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Normal-Weight Central Obesity and Mortality Risk in Older Adults With Coronary Artery Disease

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Abstract

Objective: To study the relationship between body mass index (BMI) and central obesity and mortality in elderly patients with coronary artery disease (CAD).

Patients and Methods: We identified 7057 patients 65 years or older from 5 cohort studies assessing mortality risk using either waist circumference (WC) or waist-hip ratio (WHR) in patients with CAD from January 1, 1980, to December 31, 2008. Normal weight, overweight, and obesity were defined using standard BMI cutoffs. High WHR was defined as 0.85 or more for women and 0.90 or more for men. High WC was defined as 88 cm or more for women and 102 cm or more for men. Separate models examined WC or WHR in combination with BMI (6 categories each) as the primary predictor (referent = normal BMI and normal WC or WHR). Cox proportional hazards models investigated the relationship between these obesity categories and mortality.

Results: Patients' mean age was 73.0±6.0 years (3741 [53%] women). The median censor time was 7.1 years. A normal BMI with central obesity (high WHR or high WC) demonstrated highest mortality risk (hazard ratio [HR], 1.29; 95% CI, 1.14-1.46; HR, 1.29; 95% CI, 1.12-1.50, respectively). High WHR was also predictive of mortality in the overall (HR, 2.14; 95% CI, 1.93-2.38) as well as in the sex-specific cohort. In the overall cohort, high WC was not predictive of mortality (HR, 1.04; 95% CI, 0.97-1.12); however, it predicted higher risk in men (HR, 1.12; 95% CI, 1.01-1.24).

Conclusion: In older adults with CAD, normal-weight central obesity defined using either WHR or WC is associated with high mortality risk, highlighting a need to combine measures in adiposity-related risk assessment.

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The worldwide prevalence of obesity has almost doubled between 1980 and 2008, a trend also observed in elderly adults.[1] In the United States, more than 35% of adults 65 years and older were classified as having obesity on the basis of body mass index (BMI) in the period 2007 to 2010, representing more than 13 million adults.[2] Overweight and obesity (including central obesity) not only are associated with the development of metabolic syndrome, hypertension, dyslipidemia, insulin resistance, type 2 diabetes mellitus, and obstructive sleep apnea but are also independently associated with coronary artery disease (CAD)[3] and cardiovascular (CV) mortality.[4]

Although obesity in older adults is associated with the development of functional limitations, poorer quality of life,[5] and higher rates of institutionalization,[6] its effect on CV mortality in older adults is unknown. The usefulness of various anthropometric measures of obesity as mortality predictors in older adults has generated inconsistent results.[7] Little consensus exists as to which measures are most strongly associated with CV disease risk in elderly populations. The combination of normal BMI with central obesity, termed *normal- weight central*

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obesity (NWCO),[8] confers higher mortality risk in adults with CAD[9]; however, its impact on mortality in older adults with CAD is unknown. In certain populations, BMI has been shown to be inversely related to mortality, a phenomenon described as the "obesity paradox."[10-14] Our aim was to determine whether NWCO in elderly patients with CAD confers high mortality risk and whether the obesity paradox exists in this subpopulation.

PATIENTS AND METHODS

We identified 5 cohort studies from 3 continents (Mayo Clinic, Rochester, Minnesota; University of California, San Francisco[15]; Rigshospitalet Copenhagen, Denmark[16]; INSERM U866, University of Bourgogne-Franche-Comté, Dijon, France[17]; and Yeungnam University Hospital, Daegu, Korea[18]) assessing mortality risk associated with either waist circumference (WC) or waist-hip ratio (WHR) in a sample of patients with CAD from January 1, 1980, through December 31, 2008.[19] All the individual studies included in this analysis received approval from their respective institutional review boards. Details regarding the systematic review, inclusion and exclusion criteria, origin of the cohorts included, and approach to obtain individual-level data have been previously described.[19] Of the 15,550 patients, 8765 were 65 years or older. We excluded 1708 patients in whom hip circumference data were not available, yielding a final analytical sample of 7057. All patients analyzed in the final cohort had complete data available for WC, hip circumference, and WHR. Patients were defined to have CAD at baseline on the basis of a history of myocardial infarction, percutaneous coronary intervention, and/or coronary artery bypass grafting; anthropometric and mortality measures of either WC or WHR; and a minimum follow-up of 6 months. Information on all-cause mortality was obtained from individual-level data from each study. No information was available on CV mortality in patients in our database. All-cause mortality was chosen as the primary end point for analysis.

Our predictor variables were WC, WHR, and BMI. *Body mass index* was defined as the weight in kilograms divided by the height in meters squared. Weight was measured with a standard balance beam scale in all studies. Normal weight, overweight, and obese were defined using standard BMI cutoffs (normal BMI, 18.5-24.9 kg/m^2; overweight, 25-29.9 kg/m^2; obese, $\geq$30-34.9 kg/m^2). High WC was defined using National Cholesterol Education Program Adult Treatment Panel III cutoffs of 88 cm or more for women and 102 cm or more for men.[20] Waist circumference was measured between the iliac crest and the lower ribs at a level that had the minimum circumference in 4 studies and at the level of the navel in 1 study. Hip circumference was measured horizontally over the greatest posterior extension of the buttocks in 4 studies and at the level of the major trochanter in 1 study. The WHR was calculated by dividing the WC by hip circumference, both in centimeters. High WHR was defined as 0.85 or more for women and 0.90 or more for men.[21] Patients were defined to have central obesity if they had either the WHR or the WC above sex-specific cutoff values.

Statistical Analyses

All continuous variables are expressed as mean ± SD, and categorical variables as number (%). Patients were categorized into 12 groups on the basis of combination of BMI and central obesity category: (1) normal BMI/low WHR, (2) normal BMI/high WHR, (3) overweight BMI/low WHR, (4) overweight BMI/high WHR, (5) obese BMI/low WHR, (6) obese BMI/high WHR, (7) normal BMI/low WC, (8) normal BMI/high WC, (9) overweight BMI/low WC, (10) overweight BMI/high WC, (11) obese BMI/low WC, and (12) obese BMI/high WC. Our primary aim was to assess the effect of each anthropometric category on long-term mortality. Cox proportional hazards models were used to investigate the relationship of these anthropometric categories with the mortality end point. Initially, we used the assumptions of proportional hazard modeling using the methods outlined by Grambsch and Therneau.[22] The Cox proportional hazard models were adjusted for age, sex, hypertension, diabetes, smoking status (past or current), and congestive heart failure. If the proportional hazards assumption was not met, that factor was used as a stratification factor in the adjusting model. For instance, while analyzing the mortality risk in the overall cohort, because of proportional hazard assumption violation the model was stratified on age, diabetes, hypertension, smoking status (past or current), and congestive heart failure and was adjusted for sex. When