Immunonutrition in perioperative care of COVID-19 patients: an old weapon for a new disease?

Dear Editor,

Coronavirus infection disease-2019 (COVID-19) triggers a massive immune response in certain hosts.[1] This reaction, when not adequately counterbalanced by anti-inflammatory molecules, leads to an inflammatory state that resembles the so-called systemic inflammatory response syndrome (SIRS). Involving the abnormal regulation of numerous inflammatory cytokines, this condition leads to the loss of lean mass through the breakdown of proteins, lipolysis, and an increase in oxidative stress. These factors may also impair the patient's potential to recover from surgery or chronic critical illness, increasing the COVID-19 mortality rate.[2]

During the pandemic, a proportion of COVID-19 patients have had to undergo scheduled or urgent surgery, and evidence has demonstrated these patients to be more inflamed and procoagulant. As a consequence, mortality risk is increased since they present a higher risk of developing thrombotic and postoperative respiratory complications compared with COVID-19 negative patients. In some cases, postoperative respiratory complications have resulted in symptoms of acute respiratory failure very similar to those of acute respiratory distress syndrome (ARDS), thus requiring prolonged mechanical ventilation and ICU stay.[3]

An intriguing, but as yet unanswered, question regards whether immunonutrition could constitute an adjunctive tool in the perioperative care of COVID-19 patients. Defined as the administration of nutrients able to modulate the immune system, immunonutrition has previously been demonstrated to improve clinical outcome in many scheduled oncological surgical settings. Immunonutrition includes the administration of short-chain fatty acids, ω-3 polyunsaturated fatty acids, arginine, glutamine, and nucleotides. The primary aim of immunonutrition is to improve gut function after surgery, control the systemic inflammatory response, and enhance the removal of bacteria by the innate immune response, thus avoiding postoperative infections.

A recent meta-analysis of immunonutrition versus standard nutrition for cancer patients demonstrated its efficacy in reducing postoperative infection complications, lowering the risk of anastomotic leakage and shortening the length of hospital stay.[4]

In COVID-19 patients, given their enhanced state of inflammation, ω-3 polyunsaturated fatty acids probably represent the most important component of immunonutrition: these nutrients have been demonstrated to reduce the secretion of proinflammatory cytokines by macrophages, modulate neutrophil function, and stabilize cytokines and reactive oxygen species.[5]

For this reason, we suggest immunonutrition to be started as soon as possible in cases of COVID-19 because, in addition to being malnourished, these patients present a severe negative nitrogen balance and a deregulated immune system. Although immunonutrition is usually started preoperatively in scheduled surgery, during the ongoing COVID-19 pandemic, most surgical interventions have been urgent procedures, making it difficult to initiate immunonutrition adequately in advance of surgery (an ideal time frame would be seven days).

Whenever possible, immunonutrition should be administered through the enteric route, favouring *per os* if the patient is able to swallow, or via the nasogastric route if not. There are few contraindications to the enteric route (namely, bowel obstruction, bowel ischemia, and gastrointestinal bleeding): in such cases, the parenteral route must be considered as early as possible.

In summary, considering that no adverse outcomes of immunonutrition have been reported in either the surgical or postoperative ICU setting, this adjunctive tool should not be discarded *a priori*, but instead considered and immediately applied in the perioperative care of COVID-19 patients.

Although this ''old'' therapy is not expected to provide any definitive solutions whilst new ''weapons'' are being sought, it is certainly worth a shot, in the hope that it may just tip the balance in the patients favour!

Conflicts of interest

The author declares no conflicts of interest.

References

1. Chen Y, Liu Q, Guo D. Emerging coronaviruses: Genome structure, replication, and pathogenesis. J Med Virol. 2020;92:418–23.
2. Phua J, Weng L, Ling L, et al. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. Lancet Respir Med. 2020;8:506–17.
3. Doglietto F, Vezzoli M, Gheza F, et al. Factors Associated With Surgical Mortality and Complications Among Patients With and Without Coronavirus Disease 2019 (COVID-19) in Italy. JAMA Surg. 2020;155:1–14.
4. Yu K, Zheng X, Wang G, et al. Immunonutrition vs Standard Nutrition for Cancer Patients: A Systematic Review and Meta-Analysis (Part 1). JPEN J Parenter Enteral Nutr. 2020;44:742–67.
5. Gritsenko K, Helander E, Webb MPK, et al. Preoperative frailty assessment combined with prehabilitation and nutrition strategies: Emerging concepts and clinical outcomes. Best Pract Res Clin Anaesthesiol. 2020;34:199–212.

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