



Higher Weight Variability Could Bring You a Fatty Liver

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Obesity, one of the most leading global health burdens of the 21st century, is defined as disproportionate body weight for one's height together with excess body fat accumulation, usually accompanied by systemic inflammation [1]. Nonalcoholic fatty liver disease (NAFLD) is a spectrum of disease encompassing hepatic fat accumulation, ranging from hepatocyte inflammation and necrosis to fibrosis and cirrhosis. Occurring in the background of obesity and insulin resistance, NAFLD is associated with various metabolic and cardiovascular disorders, such as metabolic syndrome, hypertension, dyslipidemia, and type 2 diabetes, as well as progressive liver disease [2]. There is currently no approved pharmacotherapy for NAFLD; the first priority of treatment is weight loss through lifestyle changes [3]. Weight loss can improve not only the hepatic histology, but also metabolic risk factors associated with obesity in a dose-related manner. Nevertheless, weight loss and its long-term maintenance are difficult to achieve, as an estimated 80% of individuals who intentionally lose more than 10% body weight regain that weight within a year [4]. This pattern of repetitive weight loss and regain is referred to as weight cycling or weight fluctuation, which could lead to adverse outcomes contrary to the original intention.

Recent studies have shown that weight cycling adversely affects the accumulation and distribution of body fat [5-7]. An increased propensity to regain fat mass after weight loss may be explained by the improved fat storage capacity of adipose tis-

sue. In a study with a rat model of weight recovery, after 1 week of refeeding, insulin-stimulated glucose utilization was lower in skeletal muscle but higher in white adipose tissue, resulting in catch-up fat accumulation [8]. These changes in insulin sensitivity and the increased insulin secretion during refeeding are explained as the main drivers of boosted lipid storage during weight cycling. In contrast, gain in muscle mass can only be achieved through the anabolic effects of a positive energy balance, whereas the large energy deficit during dieting leads to an accelerated loss of lean body mass [9]. In addition to unfavorable body fat accumulation, epidemiologic studies have shown that long-term weight fluctuations are linked to adverse health consequences such as type 2 diabetes, cardiovascular diseases, and mortality [10-12].

In this issue of *Endocrinology and Metabolism*, Jung et al. [13] published a study investigating the association between weight variability and the NAFLD in subjects without diabetes. The authors observed that subjects with higher weight fluctuations, as assessed by average successive variability and the coefficient of variation of serial weight data, showed an increased risk of developing NAFLD. Interestingly, a stepwise increased risk of NAFLD development was observed according to baseline obesity status and weight variability; the most prominent risks were noted in subjects with higher weight variability and with baseline obesity or weight gain during follow-up. A major strength of this study is that it included relatively young subjects

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for whom over 4 years of weight data were available, using a well-structured cohort at the Health Promotion Center of Kangbuk Samsung Hospital. Furthermore, study subjects were classified into various groups according to obesity status and weight variability. The consistent findings in the analyses give strong support to the link between weight fluctuation and NAFLD development.

However, we have several concerns related to the interpretation of the results of this study. As mentioned by the authors as a limitation, the cause (intentional or unintentional) and methods (e.g., dieting, exercise, or both) by which weight fluctuations occurred could not be assessed in the study. There might have been heterogeneous causes of weight variability according to baseline obesity status. As expected, subjects with higher weight variability showed more so-called “bad habits,” which might have had a greater impact on the development of NAFLD in the study than the weight cycling itself; in particular, the group of subjects with higher weight variability had higher alcohol intake and contained more smokers. These differences might have exaggerated the effects of weight fluctuation on the development of NAFLD in obese subjects. Next, the weight measurements assessed in the study were obtained through regular check-ups, which might not accurately reflect actual weight fluctuations; for instance, people often make efforts to lose weight after a health check-up, but their weight cycling might be masked by weight that is regained before the next check-up. Nevertheless, the fact that this analysis was based on a total of 15,340 relatively young healthy subjects could attenuate these concerns [14].

In summary, higher long-term weight variability was significantly associated with an increased risk of developing NAFLD in subjects without diabetes. Weight cycling is considered to be a metabolic adaptation to weight loss originally contributed to increased survival capacity during alternating periods of feast and famine, but appears to lead to adverse health outcomes in the modern obesity-pandemic period. Weight reduction is a powerful and essential solution to restore the NAFLD, a hepatic manifestation of metabolic syndrome. Developing strategies to maintain weight should be emphasized along with weight loss.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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