unit.

Tabela 4. Comparative analysis of age, nutritional and biochemical variables as a function of the clinical outcome of COVID positive patients at a University Hospital Reference in Cardiology in Recife-PE, Brazil (n=49)

Variable	Outcome				p-value*
	Discharged (n=34)		Died (n=15)		
	M ou Med	SD ou QI	M ou Med	SD ou QI	
Age (year)	61.8	14.0	68.9	11.0	0.089
AC (cm)	29.5	4.8	28.1	2.2	0.393
TSF (mm)	16.6	6.7	17.1	3.9	0.826
AMC	24.7	3.4	22.3	1.8	0.012
CC (cm)	33.8	4.6	30.4	4.8	0.066
PNI	40.8	5.6	33.4	5.3	<0.001
TLC	1125.8	819.9-1466.6	792.4	552.5-1097.0	0.010
Albumin (mg/dL)	3.5	0.5	2.9	0.6	0.006

* Student's T for comparing means and Mann Whitney U for comparing medians. M: Average; Med: Median; SD: Standard Deviation; QI: Interquartile Interval; AC: Arm Circumference; TSF: Tricipital Skinfold; AMC: Arm Muscle Circumference; CC: Calf Circumference; PNI: Prognostic Nutritional Index; TLC: Total Lymphocyte Count.

DISCUSSION

The high prevalence of malnutrition in heart disease patients with COVID-19 (more than 40%, according to AC), with greater impairment of muscle reserve (almost 50%) than adipose reserve (17.1%), was higher than that reported in the literature. Kim *et al* (2020) reported only 2.2% of malnutrition according to the Body Mass Index (BMI) in adult patients admitted to a hospital in New York. Another investigation involving 41 patients with COVID-19 and mean age of 55 years, evaluated by the Mini Nutritional Assessment (MAN) method, evidenced 14.6% of malnutrition after discharge from the Intensive Care Unit (Haraj *et al*., 2021). These differences may be due to the different parameters used and the clinical characteristics of the patients. Our study involved a group of patients with pre-existing cardiovascular disease and a high rate of associated comorbidities, which may contribute to greater susceptibility to malnutrition. Research has shown that the more types of chronic diseases combined, the worse the nutritional status of patients with coronaviruses (Cao *et al*., 2020). Furthermore, as nutritional status was assessed at hospital admission, malnutrition can be pre-existing or acute. In case it is pre-existing, it may reflect the greater vulnerability of the malnourished patient to adversely progress in the course of the disease, with greater need for hospitalization. However, one cannot fail to consider the possibility that malnutrition was suddenly installed due to the presence of active infection. Research has shown that patients with COVID-19 are under a condition that includes acute malnutrition, with a significant reduction in food intake during the days prior to hospitalization (Zhao *et al*., 2020). In addition, the inflammatory storm they endure during the course of the disease poses an inevitable tendency to lose weight (Liu, 2020). Therefore, systematically evaluating the nutritional status of patients with COVID-19, including a history of weight loss, is important to understand the acute repercussions of the disease and define prevention strategies. The greater impairment of muscle reserve (as assessed by AMC) in relation to adipose reserve may be due to muscle proteolysis caused by the acute inflammatory response of the new coronavirus infection, which increases albumin consumption for acute phase protein synthesis (Tao Li, 2020).

Moreover, the angiotensin-2 converting enzyme is the receptor for coronavirus-2 and is present in skeletal muscle, causing muscle loss in people with COVID-19 (Morley *et al*., 2020). It is also noteworthy that more than half of our patients were in intensive care, and muscle losses are extensive in patients with COVID-19 during their stay in the ICU. These losses are imposed by the immobility and hypermetabolism that accompanies the inflammatory storm of the infection (Morley *et al*., 2020). Malnutrition was not the only nutritional problem in the population of heart disease patients with COVID. Almost half of the patients were overweight, this percentage being significantly higher than in the comparison group. Other authors have reported the high frequency of obesity in patients hospitalized with COVID-19. Al Salameh *et al*. (2020), in a study with adult patients hospitalized with COVID-19 in France, found an overweight prevalence of 65.1%. Kim *et al* (2020) reported 74.7% of overweight patients according to the BMI in adult patients with COVID-19 admitted to a hospital in New York. Obese and overweight patients represent the majority of patients with COVID-19 hospitalized and admitted to the ICU (De Lorenzo *et al*., 2020). Obesity is typically associated with a restrictive ventilatory pattern due to excess adipose tissue, hindering expansion movements of the chest, diaphragm, and basal walls.

This results in airway resistance, closure of peripheral pulmonary units, ventilation-perfusion abnormalities, and arterial hypoxemia (Fedele *et al*., 2021). Thus, obesity may play an important role as a risk factor for SARS-CoV-2 infection, and may play a crucial role in the course of the disease (Fedele *et al*., 2021). Patients with COVID-19 had markedly lower levels of TLC than patients without the disease. Due to the intense inflammatory nature of COVID-19, some biomarkers often adopted as a nutritional indicator may not effectively reflect malnutrition, representing much more a biomarker for the acute phase response and an indicator of disease severity Baron *et al*. (2020). In fact, patients who progressed to death had lower levels of TLC. Gao *et al*. (2020) and Liu *et al*. (2020) showed that a reduced TLC can predict the damage caused by COVID-19 to the body. This condition correlates directly with the severity of acute respiratory failure, worsening lung injury, which is the main organ compromised by coronavirus infection. Zhao *et al*. (2020) reported that the reduction in TLC levels has a 3-fold greater risk of severity in patients with COVID-19. Studies have attributed this strong relationship between disease severity and low lymphocyte levels to the fact that the storm of inflammatory cytokines leads to lymphocyte apoptosis (Çınar *et al*., 2021). Likewise, COVID patients who died showed lower albumin levels. Li *et al*. (2020) reported a similar result, associating low serum albumin levels with a higher risk for admission to the ICU (odds ratio (OR = 0.31, 95% CI 95%: 0.1 - 0.7, $p < 0.01$)), regardless of age and C-reactive protein (CRP) levels. Furthermore, albumin levels below 2.96 mg/dL independently predicted mortality in patients with COVID-19 admitted to the ICU (Kruglikov and Scherer, 2020). Other investigations showed a relationship between low serum albumin levels and more severe disease progression, as well as higher rates of acute respiratory distress syndrome (ARDS) (Huang *et al*., 2020 and Thongprayoon *et al*., 2020). Huang *et al*. (2020) suggested that hypoalbuminemia may originate from the presence of a systemic inflammatory state in COVID-19. In fact, the literature recognizes that inflammation may be responsible for the leakage of serum albumin into the interstitial space due to increased capillary permeability Soeters *et al*. (2019). The lower PNI score in patients who died corroborates previous investigations that revealed that PNI was a useful prognostic marker in patients with COVID-19. In a study with 101 critical and noncritical patients, the authors demonstrated that PNI was a valuable biomarker to discriminate the severity of COVID-19, being an independent risk factor for an adverse outcome (Wang *et al*., 2021). A study conducted in a tertiary referral hospital for COVID care in Istanbul, involving 294 patients with a mean age of 55.4 ± 12.8 years, demonstrated that PNI was an independent predictor for all-cause hospital mortality and for cardiovascular risk factors (Çınar *et al*., 2021).

Arm muscle circumference (AMC) was also lower in patients who progressed to death. Reports on this matter show that malnutrition worsens the immune response, increasing the risk of complications (Tao *et al*., 2020). Nutritional status impairment increases viral persistence and the traffic of inflammatory cells to the lungs (De Lorenzo *et al*., 2020). In addition, malnutrition causes severe health problems since it correlates with nutrient deficiency, causing inflammation and increasing oxidative stress. As a consequence, it affects the immune system, exacerbating the inflammatory response or causing the cytokine storm inflammatory response of COVID-19. This mechanism of changes is accompanied by an increase in the rate of metabolism, requiring an energy source, substrates for biosynthesis, and molecules to regulate the inflammatory cascade. Hence, a malnourished individual will not have adequate reserves, which leads to often irreversible changes in the clinical picture (Calder, 2020). Malnutrition is thus a direct predictor of an unfavorable evolution in these patients (Arshad *et al*., 2020 and Iddir *et al*., 2020). Some limitations must be considered when interpreting our results. The relatively small sample size and the use of a single center limit the generalization of the results and allow for selection bias. In addition, the study did not include a disease severity score, nor assessed the history of weight loss, compromising some inferences. Despite this, few studies performed direct anthropometric assessment in patients infected with the new coronavirus since adaptations in the clinical-nutritional management were necessary to avoid contamination of professionals and dissemination of the virus (Martindale *et al*., 2020 and Barazzoni *et al*., 2020). Furthermore, our sample involves a specific subgroup of infected cardiac patients and included a comparison group in its design.

CONCLUSION

Heart disease patients with COVID had a high frequency of malnutrition and low levels of TLC and serum albumin. Excess weight was also high, affecting almost half of the group of infected patients and being significantly higher than in the group of heart disease patients without SARS-CoV-2 infection. Lower mean AMC, TLC, albumin, and lower PNI scores were markers of poor prognosis, regardless of age. Many issues still surround COVID-19 infection and nutritional aspects. Prospective studies that assess the effects of the infection on body compartments in the short and long term need to be undertaken to reach more definitive conclusions about the nutritional repercussions of COVID-19. However, considering the context of the disease, it is undeniable the importance of early diagnosis and nutritional management, which should be integrated into therapy.

REFERENCES

Al-Salameh A, Lanoix JP, Bennis Y, Andrejak C, Brochot E, Deschasse G, Maizel J 2020. The association between body mass index class and coronavirus disease 2019 outcomes. *Int J Obes;* doi.org/10.1038/s41366-020-00721-1.

Arshad MS, Khan U, Sadiq A, Khalid W, Hussain M, Yasmeen A, *et al* 2020. Coronavirus disease (COVID-19) and immunity booster green foods: A mini review. *Food Sci Nutr,* 8:3971–3976. DOI: 10.1002/fsn3.1719.

Barazzoni R, Bischoff SC, Breda J, Wickramasinghe K, Krznaric Z, Nitzan D, *et al* 2020. ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection. Clinical Nutrition. 39:1631-1638. https://doi.org/10.1016/j.clnu.2020.03.022.

Baron D.M., Franchini M., Goobie S.M., Javidroozi M., Klein A.A., Lasocki S., Liumbruno G.M., Muñoz M., Shander A., Spahn D.R., *et al* 2020. Patient blood management during the COVID–19 pandemic: *A narrative review. Anaesthesia*; 75:1105–1113. doi: 10.1111/anae.15095

Calder PC 2020. Nutrition, immunity and COVID-19. BMJ Nutrition, Prevention & Health. doi:10.1136/bmjnph-2020-000085.

Cao J, Wen M, Shi Y, Wu Y, He Q 2020. Study on nutritional status of patients with COVID-19 and its influencing factors. General practice, 18(9): 1073–1076. https://doi.org/10.1016/j.ijid.2020.08.018

Chumlea WC, Roche AF, SteinbaughM 1985. Estimating stature from knee height for persons 60 to 90 years age. *J Am Geriatr Soc*, 33(2): 116-120. doi: 10.1111/j.1532-5415.1985.tb02276.x.

Çınar T, Hayıroğlu Mİ, Çiçek V, Kılıç Ş, Asal S, Yavuz S, Selçuk M, Yalçınkaya E, Keser N, Orhan AL 2021. Is prognostic nutritional index a predictive marker for estimating all-cause in-hospital mortality in COVID-19 patients with cardiovascular risk factors? Heart Lung; 50(2):307-312. doi: 10.1016/ j.hrtlng.2021.01.006.

Cummings MJ, Baldwin MR, Abrams D, Jacobson SD, Meyer BJ, Balough EM, *et al* 2020. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. The Lancet; 6736(20)31189-2.

De Lorenzo, R.; Conte, C.; Lanzani, C.; Benedetti, F.; Roveri, L.; Mazza, M.G.; Brioni, E.; Giacalone, G.; Canti, V.; Sofia, V.; *et al* 2020. Residual clinical damage after COVID-19: A retrospective and prospective observational cohort study. PLoS ONE, 15, e0239570. doi: 10.1371/journal.pone.0239570

Fedele D, De Francesco A, Riso S, Collo A 2021. Obesity, malnutrition, and trace element deficiency in the coronavirus disease (COVID-19) pandemic: An overview. Nutrition; 81:111016: 1-14. doi: 10.1016/j.nut.2020.111016.

Frisancho AR 1981. New norms of upper limb fat and muscle areas for assessment of nutritional status. *Am J Clin Nutr,* 34(11): 2540–2545. doi: 10.1093/ajcn/34.11.2540.

Gao F, Zheng KI, Wang XB, Sun QF, Pan KH, Wang TY, *et al* 2020. Obesity Is a Risk Factor for Greater COVID-19 Severity. Diabetes Care. https://doi.org/10.2337/dc20-0682

Gualtieri P., Falcone C., Romano L., Macheda S., Correale P., Arciello P., Polimeni N., Lorenzo A 2020. Body Composition Findings by Computed Tomography in SARS-CoV-2 Patients: Increased Risk of Muscle Wasting in Obesity. *Int. J. Mol. Sci*; 21:4670. doi: 10.3390/ ijms21134670.

Haraj NE, El Aziz S, Chadli A, Dafir A, Mjabber A, Aissaou O, *et al* 2021. Nutritional status assessment in patients with Covid-19 after discharge from the intensive care unit. *Clinical nutrition* ESPEN, 41, 423–428. https://doi.org/10.1016/ j.clnesp.2020. 09.214.

Henriques I, Cebola M, Mendes L. Malnutrition, sarcopenia and COVID-19 in the elderly. Scientific evidence for vitamin d supplementation. *Acta Portuguesa de Nutrição*. 2020,21: 26-30. http://dx.doi.org/10.21011/apn.2020.2106.

Huang J., Cheng A., Kumar R 2020. Hypoalbuminemia predicts the outcome of COVID-19 independent of age and co-morbidity. *J Med Virol.* doi: 10.1002/jmv.26003.

Hulot JS. COVID-19 in patients with cardiovascular diseases 2020. Arch Cardiovasc Dis;113(4):225-226. doi: 10.1016/ j.acvd.2020.03.009.

Iddir M, Brito A, Dingeo G, Campo SSFD, Samouda H, FrandoMLR, *et al* 2020. Strengthening the Immune System and Reducing Inflammation and Oxidative Stress through Diet and Nutrition: Considerations during the COVID-19 Crisis. Nutrients, 12(1562): 1-39. doi:10.3390/nu12061562.

Kim T, Roslin, M, Wang JJ, Kane J, Hirsch, JS, Ji Kim E, Kozel Z 2020. Body Mass Index as a Risk Factor for Clinical Outcomes in Patients Hospitalized with COVID-19 in New York. Obesity; 28 (2), 279-84. https://doi.org/10.1002/ oby.23076

Kruglikov I.L., Scherer P.E 2020. The role of adipocytes and adipocyte-like cells in the severity of COVID-19 infections. Obesity (Silver Spring);28:1187–1190. doi: 10.1002/oby.22856.

Liu Y, YangY, Zhang C, Huang F, Wang F, Yuan J, *et al* 2020. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. Sci China Life Sci; 63(3): 364-374. https://doi.org/10.1016/S0140-6736(20)30154-9.

Liu, G., Zhang, S., Mao, Z. *et al* 2020. Clinical significance of nutritional risk screening for older adult patients with COVID-19. Eur *J Clin Nutr* 74, 876–883. https://doi.org/10.1038/s41430-020-0659-7

Martindale R, Patel JJ, Taylor B, Warren M, Mcclave AS 2020. Nutrition Therapy in the Patient with COVID-19 Disease Requiring ICU Care. ASPEN.

Morley JÁ, Kalantar-Zadeh K, Anker SD 2020. COVID-19: a major cause of cachexia and sarcopenia? ournal of Cachexia, Sarcopenia and Muscle; 11: 863–865. DOI: 10.1002/jcsm.12589.

Morley JE, Kalantar-Zadeh K, Anker SD 2020. COVID-19: a major cause of cachexia and sarcopenia?, *Journal of Cachexia, Sarcopenia and Muscle,* 11, 863– 865. https://doi.org/10.1002/ jcsm.12589

Popkin BM, Du S, Green WD, Beck MA, Algaith T, Herbst CH, *et al* 2020. Individuals with obesity and COVID-19: A global perspective on the epidemiology and biological relationships. *Obesity Reviews*, 21: 1-17. doi: 10.1111/obr.13128.

Siddiqi HK, Mehra MR 2020. COVID-19 illness in native and immunosuppressed states: a clinical-therapeutic staging proposal. *J Heart Lung Transplant;* 39:405–7. doi: 10.1016/j.healun.2020.03.012

Soeters PB, Wolfe RR, Shenkin A 2019. Hypoalbuminemia: pathogenesis and clinical significance. *JPEN J Parenter Enter Nutr;* 43:181–193. doi: 10.1002/jpen.1451.

Sohrabi C, Alsafi Z, O'Neill N, Khan M, Kerwan A, Al-Jabir A, *et al* 2020. World Health organization declares global emergency: a review of the 2019 novel coronavirus (COVID-19). *Int J Surg;* 76:71e6. doi: 10.1016/j.ijsu.2020.02.034

Tao Li, Zhang Y, Gong C, Wang J, Liu B, Shi L, *et al* 2020. Prevalence of malnutrition and analysis of related factors in elderly patients with COVID-19 in Wuhan, China. *Eur J Clin Nutr* 74, 871–875. https://doi.org/10.1038/s41430-020-0642-3

Thongprayoon C, Cheungpasitporn W, Chewcharat A, Mao MA, Thirunavukkarasu S, Kashani KB (2020). Risk of acute respiratory failure among hospitalized patients with various admission serum albumin levels, Medicine: 99(9):9. doi: 10.1097/MD.0000000000019352

Venter C, Eyerich S, Sarin T, Klatt KC 2020. Nutrition and the Immune System: A Complicated Tango. Nutrients, 12: 1-15.doi:10.3390/nu12030818.

Wang ZH, Lin YW, Wei XB, Liao XL, Yuan HQ, Huang DZ, *et al* 2021. Predictive Value of Prognostic Nutritional Index on COVID-19 Severity. Front Nutr; 14:1-9. https://doi.org/10.3389/fnut.2020.582736

Zhao Q, Meng M, Kumar R, Wu Y, Huang J, Deng Y, *et al* 2020. Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A systemic review and meta-analysis. International Journal of Infectious Diseases, 96: 131–135.https://doi.org/10.1016/j.ijid.2020.04.086

Zhao X, Li Y, Ge Y, Shi Y, Lv P, Zhang J, *et al* 2020. Evaluation of nutrition risk and its association with mortality risk in severely and critically ill COVID-19 patients.JPEN *J Parenter Enteral Nutr*. Accepted manuscript. https://doi.org/10.1002/jpen.1953.

Zhu N, Zhang D, Wang W, Xingwang L, Bo Y, Song J, *et al* (2019). A novel coronavirus from patients with pneumonia in China. N *Engl J Med* 2020; 382(8): 727e33. doi: 10.1056/NEJMoa 2001017

Zou X, Chen K, Zou J, Han P, Hao J, Han Z 2020. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. *Frontiers of Medicine;* 14(2):185–92. doi: 10.1007/s11684-020-0754-0.

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