Letter to editor

Possible cross-talk between fat tissue and immune system in COVID-19 with considering to the physical exercise

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Dear Editor-in-Chief

Coronaviruses are a very large family of viruses that are phenotypically and genetically diverse and are common in humans and animals. The Prevalence of Coronavirus disease 2019 (COVID-19) began in Wuhan, China. As of 17 March 2020, extensive human-to-human transmission mainly occurs via the respiratory particles of the infected person. Among COVID-19 cases, it seems that new pandemic complications are already well-defined in obese and overweight people with body mass indexes (BMI) over 25 kg/m2 or even higher that contribute to increased risk of SARS-CoV-2 infection. The higher BMI in COVID-19 patients, the higher risk of medical complications, hospitalization in the intensive care unit (ICU), and invasive mechanical ventilation (IMV) (Földi et al., 2020). However, BMI does not show the distribution of body fat, and therefore research results cannot show the effect of excess fat in different parts of the body on the severity of COVID-19. In confirmation of this finding, it can be said that although the ratio of total body fat in women is higher than men on average, the incidence of COVID-19 is higher in men (Simonnet et al., 2020).

The possible critical mechanism by which adipose tissue accumulation increases the risk of COVID-19 in patients is unknown. However, fatty tissue may serve as a reservoir for viral production that might contribute to the increased risk from COVID-19 for patients with obesity. It is suggested that fatty tissue is targeted by SARS-CoV-2. The mechanism by which SARS-CoV-2 enters cells is not fully elucidated. But apart from a direct fusion of the virus with the plasma membrane, it appears that various types of endocytosis might be involved in this process. These lipid membrane trafficking events include clathrin-mediated endocytosis, caveolin- mediated

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Received 29 March 2021; Accepted 7 June 2021

involved in muscle hypertrophy and strength. In this regard, OCN-deficient mice have been shown to have lower muscle mass; inversely, improved muscle mass was found in older mice with ucOCN administrations. Recent data has figured out a novel mechanism of bone-muscle crosstalk in relation to OCN and IL6 signaling (Kirk et al., 2020).

Endocytosis, macropinocytosis, and phagocytosis. Caveolin-mediated endocytosis is especially interesting to study as caveolae are abundant in fat cells, caveolins participate in fatty tissue function because caveolin was shown to interact with various viral proteins. In addition, the increased number of fat cells would increase the pool of infection susceptible cells. Fatty tissue contains not only fat cells but cells of stromal vascular fraction among which adipocyte precursors and macrophages. These cells also express ACE2 and display a potential target of SARS-Cov-2 infection and thus may contribute to increased inflammatory status (Dugail, Amri, & Vitale, 2020). Another possibility is that fatty tissue droplets could provide a platform for virus replication and production. Concerning the hypothesis that fatty tissue is an infection place for the SARS-CoV-2 virus, it has not yet been established if viral loads are proportional to fatty tissue mass in patients. The ACE2 activity leading to increased levels of angiotensin II and so increased inflammation and lung damage. It seems that fat cells play a substantial role in viral infection and the viral life cycle. Adipose tissue is directly involved in contact with the viral membrane of the host cell. For example, fats are critical to the formation and function of the viral replication complex and can provide some of the energy required for viral replication. In addition, specific fats are needed for the formation of double-membrane vesicles for viral genome amplification and the production of viral particles. Viral internalization can occur with endocytosis and viral release from cells. It is possible that fat availability and fats metabolism modifications occurring in an obese patient also contribute to improving several stages of the virus's life cycle and severity of the disease (Dugail et al., 2020).

In this regard, any approach should consider reducing the costs of intensive care units to reduce the mortality of patients. Especially wit-

-h concerning increase their number and people at higher risk in obese people. Moderate-intensity exercise can directly boost the immune system, antioxidant defenses, and anti-inflammatory responses Adipose tissue molecular adaptation always was considered as one of the mechanisms for the anti-inflammatory effects of physical exercise. Aerobic exercise is a physical activity that is moderate-intensity and does not put much pressure on the body. Regular exercise has been shown to improve infection, antibacterial and antiviral immunity, reduce inflammation, and delay immune aging (Campbell & Turner, 2018). Following the moderate-intensity physical activity, an increase in the number of neutrophils and natural killer (NK) cells is detected, and salivary IgA concentrations increase (Brolinson & Elliott, 2007). During physical exercise, rapid and general mobilization of NK cells into the bloodstream is induced by adrenergic B signaling and catecholamines. It is suggested that mobilized NK cells are affected by muscle-derived myokines, exercise-related hyperthermia, and coronary arteries, which are affected by regulation, redistribution, and activation of mobilized NK cells (Brolinson & Elliott, 2007). Moreover, adipocytes play a critical role in NK cell activations. Adipose tissue may respond to the activation of NK cells during exercise in a cross-talk with the immune system.

Moderate exercise was exercise is one of the mechanisms in NK cell activation following physical exercise. The results show a 20 to 30 percent reduction in upper respiratory tract infections in people who do moderate-intensity of physical activity in their daily lives (Brolinson & Elliott, 2007). Therefore, it can be said that moderate-intensity training can be an effective way to boosting the immune system. Possible cross-talk between fat and immune tissues was approved in some other studies. It is suggested that some exercise factors such as IL-6 and Hsp70 can be effective in the possible cross-talk between the immune system and fat tissue. Molecular and structural changes in adipose tissue following physical exercise can be effective in improving immune responses.

Fatty tissue is probably targeted by the SARS-CoV-2 virus, which causes adipose tissue dysfunction. Accumulation of fat tissue also serves as a platform for replication and production of virus. Based on the evidence, it seems that exercise activities, especially combined exercise training, reduce fat mass in obese or overweight people, reduce the risk of COVID-19, as well as the risk of severity and side effects in patients. Possible cross-talks between the immune system and adipose tissue could be one of the possible mechanisms in boosting immune responses against the virus.

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