Healthy Lifestyle: Even If You Are Doing Everything Right, Extra Weight Carries an Excess Risk of Acute Coronary Events

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Editorial

Healthy Lifestyle

Even If You Are Doing Everything Right, Extra Weight Carries an Excess Risk of Acute Coronary Events

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Epidemiological, metabolic, and clinical studies conducted over the last few decades have identified important factors that contribute to the development of cardiovascular disease (CVD). Accordingly, several modifiable (smoking, blood pressure, lipid/lipoprotein and glucose levels, diabetes mellitus, poor diet, lack of physical activity/exercise, obesity, and psychosocial factors) and nonmodifiable (age, gender, and genetic predisposition) CVD risk factors are now recognized in contemporary clinical practice.[1] The health hazards of obesity have been recognized for centuries,[2] and in 1998, obesity was reported as a major modifiable risk factor for CVD by the American Heart Association.[3]

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In this issue of *Circulation*, Jensen et al[4] report an analysis of the associations of obesity (defined by body mass index [BMI]) in combination with physical activity, smoking, and a Mediterranean diet with the risk of acute coronary syndrome (ACS; defined as unstable angina pectoris and nonfatal and fatal acute myocardial infarction) in a prospective, population-based study of 54 783 middle-aged men and women. The investigators found that the association between BMI and ACS was strong and graded, and the absolute risk was substantially higher among men. Behavioral risk factors such as smoking, relative physical inactivity, low adherence to the Mediterranean diet, and having the lowest alcohol intake were all associated with a higher risk of ACS. Of importance, BMI was associated with risk of ACS at all levels of classic behavioral lifestyle risk factors: physical inactivity, smoking, and unhealthy diet. These findings suggest that obesity is important even in subjects who adhere to an otherwise healthy lifestyle.

Adiposity Indices

In the present study, adiposity status was assessed by BMI, and physical activity was self-reported. Although this prospective study used validated end points, one must consider that assessments of adiposity and physical activity may have introduced biases, which are probably overcome by the size of the study. In the past, lack of statistical power, especially small numbers of outcome events and inadequate length of follow-up, have been potential explanations for studies that failed to find relationships between obesity and morbidity/mortality. Other considerations include the potential for unmeasured confounders in observational studies and potential misclassification bias from the use of surrogate markers of body fat such as BMI, the impact of which varies across population groups. Thus, inconsistencies of findings between studies may be related to differences in study populations and sampling, measures of adiposity or obesity, and statistical approaches. The present study went to great lengths to avoid such pitfalls.

Obesity as defined by BMI is undoubtedly associated with an increased rate of comorbidities and cardiovascular morbidity/mortality, including ACS.[2] Current definitions designate overweight in adults as a BMI of 25.0 to $<$30.0 kg/m^2 and obesity as a BMI of $\geq$30.0 kg/m^2. Numerous studies have found no significant relationship between BMI in the overweight range and cardiovascular morbidity/mortality, such as ACS, which has led to confusion and controversy. Some have interpreted the data to mean that "overweight" is not detrimental to health. Overweight/obesity is a remarkably heterogeneous condition, and the distribution of the adipose tissue is of importance in determining the presence/absence of metabolic dysfunctions that predispose to chronic diseases.[5] Body fat distribution, especially visceral adipose tissue accumulation, has been found to be a major correlate of a cluster of diabetogenic and atherogenic abnormalities described as the "metabolic syndrome," which should be considered clinically as obesity "at risk" of morbidity/mortality.[6] BMI, a crude measure of overall obesity, is often not the best predictor of obesity-related outcomes,[7,8] and there is evidence that measures of abdominal adiposity are associated with CVD independent of overall body adiposity.[9] Waist circumference (WC) or waist-to-hip ratio measures are useful proxies for body fat distribution, and in several studies, they have been more important indicators of CVD risk than BMI. Large epidemiological studies have demonstrated evidence supporting the abdominal adiposity assessment.[10,11] The International Day for the Evaluation of Abdominal obesity (IDEA study) was a very large cross-sectional evaluation of almost 170 000 patients seen by primary care physicians in $>$60 countries.[10] After a simple and brief video-based training session, the 6400 study physicians measured weight, height, and WC and reported on the clinical status of the patients evaluated. Results showed that WC predicted CVD and diabetes at every

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BMI level and confirmed the clinical relevance of measuring WC as a further refinement of excess adiposity; however, the cross-sectional nature of the study was not designed as a prospective evaluation of which were the superior indices of adiposity. Investigators of the European Prospective Investigation of Cancer (EPIC)-Norfolk study reported the relationships of WC and hip circumferences with the incidence of coronary heart disease.[11] EPIC-Norfolk is a large prospective study of a population-based sample of 24 508 men and women who were followed up for 9.1 years for coronary heart disease incidence, including ACS. The authors reported that an increased WC was associated with an elevated risk of coronary heart disease, whereas a large hip circumference appeared to protect against coronary heart disease after adjustment for BMI, age, systolic blood pressure, cholesterol, cigarette smoking, physical activity, and alcohol intake.[11] Waist-to-height ratio has been suggested as an alternative to waist-to-hip ratio because it provides a correction for body frame size, which may be more conveniently measured than hip circumference.[12] The relationship of indices of adiposity (BMI, WC, waist-to-hip ratio, and waist-to-height ratio) to CVD mortality has been reported recently in women.[8] An association was described between increasing WC and all-cause mortality, which became stronger after adjustment for BMI. Indeed, even among normal-weight women, defined as BMI <25 kg/m^2, abdominal obesity was associated with a significantly higher risk of CVD mortality. A graded dose-response relationship was observed between abdominal adiposity and the risk of death whether evaluated by WC, waist-to-hip ratio, or waist-to-height ratio.[8]

Given this evidence, it has become important to consider which measure of adiposity should be applied for clinical use. In fact, excess weight and adiposity indices are not evaluated routinely in a real-life cardiology practice.[13,14] In this context, BMI and WC might both prove useful to clinical practice simply to make clinicians aware of the presence of obesity.

Physical Fitness

It is well known that self-assessed physical activity and objective measures of fitness may not concur. Blair et al at the Cooper Aerobics Center in Dallas, Tex, have published seminal evidence that low cardiorespiratory fitness is among the strongest risk factors for CVD and related mortality. This group also pioneered the interesting notion that being apparently fat yet fit could nevertheless be associated with a substantially reduced risk of metabolic complications and CVD compared with unfit, normal-weight individuals.[15] However, there is evidence that the poor metabolic risk profile of men with low cardiorespiratory fitness is associated with greater visceral adipose tissue accumulation after controlling for BMI.[16] Because physical inactivity and excess weight have been independently associated with mortality, there are potentially incremental benefits for overweight and obese individuals to adopt an active lifestyle in addition to healthy eating habits. In the study by Jensen et al,[4] only 8% of study participants were in the healthiest group for all 4 behavioral lifestyle risk factors (physically active 3.5 hours/week or more, nonsmoking, highest score on the Mediterranean diet scale, and a light-to-moderate alcohol intake), and only 47 cases (4.1%) of ACS occurred in this group during follow-up. Among these participants characterized by an overall healthy lifestyle, the hazard ratio for ACS was 1.65 (95% CI 0.82 to 3.22) for the overweight subjects and 2.65 (95% CI 1.12 to 6.27) for the obese subjects.[4] As a caveat, because body fat distribution was not assessed and physical activity was self-reported, some individuals may have been misclassified.

In the long term, because weight gain is progressive and weight loss is difficult to maintain, it is critically important that effective weight maintenance and obesity prevention approaches be developed and implemented for all individuals above normal weight. In addition, "healthy weight" should be defined from a perspective of both total fat and body fat distribution, because metabolically obese normal-weight individuals do exist,[17] and this concept is being reinforced in recent literature.[8] Actually, a substantial number of nonobese overweight patients with excess visceral adiposity, who are thus at higher risk of CVD, would not be detected on the basis of BMI alone.[18]

Most physicians are convinced that diet and physical activity/exercise are the cornerstone of therapy for the management of "at-risk" obesity and related cardiometabolic abnormalities. However, hoping to change nutritional and physical activity in clinical practice may be overly optimistic under the current healthcare provider model. Unfortunately, physicians have little time and support to implement successful lifestyle modification interventions, which require the support of an interdisciplinary team in regular contact with the patient, as shown by findings of landmark studies.[19,20] The fight against at-risk obesity as a major cause of CVD morbidity and mortality will require major societal changes and the involvement of dietitians, kinesiologists, and behavioral specialists interacting in clinical practice to help clinicians achieve optimal management of behavioral CVD risk factors. In addition to improving the clinical environment by providing more interdisciplinary support, public health policies should focus on early prevention of overweight/obesity by creating favorable and permissive environments for healthy eating habits and more physical activity/exercise, which should be implemented very early in life. Sadly, the improvement in risk factor recognition and management that has developed through the last decades in cardiology may be challenged by today's youth, who will carry their elevated risk of CVD for many more years. Undeniably, with obesity occurring at younger ages, the children and young adults of today will carry and express obesity-related risk for a longer time span than previous generations. From a public health perspective, increases in physical activity along with the establishment of healthy eating habits early in life may become the best, most cost-effective avenue to combat obesity and contain cardiometabolic risk.

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