Possible role of intermittent fasting against SARS-CoV-2 infection: Crosstalk among calorie restriction, autophagy and immune response

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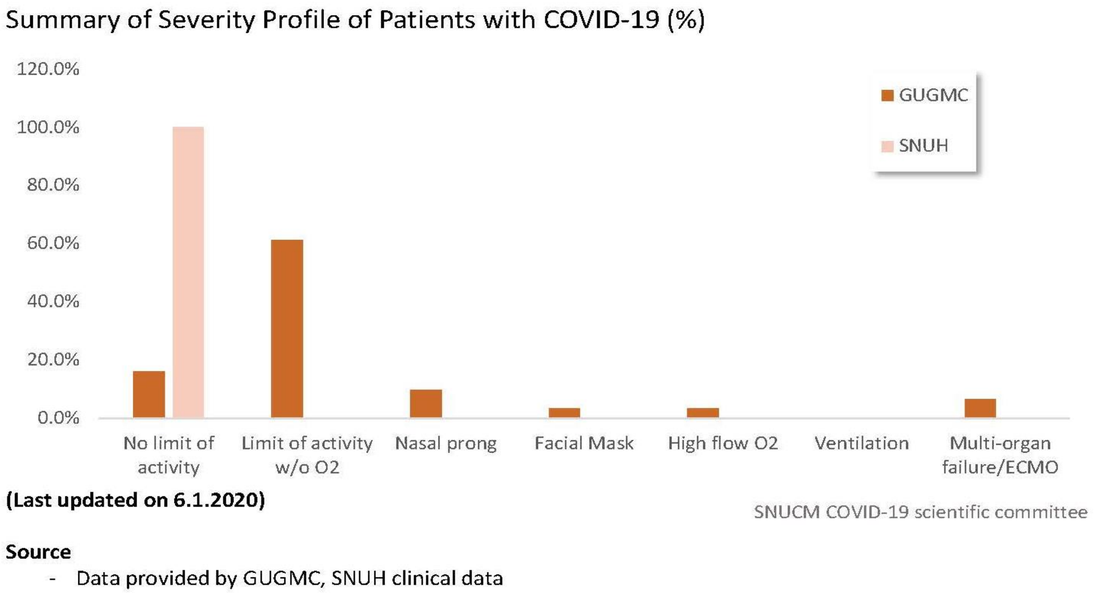
Abstract

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the causative pathogen of deadly Coronavirus disease-19 (COVID-19) pandemic, which emerged as a major threat to public health across the world. Although there is no clear gender or socioeconomic discrimination in the incidence of COVID-19, individuals who are older adults and/or with comorbidities and compromised immunity have a relatively higher risk of contracting this disease. Since no specific drug has yet been discovered, strengthening immunity along with maintaining a healthy living is the best way to survive this disease. As a healthy practice, calorie restriction in the form of intermittent fasting (IF) in several clinical settings has been reported to promote several health benefits, including priming of the immune response. This dietary restriction also activates autophagy, a cell surveillance system that boosts up immunity. With these prevailing significance in priming host defense, IF could be a potential strategy amid this outbreak to fighting off SARS-CoV-2 infection. Currently, no review so far available proposing IF as an encouraging strategy in the prevention of COVID-19. A comprehensive review has therefore been planned to highlight the beneficial role of fasting in immunity and autophagy, that underlie the possible defense against SARS-CoV-2 infection. The COVID-19 pathogenesis and its impact on host immune response have also been briefly outlined. This review aimed at revisiting the immunomodulatory potential of IF that may constitute a promising preventive approach against COVID-19.

Introduction

Severity of SARS-CoV-2 infection

- Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the causative pathogen of deadly Coronavirus disease-19 (COVID-19) pandemic, which emerged as a major threat to public health across the world.
- As newly emerged, no suitable therapy against COVID-19 has yet been discovered, nor even a clear concept about the pathogenesis of this disease.

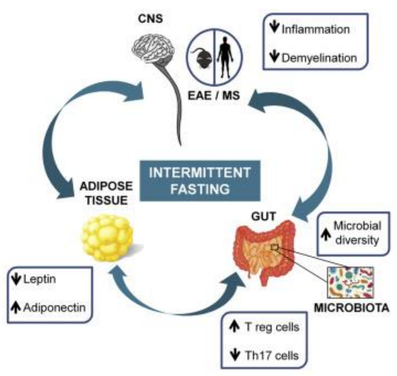


Interplay among immune system, autophagy, and SARS-CoV-2 infection

- The immune system plays a critical role in fighting off SARS-CoV-2 infection [1]
- Autophagy is a cellular protective housekeeping mechanism to eliminate damaged organelles, misfolded proteins and pathogens. Induction of autphagy can potentially promote the immune system [2].
- Modulation of autophagy is a potential therapeutic target for a diverse range of diseases.
- Targeting the immune system as well as the cellular processes (here, autophagy) that regulate immunity could offer a strategic tool against SARS-CoV-2 infection.

Role of fasting on autophagy, and immune response

- Among several stress stimuli inducers, fasting and calorie restriction are the most potent non-genetic autophagy stimulators.
- Fasting, a willful abstaining from eating for a certain period of time, is observed as a religious ritual that has known to have a myriad of health benefits, including boosting up immunity, resistance to stress, slowing down aging process, and increasing longevity without noticeable side effects.
- Fasting also has shown to activate autophagy, which in turn promotes immunity
- As the COVID-19 lacks a specific therapy, preventive measures that can prime host defense could help contain this disease.



Potential immunomodulatory effects of fasting [3]

Aim of the study

- Considering the regulatory roles of fasting on autophagy and immunity, we anticipate that fasting may become a possible preventive strategy against COVID-19.
- In this review, we revisit the current knowledge of fasting as a possible important mediator that is involved in the diverse pathophysiological phenomena, including host immune response, autophagy, and the pathogenesis of SARS-CoV-2 infection.

Methodology

A literature search was conducted using PubMed, Scopus, and Google that includes all original research articles written in English on beneficial effects of honey against various pathophysiological conditions. Searching was conducted before April 2020 using various keywords including SARS-COV-2, Fasting, Autophagy, Cytokine storm, Immune responses, COVID-19 and so on. Figures were generated using BioRender.com, an online software.

Literature interpretation

Autophagy and immune responses

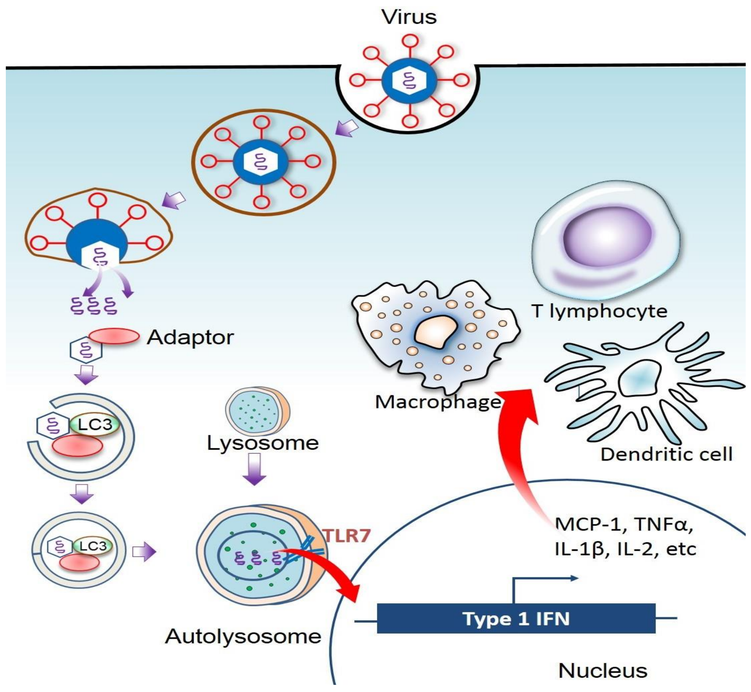


Fig. 1. Autophagy-dependent innate immune response. Autophagy may induce innate immunity by delivering viral nucleic acids to endosomes containing Toll-like receptor 7 (TLR7), which stimulates the production of type 1 interferons (IFN) that, in turn, attract immune cells to the site of infection.

Fasting and autophagy

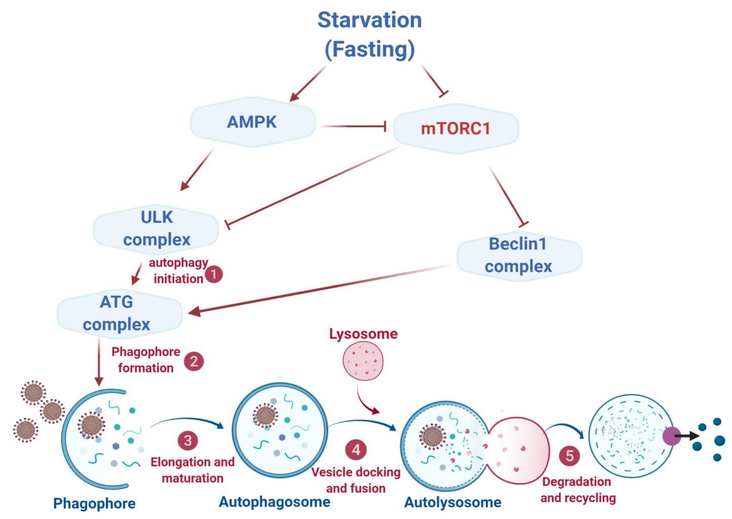


Fig. 2. Fasting mediates autophagy. Autophagy receives fasting signals through two metabolic sensors such as mTOR and AMPK. Under the condition of nutrient depletion, mTOR detaches from the ULK1 complex leading to the activation of autophagy. Whereas, AMPK negatively regulates mTOR, and also directly activates ULK1 complex, thereby acting as a positive regulator of autophagy in response to nutrient depletion. Beclin1 complex is another autophagy activator that is negatively regulated by mTOR. Once autophagy is initiated, cytoplasmic elements (cargo) to be recycled are engulfed into double-membrane vesicles, termed as autophagosomes, which fuse with lysosomes forming autolysosomes, where cargos are degraded. Autophagy is a multistep process which are regulated by ATGs. mTOR, AMPK.

Prospects of fasting-mediated autophagy and immune response against COVID-19

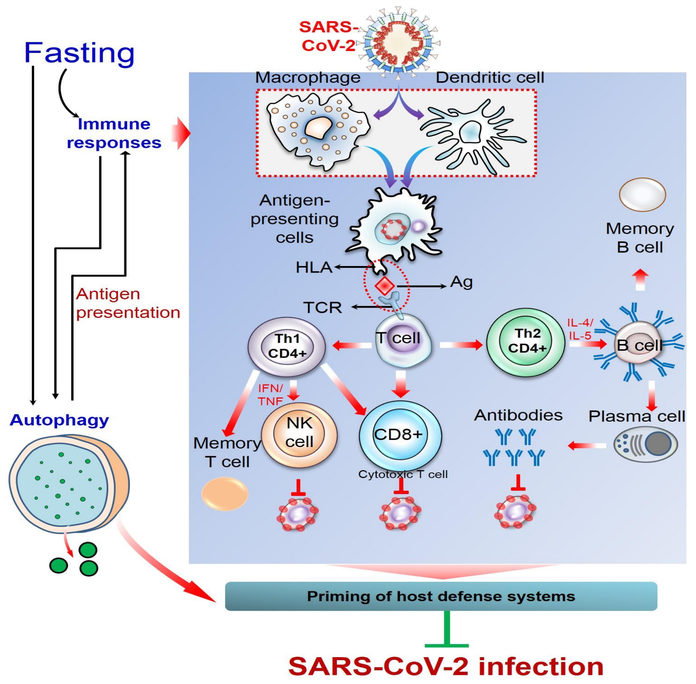


Fig. 3. Fasting as an intervention tool against SARS-CoV-2 infection. Fasting can prime the host defense system through activating multiple physiological processes, including immune responses and autophagy. In case of immune responses, the pulmonary alveolar epithelial cells that are infected with SARS-CoV-2 release pro-inflammatory cytokines and chemokines. These mediators attract inflammatory cells, including macrophages, monocytes, and T cells to the site of infection, promoting further inflammation. In protective immune response, the antigen-presenting cells (macrophages and dendritic cells) present viral antigens to T cells which stimulate both cell-mediated and humoral immunity. CD8+ T cells kill virus-infected cells. Of the two subsets of CD4+, Th1 cells either activate natural killer cells or CD8+ T cells or may remain as memory T cells. Whereas, upon stimulation from CD4+ Th2 cells, B cells are converted into plasma B cells which generate SARS-CoV-2-specific antibodies that neutralize viruses. Another fasting-mediated cellular process is autophagy that either degrades viral particles (xenophagy) or activates innate and adaptive immunity.

Conclusion

- Since the symptoms of COVID-19 are more severe in those who are already suffering from various diseases and deficient in immunocompetence, the possible preventive measures are to control prevailing diseases and to boost up defense systems.
- As already proposed, intermittent fasting could be an effective approach that may help prevent SARS-CoV-2 infection. This strategy of dietary restriction can directly (by activating immune response) or indirectly (by inducing autophagy) stimulate body surveillance system and boost up immunity, and thus prime host defense to cope with the confronting stresses.
- During fasting, care should be taken to ensure an adequate amount of essential micronutrients such as vitamin C, vitamin D, and zinc that help boost up the immunity and anti-stress mechanisms.

References

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