The Potential of Exerkines in Women's COVID-19

Subjects: Public, Environmental & Occupational Health | Others

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Exerkines are a group of promising molecules that may underlie the beneficial effects of physical exercise in diseases. The idea of exerkines is to understand the effects of physical exercise on diseases better. Exerkines have a high potential for the treatment of diseases and, considering that, there is still no study of the importance of exerkines on the most dangerous disease in the world in recent years, COVID-19.

Keywords: coronavirus disease 2019 (COVID-19) ; females ; exercise ; physical activity ; physical exercise ; exerkines ; exerkine

1. Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the acute respiratory syndrome with coronavirus that primarily affects the lungs [1]. After three years of this disease, we understand who is more exposed to the symptoms of COVID-19 and who suffers from moderate and high severity of this disease [2]. The review of previous studies showed that most people infected with COVID-19 were obese or overweight [3][4], and disease severity and mortality were higher in obese subjects than in overweight subjects [5]. Moreover, during the illness, COVID-19 patients face a decrease in muscle strength (muscle atrophy), a decrease in muscle endurance, and other physiological factors, which can affect training programs in the long term after discharge from the hospital [6][7]. It has been determined that, in the long term, COVID-19 can lead to negative physiological changes and decrease the quality of life, reducing hope and motivation for physical activity, which worsens the course of the disease [8].

Gender is an essential determinant of mortality risk and immunological responses to COVID-19 [9][10][11]. Women face a higher risk of becoming infected during a pandemic because of their societal position, as the United Nations (UN) and the World Health Organization (WHO) reported [12][13][14]. Women are over-represented in health care professions [11][15][16][17]. On the other hand, obese and overweight women are more exposed to the complications of COVID-19 than normal women [18]. Being physically active or the lack thereof plays a vital role in obesity. Indubitably, obesity ensues from physical inactivity and vice versa [19][20][21]. Hormones can also affect sexual difference in viral infections such as COVID-19. The SARS-CoV-2 spike protein binds to the human angiotensin-converting enzyme 2 (ACE2) receptor. Studies have shown that estradiol, a primary female sex hormone, likely regulates ACE2 expression in airway epithelial cells, kidneys, heart, and adipose tissues [22][23]. In obese and overweight women, estradiol function [24] is disrupted and ACE2 expression increases [22][23].

Undeniable evidence has been supporting the vital role of physical exercise in improving immune system, body composition, and reducing the complications of COVID-19 [25][26]. Although the benefits of physical exercise in improving health and reducing the severity of COVID-19 are well known, the molecular mechanisms underlying these benefits associated with physical exercise are not yet defined and are being investigated [27][28]. Physical exercise generally includes aerobic, anaerobic, or resistance training, but physical activity includes occupational, sports, conditioning, household, or other activities [29][30][31]. Promoting physical activity seems to have a more significant effect on reducing the diseases severity [27][32][33][34]. In 2020, WHO reported that all adults should aim for 150 to 300 min of moderate-intensity physical activity per week or 75 to 150 min of vigorous-intensity physical activity per week, or an equivalent combination of moderate- and vigorous-intensity physical activity [35]. However, it is important to understand how physical activity can affect the acute or chronic immune response in obese women.

To make better recommendations for immunization in women, it is needed to understand the impact of physical exercise on all organs. Studying exerkines would be the key. The word exerkines has introduced in 2016 [36]. So far, there is no exact definition of exerkines, but the best explanation for seems to be: the release of myokines, cardiokines, hepatokines, and adipokines due to physical exercise [27]. That is, physical exercise can affect these "kines" and ultimately exerts its effects through endocrine, paracrine, and/or autocrine pathways (**Figure 1**) [35].

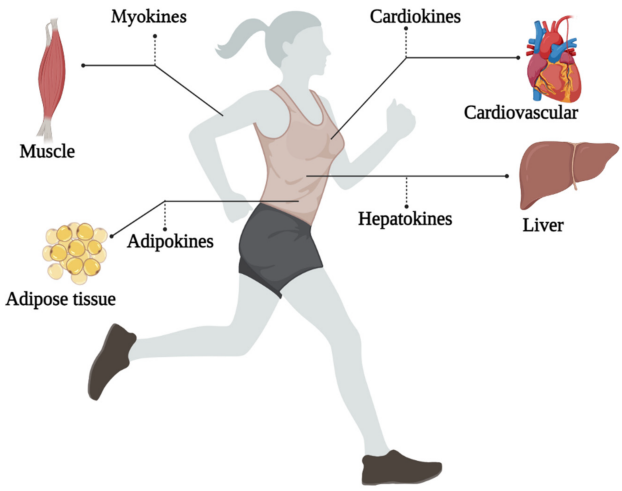

Figure 1. An overview of the exerkines investigated.

By reviewing past studies related to rehabilitation and physical exercise in the survivors of COVID-19, it can be well understood that most of those who were infected with COVID-19 were overweight and obese (**Figure 2**) [37][38][39][40][41][42][43][44][45][46][47][48][49][50][51][52][53][54][55][56].

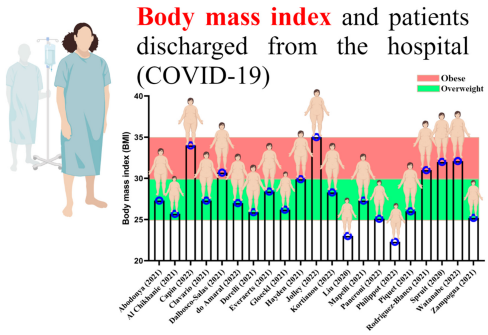

Figure 2. Body mass index of patients with COVID-19 discharged from the hospital [37][38][39][40][41][42][43][44][45][46][47][48][49][50][51][52][53][54][55][56].

2. The Potential Role of Exerkines Can Be Effective in COVID-19

It is well known that the most affected organs in COVID-19 include fat tissue, lungs, muscles, liver, and heart [57]. With the binding of SARS-CoV-2 spike protein to ACE2, physiological changes are created in the tissue, which can increase the disease process and influence the severity of the disease [58]. Moreover, the side effects of COVID-19 can stay with the patient long after discharge from the hospital and reduce the quality of life [59]. In this regard, most sports studies implementing “rehabilitation exercises” after COVID-19 had a general view of the effect of rehabilitation exercises on patients discharged from the hospital and did not investigate the fundamental mechanisms but highlighted the importance of physical exercise. Nevertheless, to provide a suitable physical exercise strategy for this disease, the mechanisms behind the curtain should be investigated. The idea of exerkines to take a more detailed look at diseases in 2022 by Chow et al. in the journal *Nature Reviews Endocrinology* gave rise to the idea that it might be possible to investigate the mechanisms behind the curtain and the effect of physical exercise in COVID-19 [27].

Exerkines look at the effect of physical exercise acutely or chronically on disease [27], and frequency, intensity, time, and type (FITT) can help to understand the effect of exerkines on disease better [27]. Exerkines are secreted in response to acute exercise (short-term physical exercise and less than 2 weeks), which is usually a part of aerobic or resistance training. Chronic exercise (long-term physical exercise and more than 2 weeks) is associated with changes in humoral factors, even at rest, suggesting that exerkine changes may reflect the effects of chronic exercise [60]. The acute exerkine response is influenced by the type of physical exercise, duration of physical exercise, background fitness, feeding–fasting status, and post-exercise sampling time [61]. Classical exerkines released during acute exercise, as found in human and animal models, include IL-6, IL-8, IL-1 receptor antagonist (IL-1ra), and IL-10. In a human study in which blood samples were collected before and after a marathon race (acute exercise), plasma levels of several cytokines (IL-6, IL-1ra, IL-10, and tumor necrosis factor (TNF)), when collected immediately, were higher than the base. Plasma levels measured after

physical exercise were found to peak and remain high for up to 4 h after exercise [62]. Notably, the acute exerkine response does not necessarily parallel the chronic exerkine response [63].

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