Does Body Mass Index Adequately Convey a Patient's Mortality Risk?

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WHAT ADULT WEIGHT BEST ADVANCES HEALTH, minimizes the risk of chronic disease, and promotes longevity? This question has engaged the interest of the public, health care professionals, and a wide range of clinical investigators. The consequences of answering this question have profound health, social, and economic implications for individuals, communities, and the population as a whole.

A Metropolitan Life Insurance Company (MLIC) statistician revealed an association between longevity and body weight in 1942. Lifespan was longest when body weight was maintained at the same level as 25-year-old adults with similar height and frame size.[1] The initial 1942 MLIC ideal body weight tables were later revised to desirable weight tables in 1959 and again in 1983 to height and weight tables. Obesity was considered present when a person's weight exceeded his or her desirable weight by 20%.

This approach was popular among researchers. However, the MLIC tables were complex, had technical limitations, and were not easily applied when evaluating patients in the clinic or when screening individuals in field settings. Because body weight increases with height, there is a need to establish normal body weight as a function of height. This is accomplished by the body mass index (BMI; calculated as weight in kilograms divided by height in meters squared), which increases with greater adiposity.[2] In 1985, a National Institutes of Health consensus panel defined overweight-obesity as a BMI of 27.8 or greater for men and 27.3 or greater for women.[1] The BMIs at these levels are approximately 20% above the MLIC desirable weights. The panel recommended weight loss for people whose BMIs exceeded these thresholds. In 1997, a World Health Organization Consultation on obesity defined preobesity (overweight) as a BMI of 25 or greater and class (grade) 1 obesity as a BMI of 30 or greater, class 2 as a BMI of 35 or greater, and class 3 as a BMI of 40 or greater.[1] One year later, a National Heart, Lung, and Blood Institute (NHLBI) expert panel recommended a similar BMI-based definition of overweight and obesity.[1] Total mortality has a U-shaped relationship with BMI. Mortality rates sharply increase at BMIs of less than 18.5 and of greater than 30.

In this issue of *JAMA*, Flegal and colleagues[3] report their findings from a systematic review and meta-analysis of associations between standard NHLBI BMI categories for overweight and obesity and all-cause mortality. Using rigorous study selection criteria and statistical methods, and based on a sample of more than 2.88 million individuals with more than 270 000 deaths, they confirmed significantly increased all-cause mortality hazard ratios (HRs) relative to normal weight (defined as a BMI of 18.5-<25) for overall obesity (grades 1, 2, and 3 combined; HR, 1.18 [95% CI, 1.12-1.25]) and grades 2 and 3 obesity (HR, 1.29 [95% CI, 1.18-1.41]). Higher all-cause mortality was not observed in individuals with grade 1 obesity. Mortality was significantly lower among those who were overweight (HR, 0.94 [95% CI, 0.91-0.96]) compared with normal weight individuals. The findings remained consistent even after adjusting for smoking status, preexisting disease, or weight and height reporting method (self or measured).

The present investigation extends a 2005 study by Flegal et al[4] based on the National Health and Nutrition Examination Survey that did not find an increased mortality risk in overweight persons. Among others with similar findings, McGee et al[5] found no increase in all-cause mortality for overweight males (relative risk, 0.965 [95% CI, 0.922-1.009]) and females (relative risk, 0.968 [95% CI, 0.925-0.987]) in a 2005 meta-analysis including 388 622 individuals with 60 374 deaths. Orpana et al[6] estimated the relationship between all-cause mortality and BMI in a nationally representative sample of 11 326 Canadian adults and found a relative mortality risk of 0.76 (95% CI, 0.58-0.99) in overweight nonsmokers.

Based on these observations,[3,5,6] are the concerns about overweight as currently defined unfounded? Answering this question requires consideration of BMI as a health risk phenotype. Body mass index accounts for about two-thirds of the between-individual variation in total adiposity.[2] Body mass index does not account for sex, race, age, and fitness differences in fat mass even at the same body weight. Race and age both influence the associations among disease risk, mortality, and BMI.[7] Moreover, fat distribution varies widely

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even among individuals at the same level of adiposity, with an abdominal fat pattern conveying the greatest health risks.[8] The NHLBI clinical guidelines[9] recognize this limitation of BMI, and waist circumference is recommended as an additional surrogate marker of the health risks associated with adiposity and adipose tissue distribution.

Body mass index is known to be an imperfect predictor of metabolic risk. Some individuals with normal BMI have an overweight-obesity metabolic pattern.[10] Others with high BMIs appear to have a healthy metabolic pattern.[11] Factors such as cardiorespiratory fitness are also independent predictors of total mortality in some groups after controlling for BMI, waist circumference, and percentage of body fat.[12] A relatively large fat mass can mask small muscle mass, which is a condition referred to as sarcopenic obesity. Sole use of BMI as a health risk phenotype aggregates people with substantial differences in nutritional status, disability, disease, and mortality risk together into similar BMI categories. Identification of at-risk individuals for overweight and grade 1 obesity is best captured by considering traditional risk factors, including blood pressure, blood lipid levels, and fasting blood glucose level, in addition to BMI, waist circumference, or both as recommended in the NHLBI report.[9] Newer markers such as those representing systemic inflammation may also extend risk prediction beyond BMI.

Apart from an imperfect relationship between BMI and phenotype, are there explanations why overweight may be associated with a lower mortality risk? Physicians are increasingly aggressive in managing risk factors among patients with overweight or obesity. Substantial declines in cardiovascular disease risk factors have been reported among persons with obesity, more so than in those with normal weight.[13] New pharmacological therapies and invasive treatments for existing disease may prolong survival and, when combined with public health measures, may account for the weakening of associations between obesity and mortality observed over time.[13] Overweight and grade 1 obesity might lead to greater morbidity that is not captured when evaluating associations between all-cause mortality and BMI.

What appears to be a reduced or very low all-cause mortality risk in overweight people may represent an artifact of applying a wide range of BMIs in the normal weight reference category established by the NHLBI. In most studies, the lowest all-cause mortality is observed between a BMI of 22 and 25.[7,14] Persons with a BMI between 18.5 and 22 have higher mortality than those with a BMI between 22 and 25. Placing these persons in a single group raises the mortality rate for the normal weight group. The average resulting from combining persons in the lowest mortality category (BMI of 22-25) with those who have greater mortality (BMI of 18.5-22) might explain why the NHLBI category of normal weight has an observed mortality similar to class 1 obesity (BMI of 25-30).

Can overweight as defined by BMI actually have a protective association with mortality? The presence of a wasting disease, heart disease, diabetes, renal dialysis, or older age are all associated with an inverse relationship between BMI and mortality rate, an observation termed the obesity paradox or reverse epidemiology.[15] The optimal BMI linked with lowest mortality in patients with chronic disease may be within the overweight and obesity range.[15] Even in the absence of chronic disease, small excess amounts of adipose tissue may provide needed energy reserves during acute catabolic illnesses, have beneficial mechanical effects with some types of traumatic injuries, and convey other salutary effects that need to be investigated in light of the studies by Flegal et al[3] and others.[3-6]

The study by Flegal et al[3] confirms that obese individuals with a BMI of 35 or greater are at increased risk of mortality, as are their underweight counterparts with a BMI less than 18.5.[5] The large BMI range between these extremes includes persons with differing adiposity, adipose tissue distribution, muscularity, nutritional status, and disease risk factors. Not all patients classified as being overweight or having grade 1 obesity, particularly those with chronic diseases, can be assumed to require weight loss treatment. Establishing BMI is only the first step toward a more comprehensive risk evaluation.

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