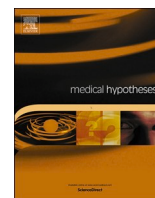




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## Letter to Editors

## Nutrition acquisition by human immunity, transient overnutrition and the cytokine storm in severe cases of COVID-19



## ARTICLE INFO

## Keywords

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## ABSTRACT

The human immunity has a pivotal role in nutrition acquisition from the pathogens and damaged body tissue during the SARS-CoV-2 virus infection, which may lead to transient overnutrition in the patients, lead to lipotoxicity and further damage in non-adipose tissues, and cause hyperinflammation and cytokine storm in severe cases of COVID-19. In view of this, high-quality clinical trials on restrictive eating should be designed to investigate the possible benefits of food intake restriction on patients' recovery from COVID-19 disease.

## Dear Editor,

We are greatly interested in the articles by Lidoriki et al. [1] and Recinella et al. [2] in which the authors suggested that nutrition status plays an important role in the progression of COVID-19 disease.

Based on their work, we would like to hypothesize that human immunity has a pivotal role in nutrition acquisition from the pathogens and damaged body tissues during the SARS-CoV-2 virus infection, which may lead to transient overnutrition, lipotoxicity and further tissue damage in overweight patients or patients with metabolic syndromes. Those patients are thus predisposed to escalated inflammation and susceptible to cytokine storm in severe cases of COVID-19.

The interactions between nutrition, microorganism infection and immunity are very complex. On the one hand, adequate nutrition and a symbiotic microbiome ensure proper function of the immune system during infection [3]; on the other hand, the human immune system also plays an important role in acquiring essential nutrients from living microbial cells during the elimination of the symbiotic microbiome and infectious pathogens [4,5]. During an infection, xenophagy as the specific type of autophagy mediating intracellular pathogen eradication [6], together with other immunological proteolytic/lipolytic processes, degrades symbiotic microbiome, pathogens, and damaged human body tissues, and turn them into nutrients. This nutrition acquisition pathway may cause transient overnutrition, lead to lipotoxicity [7], tissue damage, hyperinflammation and cytokine storm [5].

Inflammation is the physiological response of the immune system to tissue damage [8]. It is a protective reaction by the organism to remove the injurious stimuli, and remove the damaged tissue as well as initiate the healing process for the tissue [8]. Yet, during acute infection, nutrition excess will prevent the tissue healing process from happening. This is because, if the nutrition from the degradation of pathogens and the damaged body tissues exceeds the nutrition needs for tissue repair, the excessive nutrition will be mostly turned into lipid intermediates and deposited in new non-adipose tissue, causing lipotoxicity [7] in healthy non-adipose tissues and inducing further tissue damage. The breakdown of newly damaged non-adipose tissues and the formation of lipid

intermediates result in a vicious cycle. Thus, the overnutrition situation is worsened by the loss of lean body mass, coupled with escalation of inflammation, and eventually lead to cytokine storm in the severe cases of COVID-19.

Clinically, early parenteral nutrition (PN) alone or PN in combination with enteral feedings are strongly discouraged in critically ill patients, and only initiative early enteral nutrition (EEN) is recommended for patients who can be fed enterally [9]. EEN can be beneficial due to its trophic effect on gut mucosa [10] to avoid gut mucosa atrophy and bacteria translocation [11], while aggressive nutritional support may be detrimental [10] due to the transient over-nutrition discussed above. In the future, high-quality clinical trials on restrictive eating [5] in which only very small amount of enteral nutrition will be provided to support the gut mucosa, and maintain serum fasting to dissipate the transient over-nutrition during SARS-CoV-2 viral infection should be designed to investigate the possible benefits of restrictive eating to COVID-19 recovery.

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## Consent statement/Ethical approval

Not required.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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