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Article

Should we recommend weight loss for heart failure patients?

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Obesity is defined as an excess fat mass that impairs health [1], which is most commonly defined as a body mass index (BMI) 30 kg/m2. It is not only a growing health burden in the modern era but also an established risk factor for the development of heart failure (HF). Among 5,881 healthy participants in the Framingham Heart Study, HF risk increased by 5% for men and 7% for women for each single unit increase in BMI [2]. In the Physicians Health Study, among 21,094 men without known coronary artery disease, overweight and obese participants had a 49% and 180% increase in HF risk compared with lean subjects, respectively [3]. Similarly, among 59,178 Finnish participants who were 25 to 74 years of age and free of HF at baseline, not only higher BMI, but also higher waist circumference, waist-hip ratio, and waist-to-height ratio were associated with a higher risk of HF hospitalization and mortality [4]. Pro-inflammatory cytokines produced by the adipose tissue can induce cardiac dysfunction and can promote the formation of atherosclerotic plaques. In view of primary prevention, weight loss in obese people is useful to ameliorate the disease burden of obesity and its complications.

However, physicians mostly deal with chronically ill patients and those with established cardiovascular disease. In a two-year observational study enrolling 247 male veterans 65 y/o, both involuntary (unintentional) and voluntary (by diet) weight loss were independently associated with increased mortality [5], suggesting that recommendations for weight loss should be made with caution.

Previous manuscripts observed that overweight HF patients (BMI 25.0-29.9 kg/m^2) and those with mild obesity (BMI 30.0-34.9 kg/m^2) had a better survival. On the contrary, lower body weight was associated with higher mortality, presenting the J-curve effect in body weight and adverse event [6,7]. This phenomenon has been termed the "obesity paradox", and was repeated confirmed not only in patients with HF, but also in patients with other cardiovascular diseases, including coronary artery disease, cerebral stroke, and in patients receiving interventions such as percutaneous coronary intervention, bypass surgery, valvular surgery and heart transplantation [8]. In the ADHERE database enrolling more than 100,000 patients, higher BMI was associated with lower in-hospital mortality. Specifically, for every 5-unit increase in BMI, the odds of risk-adjusted mortality were 10% lower [9]. In a meta-analysis from 14 HF studies, the obesity paradox was present in both those with reduced and preserved ejection fraction. Mortality in both HF subtypes was U-shaped, with a nadir at 30.0-34.9 kg/m^2 [10]. Interestingly, the impact of body weight on mortality seems not parallel to that on re-admission. In a HF with preserved ejection fraction cohort, despite the presence of the obesity paradox with respect to survival, increasing BMI actually was associated with an increased risk of HF hospitalization [11].

Although the prevalence of obesity is lower among Asian populations (12.7%) than Hispanics (47.0%), non-Hispanic blacks (46.8%), and non-Hispanic whites (37.9%) [12], data from the Taiwan

Society of Cardiology Heart Failure with reduced Ejection Fraction registry also presented the phenomenon of "obesity paradox" in Taiwanese HF patients [13]. Of note, the Asian Sudden Cardiac Death in Heart Failure (ASIAN-HF) registry demonstrated that patients with high waist-to-height ratio but low BMI had the worst outcomes, indicating that obesity phenotype should be stratified in a more meticulous way [14].

The mechanisms of why obesity improves prognosis in patients with HF are still unclear. However, the increased lean mass in obese patients may play a crucial role [15]. The increased lean mass has been associated with greater skeletal muscle strength. Moreover, the O2 pathway utilized to calculate peak oxygen consumption highly relies on muscle diffusion capacity and mitochondrial respiration capacity at the skeletal muscle level, emphasizing the importance of lean mass [16]. In a randomized trial including 100 obese HF patients with preserved ejection fraction, peak oxygen consumption was increased significantly by exercise (1.2 mL/kg body mass/min) and diet (1.3 mL/kg body mass/min). Moreover, the combination of exercise plus diet was additive for peak oxygen consumption (joint effect, 2.5 mL/kg/min), and the change in peak oxygen consumption was positively correlated with the change in percent lean body mass [17]. It appears clear that lifestyle modifications including exercise and a healthy diet should be suggested for HF patients, whereas strict caloric restriction and body weight reduction may not be necessary. The 2016 European Society of Cardiology HF guideline still states that, in patients with HF and moderate degrees of obesity (BMI<35 kg/m^2), weight loss cannot be recommended [18]. Since there is scarce evidence regarding weight-reducing interventions in patients with HF, studies investigating the effects of such interventions on clinical outcomes are required to implement them in clinical practice.

Conflicts of Interest:
The authors declare no conflict of interest.

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