

Nutrition support in the time of SARS-CoV-2 (COVID-19)

Nutrition is a key determinant of health [1]. More importantly, nutrition is part of the treatment regimen for acute and chronic diseases and applies particularly to ailments for which an etiologic treatment has not yet been discovered and validated. The 2014–2016 Ebola virus outbreak in Western Africa demonstrated that immediate supportive care significantly reduces case fatality rates [2,3]. This may apply as well to the current SARS-CoV-2 (or COVID-19) pandemic that is ravaging the world.

Emerging evidence shows that COVID-19 is associated with negative outcomes in older, comorbid, and hypoalbuminemic patients [4]. These characteristics are not specific to the Chinese population because they have been reported also in North American patients with COVID-19 [5]. When considered together, the emerging literature on patients with COVID-19 indirectly highlights the relevance of nutrition in possibly determining their outcomes. Older age and the presence of comorbid conditions are almost invariably associated with impaired nutritional status and sarcopenia, independently of body mass index [6]. Interestingly, a high body mass index score appears to be related to a poor prognosis in comorbid patients with COVID-19, which further points to a possible role of sarcopenic obesity in influencing outcome [7]. Also, lymphopenia, which is a marker of malnutrition, is a negative prognostic factor in patients with COVID-19 [4]. Albumin circulating levels should not be considered as a nutritional marker in patients with inflammatory response, but a recent report that a low prealbumin level predicts progression to acute respiratory distress syndrome (ARDS) [8] suggests that poor nutritional intake contributes to the outcome. Finally, the timing of nutritional intervention appears to be critical because most patients rapidly progress from cough to dyspnea, and then to respiratory failure and admission to an intensive care unit (ICU) for mechanical ventilation [4,5].

Nutritional status appears a relevant factor influencing the outcome of patients with COVID-19, but not much information has emerged so far on the impact of early nutritional support in pre-ICU patients with COVID-19. The National Health Commission of the People's Republic of China and the National Administration of Traditional Chinese Medicine recommend implementing "strengthened supportive care to ensure sufficient energy intake" [9]. Zhang and Liu recently elaborated on a list of nutrients with possible anticoronavirus effects based on in vitro and clinical studies [10]. However, none of the available literature has so far discussed how to adapt the currently available guidelines for nutrition therapy during disease to the specific clinical scenario of COVID-19. A protocol based on the clinical experience learned from the daily challenges posed by patients with COVID-19 may

help stimulate discussions regarding nutrition-delivery options and lead to improvements in standardizing nutrition approaches and the identification of optimal care.

Herein, we publish a pragmatic protocol for the delivery of nutrition therapy in pre-ICU patients with COVID-19. The protocol has been devised by a multidisciplinary team of experts working in Lombardy, Italy, which is the center of the Italian COVID-19 crisis [11]. In the protocol, some procedures diverge from the available nutrition guidelines. However, discrepancies appear justified by the specific clinical characteristics of patients with COVID-19. Also, the hospital environment (i.e., shortage of doctors and nurses, increasing daily workload, and need to reduce contact with patients infected by COVID-19 which is a highly infectious pathogen) influenced the decision to prefer certain feeding routes in an apparent contradiction to international guidelines. Consequently, the protocol should not be considered as a guideline but rather an example of the strategy implemented by a team of experts to deliver nutritional care to patients at a high risk of malnutrition in a difficult working environment. We hope that this protocol will generate debates and possibly new proposals to address the clinical and organizational challenges of COVID-19. *Nutrition* is prepared to serve as a tribune for the progressive amelioration of the nutritional care of these patients.

We acknowledge that the protocol does not address the important question of its effectiveness. This appears to be relevant because baseline inflammation limits the impact of nutritional support on clinical outcome [12]. Considering that patients with COVID-19 show an increased inflammatory response upon hospital admission [4], the protocol may need adjustments to also target inflammation. In addition, the issue of blood glucose control of diabetic patients with COVID-19 may require further consideration [13]. Finally, we acknowledge that this protocol is not addressing the nutritional care of COVID-19 patients who are critically ill. This is a crucial clinical point, because once a patient needs to be intubated and mechanically ventilated, the ICU stay can be prolonged [4]. The European Society of Intensive Care Medicine and the Society of Critical Care Medicine just issued guidelines for the management of patients critically ill with COVID-19 that do not address the unmet need of nutritional care [14]. While waiting for specific recommendations on the nutritional management of patients with COVID-19 in the ICU, current available guidelines on the clinical nutrition for patients in the ICU are likely to fit the needs of patients with COVID-19. However, whether the nutritional and metabolic needs of ventilated patients with COVID-19 are similar to those of patients with ARDS remain to be proven.

According to recent ESPEN guidelines, enteral nutrition is preferred for patients in the ICU who receive mechanical ventilation [15]. However, the specific needs of patients with COVID-19 may require the adoption of prone ventilation or neuromuscular blockade [5,14]. Although enteral nutrition in the prone position has been demonstrated to be feasible and safe [16], its implementation in daily practice could be difficult. This issue may be particularly relevant for young professionals without specific expertise in clinical nutrition who are called to act and make decisions in a difficult environment and so far without specific indications and protocols.

Also, life-threatening hypoxemia requires a delay of enteral nutrition [15]. Furthermore, gastrointestinal symptoms, including vomiting and diarrhea, are frequent in patients with COVID-19 [17]. In patients with ARDS/acute lung injury, enteral diets that contain eicosapentaenoic acid, gamma-linolenic acid, and antioxidant agents may offer a clinical benefit in oxygenation and days of ventilation [15], but whether COVID-19-related pneumonia responds to specific enteral diets remains to be determined.

Another yet unanswered question regarding the nutritional care of critically ill patients with COVID-19 is whether modulation of inflammatory response by specific lipid emulsions could offer any additional benefit over corticosteroidal and anti-interleukin-6 drugs. Finally, postventilation-acquired dysphagia and ICU-acquired weakness pose enormous challenges to the successful rehabilitation of COVID-19 survivors, and need to be addressed early and comprehensively during the recovery period. International nutrition scientific societies, including the European Society for Clinical Nutrition and Metabolism, are taking up the challenge to develop updated guidelines that are specific to the needs of patients who are critically ill with COVID-19, and their efforts will be available in the next few days [18].

COVID-19 is here to stay, and will ravage countries and continents, disappear and then reemerge here and there, when environmental and social conditions allow. It is better to be prepared.

Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Covinsky K, Katz M. Supplemental nutrition assistance program - Do not take the food out of patients' mouth. *JAMA Intern Med* 2020. <https://doi.org/10.1001/jamainternmed.2019.7151>. [Epub ahead of print, Accessed March 9, 2020].
- [2] Cohen J. Saving lives without new drugs. *Science* 2014;246:911.
- [3] Bah EI, Lamah MC, Fletcher T, Jacob ST, Brett-Major DM, Sall AA, et al. Clinical presentation of patients with Ebola virus disease in Conakry, Guinea. *N Engl J Med* 2015;372:40–7.
- [4] Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. *Lancet* 2020;395:1054–62.
- [5] Arentz M, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, et al. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington state. *JAMA* 2020. <https://doi.org/10.1001/jama.2020.4326>. [Epub ahead of print, Accessed March 19, 2020].
- [6] Graf CE, Pichard C, Herrmann FR, Sieber CC, Zekry D, Genton L. Prevalence of low muscle mass according to body mass index in older adults. *Nutrition* 2017;34:124–9.
- [7] Peng YD, Meng K, Guan HQ, Leng L, Zhu RR, Wang BY, et al. Clinical characteristics and outcomes of 112 cardiovascular disease patients infected by 2019-nCoV. *Zhonghua Xin Xue Guan Bing Za Zhi* 2020;48:E004.
- [8] Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with Coronavirus Disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med* 2020. <https://doi.org/10.1001/jamainternmed.2020.0994>. [Epub ahead of print, Accessed March 13, 2020].
- [9] National Health Commission of the People's Republic of China. Chinese management guideline for COVID-19 (version 7.0). Available at: <http://www.chinadaily.com.cn/specials/diagnosisandtreatment-Africa.pdf>. Accessed March 3, 2020.
- [10] Zhang L, Liu Y. Potential interventions for novel coronavirus in China: A systematic review. *J Med Virol* 2020;92:479–90.
- [11] Caccialanza R, Laviano A, Lobascio F, Montagna E, Bruno R, Ludovisi S, et al. Early nutritional supplementation in non-ICU patients hospitalized for the 2019 novel coronavirus disease (COVID-19): Rationale and feasibility of a shared empirical protocol. *Nutrition* 2020. <https://doi.org/10.1016/j.nut.2020.110835>. [Epub ahead of print, Accessed April 3, 2020].
- [12] Merker M, Felder M, Gueissaz L, Bolliger R, Tribollet P, Kägi-Braun N, et al. Association of baseline inflammation with effectiveness of nutritional support among patients with disease-related malnutrition. *JAMA Network Open* 2020;3:e200663.
- [13] Wang A, Zhao W, Xu Z, Gu J. Timely blood glucose management for the outbreak of 2019 novel coronavirus disease (COVID-19) is urgently needed. *Diabetes Res Clin Pract* 2020. <https://doi.org/10.1016/j.diabres.2020.108118>. [Epub ahead of print, Accessed March 13, 2020].
- [14] Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving Sepsis campaign: Guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). *Intensive Care Med* 2020. <https://doi.org/10.1007/s00134-020-06022-5>. [Epub ahead of print, Accessed March 28, 2020].
- [15] Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, et al. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr* 2019;38:48–79.
- [16] Pan L, Mu M, Yang P, Sun Y, Wang R, Yan J, et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: A descriptive, cross-sectional, multicenter study. *Am J Gastroenterol* 2020. https://journals.lww.com/ajg/Documents/COVID_Digestive_Symptoms_AJG_Preproof.pdf [Epub ahead of print, Accessed March 18, 2020].
- [17] Saez de la Fuente I, Saez de la Fuente J, Quintana Estelles MD, García Gígorro R, Terceros Almanza LJ, Sanchez Izquierdo JA, et al. Enteral nutrition in patients receiving mechanical ventilation in a prone position. *JPEN J Parenter Enteral Nutr* 2016;40:250–5.
- [18] Barazzoni R, Bischoff SC, Krznaric Z, Pirlich M, Singer P. ESPEN experts statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection. *Clin Nutr* 2020. <https://doi.org/10.1016/j.clnu.2020.03.022>. [Epub ahead of print, Accessed March 31, 2020].

Alessandro Laviano M.D.*

Department of Translational and Precision Medicine, Sapienza University, Rome, Italy

Angela Koverech M.D.

Department of Physiology and Pharmacology, "Vittorio Ersparmer", Sapienza University, Rome, Italy

Michela Zanetti M.D., Ph.D.

Internal Medicine Department, University of Trieste Hospital, Trieste, Italy

Chairwoman, SINPE, Italian Society of Artificial Nutrition and Metabolism, Italy

*Corresponding author. Tel.: +390649973902; fax: +39-064440806.

E-mail address: alessandro.laviano@uniroma1.it (A. Laviano).