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COVID-19 and Nutritional Intervention: A Narrative Review

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Abstract: Throughout history, infectious diseases have caused damage among societies. Emerging and re-emerging infectious diseases are now occurring at unprecedented speed, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), commonly referred as Covid-19 pandemic. Although the majority of the population is susceptible to Covid-19, there are risk factors that are seen as clinical predictors of hospitalization, disease severity and mortality. Since the poor nutritional status of patients affects the prognosis of Covid-19, the present work was developed with the aim of presenting a view on the role of nutrition in the treatment of patients with this respiratory infection, at the level of identification of nutritional risk, assessment of nutritional status, nutritional diagnosis, nutritional treatment, monitoring and nutritional evolution. Symptoms and comorbidities reported by patients infected with SARS-CoV-2 may be determining factors in the prognosis of Covid-19. These patients should undergo a nutritional status assessment to identify complications associated with SARS-CoV-2 infection, such as increased energy requirements, malnutrition, involuntary weight loss, gastrointestinal disorders and dehydration. Recognizing these complications will allow establishing the best nutritional therapy to be applied. The inflammatory condition and the characteristic symptoms of this disease lead to an increase in catabolism and, consequently, to an increase in nutritional requirements. This clinical picture is exacerbated by hospitalization, which is why patients recovering from Covid-19 should benefit from follow-up, in order to ensure adequate rehabilitation. Nutritional intervention in patients with Covid-19 is of great importance and, despite the existence of guidelines, each case must be interpreted individually, not focusing only on nutritional therapy.

Keywords: SARS-Cov-2; Covid-19; nutrition; feeding; nutritional support; nutritional recommendations; nutritional intervention; nutritional care process.

INTRODUCTION

In December 2019, the World Health Organization (WHO) received the first information about a new coronavirus, which was beginning to gain strength in Wuhan, China (WHO, 2020). The number of known cases of infection by this virus began to grow alarmingly as early as the beginning of 2020, prompting the WHO to declare an International Public Health Emergency at the end of January. At a time when cases of infection reached 114 countries, on 11 March 2020, the WHO classified the disease as a pandemic (Cena, H., & Chieppa, M. 2020; Moscatelli, F. *et al.*, 2021). The virus responsible for causing serious infections in the respiratory system was called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), and the associated disease Covid-19 (Ochoa, J. B. *et al.*, 2020; WHO, 2020; Moscatelli, F. *et al.*, 2021; Wu, S. *et al.*, 2021).

Most of the population is susceptible to Covid-19 (Wei, P. F. 2020; Liu, J., & Liu, S. 2020). However, there are risk factors that are seen as clinical predictors of hospitalization, disease severity and mortality (Martindale, R. *et al.*, 2020; Thomas, S. *et al.*, 2021).

Age, different comorbidities such as obesity, diabetes mellitus, hypertension, cancer, cardiovascular disease, and a clinical profile of immunosuppression are the main risk factors to consider (Liu, J., & Liu, S. 2020; Martindale, R. *et al.*, 2020; Thomas, S. *et al.*, 2021).

The concomitant presence of symptoms and risk factors may be correlated with a poor nutritional status, which may be due to insufficient food consumption, decreased nutrient absorption, and/or increased energy expenditure (Cawood, A. L. *et al.*, 2020; Virgens, I. P. *et al.*, 2021; Wierdsma, N. J. *et al.*, 2021). The difficulty in meeting the nutritional needs of these patients often leads to involuntary loss of weight and muscle mass, and therefore to the development of cases of malnutrition and cachexia, this scenario being particularly reported in the elderly (Virgens, I. P. *et al.*, 2021; Wierdsma, N. J. *et al.*, 2021).

In addition to advanced age and the presence of chronic diseases being strong predictors of hospitalization and mortality from Covid-19 (Thomas, S. *et al.*, 2021), this age group is also associated with a deficient nutritional status and a clinical picture of sarcopenia (Laviano, A. *et al.*, 2020), being notorious the prevalence of malnutrition (Azzolino, D. *et al.*, 2020).

Obesity is not only one of the most common comorbidities reported by patients with Covid-19, but also a public health problem with high prevalence worldwide (Holdoway, A. 2021; Silverio, R. *et al.*, 2021). This chronic disease, in addition to its relationship with the severity and mortality of the disease, is also associated with a decrease in forced expiration volume and forced vital capacity, which, in turn, can lead to an increased need for invasive mechanical ventilation (MV) (Silverio, R. *et al.*, 2021). MV intervention is associated with the outcome of the disease (Liu, J., & Liu, S. 2020). Furthermore, patients with obesity have a higher risk of developing other chronic diseases, such as hypertension, type 2 diabetes mellitus and cardiovascular disease, which are predictors of a negative clinical outcome (Silverio, R. *et al.*, 2021).

The gastrointestinal symptoms identified among patients with Covid-19 are also associated with the risk of malnutrition, specifically undernutrition (Silverio, R. *et al.*, 2021; Thomas, S. *et al.*, 2021). Nausea, vomiting and gastrointestinal intolerance are clinical manifestations related to the digestive system, which promote a decrease in food intake, contributing to the deficiency of several nutrients (Ali, A. M., & Kunugi, H. 2021; Silverio, R. *et al.*, 2021; Thomas, S. *et al.*, 2021; Zhao, X. *et al.*, 2021). Diarrhea, as well as deficient oral intake and pharmacological therapy, may be the cause of the dehydration observed in some patients infected with SARS-CoV-2 (Silverio, R. *et al.*, 2021).

Considering the difficulty in identifying drugs that work effectively in the prevention and treatment of Covid-19, and until vaccination against this disease reaches a large proportion, it is essential to look for other ways to optimize the clinical picture of patients infected with SARS-CoV-2 (Piquet, M. A., & Dupont, B. 2021; Aguila, E. J. T., & Cua, I. H. Y. 2021; Clemente-Suárez, V. J. *et al.*, 2021). Since the poor nutritional status of patients affects the prognosis of Covid-19, the provision of nutritional care should be, together with an interdisciplinary collaboration, one of the main interventions to consider in the treatment of this disease (Chapple, L. A. S. *et al.*, 2020; Laviano, A. *et al.*, 2020; Romano, L. *et al.*, 2020; Ali, A. M., & Kunugi, H. 2021; Clemente-Suárez, V. J. *et al.*, 2021; Haraj, N. E. *et al.*, 2021).

An adequate nutritional assessment and respective nutritional treatment promote a reduction in complications associated with various diseases and also a notable improvement in outcome (Barazzoni, R. *et al.*, 2020). In this sense, the present work aims to present, based on a literature review, a vision of the intervention of nutrition in the treatment of patients with Covid-19, more specifically regarding the processes that should integrate the nutritional care to be provided to patients with this pathology: identification of nutritional risk and assessment of nutritional status, nutritional diagnosis, nutritional treatment, monitoring and nutritional assessment.

NUTRITIONAL INTERVENTION: COVID-19

Considering all the complications that can result from Covid-19, it is essential to intervene and prevent such events, promoting a positive clinical result (Liu, J., & Liu, S. 2020; Thomas, S. *et al.*, 2021). For that, the comorbidities reported by patients infected with SARS-CoV-2 must be faced with special attention, and may be determining factors in the prognosis of Covid-19 (Liu, J., & Liu, S. 2020). Therefore, it is imperative that a process be established that involves the monitoring of clinical signs indicating deterioration, as well as an early assessment of the risk in which patients are found, so that it is possible to provide the most appropriate treatment at the most suitable time (Liu, J., & Liu, S. 2020; Alves, T. C. H. S. *et al.*, 2021).

- **Nutritional Risk Identification and Nutritional Status Assessment:**

Nutritional status is a concept that can be defined as an individual's health condition, which is influenced by the consumption of nutrients and their use (Li *et al.*, 2021). Patients with a suspected or confirmed diagnosis of Covid-19 should undergo a nutritional status assessment to identify cases of malnutrition and other complications associated with SARS-CoV-2 infection (Barazzoni, R. *et al.*, 2020; Brugliera, L. *et al.*, 2020; Handu, D. *et al.*, 2021; Morán-López, J. M. 2021).

Covid-19 is a disease characterized by an inflammatory syndrome (Haraj, N. E. *et al.*, 2021), whose associated symptoms vary according to its severity. However, certain symptoms are transversal to patients with mild, severe or critical illness, such as fever, dyspnea, cough, loss of appetite, anosmia, dysgeusia, diarrhea, nausea and vomiting (Allard, L. *et al.*, 2020; Vena, A. *et al.*, 2020; de Araújo Morais, A. H. *et al.*, 2021). The inflammatory condition and the aforementioned symptoms lead to an increase in catabolism and, consequently, to nutritional needs increasement (de Araújo Morais, A. H. *et al.*, 2021). Along with the clinical manifestations described, Vena, A. *et al.* (2020) related a rate comprised between 50 and 75% of reduction in food intake in 24.3% of the Covid-19 patients in the study (Vena, A. *et al.*, 2020). Based on the concept of undernutrition, which applies in situations where the energy and macronutrient intake (carbohydrates, proteins and lipids) is inadequate and/or in which there is a deficiency in micronutrients (vitamins and minerals) (Mentella, M. C. *et al.,* 2021), these patients may have a high risk of falling into this nutritional status (Thibault, R. *et al.,* 2020).

The high prevalence of Covid-19 is found in older adults who present at least one associated comorbidity (Thibault, R. *et al.,* 2020; Ali, A. M., & Kunugi, H. 2021), as reported in the study by Vena, A. *et al.* (2020), which included the participation of a sample with a mean age of 71 years and 65.3% indicated the presence of at least one underlying disease. This age group is naturally prone to inadequate food intake and reduced muscle mass, which leads to an unbalanced nutritional status and a negative clinical prognosis (Silverio, R. *et al.,* 2021).

The proper functioning of the organism depends on the adequate supply of vitamins and minerals, especially in the presence of disease (Cervantes-Pérez, E. *et al.,* 2020). Deficiency in micronutrients, in particular vitamins C and D and selenium, appear to be associated with an increased probability of hospitalization and mortality from Covid-19 (Clemente-Suárez, V. J. *et al.,* 2021; de Faria Coelho-Ravagnani, C. *et al.,* 2021). In a study conducted by Im, J. H. *et al.* (2020), the levels of various nutrients in Covid-19 patients admitted to a hospital unit were analyzed and it was observed that vitamin D deficiency was the most prevalent: 76% of users had values of 25 - hydroxyvitamin D3 ≤ 20 ng/dl, which indicated vitamin D deficiency, and in 24% of the sample a severe deficiency of this vitamin (25-hydroxyvitamin D3 ≤ 10 ng/dl) was identified. This study further demonstrated that 82% of patients diagnosed with Covid-19 were deficient in at least one nutrient, emphasizing vitamin D and selenium deficiency (42%) (Im, J. H. *et al.,* 2020).

The deterioration of the clinical status of these patients often requires their hospitalization, in a ward or in intensive care units (ICU) (Wu, S. *et al.,* 2021). A retrospective study (Yu, Y. *et al.,* 2021) found that patients diagnosed with Covid-19 are predisposed to longer hospital stays. According to Wierdsma, N. J. *et al.* (2021), Covid-19 patients in the ward remained hospitalized for an average of 8 days, and patients in the ICU, 19 days. In the same study, it was observed that, after hospital admission, 21% of patients infected with SARS-CoV-2 experienced severe weight loss (>5 kg), of which 85% were eventually transferred to the ICU.

Admission to the ICU is often associated with the need for MV intervention (Wu, S. *et al.,* 2021), which implies patient sedation and the use of other drugs (Chapple, L. A. S. *et al.,* 2020; Turner, P. *et al.,* 2021). Pharmacological therapy administered to hospitalized Covid-19 patients, in the absence of specific treatment, involves the administration of antivirals and antibiotics. This medication can alter the intestinal microbiota, exacerbating the symptoms and gastrointestinal intolerance reported by patients (Aguila, E. J. T. *et al.,* 2020).

There are several validated indicators and tools, whose application suits Covid-19 (Azzolino, D. *et al.,* 2020; Barazzoni, R. *et al.,* 2020). According to Li *et al.* (2021), the body mass index (BMI) is an indicator of nutritional status that is associated with the severity of Covid-19. Considered a parameter of nutritional status, the BMI (kg/m^2) is a tool used in clinical practice, depending on the height and body weight of users, allowing to understand if an individual is underweight (BMI < 18.5 kg/m^2), normal weight (BMI 18.5 - 25 kg/m^2), overweight (BMI > 25 kg/m^2) or obese (BMI ≥ 30 kg/m^2) (Alves, T. C. H. S. *et al.,* 2021; Fedele, D. *et al.,* 2021). The study conducted by Wierdsma, N. J. *et al.* (2021) found that 67% of patients infected with SARS-CoV-2 admitted to hospital units were overweight; Bedock, D. *et al.* (2021) reported that approximately 24% of the study sample revealed a BMI ≥ 30 kg/m^2, indicative of obesity. The mean BMI of patients who died in the ICU was higher than the mean BMI of patients who recovered from the disease (Li *et al.,* 2021). Within Covid-19, the lack of anthropometric data on users is frequente (Zhang, P. *et al.,* 2021). The weighing of hospitalized users and the use of anthropometric measurements can be an obstacle due not only to the risk of transmission associated with the patient-health professional contact (Thibault, R. *et al.,* 2020), but also to the conditioned physical state of hospitalized patients, due to the action of MV and/ or due to the presence of edema and venous thrombi (Chen, H. *et al.,* 2021; Zhang, P. *et al.,* 2021). In these cases, nutritional screening should include interviews with the patients themselves and/or family members, so that it is possible to obtain information about the history of weight and eating habits (Thibault, R. *et al.,* 2020).

- **Nutritional Assessment and Screening Tools:**

The Nutrition Risk Screening – 2002 (NRS-2002), a nutritional status screening tool, is based on collecting information regarding age, intentional weight loss, BMI, recent food intake and disease severity (Azzolino, D. *et al.,* 2020; Zhao, X. *et al.,* 2021). Each parameter is assigned a rating from 0 to 3, and for individuals aged ≥ 70 years, one point is added. It was proposed that an individual whose Covid-19 is severely expressed should be rated 2 points and a critical illness frame rated 3. A total score ≥ 3 corresponds to a nutritional status at risk. Zhao, X. *et al.* (2021) identified 92% of the patients included in the study at nutritional risk and 16% at high nutritional risk. This study also shows that patients who obtained a higher score are those who present a more critical condition, which results in higher mortality and longer hospital stay. Patients with a score > 5 on the NRS-2002 were at a significantly increased risk of death in a hospital setting compared with patients with a lower score (Li *et al.,* 2021).

The Geriatric Nutritional Risk Index (GNRI) is a clinical outcome predictor tool based on serum albumin (ALB) levels and the BMI value. A GNRI ≤ 100 seems to be associated with a negative outcome and an increased incidence of death in the hospital environment, as demonstrated by Song, F. *et al.* (2021).

The Controlling Nutritional Status (CONUT) score is an indicator that aims to estimate protein reserves, energy expenditure and immune defenses based on ALB, total cholesterol and lymphocyte levels (Song, F. *et al.*, 2021). Through the rating obtained by this tool, an individual may have a normal nutritional status (CONUT score 0-1), mild undernutrition (CONUT score 2-4), moderate undernutrition (CONUT score 5-8) and severe undernutrition (CONUT score 9 -12). A study guided by Song, F. *et al.* (2021) concluded that critically ill Covid-19 patients exhibited a high CONUT score, which is associated with an increased risk of mortality in the hospital setting.

The Prognostic Nutritional Index (PNI) conveys the immunological nutritional status considering ALB and lymphocyte count values (Song, F. *et al.*, 2021). According to this tool, a score > 38 is indicative of a normal nutritional status, the range between 35 and 38 is assigned to patients at moderate risk of undernutrition, and a score <35 is a severe risk of undernutrition. Patients with Covid-19 in the severe form had lower PNI scores and, consequently, an increased risk of in-hospital mortality (Song, F. *et al.*, 2021).

The Nutrition Risk in the Critically Ill (NUTRIC) is a nutritional risk assessment tool developed for application to patients hospitalized in the ICU (Azzolino, D. *et al.*, 2020; Zhang, P. *et al.*, 2021; Wu, S. *et al.*, 2021). Recently, a short version, Modified Nutrition Risk in the Critically Ill (mNUTRIC), was created with greater ease of application, where the variable interleukin (IL)-6 was removed, due to the reduced frequency of its measurement in the routine of the ICU (Zhang, P. *et al.*, 2021; Wu, S. *et al.*, 2021). mNUTRIC consists of the sum of scores obtained in 5 domains: age, score obtained at the time of hospital admission in the Acute Physiology and Chronic Health Evaluation II (APACHE II), result obtained at the time of hospital admission in the Sequential Organ Failure Assessment (SOFA), number of comorbidities and length of stay in the ward. The range of values can range from 0 to 9, with a score ≥ 5 indicating high nutritional risk. The use of mNUTRIC in the study by Zhang, P. *et al.* (2021) found that 61% of critically ill Covid-19 patients admitted to the ICU exhibited a high nutritional risk. The 28-day mortality rate in patients at higher nutritional risk appears to be increased compared to the group of Covid-19 patients with a lower mNUTRIC score (87% versus 49%).

Global Leadership Initiative on Malnutrition (GLIM) is a tool to assess the nutritional status of adults in a hospital context, which allows for the identification of the presence of undernutrition and comprises two phases (Thibault, R. *et al.*, 2020; Mentella, M. C. *et al.*, 2021; Yu, Y. *et al.*, 2021). The first step corresponds to the screening of nutritional status (Mentella, M. C. *et al.*, 2021; Yu, Y. *et al.*, 2021; Zhang, P. *et al.*, 2021). The second phase, referring to nutritional assessment, allows for the determination of undernutrition in an individual if there is at least one phenotypic criterion and at least one etiological criterion present. The established phenotypic criteria are: BMI < 20 kg/m^2 (or BMI < 22 kg/m^2 for individuals aged ≥ 70 years), or involuntary weight loss > 5% in the last 6 months or > 10% in a period longer than 6 months, or loss of muscle mass. The determined etiological criteria are: reduction of food intake by at least 50% for more than one week, or reduced absorption of nutrients, or presence of disease or acute or chronic injury associated with inflammation (Thibault, R. *et al.*, 2020; Mentella, M. C. *et al.*, 2021; Yu, Y. *et al.*, 2021). The degree of undernutrition can be classified as moderate or severe (Mentella, M. C. *et al.*, 2021; Yu, Y. *et al.*, 2021). According to GLIM, hospitalized Covid-19 patients, either in the ward or in the ICU, present two phenotypic criteria from the outset, namely, acute illness and reduced ALB levels, the latter being associated with decreased muscle mass (Thibault, R. *et al.*, 2020; Formisano, E. *et al.*, 2021).

The high scores obtained in the NUTRIC and NRS2002 tools have been shown to be associated with a negative outcome, so that, simultaneously with the GLIM, they are validated as convenient, objective and adequate tools in the assessment of nutritional risk in patients with Covid-19 (Pardo, E. *et al.*, 2020; Li *et al.*, 2021). The results obtained based on the assessment of nutritional status using the GNRI, CONUT and PNI tools demonstrated to be significantly associated with in-hospital mortality of Covid-19 patients (Song, F. *et al.*, 2021).

- **Biochemical Markers:**

ALB and prealbumin (PA) are biochemical markers frequently used in nutritional assessment. These indicators express an approximation of the nutritional status of the most critical patients or the severity of the disease (Li *et al.*, 2021).

ALB is the main protein in human plasma and the most abundant element in the extracellular environment. Its synthesis is stimulated by food intake and insulin levels, so a sharp decrease in the levels of these biochemical markers reflect an insufficient protein intake, which may culminate in nutritional problems such as malnutrition, more specifically, undernutrition, cachexia and inflammation (Alves, T. C. H. S. *et al.*, 2021; Song, F. *et al.*, 2021). There is some divergence regarding the analysis of ALB levels as an indicator of nutritional status (Abate, S. M. *et al.*, 2021; Thomas, S. *et al.*, 2021; Wierdsma, N. J. *et al.*, 2021). This laboratory data undergoes a reduction in its levels in the presence of inflammation in the acute phase, regardless of the individual's nutritional status. However, a clinical picture in which there is inflammation in the acute phase and the presence of a disease in the critical phase will require that protein synthesis undergoes alterations, resulting in a marked decrease in ALB levels. As a result, hypoalbuminemia leads to a less favorable clinical outcome, compromising gastrointestinal functionality (Thomas, S. *et al.*, 2021). Thus, ALB seems to establish a close association with a negative outcome, and should not be seen as an indicator of nutritional status (Thomas, S. *et al.*, 2021; Wierdsma, N. J. *et al.*, 2021). However, ALB should be used in nutritional assessment as an inflammatory marker associated with nutritional risk, and decreased ALB is an indicator of an unfavorable clinical outcome (Pironi, L. *et al.*, 2021; Thomas, S. *et al.*, 2021). The positive relationship of this biomarker with muscle mass is referenced in the literature (Virgens, I. P. *et al.*, 2021). Pironi, L. *et al.* (2021) found a positive correlation between ALB levels and protein-energy intake, which translates into the relevance of nutritional treatment to meet the needs of patients. Furthermore, laboratory data from critically ill patients demonstrated substantially lower levels of total protein, ALB and PA when compared to data collected from critically ill patients (Zhao, X. *et al.*, 2021).

PA is a useful tool in the assessment of malnutrition in hospitalized patients. In the study conducted by Li *et al.* (2021), the mean values of ALB and PA, recorded upon admission to hospital of users with Covid-19, showed a state of moderate malnutrition. Li *et al.* (2021) showed that the levels of ALB in patients diagnosed with severe Covid-19, at the time of hospital admission, was significantly lower than the levels observed in groups of individuals with moderate or severe disease (Alves, T. C. H. S. *et al.*, 2021). Allard, L. *et al.* (2020) evaluated some metabolic parameters of patients with Covid-19 and found that the levels of plasma proteins, ALB and PA are related to nutritional risk. Simultaneously, this study also demonstrated that decreased levels of ALB, PA, plasma proteins and zinc, and high levels of magnesium, are related to disease severity. The results obtained by Zhang, P. *et al.* (2021) are similar, with the patients, upon admission, showing signs of a weakened nutritional status through low levels of ALB and PA.

There are also other biochemical markers that reflect the nutritional status of patients with Covid-19, such as lactic dehydrogenase and serum creatinine, which have been shown to have an important relationship with disease severity (Alves, T. C. H. S. *et al.*, 2021). Myoglobin, creatinine kinase and lactic dehydrogenase levels are biochemical markers that are found at high levels in cases of muscular dystrophy (Ali, A. M., & Kunugi, H. 2021). These data are reported particularly by Covid-19 patients admitted to the ICU, which suggests that these individuals are susceptible to weight loss, more specifically, skeletal muscle mass (Ali, A. M., & Kunugi, H. 2021; Alves, T. C. H. S. *et al.*, 2021). This situation compromises glucose regulation and all body homeostasis (Ali, A. M., & Kunugi, H. 2021). Some studies report that blood glucose levels in critically ill patients may be reduced, which seems to be associated with the development of hypoglycemia and a higher mortality rate, following Covid-19 (Chen, H. *et al.*, 2021; Zhao, X. *et al.*, 2021).

SARS-CoV-2 infection is also characterized by lymphopenia at an early stage of Covid-19 (Liu, J., & Liu, S. 2020; Alves, T. C. H. S. *et al.*, 2021) with patients suffering from the more severe form of the disease having lower values than those with the milder form of Covid -19 (Alves, T. C. H. S. *et al.*, 2021).

There was also an above-normal value of nitrogenous urea in the blood, creatinine, glucose and total bilirubin in critically ill patients (Zhao, X. *et al.*, 2021). In this study, the biomarkers of nitrogenous blood urea, creatinine and glucose revealed a positive association with the NRS-2002. On the other hand, with regard to total protein, ALB and PA, these markers showed a negative correlation with the NRS-2002 tool, showing the high nutritional risk these patients may be subject to.

- **Nutritional Diagnosis:**

Nutritional assessment is a step that should integrate the nutritional care provided to patients infected with SARS-CoV-2 (Cawood, A. L. *et al.*, 2020; Thibault, R. *et al.*, 2020; Handu, D. *et al.*, 2021) and plays an important role in identifying the origin of nutritional problems (Handu, D. *et al.*, 2021). The recognition of these complications inherent to Covid-19 will subsequently allow the establishment of the best nutritional therapy to be applied (Thomas, S. *et al.*, 2021; Handu, D. *et al.*, 2021).

Covid-19 is often associated with the following diagnoses: increased energy needs, malnutrition, which includes undernutrition and overnutrition (obesity), involuntary weight loss, gastrointestinal disorders and dehydration. These diagnoses are based on the assessment of nutritional status (Handu, D. *et al.*, 2021).

- **Increased Energy Needs:**

During the lockdown, in 2020, (i.e. limited restrictions, partial lockdown or full lockdown), curtailment in several activities, such as mobility, physical activity, emotional changes, amoung others ounced the energy demand. The inflammatory condition related to Covid-19 in its severe form, translates into a situation of hypercatabolism, characterized by fever, fatigue, loss of appetite and which is reflected in increased energy needs (Clemente-Suárez, V. J. *et al.*, 2021; Li *et al.*, 2021). This nutritional diagnosis is also associated with the need for MV, which consequently affects nutrient intake, enhancing undernutrition (Clemente-Suárez, V. J. *et al.,* 2021).

➢ **Malnutrition:**

As previously mentioned, malnutrition is defined as inadequate intake of energy and nutrients, preventing the preservation of an adequate body composition, in particular of lean mass (Barazzoni, R. *et al.,* 2020; Brugliera, L. *et al.,* 2020; Mentella, M. C. *et al.,* 2021). Since this condition is associated with the set of tissues that make up the body mass, BMI is a tool that should be read with caution, as it may not directly transmit malnutrition and, therefore, this diagnosis may occur either in cases of undernutrition or in situations of overnutrition (Barazzoni, R. *et al.,* 2020; Brugliera, L. *et al.,* 2020; Handu, D. *et al.,* 2021).

➢ **Undernutrition:**

Undernutrition is defined as a pathology implicit in a diet that is unable to meet the nutritional and/or energy needs of an individual (Mentella, M. C. *et al.,* 2021; Thomas, S. *et al.,* 2021). It is a nutritional condition with high prevalence, particularly among patients infected with SARS-CoV-2 hospitalized and admitted to the ICU (Haraj, N. E. *et al.,* 2021). Pironi, L. *et al.* (2021) observed that 77.2% of hospitalized patients were at risk of undernutrition and 49.7% were diagnosed with undernutrition.

This diagnosis can result from an increase in energy expenditure, insufficient intake of macro and/or micronutrients, deficient absorption of nutrients and metabolic dysfunctions inherent to Covid-19 (Barazzoni, R. *et al.,* 2020; Mentella, M. C. *et al.,* 2021, Silverio, R. *et al.,* 2021; Thomas, S. *et al.,* 2021). In turn, the increase in energy requirements is due to the feverish state, MV, intense activity of the muscles of the respiratory system and the hypercatabolic condition (Stachowska, E. *et al.,* 2020; Haraj, N. E. *et al.,* 2021; Mentella, M. C. *et al.,* 2021). Insufficient nutrient intake can arise as a consequence of loss of appetite, ageusia and anosmia, shortness of breath, need for MV and gastrointestinal symptoms (nausea, vomiting and diarrhea) (Stachowska, E. *et al.,* 2020; Haraj, N. E. *et al.,* 2021; Mentella, M. C. *et al.,* 2021; Thomas, S. *et al.,* 2021; Zhao, X. *et al.,* 2021). Impaired nutrient absorption is associated with an imbalance in the intestinal microbiota (dysbiosis) (Cena, H., & Chieppa, M. 2020; Mentella, M. C. *et al.,* 2021). These patients demonstrated metabolic disturbances at various levels (Stachowska, E. *et al.,* 2020; Zhao, X. *et al.,* 2021). Glucose metabolism is affected by increased blood glucose and insulin resistance (Stachowska, E. *et al.,* 2020). At the level of protein metabolism, the inflammatory condition promotes an increase in the synthesis of acute phase proteins, which leads to an increase in proteolysis, resulting in a negative nitrogen balance (Stachowska, E. *et al.,* 2020; Anker, M. S. *et al.,* 2021; Virgens, I. P. *et al.,* 2021). Critically ill patients diagnosed with Covid-19 may still be subject to fat mobilization and decomposition (Stachowska, E. *et al.,* 2020).

➢ **Obesity:**

Obesity increased the risk of severe disease, mortality and infection with COVID-19. Although the diagnosis of this disease, characterized by an accumulation of fat mass (Barazzoni, R. *et al.,* 2021) precedes infection by SARS-CoV-2, in the context of this new pathology it is considered not only a risk factor, but also a relevant factor in its progression (Angelidi, A. M. *et al.,* 2021; Fedele, D. *et al.,* 2021). The prevalence of obesity among patients with Covid-19 at the time of hospital admission is high, as noted by (Lakenman, P. L. M. *et al.,* 2021), whose study included a sample in which 57% of patients were obese (BMI > 30 kg/m^2).

Obese individuals, with advanced age, other comorbidities and/or metabolic complications, present a high risk of loss of skeletal muscle mass (Barazzoni, R. *et al.,* 2021). Involuntary weight loss in these patients could even be seen as a positive aspect; however, the loss of muscle mass inherent to weight loss promotes the development of other complications, compromising recovery (Holdoway, A. 2021). One of these complications can appear in the form of sarcopenic obesity, which occurs in a context of high fat mass with reduced muscle strength (Fedele, D. *et al.,* 2021; Silverio, R. *et al.,* 2021).

➢ **Involuntary Weight Loss:**

Covid-19 is characterized by a clinical picture of inflammation, with an exacerbated production of acute phase proteins that, in turn, cause a dysregulation of metabolism (Anker, M. S. *et al.,* 2021). In parallel, SARS-CoV-2 infection causes some symptoms such as, anorexia, anosmia, ageusia, dyspnea, fatigue and fever, which enhance the decrease in food consumption, contributing to the development of other pathologies, namely, undernutrition and sarcopenia (Anker, M. S. *et al.,* 2021; Virgens, I. P. *et al.,* 2021; Wierdsma, N. J. *et al.,* 2021). The catabolic situation developed under these circumstances stimulates the loss of body weight in these patients (Anker *et al.,* 2021). Furthermore, the recovery of Covid-19 requires rest and, as a disease that mainly affects the respiratory system, MV intervention may be necessary and, consequently, greater immobilization of the patient, which leads to exacerbated degradation of the skeletal muscle in a short period of time (Ali, A. M., & Kunugi, H. 2021; Anker, M. S. *et al.,* 2021; Silverio, R. *et al.,* 2021).

Sarcopenia is characterized by a progressive and generalized dysfunction of the skeletal muscle, reflected in impairment of muscle strength, reduction in muscle quantity and/or quality, and impairment of physical capacity (Fedele, D. *et al.,* 2021; Silverio, R. *et al.,* 2021). Wierdsma, N. J. *et al.* (2021) reported that 73%

of patients, upon admission to the hospital, were at risk for sarcopenia. This clinical condition is associated not only with an insufficient supply of energy and nutrients, but also with a reduced bioavailability of nutrients resulting from gastrointestinal symptoms and an increase in energy requirements (Fedele, D. *et al.,* 2021).

Cachexia is defined as a complex metabolic syndrome underlying a pathology and is characterized by the loss of fat-free mass (≥ 5%), with or without loss of fat mass (Mentella, M. C. *et al.,* 2021; Thomas, S. *et al.,* 2021; Virgens, I. P. *et al.,* 2021). There is still another way of diagnosing this clinical condition, which is based on weight loss associated with the disease, combined with at least three of the following factors: decreased hand grip strength, fatigue, anorexia, low fat-free mass index and biochemical data altered (Thomas, S. *et al.,* 2021; Virgens, I. P. *et al.,* 2021). Most of these criteria are frequent symptoms of Covid-19 (Li *et al.,* 2021; Zhang, P. *et al.,* 2021). Cachexia caused by Covid-19 may contribute to an unfavorable progression of the clinical condition of patients, especially in the elderly, in which the loss of muscle mass is already prevalent (Thomas, S. *et al.,* 2021).

- **Gastrointestinal Changes:**

Although the gastrointestinal disorders reported by patients with Covid-19 have a multifactorial etiology, it is believed that the use of drugs such as sedatives, antivirals and antibiotics, the acute phase of the disease and the need to place patients in a prone position are the main related causes (Aguila, E. J. T., & Cua, I. H. Y. 2021). Several studies assume that the development of dysbiosis in patients with Covid-19 may be an impact of the use of these drugs (Cena, H., & Chieppa, M. 2020; Chen, H. *et al.,* 2021; Silverio, R. *et al.,* 2021). Furthermore, morphine, specifically, seems to be the cause of some symptoms, such as nausea and constipation, which affect intestinal motility (Osuna-Padilla, I. *et al.,* 2021; Wierdsma, N. J. *et al.,* 2021). These gastrointestinal disturbances associated with the administration of drugs contribute to another clinical obstacle: the difficulty in meeting the nutritional needs of these patients, particularly at the protein-energy level, which translates into an insufficient supply of energy and protein (Chen, H. *et al.,* 2021; Silverio, R. *et al.,* 2021). This scenario enhances the development of undernutrition and muscle catabolism (James, P. T. *et al.,* 2021; Mentella, M. C. *et al.,* 2021). Gastrointestinal manifestations caused by SARS-CoV-2 infection may be the cause of the decrease in nutrients observed in these patients, contributing to the progression of undernutrition (Virgens, I. P. *et al.,* 2021).

- **Dehydration:**

Dehydration is highly prevalent upon admission of Covid-19 patients to the ICU (Pardo, E. *et al.,* 2020). Diarrhea, insufficient oral food intake and the side effects of certain drugs seem to be the causes that most contribute to this circumstance (Vena, A. *et al.,* 2020).

- **Nutritional Treatment:**

Patients diagnosed with mild Covid-19, able to control and recover from the disease at home, should benefit from nutritional treatment, implemented remotely. For these patients, guidelines indicate that the recommended daily intake of energy and protein should, at a minimum, be met; the incorporation of high-calorie and high-protein snacks and meals should be a strategy to be adopted; the inclusion of nutritionally rich foods, beverages and oral nutritional supplements (ONS) in the daily diet can be a way to increase protein-energy intake; replacing solid foods by liquids can be an asset for individuals with chewing difficulties; micronutrient supplementation can be a way to compensate for unbalanced food intake and possible nutritional deficiencies; symptoms associated with the disease, such as nausea, vomiting and shortness of breath, can be alleviated by offering more frequent snacks and meals with smaller portions; the food to be supplied must not be subject to great preparation, nor must it require much effort to be consumed; water needs must be met, and the use of electrolyte drinks is recommended in the presence of vomiting and diarrhea (Handu, D. *et al.,* 2021).

The nutritional therapy to be implemented in hospitalized patients requires the determination of the patients' energy and nutritional needs (Barazzoni, R. *et al.,* 2020). The guidelines developed so far indicate that nutritional support for Covid-19 patients, particularly those in critical condition, should benefit from a slow and progressive approach during the first 5-7 days (Turner, P. *et al.,* 2021).

The recommended energy intake for patients aged > 65 years and with more than two comorbidities (polymorbid) is a maximum of 27 kcal/kg of body weight/day, having been established as the maximum energy supply ceiling for patients Covid-19 polymorbids with very low weight and as a reference value for the elderly, 30 kcal/kg of body weight/day. The prescription of nutritional therapy based on an energy intake of 30 kcal/kg/day for underweight patients should take into account the propensity of these individuals to the re-feeding syndrome (Barazzoni, R. *et al.,* 2020). The risk of developing this syndrome should be assessed and identified in Covid-19 patients, especially in users who are undernourished upon admission to hospital, who have not received nutritional support for more than a week and/or have electrolyte imbalances (Wells Mulherin, D. *et al.,* 2020; Pardo, E. *et al.,* 2020; Thibault, R. *et al.,* 2020). In these cases, it is recommended that nutritional support be initiated with 25% of the established energy requirements, either through enteral nutrition (EN) or parenteral nutrition (PN), and progressed to 70-80% within a period of 4 to 7 days (Martindale, R. *et al.,* 2020; Thibault, R. *et al.,* 2020). At the same time, careful monitoring of serum phosphate, magnesium and potassium levels (Martindale, R. *et al.*, 2020; Pardo, E. *et al.*, 2020; Thibault, R. *et al.*, 2020) must be maintained. In a clinical picture of re-feeding syndrome, supplementation with vitamins, minerals and electrolytes is essential, particularly the supply of thiamine (Pardo, E. *et al.*, 2020).

The protein intake of elderly, polymorbid and/or hospitalized patients, according to the recommendations, should ensure 1 g/kg of body weight/day, aiming to prevent involuntary weight loss and reduce the risk of complications and, thus, improving the outcome (Barazzoni, R. *et al.*, 2020; Barazzoni, R. *et al.*, 2021). Regarding the needs of carbohydrates and lipids, the management of the intake of these macronutrients should be made taking into account the energy intake and the ratio 30:70 for Covid-19 patients without respiratory difficulties and 50:50 for ventilated patients (Barazzoni, R. *et al.*, 2020).

Nutritional support aimed at Covid-19 patients should be started as early as possible, preferably within the first 24 to 48 hours after hospital admission (Barazzoni, R. *et al.*, 2020; Martindale, R. *et al.*, 2020; Minnelli, N. *et al.*, 2020; Wells Mulherin, D. *et al.*, 2020). Oral nutritional intake, whenever possible, should be privileged (Aguila, E. J. T. *et al.*, 2020; Barazzoni, R. *et al.*, 2020). Thus, for users who, despite nutritional guidance and the incorporation of fortified foods into their daily diet, do not meet their protein-energy requirements, oral nutritional supplementation (ONS) is a solution (Aguila, E. J. T. *et al.*, 2020; Barazzoni, R. *et al.*, 2020; Terblanche, E., & Bear, D. 2020). The use of ONS is intended to enhance the achievement of nutritional needs, through an alternative rich in energy and/or protein, vitamins and minerals, so it must provide at least 400 kcal and 30 g or more of protein (Aguila, E. J. T. *et al.*, 2020; Barazzoni, R. *et al.*, 2020). In situations where nutritional needs are not met through oral intake, EN should be prioritized, particularly in hospitalized polymorbid SARS-CoV-2 infected patients and elderly people with a reasonable prognosis. The oriented nutritional support for patients with Covid-19 admitted to the ICU can be differentiated depending on whether the patients are non-ventilated, under MV, or after the ventilation period (Barazzoni, R. *et al.*, 2020). Nutritional therapy for non-ventilated patients, who are not able to meet protein-energy requirements through oral feeding, should consider, in the first instance, the administration of ONS and only after that, EN (Barazzoni, R. *et al.*, 2020; Terblanche, E., & Bear, D. 2020). If there are limitations to the administration of EN, it is recommended to start PN peripherally (Barazzoni, R. *et al.*, 2020; Martindale, R. *et al.*, 2020).

Patients infected with SARS-CoV-2 who require MV intervention should first undergo an energy needs assessment, as mentioned above (Barazzoni, R. *et al.*, 2020). The administration of hypocaloric nutritional support at an early stage of the acute disease is recommended, and the energy intake should gradually increase until reaching 80 to 100% of energy requirements (Barazzoni, R. *et al.*, 2020; Martindale, R. *et al.*, 2020). In case the energy requirements were obtained through predictive equations, it is advisable to maintain isocaloric nutrition in the first week, due to the overestimation of energy requirements (Barazzoni, R. *et al.*, 2020). Given the need to preserve skeletal muscle mass and the hypercatabolic condition associated with the severity of Covid-19, it is recommended that the protein intake, in critically ill Covid-19 patients, progressively reach 1.2 to 2 g/kg of body weight/day (Aguila, E. J. T. *et al.*, 2020; Barazzoni, R. *et al.*, 2020; Martindale, R. *et al.*, 2020; Turner, P. *et al.*, 2021).

European Society for Clinical Nutrition and Metabolism (ESPEN) advocates that the administration of EN in intubated and ventilated Covid-19 patients should start with a nasogastric tube and that nutritional support be provided continuously, with a view to reduce the incidence of diarrhea (Aguila, E. J. T. *et al.*, 2020; Barazzoni, R. *et al.*, 2020; Martindale, R. *et al.*, 2020; Patel, J. J. *et al.*, 2020). In these patients, intolerance to EN is a frequent complication, so ESPEN established the residual gastric volume > 500 ml as a cutoff point for another strategy to be implemented (Aguila, E. J. T. *et al.*, 2020; Barazzoni, R. *et al.*, 2020). In view of this situation, prokinetic treatment is advised, with a view to improving intestinal motility (Martindale, R. *et al.*, 2020), and the formula to be administered must be concentrated and of reduced volumen (Aguila, E. J. T. *et al.*, 2020). After prokinetic treatment, if gastrointestinal intolerance persists or a high-risk situation for aspiration occurs, it may be prudent to resort to post-pyloric access (Aguila, E. J. T. *et al.*, 2020; Barazzoni, R. *et al.*, 2020; Terblanche, E., & Bear, D. 2020; Martindale, R. *et al.*, 2020; Patel, J. J. *et al.*, 2020). In a scenario where enteral nutrition is not a viable option, even after all strategies to enhance EN tolerance have been put in place, PN should be started (Barazzoni, R. *et al.*, 2020; Terblanche, E., & Bear, D. 2020; Wells Mulherin, D. *et al.*, 2020). From another perspective, ASPEN (Martindale, R. *et al.*, 2020; Wells Mulherin, D. *et al.*, 2020) proposes starting nutritional support with PN and, after improving gastrointestinal symptoms, transitioning to EN.

Placing individuals in the prone position seems to benefit the oxygenation of Covid-19 patients, however this strategy presents a risk of aspiration (Aguila, E. J. T. *et al.*, 2020; Martindale, R. *et al.*, 2020; Minnelli, N. *et al.*, 2020; Patel, J. J. *et al.*, 2020). In this sense, the British Dietetic Association (BDA) advises the administration of EN via nasogastric during the adoption of this practice, provided that there is no gastrointestinal intolerance, nor the use of high volumes (≥ 2 kcal/ml), that should be avoided, because potentiate the increase of gastric residual volume. The maximum gastric emptying volume should be 300 ml/4 hours, in order to reduce the risk of aspiration (Terblanche, E., & Bear, D. 2020). The ESPEN recommendations (Barazzoni, R. *et al.,* 2020) for Covid-19 patients placed in the prone position are similar to those recommended for intubated and ventilated patients, adding that the beginning of EN should suppress 30% of the determined energy needs and the energy supply must have a progressive increase.

With regard to micronutrient supplementation, ESPEN advises that the recommended daily intake of vitamins and minerals be adhered, especially for Covid-19 patients diagnosed with undernutrition. If micronutrient deficiencies are detected, a higher intake should be provided (Barazzoni, R. *et al.,* 2020; Holdoway, A. 2020).

❖ **Nutritional Monitoring and Assessment:**

Patients recovering from Covid-19 should benefit from follow-up for 3 to 6 months, in order to ensure adequate rehabilitation, taking into account the same parameters previously evaluated (Barazzoni, R. *et al.*, 2020; Bedock, D. *et al.*, 2021; Zhao, X. *et al.*, 2021).

Muscle catabolism, exacerbated by hospitalization in the ICU, contributes to an increase in energy requirements (Handu, D. *et al.,* 2021). Simultaneously, symptoms such as shortness of breath, fatigue, dysphagia, anosmia and ageusia were reported by these patients, even after the acute phase of the disease (Holdoway, A. 2021), which leads to insufficient oral intake and a decrease in body weight, enhancing the risk of undernutrition or aggravating this clinical picture (Barazzoni, R. *et al.,* 2020; Terblanche, E., & Bear, D. 2020; Formisano, E. *et al.,* 2021; Haraj, N. E. *et al.*, 2021). Bedock, D. *et al.* (2021) followed Covid-19 patients thirty days after hospital discharge. For the assessment of body composition, bioempedacia was used and muscle strength was assessed by measuring the hand grip strength. This study found that after 30 days, patients did not return to their usual body weight. In the study developed by Lakenman, P. L. M. *et al.* (2021), 60% of the sample benefited from monitoring, given the marked muscle weakness after medical discharge. In this follow-up, it becomes necessary to review the nutritional therapy to be provided to these individuals (Barazzoni, R. *et al.,* 2020).

Patients whose oral feeding is compromised by difficulty in swallowing must be provided with food with altered texture and adequate to the degree of dysphagia (Barazzoni, R. *et al.,* 2020; Thibault, R. *et al.,* 2020). If, after medical discharge from the ICU, the oral intake of nutrients is insufficient, an isocaloric diet with a high protein content should be maintained (Pardo, E. *et al.,* 2020). Given these circumstances, ESPEN recommends that nutritional support be administered via EN, using ONS if necessary, until exclusive oral food intake is able to respond to protein-energy needs (Barazzoni, R. *et al.*, 2020; Handu, D. *et al.,* 2021). If dysphagia persists and/or nutritional needs are not met, EN should be administered and, in conditions of high risk of aspiration, EN with post-pyloric access should be an option, with PN being the last resort and only during the swallow training period (Barazzoni, R. *et al.*, 2020; Terblanche, E., & Bear, D. 2020; & Handu, D. *et al.*, 2021).

CONCLUSION:

The disease that is at the origin of the current pandemic, Covid-19, is a worldwide concern, since, in the absence of an effective treatment and with the process of vaccination against SARS-CoV-2 underway, the number of deaths continues to rise.

The population groups most affected by Covid-19 are mostly elderly and individuals diagnosed with chronic diseases. Covid-19 can reach more severe proportions, requiring hospitalization of infected individuals, who report symptoms that require the attention of health professionals due to the repercussions that they may have on the clinical picture. In this sense, several studies have shown that nutritional intervention in the care of patients with Covid-19 is essential, favoring a positive outcome for these individuals. The identification of nutritional problems, based on an assessment of the nutritional status, will allow the development of the most adequate nutritional treatment for the user. However, there are some obstacles that must be analyzed in order to take the best approach.

First, determining the energy requirements of patients with Covid-19 is essential for the development of the most appropriate nutritional therapy. However, due to the high rate of spread of SARS-CoV-2, the use of indirect calorimetry, the method recommended for this procedure, seems to increase the risk of contagion of the virus. Although ESPEN recommends, as long as hygiene and safety conditions are ensured, the use of indirect calorimetry to measure energy expenditure, this practice is not recommended by ASPEN. In this follow-up, predictive equations, such as the Harris-Bennedict one, may appear as an alternative.

Experienced professional associations, such as ESPEN, ASPEN and BDA, have developed recommendations and guiding guides regarding how nutritional therapy can be implemented in this setting. However, the application of these indications recommended for Covid-19 patients in several studies allowed us to conclude that they do not meet the needs demanded by these patients. The negative energy balance is considered the greatest difficulty identified in the nutritional support of patients infected with SARS-CoV-2, since, despite the protein intake provided being very close to the target value, there is still a deficiency of this nutrient in the ICU. Consequently, Covid-19 patients capable of surviving the adversities inherent to hospitalization in the ICU are subject during this period to a loss of skeletal muscle mass and muscle functionality. Considering that malnutrition, particularly undernutrition, often precedes the contamination by this virus, the application of screening tools in patients with Covid-19 is an important step inserted in nutritional intervention, which helps in the assessment of nutritional status and plays a role in the nutritional therapy to be implemented.

Given the fact that the guidelines developed so far are based on nutritional therapy applied to users in critical condition or with severe acute respiratory syndrome, it is necessary to understand which nutritional strategies can be applied in order to optimize the protein balance -energetic of patients with Covid-19.

Although there are guidelines, each Covid-19 case must be interpreted individually. Thus, the nutritional care to be provided to these patients should not only focus on nutritional therapy. It is essential to carry out an early assessment of the nutritional status and nutritional problems that may compromise recovery from the disease.

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