Metabolically Healthy Obesity: Is It Really A Benign Condition?

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Obesity is associated with various cardiometabolic diseases and increased mortality. However, a select group of obese individuals, the metabolically healthy obese (MHO), characterized by absence of metabolic disturbances, appear to be spared from the ominous complications of obesity. In South Korea, the prevalence of obesity has increased in all age groups over the last decade, reaching 35.7% in 2018. According to a previous meta-analysis, the prevalence of MHO reported in previous studies was largely variable depending on the definition of MHO used and ranged from 13% to 86%. There are also regional and sex differences in the prevalence of MHO. Although the mechanism of preservation of metabolic health in the MHO group has been investigated in both human and animal studies, it remains unknown. The suggested mechanisms include subcutaneous fat distribution, adipose tissue expandability, sustained insulin sensitivity, preserved adipocyte function, chronic inflammation, and genetic associations. Environmental and behavioral factors, such as an individual’s physical activity level and self-rated health (SRH), also have also been proposed.

The prognosis of MHO in association with type 2 diabetes and cardiovascular disease (CVD) is controversial. Some studies have demonstrated that MHO individuals show a favorable prognosis and advocated that MHO be classified as a “benign condition.” However, some studies have opposed this concept and reported that MHO individuals have higher risk of type 2 diabetes, CVD, and mortality. Accumulated evidence regarding the increased risk of type 2 diabetes and CVD among MHO individuals compared to that in metabolically healthy normal weight (MHNW) individuals suggests that MHO is not a “benign condition.”

In a previous study, the SRH of subjects with obesity and metabolic syndrome was worse than that reported by non-obese subjects. In addition, low SRH in MHO individuals was associated with progression to metabolically unhealthy obese (MUO) status. In another study, impaired glucose tolerance was associated with low SRH. In line with these results, a recent study by Hjelmgren et al. published in *Journal of Obesity & Metabolic Syndrome* reported that obese individuals rated their health worse than non-obese individuals. That study reported a novel finding that MHO subjects rated their health similar to other individuals of the same age. Moreover, the SRH of the MUO group was
significantly worse than those of the MHNW and MHO groups. These findings imply that metabolic health has a more critical influence on one’s health rating than does obesity itself.

Previous studies on the level of physical activity of MHO individuals have reported inconsistent results. A study by de Winter et al. reported no difference in the level of physical activity between MHO and MUO groups; however, a study by de Rooij et al. concluded that the MHO group performed more physical activity than the MUO group. A study by Hjelmgren et al. provided evidence supporting the study by de Winter et al.; the number of individuals performing leisure-time physical activity for >30 minutes at least 1–2 times a week was not significantly different between MHO and MUO groups. In addition, the level of physical activity in the MHNW group was similar to that in obese groups, possibly because the study was a cross-sectional analysis of a relatively small number of obese subjects. Therefore, it seems premature to purport a conclusion on the effect of the level of physical activity on metabolic health and body weight based on the abovementioned results alone.

However, Hjelmgren et al. showed that the MHO group had intermediate levels of beta-cell dysfunction (indirectly measured by plasma proinsulin and C-peptide levels) and insulin resistance assessed by homeostatic model assessment for insulin resistance. Currently, MHO subjects are considered metabolically heterogeneous in terms of risk of type 2 diabetes, although they are classified using different diagnostic criteria. Our group demonstrated that elevated high-sensitivity C-reactive protein level or increased hepatic steatosis can stratify the risk of type 2 diabetes among MHO subjects. Although the study by Hjelmgren et al. confirmed the intermediate status of MHO subjects in terms of beta-cell function and insulin resistance, the heterogeneous nature of MHO should be considered when assessing the risk of type 2 diabetes in such a population.

The homogenous population of this study is both a strength and a limitation. Another limitation of this study is the cross-sectional study design, whereas metabolic health and obesity status should be considered dynamic concepts. Nevertheless, the present study provides valuable information on SRH, level of physical activity, and insulin resistance in MHO individuals. This study also supplements evidence that MHO status is not comparable to MHNW status, as various studies have categorized MHO as an intermediate phenotype between MHNW and MUO phenotypes. The debate on the MHO
phenotype and its relationship with possible causes and consequences of obesity persists. Further studies are needed to provide a risk-stratified obesity treatment in MHO patients.

CONFLICTS OF INTEREST

Chang Hee Jung has worked as an Assistant Editor of *Journal of Obesity & Metabolic Syndrome*; however, he was not involved in peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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AUTHOR CONTRIBUTIONS

Study concept and design: ***; acquisition of data: ***; analysis and interpretation of data: ***; drafting of the manuscript: ***; critical revision of the manuscript: ***; statistical analysis: ***; obtained funding: ***; administrative, technical, or material support: ***; and study supervision: ***.
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