

# Metabolically Healthy Obesity: Is It Really a Benign Condition?

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Obesity is associated with various cardiometabolic diseases and increased mortality.<sup>1</sup> 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.<sup>2,3</sup> In South Korea, the prevalence of obesity has increased in all age groups over the last decade and reached 35.7% in 2018.<sup>1</sup> According to a meta-analysis, the prevalence of MHO reported in previous studies was largely variable depending on the definition of MHO used, ranging from 13% to 86%.<sup>2</sup> There are also regional and sex differences in the prevalence of MHO.<sup>2</sup> Although the mechanism of preservation of metabolic health in the MHO group has been investigated in both human and animal studies, it remains unknown.<sup>3,4</sup> The suggested mechanisms include subcutaneous fat distribution, adipose tissue expandability, sustained insulin sensitivity, preserved adipocyte function, chronic inflammation, and genetic associations.<sup>3,5</sup> Environmental and behavioral factors, such as an individual's physical activity level and self-rated health (SRH), also have been proposed.<sup>6</sup>

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."<sup>5</sup>

However, some studies have opposed this concept and reported that MHO individuals have higher risk of type 2 diabetes, CVD, and mortality.<sup>7</sup> 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."<sup>3,7</sup>

In a previous study, the SRH of subjects with obesity and metabolic syndrome was worse than that reported by non-obese subjects.<sup>6</sup> In addition, low SRH in MHO individuals was associated with progression to metabolically unhealthy obese (MUO) status.<sup>6</sup> In another study, impaired glucose tolerance was associated with low SRH.<sup>8</sup> In line with these results, a recent study by Hjelmgren et al.<sup>9</sup> published in *Journal of Obesity & Metabolic Syndrome* reported that obese individuals rated their health worse than non-obese individuals. This 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.<sup>10,11</sup> A study by de Winter

et al.<sup>11</sup> reported no difference in the level of physical activity between MHO and MUO groups; however, de Rooij et al.<sup>10</sup> concluded that the MHO group performed more physical activity than the MUO group. A study by Hjelmgren et al.<sup>9</sup> provided evidence supporting the study by de Winter et al.<sup>11</sup>; 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.<sup>9</sup> 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.<sup>12</sup> Our group demonstrated that elevated high-sensitivity C-reactive protein level or increased hepatic steatosis could stratify the risk of type 2 diabetes among MHO subjects.<sup>13,14</sup> Although the study by Hjelmgren et al.<sup>9</sup> 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 a dynamic concept.<sup>15</sup> 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 Associate 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, and analysis and interpretation of data: all authors; drafting of the manuscript: HSK; critical revision of the manuscript: CHJ; statistical analysis: HSK; obtained funding, administrative, technical, or material support, and study supervision: CHJ.

## REFERENCES

1. Nam GE, Kim YH, Han K, Jung JH, Rhee EJ, Lee SS, et al. Obesity fact sheet in Korea, 2019: prevalence of obesity and abdominal obesity from 2009 to 2018 and social factors. *J Obes Metab Syndr* 2020;29:124-32.
2. Lin H, Zhang L, Zheng R, Zheng Y. The prevalence, metabolic risk and effects of lifestyle intervention for metabolically healthy obesity: a systematic review and meta-analysis: a PRISMA-compliant article. *Medicine (Baltimore)* 2017;96:e8838.
3. Stefan N, Häring HU, Hu FB, Schulze MB. Metabolically healthy obesity: epidemiology, mechanisms, and clinical implications. *Lancet Diabetes Endocrinol* 2013;1:152-62.
4. Loos RJ, Kilpeläinen TO. Genes that make you fat, but keep

- you healthy. *J Intern Med* 2018;284:450-63.
5. Primeau V, Coderre L, Karelis AD, Brochu M, Lavoie ME, Messier V, et al. Characterizing the profile of obese patients who are metabolically healthy. *Int J Obes (Lond)* 2011;35:971-81.
  6. Kim MH, Chang Y, Jung HS, Shin H, Ryu S. Impact of self-rated health on progression to a metabolically unhealthy phenotype in metabolically healthy obese and non-obese individuals. *J Clin Med* 2019;8:34.
  7. Kramer CK, Zinman B, Retnakaran R. Are metabolically healthy overweight and obesity benign conditions? A systematic review and meta-analysis. *Ann Intern Med* 2013;159:758-69.
  8. Andersson S, Ekman I, Friberg F, Daka B, Lindblad U, Larsson CA. The association between self-rated health and impaired glucose tolerance in Swedish adults: a cross-sectional study. *Scand J Prim Health Care* 2013;31:111-8.
  9. Hjelmgren O, Gummesson A, Bergström G, Schmidt C. Beta-cell function, self-rated health, and lifestyle habits in 64-year-old Swedish women with metabolically healthy obesity phenotype. *J Obes Metab Syndr* 2020;29:39-46.
  10. de Rooij BH, van der Berg JD, van der Kallen CJ, Schram MT, Savelberg HH, Schaper NC, et al. Physical activity and sedentary behavior in metabolically healthy versus unhealthy obese and non-obese individuals: the Maastricht study. *PLoS One* 2016;11:e0154358.
  11. de Winter M, Rioux BV, Boudreau JG, Bouchard DR, Sénéchal M. Physical activity and sedentary patterns among metabolically healthy individuals living with obesity. *J Diabetes Res* 2018;2018:7496768.
  12. Bell JA, Kivimaki M, Hamer M. Metabolically healthy obesity and risk of incident type 2 diabetes: a meta-analysis of prospective cohort studies. *Obes Rev* 2014;15:504-15.
  13. Jung CH, Lee MJ, Kang YM, Jang JE, Leem J, Hwang JY, et al. The risk of incident type 2 diabetes in a Korean metabolically healthy obese population: the role of systemic inflammation. *J Clin Endocrinol Metab* 2015;100:934-41.
  14. Jung CH, Kang YM, Jang JE, Hwang JY, Kim EH, Park JY, et al. Fatty liver index is a risk determinant of incident type 2 diabetes in a metabolically healthy population with obesity. *Obesity (Silver Spring)* 2016;24:1373-9.
  15. Soriguer F, Gutiérrez-Repiso C, Rubio-Martín E, García-Fuentes E, Almaraz MC, Colomo N, et al. Metabolically healthy but obese, a matter of time? Findings from the prospective Pizarra study. *J Clin Endocrinol Metab* 2013;98:2318-25.