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Overweight and obese cardiac patients have better prognosis despite reporting worse perceived health and more conventional risk factors

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ABSTRACT

Objective. The obesity paradox in patients with cardiovascular disease (CVD) remains unexplained. We examined the role of self-rated health, behavioral and objectively assessed risk factors, in order to further explore mechanisms that might influence the association between body mass index (BMI) and mortality in CVD patients.

Methods. Participants were 4417 community dwelling adults from the Health Survey for England and Scottish Health Survey from 1994–2004 (aged 65.9 ± [Standard deviation (SD) 10.6 yrs], 56.2% men) with clinically diagnosed CVD at baseline.

Results. There were 570 CVD and 1441 and all-cause deaths, over an average of 7.3 yrs of follow-up. Overweight and obese patients reported worse self-rated health, more co-morbidities and biological risk factors. However, compared with non-obese participants (BMI < 25 kg/m^2), a lower risk of all-cause mortality was observed in overweight (BMI 25 < 30 kg/m^2) (Hazard ratio [HR] = 0.73, 95% confidence intervals [CI], 0.64–0.82), and obese (BMI ≥ 30 kg/m^2) participants (HR = 0.84, 95% CI, 0.73–0.97) after adjustment for age, sex, smoking, physical activity, and various co-morbidities.

Conclusions. Overweight and obese CVD patients have better prognosis despite reporting worse health, more co-morbidities and risk factors, and poorer adherence to lifestyle advice.

Introduction

There is convincing evidence to show adverse effects of obesity on health in the general population (Kopelman, 2000; Whitlock et al., 2009). In a recent comprehensive systematic review of more than 2.88 million healthy individuals at baseline, overweight was associated with slightly reduced risk of all-cause mortality although obesity was associated with up to 30% increased risk (Flegal et al., 2013). However, a paradoxical association between body mass index (BMI) and survival has been demonstrated in patients with cardiovascular disease (CVD) (Oreopoulos et al., 2008; Romero-Corral et al., 2006), showing that both overweight and mildly obese patients have better prognosis. Some data suggests a linear reduction in risk with increasing BMI (Oreopoulos et al., 2009), while others have demonstrated a U-shaped relationship between BMI and mortality with the highest mortality in underweight and obese class II, but lowest in the other BMI classes (Abdulla et al., 2008). Indeed others have also confirmed poorer prognosis in class 3 obesity (Das et al., 2011), as well as showing that only those with both low BMI and low fat have the worse prognosis, suggesting that this is as much a “lean paradox” as it is an “obesity paradox” (Lavie et al., 2011). The reasons for this obesity paradox remain unclear, although patients with obesity may present earlier and be particularly targeted to receive more aggressive treatment compared to those with normal BMI. Indeed, some data have shown that overweight and mildly obese patients are more likely to be revascularized compared with underweight (Oreopoulos et al., 2009).

Self-rated health can be conceptualized as marker of overall wellbeing that may incorporate numerous constructs of health including psychological, behavioral and clinical risk factors. The role of perceived health remains unexplored in the context of the obesity paradox, but may be potentially important as self-rated health has demonstrated predictive utility for overall health status and mortality (DeSalvo et al., 2006). Related mechanisms might involve lifestyle risk factors. Contemporary reviews in cardiovascular medicine have emphasized the strong influence of lifestyle on established risk factors (Mozaffarian et al., 2008). Smoking cessation and physical activity are key aspects of secondary prevention programs (Clark et al., 2005; Smith et al., 2011), although it is unclear if better uptake and adherence to lifestyle advice might partly explain the obesity paradox in CVD patients. Several papers, for example, show that an obesity paradox does not persist in coronary patients with high levels of physical fitness (Goel et al., 2011; McAuley et al., 2010). The aim of this study was to examine the role of self-rated health, behavioral and objectively assessed risk factors, in order to further explore mechanisms that might influence the association between BMI and mortality in a community sample with established CVD.

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Methods

Study design and participants

Participants were recruited into the Health Survey for England (HSE) and Scottish Health Survey (SHS), both general population-based studies that sample individuals living in households (The Scottish Government Statistics). HSE/SHS samples are selected using multi-stage stratified probability design to give a representative sample of the target population. Stratification is based on geographical entities and not on individual characteristics: postcode sectors selected at the first stage and household addresses selected at the second stage. The overall response rate (interviewer home visit) ranged between 60 and 90% for different survey years. Participants for the present analysis were merged together from a range of different survey years and were linked prospectively to the National Health Service mortality data, thus the analyses were based on a prospective cohort design. Study participants gave full written informed consent and ethical approval was obtained from the London Research Ethics Council.

Demographic and clinical variables

During the household visit, interviewers collected information using computer-assisted personal interviewing (CAPI) modules. Various self-reported information was collected, including smoking (current/ex-smoker/never) and participation in moderate to vigorous leisure time physical activity including walking and cycling for any purpose (number of sessions per week lasting at least 30 min for walking and 15 min for sports and exercise). The physical activity questionnaire has been validated using objective accelerometry recordings (Joint Health Surveys Unit, 2007). Participants were asked to rate their health on a five point scale ranging from very good to very poor, which has demonstrated predictive utility for overall health status and mortality (DeSalvo et al., 2006). Trained interviewers collected information about physician diagnosed CVD (stroke, angina, heart attack), hypertension, and diabetes mellitus (types I and II), and trained nurses collected information on prescribed medication (including beta-blockers, ACE inhibitors, diuretics, calcium blockers, lipid lowering agents) and collected bloods in a sub-sample of patients. Participants' body weight was measured by the interviewers using Tanita electronic scales without shoes in light clothing, and height was measured using a Stadiometer with the Frankfort plane in the horizontal position. Body mass index was calculated as [BMI: weight (kilograms)/height (meters) squared]. Blood samples were analyzed for C-reactive protein (CRP), fibrinogen, hemoglobin, glycated hemoglobin, total and HDL-cholesterol. Detailed information on the technicalities of the blood analysis, the internal quality control, and the external quality assessment for the laboratory have been described elsewhere (Graig et al., 2006). Systolic and diastolic blood pressures were measured with an Omron HEM-907 blood pressure monitor three times in the sitting position after 5-minute rest between each reading. The initial reading was discarded and an average of the second and third BP recordings was used for the present analyses. In order to avoid shrinkage in effect estimates from treatment we applied a constant of 10 mm Hg to systolic blood pressure values in all participants treated with anti-hypertensive medication (diuretics, ACE-inhibitors, beta-blockers, calcium blockers) (Tobin et al., 2005).

Mortality follow-up

Classification of the primary (underlying) cause of death was based on information collected from the death certificate together with any additional information provided subsequently by the certifying doctor (e.g., secondary death cause). Diagnoses for primary cause of death were recorded using the International Classification of Diseases, Ninth (ICD-9) and Tenth (ICD-10) Revisions. Cardiovascular disease codes were 390–459 for ICD-9 and I01–I99 for ICD-10.

Statistical analyses

Body mass index was categorized into three groups (<25 kg/m^2; 25 to <30 kg/m^2; ≥ 30 kg/m^2) for the main analysis, although in sensitivity analysis we created further categories corresponding to underweight (BMI $<$ 18.5 kg/m^2) and morbid obesity (≥ 35 kg/m^2). Having first ascertained that the proportional hazards assumption had not been violated, CVD or all-cause death as the outcome of interest, we used Cox proportional hazards models to compute hazard ratios (HR) with accompanying 95% confidence intervals (CI) for the association with BMI categories. The proportional hazards assumption was examined by comparing the cumulative hazard plots grouped on the various exposure variables, although no appreciable violations were noted. Months were the time scale, and for participants with no record of an event, the data were censored at 15th February 2008 (HSE) and 31st December 2008 (SHS). Each model was adjusted for age and sex and we also ran additional models that included further adjustment for physical activity (none; <1; 1–2; ≥ 3 sessions/week lasting at least 30 min for walking and at least 15 min for sports and exercises including cycling), smoking (never; previous; current), socioeconomic status (I/II professional/intermediate, III skilled non-manual/skilled manual, IV/V part-skilled/unskilled), self-rated health, CVD medication, diabetes, and hypertension (defined as clinic blood pressure reading above 140/90 mm Hg; self-reported clinician's diagnosis; prescribed anti-hypertensive medication). In order to examine the influence of lifestyle we stratified participants according to whether they adhered to two key health behaviors (non-smoking and moderate to vigorous physical activity at least 1 session/week) and repeated the survival models described above. Although the present guidelines recommend at least 30 min of physical activity on 7 days/week (Smith et al., 2011), we used a lower threshold of 1 session/week as only 4.3% of the present sample adhered to daily exercise and in a previous analysis of this cohort we have demonstrated protective effects of activity at this lower threshold (Hamer and Stamatakis, 2012). All analyses were conducted using SPSS version 20 and a significance level of $p < 0.05$ was used.

Results

We initially identified 6715 adults with physician diagnosed CVD, although 7% (n = 444) did not consent to mortality follow up and were therefore removed from any analysis. Non-consenting adults were older than those consenting (71.9 vs. 67.7 yrs, $p < 0.001$). After the exclusion of participants with missing BMI data (n = 1207) and missing data on covariables (n = 647), the final analytic sample comprised 4417 participants (aged 65.9 ± [SD 10.6 yrs], 56.2% men).

Thirty one percent of the sample was defined as obese. Obese participants were on average younger, reported worse self-rated health and more co-morbidities compared with the normal weight and overweight (Table 1). In a sub-sample of participants with available biochemical data, obese participants displayed more risk factors including lower HDL cholesterol, elevated C-reactive protein, glycated hemoglobin, and blood pressure (Table 2). However, whole blood hemoglobin levels were higher in overweight and obese participants compared with normal weight. Only 13.1% of the sample adhered to two key health behaviors (non-smoking and moderate to vigorous physical activity at least 1/wk), and adherence was more likely in the normal weight (odds ratio [OR] = 1.31, 95% CI, 1.02–1.68) and overweight (OR = 1.54, 95% CI, 1.24–1.92) compared with obese participants.

There were 570 CVD and 1441 and all-cause deaths, over an average of 7.3 yrs of follow-up. Compared with normal weight participants, a lower risk of all-cause mortality was observed in overweight (Hazard ratio [HR] = 0.73, 95% CI, 0.65–0.83), and obese participants (HR = 0.86, 95% CI, 0.74–0.99) after adjustment for age, sex, smoking, physical activity, self-rated health, medication, and various co-morbidities (Table 3). We further disaggregated the BMI categories

Table 1
Characteristics of the study population at baseline (N = 4,417). Values are means ± SD unless otherwise stated.

Variable	BMI < 25 (n = 1090)	BMI 25 < 30 (n = 1964)	BMI ≥ 30 (n = 1363)
Age (yrs)	67.0 ± 11.9	66.8 ± 10.0	63.7 ± 9.9
Men (%)	51.9	62.5	50.4
Physically active at least 1/wk (%)	15.9	17.3	12.2
Current smokers (%)	32.7	20.7	20.0
Lowest SES (%)	29.5	25.6	31.9
Poor self-rated health (%)	26.6	22.7	31.3
CVD medication[a] (%)	80.3	83.7	86.6
Diabetes diagnosis (%)	6.8	11.0	18.0
Hypertension diagnosis (%)	46.2	53.1	67.0

[a] Includes; beta-blockers, ACE inhibitors, diuretics, calcium blockers, and lipid lowering agents.