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Original article

Young adulthood obesity and risk of acute coronary syndromes, stable angina pectoris, and congestive heart failure: a 36-year cohort study

Morten Schmidt MD [a,b,*], Hans Erik Bøtker DMSc [b], Lars Pedersen PhD [a], Henrik Toft Sørensen DMSc [a]

[a] Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark
[b] Department of Cardiology, Aarhus University Hospital, Skejby, Denmark

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ABSTRACT

Purpose: To examine the association between young adulthood obesity and long-term risk of ischemic heart disease (IHD) and nonischemic congestive heart failure (CHF).
Methods: We conducted a population-based cohort study of 12,850 male conscripts whose fitness for military service was examined by Draft Boards in Northern Denmark. Outcomes were obtained from the Danish National Patient Registry, covering all Danish hospitals since 1977. Follow-up began on the 22nd birthday of each subject and continued until occurrence of an outcome, emigration, death, or on December 31, 2012, whichever came first. We used Cox regression to compute hazard ratios (HRs).
Results: The 36-year risk was 7.3% for IHD and 0.8% for CHF without pre-existing IHD among men of normal weight and 11.1% and 4.0% among obese men, respectively. Comparing obese men with men of normal weight, the adjusted HR was 1.63 (95% confidence interval [CI], 0.98–2.73) for IHD overall, 2.86 (95% CI, 1.56–5.25) for myocardial infarction, 5.52 (95% CI, 2.38–12.82) for unstable angina, 1.29 (95% CI, 0.69–2.41) for stable angina, and 6.68 (95% CI, 2.85–15.66) for CHF without pre-existing IHD.
Conclusions: Young adulthood obesity was an important risk factor for IHD but also for CHF without pre-existing IHD.

Introduction

The prevalence of young adulthood obesity, now exceeding 30% in the Untied States, is a major public health concern [1]. It is likely to counterbalance the current trend of declining cardiovascular mortality rates [1,2]. Development of obesity at a young age versus later in life is of particular concern due to early clustering of cardiovascular risk factors, particularly the metabolic syndrome [3,4], which increases risk of cardiovascular death [5]. Through ischemic heart disease (IHD), obesity is also associated with congestive heart failure (CHF). However, obesity may also lead to nonischemic CHF through hemodynamic [6], anatomic cardiac [6], metabolic [3], inflammatory [7,8], and hormonal changes [7–9]. The impact of young adulthood obesity on long-term risk of nonischemic CHF has not yet been examined.

We, therefore, followed a cohort of 22-year-old otherwise healthy men for up to 36 years to examine the association between body mass index (BMI) in young adulthood and IHD and nonischemic CHF.

Methods

Setting

This population-based cohort study was set in Denmark's Fifth Military Conscription District, with approximately 700,000 inhabitants [10]. The Danish National Health Service provides universal tax-supported health care, guaranteeing unfettered access to general practitioners and hospitals and partial reimbursement for prescribed medications [11]. Accurate and unambiguous individual-level linkage of all Danish registries is possible using the unique central personal registration number assigned to all residents at birth or on immigration [12]. The Danish Civil Registration System has recorded all changes in vital status and migration for the entire Danish population since 1968, with daily electronic updates [12].

Study cohort

Nearly all Danish men are required to register with their Draft Board and undergo an examination of fitness for military service on

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* Corresponding author. Department of Clinical Epidemiology, Aarhus University Hospital, Olof Palmes Allé 43-45, DK-8200, Aarhus N, Denmark. Tel.: +45 871 68063; fax: +45 871 67215.
E-mail address: morten.schmidt@dce.au.dk (M. Schmidt).

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reaching 18 years of age or shortly thereafter (median age: 19 years) [13]. During this process, the young men complete a health questionnaire in which they report chronic diseases that could preclude military service, for example, asthma, epilepsy, or spinal osteochondrosis [14]. The Draft Board verifies such reports with health care providers, and men deemed ineligible for military service are exempted at this point (approximately 15%) [15]. Information obtained during the examinations is stored electronically [10]. We used a conscription research database to identify all persons in the 1955 ($n = 6502$) and 1965 ($n = 6358$) birth cohorts who later appeared before their Draft Board in Northern Denmark. Persons with missing data on BMI were excluded ($n = 10$).

Body mass index

All potential conscripts undergo a physical and mental examination. The physical examination includes measurements of height (without shoes) and body weight (wearing trunks only and using sliding scales and calibrated balances). We used these height and weight measurements to compute BMI. We categorized BMI as underweight ($<$18.5 kg/m^2), normal (18.5 to $<$25.0 kg/m^2), overweight (25.0 to $<$30.0 kg/m^2), or obese ($\geq$30 kg/m^2).

Outcomes

The Danish National Patient Registry (DNPR) contains information on patients discharged from all Danish nonpsychiatric hospitals since 1977 and from all emergency room and outpatient specialty clinic visits since 1995 [16]. Each hospital discharge or outpatient visit is recorded in the DNPR with one primary diagnosis and one or more secondary diagnoses classified according to the *International Classification of Diseases*, Eighth Revision until the end of 1993 and Tenth Revision thereafter [16].

We used the DNPR to identify all first-time inpatient or outpatient diagnosis of IHD and CHF. IHD was defined as myocardial infarction, unstable angina pectoris, or stable angina pectoris. Patients with myocardial infarction are included in the DNPR also if they died in the ambulance on the way to the hospital or during the hospital admission but not if they died at home [2]. As measures of CHF with and without pre-existing IHD, we subcategorized CHF according to whether or not the diagnoses of IHD coexisted either before or within 30 day after the initial CHF diagnosis. To increase the completeness of the IHD variable, we also retrieved information from the DNPR on all registered coronary interventions (percutaneous coronary intervention or coronary artery bypass grafting).

Other characteristics

The conscription database also provided information on years of education at the time of examination. Based on quartiles, we categorized length of education as short, moderate, long, and very long. Quartiles of height were also computed because short stature, independent of BMI, has been associated with increased risk of myocardial infarction and CHF [17].

From the DNPR, we obtained information on diabetes mellitus and hypertension as potential mediators of the association between BMI and the outcomes [16]. We also searched the Aarhus University Prescription Database, covering the study region, for any use of oral antidiabetic or antihypertensive medication from January 1, 1989 onward [18]. Antihypertensive medication use was defined as redemption of prescriptions for at least two different antihypertensive agents (angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists, beta-blockers, calcium channel blockers, diuretics, or other antihypertensive drugs). To increase specificity, hypertension identified only on the basis of drug use was restricted to examinees without previously diagnosed IHD at the time of prescription redemption for the antihypertensive medication.

Statistical analyses

We first used descriptive statistics to characterize the study population using categories of BMI, years of education, and height. To ensure that the DNPR (established in 1977) would capture all events, we began follow-up on the 22nd birthday of each subject. We excluded all men who were censored between their examination date and their 22nd birthday (32 men died and 18 emigrated). Follow-up continued until the first occurrence of a study outcome, death, emigration, or on December 31, 2012, whichever came first.

We first illustrated graphically the association between BMI and the predicted cumulative incidence of each outcome using Fine and Gray's proportional subhazards model [19,20]. We computed the 36-year risk (i.e., risk at age 58 years) for each outcome according to BMI category. Death was treated as a competing risk in all analyses.

We used Cox proportional hazards regression, with age as the underlying time scale, to compute hazard ratios (HRs) with 95% confidence intervals (CIs) associating BMI with each outcome [20]. BMI was analyzed both as a categorical (quartiles) and continuous (per 1-unit increase) variable. For the categorical variable, the proportional hazards assumption was assessed using log-log plots and Schoenfeld test and found valid. We assessed the scale of the continuous BMI variable using fractional polynomials and found no evidence of nonlinearity in the log hazard. We repeated all regression analyses adjusting for years of education and body height.

To assess the degree to which an association between BMI and the outcomes was mediated through other important risk factors for IHD and CHF, we performed a subanalysis including diabetes and hypertension as categorical variables in the model. If the associations were mediated through these risk factors, we would expect the effect estimates to move toward unity when they were included in the regression model.

The study was approved by the Danish Data Protection Agency (2011-41-5807). All analyses were conducted using STATA software version 12.1 (STATA, College Station, TX).

Results

Characteristics

The characteristics of the study population are presented in Table 1. We identified 12,850 males from the 1955 and 1965 birth cohorts in Northern Denmark who were examined by their Draft Boards and who had complete data on BMI. Among these, 10,639 (83%) were of normal weight, 617 (5%) were underweight, 1368 (11%) were overweight, and 226 (2%) were obese. BMI ranged from a minimum of 14.4 kg/m^2 to a maximum of 42.7 kg/m^2. The median BMI was 21.8 kg/m^2 (interquartile range: 20.4–23.5 kg/m^2). There was no substantial difference in height quartiles among BMI categories.

The cohort contributed a total of 374,036 person-years of follow-up for IHD and 376,686 person-years of follow-up for CHF, providing a median follow-up time of 26 years (mean: 29 years). Maximum follow-up time in the cohort was 36 years (35 years and 364 days). The cumulative incidence functions for IHD and CHF without pre-existing IHD are shown in Figure 1.

Ischemic heart disease

We identified a total of 619 first-time diagnoses of IHD in the cohort, among which 221 were myocardial infarctions, 34 were