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Carrying a Heavier Weight is Healthy: Obesity-Reinforced Fitness and Favorable Outcomes in Metabolically Healthy Obesity

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Over 50 years ago the Framingham Heart Study linked obesity with coronary heart disease and cardiovascular death. Two decades later, the term “metabolic syndrome” was coined to explain the association of obesity, diabetes mellitus and a few other risk factors with atherosclerosis. The link between obesity and cardiovascular disease is believed to be through a number of metabolic pathways and their complications such as atherogenic dyslipidemia, elevated blood pressure, and elevated plasma glucose. However, recent data suggest that in some people obesity may be devoid of metabolic complications and without increased risk for cardiovascular morbidity and mortality, the so-called “metabolically healthy obesity” (MHO). Indeed higher body mass index values in the overweight to mild obesity range (25 to 35 kg/m²) may confer certain survival advantages in both the general population¹ and certain chronic disease states such as chronic kidney disease² and heart failure³ as well as among the elderly.⁴ Nevertheless, MHO may still be linked to a higher risk of type 2 diabetes mellitus.⁵ In addition, heavy weight is associated with other non-cardiovascular sequelae such as osteoarthritis, chronic back pain, gallbladder disease, asthma, and various cancers. Nonetheless, evidence is overwhelming that there may be biologic plausibility beyond statistical findings.

In this issue, Guo and Garvey⁵ showed that, while MHO was associated with a small increase in the risk of type 2 diabetes mellitus, it was not associated with an increased risk of cardiovascular events or mortality. Their data was from two large cohort studies: the Atherosclerosis Risk of Communities Study (ARIC) and the Coronary Artery Risk

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Potential Conflicts of Interest:

KKZ has received honoraria from Abbott, Abbvie, Alexion, Amgen, American Society of Nephrology, Astra-Zeneca, Aveo, Chugai, DaVita, Fresenius, Genetech, Haymarket Media, Hospira, Kabi, Keryx, National Institute of Health, National Kidney Foundation, Relypsa, Resverlogix, Sanofi, Shire, Vifor, ZS-Pharma. The other authors declare that they have no other relevant financial interests.

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Development in Young Adults (CARDIA). However, the analysis of MHO–outcome relationship was limited to 4,990 ARIC participants. Use of ARIC for these analyses was a smart choice given its representativeness considering the fact that the study participants were randomly selected from four diverse geographical areas comprising both sexes and diverse race/ethnicities. In addition, the study’s 18.7-year follow-up duration harbors to a large number of end point events, which has yielded a large statistical power, adding to the scientific merit of this study.

A potential explanation for the Guo and Garvey⁵ results is the potential cardiovascular protection conferred by cardiorespiratory fitness that can reduce the adverse effects of obesity on cardiovascular and all-cause mortality. Higher cardiorespiratory fitness is associated with a healthier metabolic profile including in the obese population, in whom the obesity sequelae are vastly attenuated by the fitness status. Hence, we argue that carrying a heavier body weight constantly may lead to a higher level of fitness in obese but ambulatory and physically active people as compared to thinner persons with the same activity level. We believe that walking with a heavier weight leads to a larger muscle mass along with higher muscle strength and hence resulting in an overall healthier muscle profile. Muscle mass is the likely source of protective cytokines including myormone and irisin.⁶ Moreover, there are known benefits of subcutaneous fat – as opposed to visceral fat – such as higher levels of circulating adiponectin and other anti-inflammatory adipokines and cytokines⁷ that may aggravate the muscle enhancement of heavier-body-ambulation. The potential effect of our hypothetical “Obesity-Reinforced Fitness” (Figure 1) on the obesity–mortality association is supported by several studies including a meta-analysis of 10 studies (total sample size: 92,986) in which the risk of death was dependent upon fitness rather than BMI.⁸ In this study, unfit obese individuals had a 2.5 fold higher risk of death, while fit obese individuals had a similar death risk as in fit normal-weight individuals.⁸ Similarly, a cohort study of 10,498 individuals has shown the strong relationship between fitness and metabolic health.⁹ In this study, the second and third tertiles of cardiopulmonary fitness were respectively associated with 26% and 53% decreased risk of metabolic syndrome in men and 20% and 63% decreased risk in women, compared to the first tertiles of cardiopulmonary fitness in each sex.⁹ Moreover, a collective analysis of eight studies examining cardiorespiratory fitness concluded that fitness was higher in individuals with MHO compared to those with metabolically abnormal obesity.¹⁰

In summary, the study by Guo and Garvey⁵ sheds some light to the contentious relationship between MHO and cardiovascular morbidity and mortality and corroborate to our obesity-reinforced fitness hypothesis. Heavier but mobile individuals carry larger weight and hence may have larger muscle mass and somewhat favorable metabolic profile, while inflammatory cytokines derived from visceral fat may also be elevated. Studies of this kind have a crucial role in exploring the consequences associated with such important subgroups as MHO and directing the appropriate preventive interventions to the affected individuals. In addition, this report paves the way for further investigations of the interplay between body weight, metabolic health and cardiopulmonary fitness and their potential roles in cardiovascular outcomes and longevity in the obese population.

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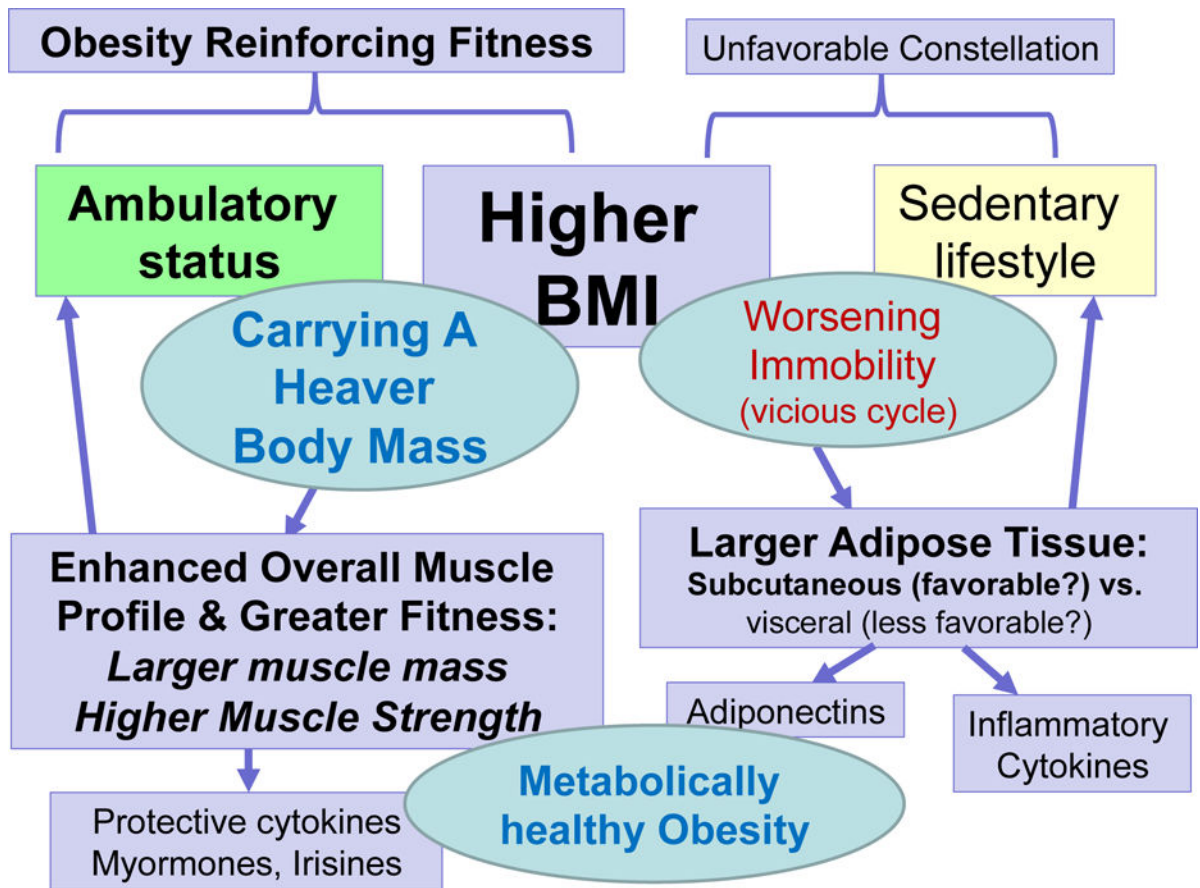


Figure 1. The Obesity-Reinforced Fitness Hypothesis

In non-sedentary obese population who are mobile, carrying heavier weight leads to enhanced fitness and greater muscle mass and strength along with more favorable cytokines and adipokine profile. Fit obese individuals are at little or no risk for cardiovascular sequelae.