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Adiposity Throughout Adulthood and Risk of Sudden Cardiac Death in Women

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ABSTRACT

OBJECTIVES This study examined the association of BMI repeatedly measured over 32 years and BMI during early and mid-adulthood with risk of sudden cardiac death (SCD) in the Nurses' Health Study.

BACKGROUND SCD is often the first manifestation of coronary heart disease among women. Data regarding body mass index (BMI) and risk of SCD are limited and conflicting.

METHODS We prospectively followed 72,484 women free of chronic disease from 1980 to 2012. We ascertained adult height, current weight, and weight at age 18 years at baseline, and updated weight biennially. The primary endpoint was SCD (n = 445).

RESULTS When updated biennially, higher BMI was associated with greater SCD risk after adjusting for confounders (p linear trend <0.001). Compared with a BMI of 21.0 to 22.9 kg/m^2, the multivariate relative risk (RR) of SCD was 1.46 (95% confidence interval [CI]: 1.05 to 2.04) for BMI 25.0 to 29.9 kg/m^2, 1.46 (95% CI: 1.00 to 2.13) for BMI 30.0 to 34.9 kg/m^2, and 2.18 (95% CI: 1.44 to 3.28) for BMI ≥35.0 kg/m^2. Among women with a BMI ≥35.0 kg/m^2, SCD remained elevated even after adjustment for interim development of coronary heart disease and other mediators (RR: 1.72; 95% CI: 1.13 to 2.60). In contrast, the association between BMI and fatal coronary heart disease risk was completely attenuated after adjustment for mediators. The magnitude of the association between BMI and SCD was greater when BMI was assessed at baseline or at age 18 years, at which time SCD risk remained significantly elevated at BMI ≥30 kg/m^2 after adjustment for mediators.

CONCLUSIONS Higher BMI was associated with greater risk of SCD, particularly when assessed earlier in adulthood. Strategies to maintain a healthy weight throughout adulthood may minimize SCD incidence. (J Am Coll Cardiol EP 2015;1:520–8) © 2015 by the American College of Cardiology Foundation.

Sudden cardiac death (SCD) accounts for approximately 300,000 deaths in the United States annually (1). Clinical guidelines focus prevention efforts on medical therapies in high-risk patients, yet up to 75% of all SCDs occur in patients not classified as high-risk by current guidelines (2). Broader prevention strategies are crucial for reducing the burden of SCD in the general population where most SCDs occur.

Obesity (body mass index [BMI] ≥30 kg/m^2) is associated with greater risk of coronary heart disease (CHD) (3), a major risk factor for SCD (4). However,

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data regarding the association between BMI and SCD have been conflicting. Obesity has been associated with higher risk of SCD in some studies (5-8), but not in others (9,10). Aging alters body composition (11), and age may modify the relationship between BMI and risk of SCD. For example, BMI was linearly associated with risk of SCD in middle-aged persons (7,8). In contrast, BMI was associated with SCD in a U-shaped fashion among older men and women, and the nadir in risk occurred in the overweight range (6).

In this investigation, we quantified the association between BMI repeatedly measured over 32 years and risk of SCD among women in the Nurses' Health Study. Additionally, we compared the relationship between BMI and risk of SCD with the relationship of BMI and risk of nonfatal and fatal CHD outcomes. Finally, we quantified the association of BMI and weight gain in early adulthood with risk of SCD.

METHODS

STUDY POPULATION. The Nurses' Health Study began in 1976 when 121,700 female nurses in the United States age 30 to 55 years responded to a mailed questionnaire about demographics, lifestyle, and medical history (12). Follow-up questionnaires are administered biennially to update this information and obtain information about newly diagnosed diseases. Diet was assessed initially in 1980 with a semiquantitative food frequency questionnaire. Return of the baseline questionnaire implied informed consent and the institutional review board at Brigham and Women's Hospital approved the study protocol. The overall follow-up rate was 96% through 2013.

The baseline for this analysis was 1980 when information on weight at age 18 years and important potential confounders (diet and physical activity) were first reported (n = 92,468 women). We excluded women with a history of cardiovascular disease (CVD) and cancer (n = 5,076) or missing information on age (n = 46), current weight (n = 560), or diet (n = 439) at baseline. We excluded women who were underweight (BMI <18.5 kg/m^2) during follow-up (n = 12,781) or who had chronic obstructive pulmonary disease (n = 980), Parkinson disease (n = 6), or multiple sclerosis (n = 96) at baseline to reduce potential reverse causation due to underlying illness. The final analysis included 72,484 women.

EXPOSURE ASSESSMENT. We calculated BMI as weight in kilograms divided by height in meters squared (kg/m^2). Self-reported adult height and weight were ascertained on the 1976 questionnaire. Self-reported weight was highly correlated with directly measured weight in a previous validation study (r = 0.96) (13). Women reported weight at age 18 on the 1980 questionnaire (<1% missing). This recalled weight was highly correlated with measured weight from physical examination records during that period (r = 0.87) (14).

OUTCOME ASSESSMENT. The primary study endpoint was SCD and specific details for the classification of SCD in this population have been published previously (5). Deaths were reported by next of kin or postal authorities or identified through a search of the National Death Index (98% follow-up rate). For deaths occurring outside of the hospital or in the emergency department, where the death certificate or National Death Index search indicated possible CVD, we sought further information about the circumstances and timing surrounding the death from medical records or through interviews with the next of kin. We confirmed the endpoint of SCD through review of medical records, autopsy reports, and interviews with family members regarding the circumstances surrounding the death.

A cardiovascular death was considered sudden if the death or cardiac arrest occurred within 1 hour of symptom onset as documented by medical records or through reports from witnesses and next of kin. We excluded women with evidence of circulatory collapse (hypotension, exacerbation of congestive heart failure, or neurologic dysfunction) before the disappearance of the pulse to increase the specificity for an "arrhythmic" death (15). SCDs were defined as probable if the death was unwitnessed or occurred during sleep where the participant was documented to be symptom-free when last observed within the preceding 24 h without obvious extracardiac cause. We included both definite and probable cases in our analysis because results were not altered when we excluded probable cases.

The secondary endpoints were fatal CHD and nonfatal myocardial infarction (MI). We confirmed fatal CHD events by hospital records or autopsy reports (International Classification of Disease-8th and 9th Revision codes 410-412; International Classification of Disease-10th Revision codes I21-I22) or if CHD was listed as the underlying and most plausible cause of death on the death certificate and there was prior evidence of CHD. We also included probable fatal CHD events, which included deaths for which medical records were unavailable but CHD was the underlying cause of death on the death certificate or a search of the National Death Index, or a family member provided supporting information.

ABBREVIATIONS AND ACRONYMS

BMI = body mass index
CHD = coronary heart disease
CI = confidence interval
CVD = cardiovascular disease
MI = myocardial infarction
RR = relative risk
SCD = sudden cardiac death