Short Communication

Influence of nutritional assistance on mortality by COVID-19 in critically ill patients

Thaisy Cristina Honorato Santos Alves [a, b], Renata Santos Guimarães [a, e],
Sineide Freitas de Souza [a], Najara Amaral Brandão [d, e], Carla Hilário da Cunha Daltro [c],
Maria Ester Pereira Conceição-Machado [c], Lucivalda Pereira Magalhães de Oliveira [c],
Carla de Magalhães Cunha [c, *]

[a] Federal University of Bahia, Nutrition School, Food, Health and Nutrition Postgraduate, Basilio da Gama Street, 40.110-040, Bahia, Brazil
[b] State University of Bahia, Science of Life Department, Silveira Martins Street, 2555, 41.150-000, Bahia, Brazil
[c] Federal University of Bahia, Nutrition School, Basilio da Gama Street, 40.110-040, Bahia, Brazil
[d] Federal University of Bahia, Science Health Institute, Interactive Organ and System Processes Postgraduate, Reitor Miguel Calmon Avenue, 40.110-902, Bahia, Brazil
[e] Couto Maia Institute, Coronel Azevedo Street, 41.332-010, Bahia, Brazil

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SUMMARY

Background & aims: Evidence suggests the existence of an association between the institution of nutritional therapy and clinical outcomes in patients with critical COVID-19. Thus, the aim of this study was to evaluate the influence of nutritional assistance on COVID-19 mortality in patients admitted to intensive care units (ICU).

Methods: This is a subset of the cohort "Influence of nutritional therapy on clinical prognosis in patients with COVID-19: a multicenter retrospective cohort study". Clinical and nutrition assistance information (type of assistance, evaluation of anthropometric status, and time of introduction of nutritional therapy) and presence of diabetes, hypertension and previous respiratory disease were collected from electronic medical records. To evaluate the association between the variables of interest and mortality, the hazard ratio was estimated.

Results: We evaluated 153 critically ill patients $\geq$18 years old, affected by COVID-19, with a rate of mortality of 77.8%. Among non survivors 58.8% were female, 52.9% aged <65 years, 66.4% had arterial hypertension, 46.2% diabetes mellitus and 81.5% had an early onset of nutritional support. Initiation of nutritional therapy after 48 h (HR: 2.57; 95% CI: 1.57—4.20) and the presence of obesity (HR: 1.55; 95% CI: 1.04—2.31) were associated with higher mortality, even after adjustment for potential confounders.

Conclusions: Our data suggests that the provision of early nutritional therapy should be prioritized, with greater attention directed to obese patients, and the nutritional assistance can contribute favorably to the clinical evolution and prognosis of critically ill patients with COVID-19.

1. Introduction

The clinical implications of COVID-19 have yet to be elucidated, while strategies are sought to minimize its various effects on the body. Studies suggest that the implementation of early nutritional therapy is related to immune response modulation and the prevention of lean mass loss and is associated with positive clinical outcomes for critically ill patients [1,2].

Adequate prescription of nutritional therapy is dependent on a correct nutritional assessment and diagnosis. Thus, the identification of risk and presence of malnutrition should be an initial step in the assessment of all patients [1]. In Brazil, under normal conditions, a nutritionist is part of the direct care team for critically ill patients. However, changes in therapeutic care routines in order to contain viral spread have modified the nutritional care modality to remote assistance in many COVID reference institutions. Furthermore, the

* Corresponding author.
  E-mail address: carlamagalhaesc@gmail.com (C.M. Cunha).

insufficient quantity of trained professionals, may result in deficiency in provided nutritional care, that may contribute to unfavorable clinical outcomes [3]. Thus, this work aimed to evaluate the influence of nutritional care on mortality by COVID-19 in patients admitted to intensive care units (ICU).

2. Materials and methods

This is a subset of the cohort "Influence of Nutritional Therapy on Clinical Prognosis in Patients with COVID-19: A Multicenter Retrospective Cohort Study", including individuals aged ≥18 years admitted to ICUs at a public COVID reference hospital in the State of Bahia, Brazil, in 2020. Critical patients with a diagnosis of COVID-19 confirmed by specific tests and a minimum hospital stay of 48 h were included. This study was approved by the Ethics and Research Committee of the Nutrition School of the Federal University of Bahia (protocol 4.139.951) and of the hospital's unit. The data collected is part of a multicenter cohort and the team has given permission for partial results to be presented.

The hospital admitted 448 critically ill eligible patients but only 34.2% of these had anthropometric diagnosis at admission, constituting a sample of 153 patients for this study. Data were collected retrospectively from electronic medical records. Gender, age, length of stay and clinical outcome (discharge/ transfer or death), anthropometric diagnosis according to body mass index (BMI), time of introduction of nutritional therapy (up to 48 h from ICU admission – early and if started after this period - late) and presence of diabetes, hypertension and previous respiratory disease were collected. Nutritional assistance was performed remotely.

The sample was characterized by measures of central tendency for continuous variables and absolute and relative frequencies for categorical variables. The variable age was categorized into ≥65 years and <65 years. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test, when appropriate. Cox proportional hazards models were used to evaluate the influence of early nutritional therapy and obesity on mortality by estimating the hazard ratio (HR) [4].

For all modeling, bivariate analysis was first performed to select candidate variables for the multivariate model, and those with a p value < 0.20 were selected. These variables, along with other potentially confounding variables, even if the p-value was> 0.20, were included in the multivariate model, and in the final model variables with p < 0,05 were considered significant. All statistical analyses were performed in the Statistical Package for Social Sciences (SPSS) for Windows, version 21.0.

3. Results

In this study 119 (77.8%) patients died, and among non survivors 58.8% were female, 52.9% aged <65 years (p = 0.014), 66.4% had arterial hypertension (p = 0.040), 46.2% diabetes mellitus (p = 0.018) and 81.5% received early nutritional support (p = 0.025). The median hospital length of stay was 8.0 (3.0–15.0) days.

The multivariate analysis, adjusted for potential confounders, showed that late nutritional therapy (HR: 2.57; 95% CI: 1.57–4.20), as well obesity (HR: 1.55; 95% CI: 1.04–2.31) were associated with increased mortality. The other exposures variables tested were not associated with mortality among critically ill patients evaluated (Table 1).

4. Discussion

The present study demonstrates that nutrition therapy started 48 h after admission and presence of obesity should be considered as risk factors for mortality by COVID-19. A significant absence of information on anthropometric status at admission was also observed. Although nutritional assessment is clearly recommended in hospitalized patient care, this aspect has lost priority, especially during the COVID-19 pandemic [5].

With the standardization of in-hospital procedures focused on containing viral spread and its consequences, health professional teams are not always able to perform nutritional assistance within the desired parameters [2,3,6]. Thus, the low number of frontline professionals in ICUs, the need to restrict the access of nutritionists in the units, and the lack of other professionals on the team trained to provide nutritional assistance seem to have culminated in little focus on nutritional status during the care of critically ill patients.

The absence of nutritional data may impede the institution and monitoring of nutritional therapy, which are indispensable for good clinical evolution and favorable prognosis for patients, especially those affected by COVID-19 [2,6]. It is noteworthy that prolonged ICU stay, combined with reduced food intake caused by COVID-19 symptoms, may worsen the nutritional status, with severe loss of skeletal muscle mass and function that may lead to additional morbidity, increasing the length of stay and worsening prognosis. Therefore, the prevention, diagnosis, and treatment of nutritional risk should be included in the management of hospitalized patients with COVID-19, aiming to contribute to positive clinical outcomes [1,7].

It is worth noting the high prevalence of obesity patients in this study, and its association with increased mortality. As the absence of information on anthropometric status was high, this data may be

Table 1
Demographic, clinical and nutritional characteristics and Cox regression analysis of the factors associated with COVID-19 mortality in critically ill patients.

Characteristics	Non-Survivors 119 (77.8%)	Survivors 34 (22.2%)	p-value[a]	HR[b] (95% CI)
Age			0.014	1.37 (0.94–2.00)
<65 years	63 (52.9)	26 (76.5)		
≥65 years	56 (47.1)	8 (23.5)		
Sex			1.000	1.17 (0.78–1.74)
Female	70 (58.8)	20 (58.8)		
Male	49 (41.2)	14 (41.2)		
Arterial hypertension	79 (66.4)	16 (47.1)	0.040	0.96 (0.61–1.48)
Diabetes mellitus	55 (46.2)	8 (23.5)	0.018	1.20 (0.81–1.77)
Obesity	63 (52.9)	14 (41.2)	0.226	**1.55 (1.04–2.31)**
Previous respiratory disease	10 (8.4)	3 (8.8)	1.000	1.22 (0.62–2.41)
Nutritional support			0.025	**2.57 (1.57–4.20)**
Early	97 (81.5)	33 (97.1)		
Delayed	22 (18.5)	1 (2.9)		

[a] Calculated by Pearson's Chi square or Fishers exact test as appropriate.
[b] Multivariate Cox Regression was performed with the variables age, sex, high blood pressure, diabetes, respiratory disease, obesity and nutritional support.

overestimated, considering that obesity may have been recorded because it is a comorbidity of higher risk for COVID-19. It is worth noting that, in the patients affected by COVID-19, an impaired innate immune response, associated with an inadequate nutritional status and lack of early and adequate nutritional therapy, may cause rapid deterioration of immune and respiratory muscle function, aggravating the consequences of lung damage caused by coronavirus [6].

Although nutritional assistance in the present study happened remotely, the frequency of early introduction of nutritional therapy was high. Moreover, initiation of nutritional therapy 48 h after admission was associated with increased mortality. As reported in the literature, early enteral nutrition seems to stimulate the innate immune response and favor a protective intestinal microbiota, providing benefits to patients with COVID-19. Due to the relationship between the gut mucosa and the lung, damage to the gut microbiota may promote modifications to the lung microbiota, further compromising lung function. Thus, early nutritional therapy is of utmost importance in the care of patients with COVID-19 [6,8].

It is important to mention that, even though the early initiation of nutritional therapy is essential for a good clinical prognosis, it seems even more relevant to evaluate and monitor the characteristics of the nutritional therapy, regarding route, nutritional composition, and volume, taking into account the individual needs of each patient [3,9]. Considering that critically patients with COVID-19 have been directly managed by teams overloaded with different attributions, a limitation in the recording of nutritional information and in the performance of professionals who need to perform remote assistance has been observed [6], and the fear of maintaining nutritional therapy may be common, due to insecurity in monitoring.

Thus, the registration and surveillance of nutritional data is relevant to ensure an adequate nutritional supply in the critical phase. Therefore, further steps of our cohort will evaluate in more detail the influence of the quantitative and qualitative composition of the nutritional therapy offered on the clinical prognosis of critically ill patients in the context of the COVID-19 pandemic. It is expected that the results will support the development of protocols that better enable the nutritional management of critically ill patients with COVID-19, despite the difficulties of the current scenario. This manuscript has some limitation as the absence of SOFA and APACHE data to be used as an additional parameter to estimate the severity of the disease. However, the estimated association included the adjustment for potential confounders for COVID mortality as part of models.

5. Conclusion

The clinical severity of patients affected by COVID-19 demands the implementation of adequate nutritional supply management, aiming at minimizing the compromise of nutritional status and favoring clinical recovery. Thus, assessing nutritional status beforehand, as well as instituting early and adequate nutritional therapy are indispensable for the good clinical evolution of critically ill patients affected by COVID-19. Considering that nutrition is a determining factor for health, early nutritional therapy should be prioritized, whenever possible, especially among individuals with obesity, contributing favorably to the clinical evolution of patients with COVID-19.

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