Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 52, No. 12, 2008
ISSN 0735-1097/08/$34.00
doi:10.1016/j.jacc.2008.05.052

EDITORIAL COMMENT

Obesity, Cardiology, and Beyond*

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Clinical trials and registries create extensive databases that might be explored by different analyses apart from the original purpose for which the databases were created. Such analyses often address the pathophysiology of the disease that has been studied or the mechanisms of specific drugs tested in a trial. Necessarily, the additional analyses are restricted to the data that have been collected or additional measurements from serum samples, and so on.

See page 979

The CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the American College of Cardiology/American Heart Association Guidelines) registry provided an opportunity to investigate the relation between obesity (body mass index [BMI]) and age in patients admitted with a non–ST-segment elevation myocardial infarction (NSTEMI) (1). For this analysis 111,847 (59.2%) of the total of 189,075 patients in the databases were available. No data were available on patients with ST-segment elevation myocardial infarction. Body mass index was calculated from weight and height.

It should be appreciated that BMI is a poor predictor of mortality risk. A combination of waist circumference or waist-hip ratio as a marker for adiposity and middle arm muscle circumference as a marker for muscle mass is a far better predictor of mortality (2–4). However, such measurements were not available in the CRUSADE database.

The analysis from the CRUSADE registry in this issue of the *Journal* (1) reports a striking, stepwise lower age at first NSTEMI in patients with increasing BMI. Patients admitted with NSTEMI and BMI >40 kg/m^2 (extreme obesity) were 15.9 years younger than patients with a first NSTEMI and BMI ≤18.5 kg/m^2 (underweight) or 12.5 years younger than those with a normal weight (BMI 18.6 to 25.0 kg/m^2). The relation between higher BMI and younger age at first NSTEMI was consistent after adjustment for other risk factors. These observations are in agreement with earlier reports of a higher risk for myocardial infarction and death from a cardiovascular cause in subjects with increasing body weight or BMI in different parts of the world (4–7). Also, in patients with known coronary artery disease, obesity—but only severe obesity (BMI >35 kg/m^2)—has been associated with subsequent cardiovascular mortality (8,9). In fact, overweight and mild obesity showed better outcomes in many cardiovascular conditions (10–14).

Moreover, however important the heart might be to health, there is more to health than the heart.

In earlier times, overweight and mild obesity were symbols of well being, good health, and the blessing of the gods. Although the relationships among increasing body weight, BMI, hypertension, diabetes, and manifestations of cardiovascular disease are consistent, the relationships among body weight, BMI, and total mortality are far more complex, particularly in elderly persons. In many studies the mortality risk from any cause is approximately the same for subjects with BMI between 18.9 and 30.0 kg/m^2 (normal and overweight) or even 35.0 kg/m^2 (normal, overweight, and obese) (15,16). The mortality risk is increased in subjects with a low BMI (underweight, ≤18.5 kg/m^2) not only in India (17) and China (6,7) but also in Europe (5) and the U.S., as shown in Figure 1 (16,18). For men, smokers, and patients with a clinical history of disease, mortality starts to increase at low normal weights of a BMI <23 kg/m^2.

The mortality risk also rises in severe obesity: BMI >35 kg/m^2 in men or BMI >33 kg/m^2 in women.

Our occupation as cardiologists, focusing on prevention, detection, and management of cardiovascular disease, should not lead to a preoccupation. Overweight and mild obesity increase the risk for hypertension, diabetes, and cardiovascular disease but also lower the risk for hip fracture (19). Overweight and obesity lower the risk of death in a wide range of conditions, including heart disease, where it is known as the obesity paradox (10–14). It should be appreciated that, when identified in a timely manner, the increased cardiovascular risk in overweight and obese subjects can be effectively reduced by lowering blood pressure, low-density lipoprotein cholesterol, and elevated glucose levels and by refraining from smoking.

The "ideal" BMI is different by age, gender, and disease status. It is different if we look at disability, mortality, or various causes of death. Indeed, in a large individual record meta-analysis, overweight increased cardiovascular mortality but lowered all-cause mortality (5). Overweight might, at the same time, extend total life expectancy but shorten life expectancy free from disability.

The CRUSADE registry provided an opportunity to once more call attention to the cardiovascular risks of

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

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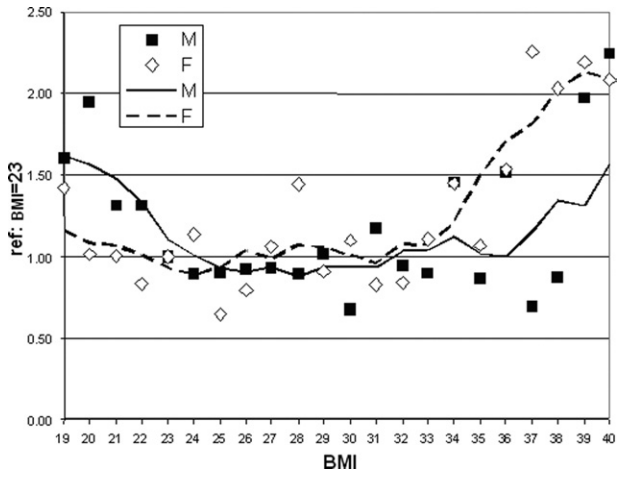

Figure 1 **Proportional Mortality Hazard Ratios by BMI**

Proportional mortality hazard ratios by body mass index (BMI) (BMI 23 kg/m^2 as reference), adjusted for age, smoking, and level of education. **Symbols** are BMI, **lines** are 5-point central moving averages weighted by SEMs. Willis J. Health and retirement study. Institutional Review Board (IRB) information. Sponsor: NIA U01 AG 09740: UM Health Sciences IRB Protocol H03-00002774-M8, 2005. Reprinted with permission from Bonneux and Reuser (18).

obesity, in particular the risk for premature NSTEMI. This is appropriate, indeed, but also opportunistic. In aging populations, the measuring tape should complement the balance, because age-related muscle wasting might mask high body fat mass. Future research should aim to gain insight into the pathophysiology of obesity and the mechanisms that result in excess cardiovascular morbidity and mortality but at the same time reduce the risk for other (fatal) diseases. Particularly at older ages, enhancing moderate physical activity seems a more rewarding policy target than decreasing population BMI.

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Key Words: obesity ■ mortality ■ atherosclerosis.