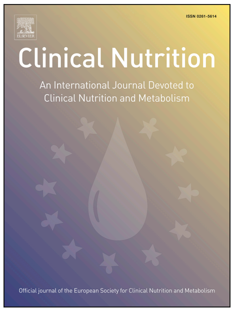

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Rocco Barazzoni, Stephan C. Bischoff, Zeljko Krznaric, Matthias Pirlich, Pierre Singer, endorsed by the ESPEN Council

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ESPEN EXPERT STATEMENTS AND PRACTICAL GUIDANCE FOR NUTRITIONAL MANAGEMENT OF INDIVIDUALS WITH SARS-CoV-2 INFECTION

Rocco Barazzoni[1*], Stephan C Bischoff[2*], Zeljko Krznaric[3], Matthias Pirlich[4], Pierre Singer[5]; endorsed by the ESPEN Council

[1]Department of Medical, Surgical and Health Sciences, University of Trieste, Italy

[2]Institute of Nutritional Medicine, University of Hohenheim, Stuttgart, Germany

[3]Department of Gastroenterology, Hepatology and Nutrition, University Hospital Centre Zagreb, University of Zagreb, Croatia

[4]Imperial Oak Outpatient Clinic, Endocrinology, Gastroenterology & Clinical Nutrition, Berlin, Germany

[5]Department of General Intensive Care and Institute for Nutrition Research, Rabin Medical Center, Beilinson Hospital, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

*contributed equally to the manuscript.

Corresponding author:
Prof. Rocco Barazzoni
Dept. of Medical Sciences – University of Trieste
Strada di Fiume, 447
34149 Trieste
Italy

Email: barazzon@units.it
Tel. +39 040 399 4416

ABSTRACT

The COVID-19 pandemics is posing unprecedented challenges and threats to patients and healthcare systems worldwide. Acute respiratory complications that require intensive care unit (ICU) management are a major cause of morbidity and mortality in COVID-19 patients. Patients with worst outcomes and higher mortality are reported to include immunocompromised subjects, namely older adults and polymorbid individuals and malnourished people in general. ICU stay, polymorbidity and older age are all commonly associated with high risk for malnutrition, representing per se a relevant risk factor for higher morbidity and mortality in chronic and acute disease. Also importantly, prolonged ICU stays are reported to be required for COVID-19 patients stabilization, and longer ICU stay may per se directly worsen or cause malnutrition, with severe loss of skeletal muscle mass and function which may lead to disability, poor quality of life and additional morbidity. Prevention, diagnosis and treatment of malnutrition should therefore be routinely included in the management of COVID-19 patients. In the current document, the European Society for Clinical Nutrition and Metabolism (ESPEN) aims at providing concise guidance for nutritional management of COVID-19 patients by proposing 10 practical recommendations. The practical guidance is focused to those in the ICU setting or in the presence of older age and polymorbidity, which are independently associated with malnutrition and its negative impact on patient survival.

INTRODUCTION

The breaking of a COVID-19 pandemic is posing unprecedented challenges and threats to patients and healthcare systems worldwide (1-5). The disease primarily involves the respiratory tract (1-5) but it may deteriorate to multi-organ failure and be fatal (3). Acute respiratory complications that are reported to require prolonged ICU stays are a major cause of morbidity and mortality in COVID-19 patients, and older adults and polymorbid individuals have worst outcomes and higher mortality (1-5). ICU stays, and particularly their longer duration, are per se well-documented causes of malnutrition, with loss of skeletal muscle mass and function which in turn may lead to poor quality of life, disability and morbidities long after ICU discharge (6). Many chronic diseases such as diabetes and cardiovascular diseases and their clustering in polymorbid individuals (7) as well as older age per se (8) are also very commonly associated with high risk and prevalence of malnutrition and worse outcomes. Causes of ICU- and disease-related malnutrition include reduced mobility, catabolic changes particularly in skeletal muscle as well as reduced food intake, all of which may be exacerbated in older adults (6-8). In addition, inflammation and sepsis development may further and primarily contribute to enhance all the above alterations in the presence of SARS-CoV-2 infections. Most importantly, appropriate nutritional assessment and treatment are well-documented to effectively reduce complications and improve relevant clinical outcomes under various conditions including ICU stays, hospitalization, several chronic diseases and in older adults (6-8).

Based on the above observations prevention, diagnosis and treatment of malnutrition should be considered in the management of COVID-19 patients to improve both short- and long-term prognosis. In the current document, the European Society for Clinical Nutrition and Metabolism

(ESPEN) aims at providing concise experts statements and practical guidance for nutritional management of COVID-19 patients, with regard to those in the ICU setting or in the presence of older age and polymorbidity, which are all independently associated with malnutrition and its negative impact on patient survival. The recommendations are based on current ESPEN guidelines and further expert advice. As there are no dedicated studies on nutrition management in COVID-19 infection, the following considerations can currently only be based on the best of knowledge and clinical experience.

PREVENTION AND TREATMENT OF MALNUTRITION IN INDIVIDUALS AT RISK OR INFECTED WITH SARS-COV-2

Statement 1

Patients at risk for poor outcomes and higher mortality following infection with SARS-COV-2, namely older adults and polymorbid individuals, should be checked for malnutrition through screening and assessment. The check should initially comprise the MUST criteria* or, for hospitalized patients, the NRS-2002 criteria.

****Must criteria: see https://www.bapen.org.uk/screening-and-must/must-calculator***

*****NRS-2002 criteria: https://www.mdcalc.com/nutrition-risk-screening-2002-nrs-2002***

Identification of risk and presence of malnutrition should be an early step in general assessment of all patients, with regard to more at-risk categories including older adults and individuals suffering from chronic and acute disease conditions. Since malnutrition is defined not only by low body mass but also by inability to preserve healthy body composition and skeletal muscle mass, persons with obesity should be screened and investigated according to the same criteria.

Sets of criteria such as MUST or NRS-2002 have been long used and validated in general clinical practice or in specific disease settings or conditions for malnutrition risk screening. For further assessment of positive patients various tools have been used and are accepted in clinical practice. These include but not limited to the Subjective Global Assessment criteria, the Mini Nutritional Assessment criteria validated for geriatric patients, the NUTRIC score criteria for ICU patients (8,9). A recent document globally endorsed by clinical nutrition Societies worldwide has introduced the GLIM (Global Leadership Initiative on Malnutrition) criteria for malnutrition diagnosis (10). GLIM proposed a two-step approach for the malnutrition diagnosis, i.e., first screening to identify "at risk" status by the use of validated screening tools such as MUST or NRS-2002, and second, assessment for diagnosis and grading the severity of malnutrition (Table 1). According to GLIM, diagnosis of malnutrition requires at least 1 phenotypic criterion and 1 etiologic criterion.

The above considerations appear to be fully applicable to patients at risk for severe SARS-CoV-2 infection or hospitalized for COVID-19 infection, since poor outcomes in COVID-19 are reported in patients that are most likely to present with malnutrition (such as older adults and comorbid individuals). Preserving nutritional status and preventing or treating malnutrition also importantly has the potential to reduce complications and negative outcomes in patients at nutritional risk who might incur in COVID-19 in the future. In particular, COVID-19 can be accompanied by nausea, vomiting and diarrhea impairing food intake and absorption (2), thus a good nutritional status is an advantage for people at risk for severe COVID-19. In a recent review about potential interventions for novel coronavirus based on the Chinese experience authors suggested that the nutritional status of each infected patient should be evaluated before the administration of general treatments (11).

Looking at influenza infections, particular predictors of mortality could be identified by multivariate analysis such as type of virus (OR 7.1), malnutrition (OR 25.0), hospital-acquired infection (OR 12.2), respiratory insufficiency (OR 125.8) and pulmonary infiltrate on X-ray (OR 6.0) were identified as predictors (12). It should be considered that also malnourished children are at increased risk for viral pneumonia and life-threatening outcome of infection. For example, it has been shown that pneumonia and malnutrition are highly predictive of mortality among children hospitalized with HIV infection (13).

Statement 2

Subjects with malnutrition should try to optimize their nutritional status, ideally by diet counseling from an experienced professionals (registered dieticians, experienced nutritional scientists, clinical nutritionists and specialized physicians).

Retrospective analysis of data available on the 1918 influenza pandemic revealed that disease severity depended on viral and host factors. Among the host factors associated with variations in influenza morbidity and mortality age, cellular and humoral immune responses, genetics and nutrition played a role (11). Malnutrition and famine were associated with high disease severity and was related to mortality also in the younger population. Undernutrition remains a problem for viral pandemics of the twenty-first century and beyond. Indeed, chronic malnutrition was thought to have contributed to the high morbidity and mortality seen in Guatemalan children during the 2009 influenza pandemic (12). In a future virus pandemic, we might face a “double burden” of malnutrition, when both undernutrition and overnutrition will promote severity of disease. It is now well accepted that obesity increases one’s risk of being hospitalized with, and dying from, an influenza virus infection, and that obesity inhibits both virus-specific CD8+ T cell responses and antibody responses to the seasonal influenza vaccine (11). The challenge for future virus pandemics is therefore not only to protect those affected by undernutrition, but also the growing number of people living with obesity (11). This is particularly important for the WHO European Region as in many European countries obesity and overweight affects 30-70% of the population. (14) In a recent Japanese study, malnutrition and pneumonia were identified as the prognostic factors in influenza infection, which are amenable to medical intervention. Using Cox proportional hazards modeling with prescribed independent variables, male sex, severity score, serum albumin levels, and pneumonia were associated with survival 30 days from the onset of influenza (13).

We provide suggestions based on various ESPEN Guidelines, with particular regard to those on polymorbid internal medicine patients (7) and those on geriatrics (8). We refer the reader to the full guidelines for specific recommendations in various specific conditions that could be encountered in association with COVID-19. The presence of at least two chronic diseases in the same individual can be defined as polymorbidity and is also characterized by high nutritional risk. Older adults are at higher risk due to combinations of higher prevalence of comorbidities, aging-associated changes in body composition with gradual loss of skeletal muscle mass and function (sarcopenia), additional factors including oral and chewing problems, psycho-social issues, cognitive impairment, low financial income. Obese individuals with chronic diseases and older age are at risk for reduced skeletal muscle mass and function and should therefore be fully included in the above recommendations. Dietary restrictions that may limit dietary intake should be avoided. For COVID-19 patients the counseling process could be performed using teleconference, telephone or other means when appropriate and possible, in order to minimize the risk of operator infection that could lead to infection of further patients and operators.

Energy needs can be assessed using indirect calorimetry if safely available with ensured sterility of the measurement system, or as alternatives by prediction equations or weight-based formulae such as:

(1) 27 kcal per kg body weight and day; total energy expenditure for polymorbid patients aged >65 years (recommendation 4.2 in ref. 7)

(2) 30 kcal per kg body weight and day; total energy expenditure for severely underweight polymorbid patients (recommendation 4.3. in ref. 7)*

(3) 30 kcal per kg body weight and day; guiding value for energy intake in older persons, this value should be individually adjusted with regard to nutritional status, physical activity level, disease status and tolerance (recommendation 1 in ref. 8)

*The target of 30 kcal/kg body weight in severely underweight patients should be cautiously and slowly achieved, as this is a population at high risk of refeeding syndrome.

Protein needs are usually estimated using formulae such as:

(1) 1 g protein per kg body weight and day in older persons; the amount should be individually adjusted with regard to nutritional status, physical activity level, disease status and tolerance (recommendation 2 in ref. 8).

(2) ≥ 1 g protein per kg body weight and day in polymorbid medical inpatients in order to prevent body weight loss, reduce the risk of complications and hospital readmission and improve functional outcome (Recommendation 5.1 in ref. 7).

Fat and carbohydrate needs are adapted to the energy needs while considering an energy ratio from fat and carbohydrates between 30:70 (subjects with no respiratory deficiency) to 50:50 (ventilated patients, see below) percent.

Statement 3

Subjects with malnutrition should ensure sufficient supplementation with vitamins and minerals.

Part of the general nutritional approach for viral infections prevention is supplementation and/or adequate provision of vitamins to potentially reduce disease negative impact (15).

As potential examples, vitamin D deficiency has been associated with a number of different viral diseases including influenza (16-19), human immunodeficiency virus (HIV) (20) and hepatitis C (21), while other studies questioned such a relation for influenza (22,23). The COVID-19 was first identified in Winter of 2019 and mostly affected middle-aged to older adults. Future investigations should confirm whether insufficient vitamin D status more specifically characterizes COVID-19 patients and is associated to their outcome. In support to this hypothesis, decreased vitamin D levels in calves have been reported to enhance risk for bovine coronavirus infection (24).

As another example, vitamin A has been defined as “anti-infective” vitamin since many of the body's defenses against infection depend on its adequate supply. For example, vitamin A deficiency is involved in measles and diarrhea and measles can become severe in vitamin A-deficient children. In addition, it has been reported that vitamin A supplementation reduced morbidity and mortality in different infectious diseases, such as measles, diarrheal disease, measles-related pneumonia, HIV infection, and malaria. Vitamin A supplementation also may offer some protection against the complications of other life-threatening infections, including malaria, infectious lung diseases, and HIV. In experimental models, the effect of infection with infectious bronchitis virus (IBV), a kind of coronaviruses, was more pronounced in chickens fed a diet marginally deficient in vitamin A than in those fed a diet adequate in vitamin A (25).

In general, low levels or intakes of micronutrients such as vitamins A, E, B6 and B12, Zn and Se have been associated with adverse clinical outcomes during viral infections (26). This notion has been confirmed in a recent review from Lei Zhang and Yunhui Liu (15) who proposed that besides vitamins A and D also B vitamins, vitamin C, omega-3 polyunsaturated fatty acids, as well as selenium, zinc and iron should be considered in the assessment of micronutrients in COVID-19 patients.

While it is important to prevent and treat micronutrient deficiencies, there is no established evidence that routine, empirical use of supraphysiologic or supratherapeutic amount of micronutrients may prevent or improve clinical outcomes of COVID-19. Based on the above combined considerations, we suggest that provision of daily allowances for vitamins and trace elements be ensured to malnourished patients at risk for or with COVID-19, aimed at maximizing general anti-infection nutritional defense.

Statement 4

Patients in quarantine should continue regular physical activity while taking precautions.

Reducing infectious risk is achieved best by quarantine at home, which is heavily recommended presently for all people at risk of COVID-19 and also for those infected with a rather moderate disease course. However, prolonged home stay may lead to increased sedentary behaviors, such as spending excessive amounts of time sitting, reclining, or lying down for screening activities (playing games, watching television, using mobile devices); reducing regular physical activity and hence lower energy expenditure. Thus quarantine can lead to an increased risk for and potential worsening of chronic health conditions, weight gain, loss of skeletal muscle mass and strength and possibly also loss of immune competence since several studies have reported positive impact of aerobic exercise activities on immune function. In a recent paper. Chen et al (27) conclude: "… there is a strong rationale for continuing physical activity at home to stay healthy and maintain immune system function in the current precarious environment. Exercise at home using various safe, simple, and easily implementable exercises is well suited to avoid the airborne coronavirus and maintain fitness levels. Such forms of exercise may include, but are not limited to, strengthening exercises, activities for balance and control, stretching exercises, or a combination of these. Examples of home exercises include walking in the house and to the store as necessary, lifting and carrying groceries, alternating leg lunges, stair climbing, stand-to-sit and sit-to-stand using a chair and from the floor, chair squats, and sit-ups and pushups. In addition, traditional Tai Ji Quan, Qigong exercises, and yoga should be considered since they require no equipment, little space, and can be practiced at any time. The use of eHealth and exercise videos, which focuses on encouraging and delivering physical activity through the Internet, mobile technologies, and television are other viable avenues for maintaining physical function and mental health during this critical period." Under particular precautions, even outdoor activities can be considered such as garden work (if a own garden is present), garden exercise (i.e. badminton), or walking/running in the forest (alone or in small family groups while maintaining a distance of 2 m minimum to others). Every day > 30 min or every second day > 1h exercise is recommended to maintain fitness, mental health, muscle mass and thus energy expenditure and body composition.

Statement 5

Oral nutritional supplements (ONS) should be used whenever possible to meet patient's needs, when dietary counseling and food fortification are not sufficient to increase dietary intake and reach nutritional goals, ONS shall provide at least 400 kcal/day including 30 g or more of protein/day and shall be continued for at least one month. Efficacy and expected benefit of ONS shall be assessed once a month.

We suggest that general guidance on prevention and treatment of malnutrition by using ONS is fully applicable to the context of COVID-19 infection (see also recommendations 2.1-2.3 in ref. 7 and recommendations 23, 26 and 27 in ref. 8). Individuals infected with SARS-Cov2 outside of the ICU should therefore be treated to prevent or improve malnutrition. The oral route is always preferred when practicable. We refer to individual guidelines for optimization of calorie targets. Nutritional treatment should start early during hospitalization (within 24-48 hours). Especially for older and polymorbid patients whose nutritional conditions may be already compromised, nutritional treatment and targets should be met gradually to prevent refeeding syndrome. ONS provide energy-dense alternatives to regular meals and may be specifically enriched to meet targets in terms of protein as well as micronutrients (vitamins and trace elements) whose daily estimated requirements should be regularly provided. When compliance is questioned, more frequent evaluation of treatment and potential indication to modify ONS could be needed (e.g. weekly). Nutritional treatment should continue after hospital discharge with ONS and individualized nutritional plans; this is particularly important since pre-existing nutritional risk factors continue to apply and acute disease and hospitalization are likely to worsen the risk or condition of malnutrition.

Statement 6

In polymorbid medical inpatients and in older persons with reasonable prognosis, whose nutritional requirements cannot be met orally, enteral nutrition (EN) should be administered. Parenteral nutrition (PN) should be considered when EN is not indicated or unable to reach targets.

Enteral nutrition should be implemented when nutritional needs cannot be met by the oral route, e.g if oral intake is expected to be impossible for more than three days or expected to be below half of energy requirements for more than one week. In these cases, the use of EN may be superior to PN, because of a lower risk of infectious and non-infectious complications (see also recommendation 3.1 in ref. 7 and recommendation 29 in ref. 8). Monitoring for EN potential complications should be performed. There are no limitations to the use of enteral or parenteral nutrition based on patient age or diagnosis, in the presence of expectable benefit to improve nutritional status.

NUTRITIONAL MANAGEMENT IN ICU PATIENTS INFECTED WITH SARS-COV-2

We provide here recommendations based on the recent ESPEN guidelines on nutritional therapy in the ICU (6) and on the respiratory therapy stages guided by the patient's condition (4). The nutritional consideration should consider the respiratory support allocated to the ICU patient as shown in Table 2.

Pre intubation period

Statement 7

In COVID-19 non-intubated ICU patients not reaching the energy target with an oral diet, oral nutritional supplements (ONS) should be considered first and then enteral nutrition treatment. If there are limitations for the enteral route it could be advised to prescribe peripheral parenteral nutrition in the population not reaching energy-protein target by oral or enteral nutrition.

NIV: In general, only a minority (25-45%) of patients admitted in the ICU for monitoring, NIV and post extubation observation are reported to be prescribed with oral nutrition as shown in the Nutrition Day ICU survey (28). Reeves et al. (29) also reported energy-protein intake in ARDS patients treated with NIV to be inadequate. It should be pointed out that airway complications may occur with longer median non-invasive ventilation duration in NIV patients treated with enteral feeding (30). The recommendation to start enteral feeding could be impaired by the fact that placement of nasal gastric tube (NGT) for nutrition may result in 1) air leakage that may compromise the effectiveness of NIV; 2) stomach dilatation that may affect diaphragmatic function and affect NIV effectiveness (31). The above observations may account at least in part for highly inadequate implementation of enteral nutrition which may result in patient starvation especially in the first 48 hours of ICU stay and higher risk of malnutrition and related complications (32). Peripheral parenteral nutrition may be therefore considered under these conditions.

FNC and HFNC: Patients oxygenated through nasal cannula may be commonly deemed medically appropriate to resume oral alimentation (33). Few studies described the implementation of nutritional support when this technique is used. However limited evidence indicates that calorie and protein intake may remain low and inadequate to prevent or treat malnutrition in HFNC patients (34, and own unpublished data). Overlooking administration of adequate calorie-protein may result in worsening of nutritional status with malnutrition and related complications. Adequate assessment of nutrient intake is recommended with treatment with oral nutrition supplements or with enteral nutrition if oral route is insufficient.

Ventilated period

When HFNC or NIV have been applied for more than two hours without successful oxygenation, it is recommended to intubate and ventilate the patient. The ESPEN recommendations (6) are fully applicable with the same goal to prevent deterioration of nutritional status and malnutrition with related complications. In agreement with the ESPEN guidelines on nutrition in ICU (6), we summarize suggestions for COVID-19 intubated and ventilated patients as follows:

Statement 8

In COVID-19 intubated and ventilated ICU patients enteral nutrition (EN) should be started through a nasogastric tube; post-pyloric feeding should be performed in patients with gastric

intolerance after prokinetic treatment or in patients at high-risk for aspiration; the prone position per se does not represent a limitation or contraindication for EN.

Energy requirements: Patient energy expenditure (EE) should be determined to evaluate energy needs by using indirect calorimetry when available. Isocaloric nutrition rather than hypocaloric nutrition can then be progressively implemented after the early phase of acute illness. If calorimetry is not available, VO_2 (oxygen consumption) from pulmonary arterial catheter or VCO_2 (carbon dioxide production) derived from the ventilator will give a better evaluation on EE than predictive equations.

Energy administration: hypocaloric nutrition (not exceeding 70% of EE) should be administered in the early phase of acute illness with increments up to 80-100% after DAY 3. If predictive equations are used to estimate the energy need, hypocaloric nutrition (below 70% estimated needs) should be preferred over isocaloric nutrition for the first week of ICU stay due to reports of overestimation of energy needs

Protein requirements: During critical illness, 1.3 g/kg protein equivalents per day can be delivered progressively. This target has been shown to improve survival mainly in frail patients. For persons with obesity, in the absence of body composition measurements 1.3 g/kg “adjusted body weight” protein equivalents per day is recommended. Adjusted body weight is calculated as ideal body weight + (actual body weight - ideal body weight) * 0.33 (6). Considering the importance of preserving skeletal muscle mass and function and the highly catabolic conditions related to disease and ICU stay, additional strategies may be considered to enhance skeletal muscle anabolism. In particular, controlled physical activity and mobilization may improve the beneficial effects of nutritional therapy.

Statement 9

In ICU patients who do not tolerate full dose enteral nutrition (EN) during the first week in the ICU, initiating parenteral nutrition (PN) should be weighed on a case-by-case basis. PN should not be started until all strategies to maximize EN tolerance have been attempted.

Limitations and precautions: Progression to full nutrition coverage should be performed cautiously in patients requiring mechanical ventilation and stabilization.

- *Contraindications*: EN should be delayed:

- in the presence of uncontrolled shock and unmet hemodynamic and tissue perfusion goals;
- in case of uncontrolled life-threatening hypoxemia, hypercapnia or acidosis,

- *Precautions during the early stabilization period*: low dose EN can be started:

- as soon as shock is controlled with fluids and vasopressors OR inotropes, while remaining vigilant for signs of bowel ischemia;
- in patients with stable hypoxemia, and compensated or permissive hypercapnia and acidosis;

General comments: When patients are stabilized and even in prone position, enteral feeding can be started ideally after measuring indirect calorimetry targeting energy supply to 30% of the measured energy expenditure. Energy administration will be increased progressively. During emergency times, the predictive equation recommending 20 kcal/kg/day could be used and energy increased to 50-70% of the predictive energy at day 2 to reach 80-100% at day 4.

The protein target of 1.3 g/kg/day should also be reached by day 3-5. Gastric tube is preferred but in case of large gastric residual volume (above 500 mL), duodenal tube should be inserted quickly. The use of enteral omega-3 fatty acids may improve oxygenation but strong evidence is missing. If intolerance to enteral nutrition is present, parenteral nutrition should be considered. Blood glucose should be maintained at target levels between 6-8 mmol/l, along with monitoring of blood triglycerides and electrolytes including phosphate, potassium and magnesium (6).

Post-mechanical ventilation period and dysphagia

Patients no longer needing mechanical ventilation have high incidence of swallowing problems and consequent dysphagia which may strongly limit oral nutrient intake, even at a time of general improvement of clinical conditions. The following considerations therefore can be applied also to the COVID-19 patient population after extubation.

Statement 10

In ICU patients with dysphagia, texture-adapted food can be considered after extubation. If swallowing is proven unsafe, EN should be administered. In cases with a very high aspiration risk, postpyloric EN or, if not possible, temporary PN during swallowing training with removed nasoenteral tube can be performed.

The post-extubation swallowing disorder could be prolonged for to up to 21 days mainly in the elderly and after prolonged intubation (35, 36), which makes this complication particularly relevant for COVID-19 patients. As much as 24% of older patients were reported to be feeding tube-dependent three weeks after extubation (37). The presence of severe post extubation dysphagia was associated with severe outcome including pneumonia, reintubation and hospital mortality. Recently, 29% of 446 ICU patients had prolonged postextubation swallowing disorder at discharge and some postextubation swallowing disorder has been shown 4 months after discharge (38). Authors have recommended referring patients recognized to have swallowing issues for swallowing evaluation, in order to prevent oral nutrition complications (39, 40). Considering tracheostomy, most of the patients may be able to return to oral intake after this procedure although prolonged tracheal cannula may delay the start of adequate oral nutrient intake (41). Supplemental PN has not been extensively studied in this population but could be considered if energy protein targets are not reached.

ICU-acquired weakness (ICUAW)

The long-term prognosis of patients surviving intensive care is affected by physical, cognition and mental impairment that occur following ICU stay (42). Loss of skeletal muscle mass and muscle function may be tremendous and a major problem in ICU survivors (43). This may particularly apply to older adults and comorbid patients that are more prone to present with pre-existing catabolic conditions and impaired skeletal muscle mass and function; in addition, these patient groups may be more presumably prone to develop more intense catabolic responses due to COVID-19 and to ICU conditions at large. Prolonged reported duration of ICU stay above two weeks for many COVID-19 patients is likely to further enhance muscle-catabolic conditions. Appropriate energy delivery avoiding overfeeding and adequate protein administration are critical to prevent this severe loss of muscle mass and function (see Statement 2 and related commentary). Although definitive guidance cannot be made on additional specific treatments potentially due to lack of high-quality studies, recent evidence seems to indicate potential positive impact of physical activity with supplemental amino acids or their metabolites (44,45).

Final considerations

Nutrition intervention and therapy needs to be considered as an integral part of the approach to patients victim of SARS-CoV-2 infection in the ICU setting, internal medicine ward setting as well as in general healthcare. Ten recommendations are proposed to manage nutritional care in COVID-19 patients (Figure 1). At each step of the treatment, nutritional therapy should be part of patient care, with regard for older adult, frail and comorbid individuals. Optimal outcome can be improved implementing adherence to recommendations to ensure survival of this life-threatening disease as well as better and shorter recovery, particularly but not limited to the post-ICU period. A comprehensive approach associating nutrition to life-support measures has potential to improve outcomes particularly in the recovery phase.

While healthcare workers are busy providing personal protective equipment (PPE) for their staff and training on how to use them or increasing the number of ventilators, it is also important to train them on how to address the nutritional aspects of these patients. We suggest stakeholders such as WHO, Ministry of Health, Nutritionists, Public Health experts develop a mechanism to share this knowledge with relevant healthcare workers. Also hospital procurement officers and others could consider these nutritional requirements as essential needs in resource allocation process. Patients with malnutrition are more likely to be from lower socio-economic groups and addressing malnutrition is an essential step in leaving no one behind in this fight against the COVID 10 pandemic.

Conflict of interests

The authors declare that they have no competing interests for the content of this paper.

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Table 1. Phenotypic and etiologic criteria for the diagnosis of malnutrition, adapted from (9).

Phenotypic Criteria		**Etiologic Criteria**	
Weight loss (%)	>5% within past 6 months or >10% beyond 6 months	Reduced food intake or assimilation**	50% of ER > 1 week, or any reduction for >2 weeks, or any chronic GI condition that adversely impacts food assimilation or absorption
Low body mass index (kg/m2)	<20 if < 70 years, or <22 if >70 years Asia: <18.5 if < 70 years, or <20 if >70 years	Inflammation***	Acute disease/injuryd, or chronic disease-related
Reduced muscle mass	Reduced by validated body composition measuring techniques*		

Abbreviations: GI, gastro-intestinal; ER, energy requirements.

*Muscle mass can be assessed best by dual-energy absorptiometry (DXA), bioelectrical impedance analysis (BIA), CT or MRI. Alternatively, standard anthropometric measures like mid-arm muscle or calf circumferences may be used (see https://nutritionalassessment.mumc.nl/en/anthropometry). Thresholds for reduced muscle mass need to be adapted to race (Asia). Functional assessments like hand-grip strength may be considered as a supportive measure.

**Consider gastrointestinal symptoms as supportive indicators that can impair food intake or absorption e.g. dysphagia, nausea, vomiting, diarrhea, constipation or abdominal pain. Reduced assimilation of food/nutrients is associated with malabsorptive disorders like short bowel syndrome, pancreatic insufficiency and after bariatric surgery. It is also associated with disorders like esophageal strictures, gastroparesis, and intestinal pseudo-obstruction.

***Acute disease/injury-related: Severe inflammation is likely to be associated with major infection, burns, trauma or closed head injury. Chronic disease-related: Chronic or recurrent mild to moderate inflammation is likely to be associated with malignant disease, chronic obstructive pulmonary disease, congestive heart failure, chronic renal disease or any disease with chronic or recurrent Inflammation. Note that transient inflammation of a mild degree does not meet the threshold for this etiologic criterion. C-reactive protein may be used as a supportive laboratory measure.

617 **Table 2.** Nutritional support depending on the respiratory support allocated to the ICU patient.

Setting	**Ward**	**ICU** **Day 1-2**	**ICU** **Day 2-**	**Ward** **rehabilitation**
Oxygen Therapy and mechanical ventilation	No or consider O2 support (High) Flow Nasal Cannula	FNC followed by mechanical ventilation	Mechanical ventilation	Possible extubation and transfer to ward
Organ Failure	Bilateral pneumonia, thrombopenia	Deterioration of respiratory status; ARDS; possible shock	MOF possible	Progressive recovery after extubation
Nutritional support	**Screening for malnutrition; oral feeding/ONS, enteral or parenteral nutrition if needed**	**Define energy and protein target** **In case of FNC or NIV, administer energy/protein orally or enterally and if not possible**	**Prefer early enteral feeding** **Protein and mobilization**	**Assess dysphagia and use oral nutrition if possible; if not: enteral or parenteral nutrition** **Increase protein intake and add**

		parenterally		**exercise**

According to the progression of the infection, a medical nutritional therapy is proposed in association with the respiratory support in the intensive care setting. Abbreviations: ICU, intensive care unit; FNC, flow nasal cannula; MV, mechanical ventilation; ARDS, acute respiratory distress syndrome; MOF, multiorgan failure; ONS, oral nutritional supplement.

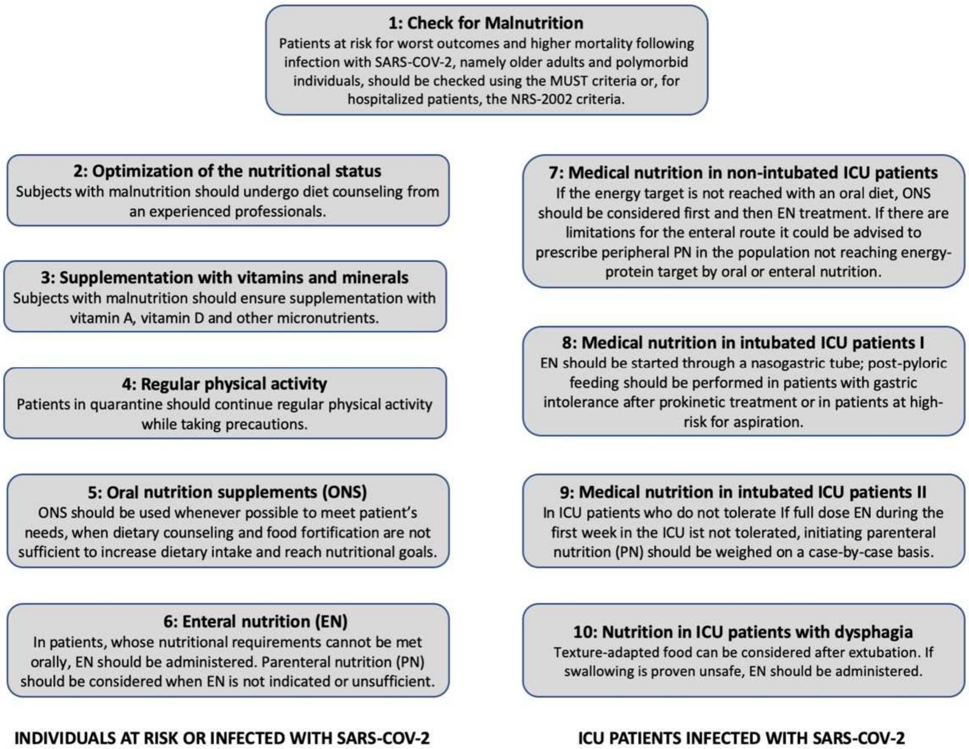

Figure 1. Nutritional management in in individuals at risk for severe COVID-19, in subjects suffering from COVID-19, and in COVID-19 ICU patients requiring ventilation. For details, see text.