Letter to the Editor: Obesity Severity and Duration Are Associated With Incident Metabolic Syndrome: Evidence Against Metabolically Healthy Obesity From the Multi-Ethnic Study of Atherosclerosis

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The notion that being obese can be “healthy” has gained emerging interest in the past decade. The term “metabolically healthy obesity” (MHO) refers to a subgroup of obese individuals suggested to have a favorable metabolic profile in comparison to those with metabolically unhealthy obesity (MUO) (1). However, MHO is not a benign condition. A recent meta-analysis showed that compared to their nonobese counterparts, MHO individuals are 1.5 times more likely to develop cardiovascular events, although there is no marked difference in all-cause mortality risk (2). A growing perspective sees MHO as a transient state toward metabolic syndrome rather than a distinct phenotype (3, 4), but until recently, there had not been exhaustive evidence supporting this claim.

The past month saw two major publications challenging the existence of MHO that we consider pivotal important to the field. Mongraw-Chaffin et al (5) performed an analysis using repeated body mass index measurements in the Multi-Ethnic Study of Atherosclerosis (MESA) and reported a positive association between both obesity duration and obesity severity and incident metabolic syndrome among obese individuals. Rydén et al (6) performed a transcriptomic analysis on the sc white adipose tissue of 51 obese participants in a clinical trial evaluating gastric bypass surgery outcomes and reported similar gene expression response to insulin in metabolically healthy and unhealthy obese individuals. Despite the different approaches used, these two studies arrived at a similar conclusion—that metabolically healthy and unhealthy obese individuals are not essentially different.

Several challenges arise when interpreting these findings. First, criteria used to classify individuals into metabolically healthy and unhealthy groups vary. MESA used the presence of metabolic syndrome, whereas the study by Rydén et al (6) classified obese individuals by insulin sensitivity measured during a hyperinsulinemic euglycemic clamp. Given the wide range of MHO prevalence in adult populations worldwide (6–75%), depending on the definition (7), a consensus is needed to define metabolic health. Furthermore, Mongraw-Chaffin et al (5) included all participants with any documented MHO at any point of observation, with a lack of information on metabolic health status before study enrollment. This limitation of capturing incident metabolic syndrome may be addressed by a life course approach in future studies (8).
In the other study (6), only severely obese individuals were included, thereby limiting its generalizability to lower levels of obesity.

Secondly, the role of lifestyle, such as smoking and physical activity, has not been explicitly addressed, although nicotine consumption did not differ between insulin-sensitive and insulin-resistant patients in the study by Rydén et al (6). Given the indication that physical activity may differentiate MHO and MUO (10), it is of interest to evaluate whether obesity-related lifestyle contributes to the mechanism linking obesity duration or severity and metabolic syndrome.

If MHO and MUO only differ by cumulative obesity exposure, as suggested by Mongraw-Chaffin et al (5), while sharing similar adipose insulin response (6), one may speculate individual variation in the extent of which accumulation of obesity elicits metabolic responses. Combining longitudinal and experimental approaches may provide more insight into this topic and answer whether a “one-for-all” intervention against obesity is indeed plausible.

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Abbreviations:

MHO metabolically healthy obesity
MUO metabolically unhealthy obesity

Reference


