CARDIOVASCULAR MEDICINE

Obesity and overweight in relation to disease-specific mortality in men with and without existing coronary heart disease in London: the original Whitehall study

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Objective: To examine the relations between obesity or overweight and coronary heart disease (CHD) mortality in men with and without prevalent CHD in a prospective cohort study.
Methods: In the Whitehall study of London-based male government employees, 18 403 middle age men were followed up for a maximum of 35 years having participated in a medical examination in the late 1960s in which weight, height, CHD status, and a range of other social, physiological, and behavioural characteristics were measured.
Results: In age-adjusted analyses of men with baseline CHD there was a modest raised risk in the overweight relative to normal weight groups for all cause mortality (hazard ratio 1.10, 95% confidence interval (CI) 1.00 to 1.20) and CHD mortality (1.28, 95% CI 1.11 to 1.47) but not for stroke mortality (1.01, 95% CI 0.73 to 1.40). Mortality was similarly raised in the obese group. While these slopes were much steeper in men who were apparently CHD-free at study induction, the difference in the gradients according to baseline CHD status did not attain significance at conventional levels (p value for interaction $\geqslant$ 0.24). The weight–mortality relations were somewhat attenuated when potential mediating and confounding factors were added to the multivariable models in both men with and men without a history of CHD.
Conclusions: Avoidance of obesity and overweight in adult life in men with and without CHD may reduce their later risk of total and CHD mortality.

In England, as in other industrialised societies, the decline in case fatality associated with acute coronary syndromes—seemingly attributable to advances in treatment—has led to an increased prevalence of coronary heart disease (CHD).[1 2] In comparison with their disease-free counterparts, patients with existing CHD experience raised rates of total mortality, recurrent CHD, and stroke.[3] There is therefore a need to identify risk factors for these health outcomes in patients with prevalent CHD.

In large scale prospective cohort studies of people who are apparently healthy at study induction, obesity and overweight are established risk factors for total mortality, CHD, and probably stroke.[4–6] To simplify data interpretation in studies in which CHD is the outcome of interest, investigators generally, although not always,[7 8] either exclude from their analyses patients with existing CHD at study induction or make statistical adjustment for CHD status.[9–11] As a consequence, much less is understood about the influence, if any, of adiposity on these outcomes in patients with a history of CHD.

We located five studies with longer term follow up (defined as $\geqslant$ 1 year) that had reported on the relation of obesity or overweight (as indexed by body mass index (BMI)) with total mortality, cardiovascular disease, CHD, or stroke (table 1) in patients with prevalent CHD.[12–16] For all cause mortality, findings are inconsistent with inverse,[14] "U" shaped,[12] and reverse "J" shaped[13 15 16] relations observed with adiposity. Results for weight and reinfarction are similarly discrepant such that positive,[12] null,[14] and "J" shaped[15] associations have been found. While only one study has examined the influence of adiposity on stroke risk in patients with CHD, effect estimates for the apparent null relation were not reported.[15] This discordance in findings across studies may be attributable, at least in part, to limited statistical power in some studies owing to a low number of cases; variability in the definition of obesity and overweight across reports, so complicating comparison; and a failure in some studies to adjust for potentially important covariates in the weight–mortality relation, particularly socioeconomic position.[17]

Extended mortality surveillance of the Whitehall study cohort affords us the opportunity to address these issues of data paucity and methodological shortcomings. In the late 1960s, over 18 000 middle aged London based government employees participated in a medical examination in which CHD status, BMI, and a range of covariate data were assessed.[18] For the purposes of comparison, in the present analyses we present the obesity–mortality gradients separately in men with and without baseline CHD.

METHODS

In the Whitehall study, data were collected on 18 403 non-industrial London-based male government employees aged from 40–64 years when examined between September 1967 and January 1970, representing a 74% response. This involved the completion of a study questionnaire and participation in a medical examination, both of which have been described in detail elsewhere.[18] In brief, the questionnaire inquired about civil service employment grade (an indicator of socioeconomic position), smoking habits, chronic

Abbreviations: BMI, body mass index; CHD, coronary heart disease; CI, confidence interval; FEV_1, forced expiratory volume in one second; ICD, *International classification of diseases*

Table 1 Studies examining the relation of obesity and overweight with longer term mortality, recurrent coronary heart disease (CHD), and stroke in patients with existing CHD

Study (reference)	Study description	Outcome	Main findings
Physicians' health study[13]	5010 men (age not reported) with self reported CHD or stroke; BMI categorised into 4 groups	913 deaths comprising 703 CVD deaths after mean of 5 years' surveillance	Reverse ''J'' shaped relation of BMI groups with total and CVD mortality
Group health cooperative[15]	2677 men and women aged 30 to 79 years with a hospital admission for MI; BMI categorised into quintiles	431 deaths; 445 reinfarctions (fatal and non-fatal); 124 strokes (fatal or non-fatal) after mean of 3.4 years' surveillance	Relation of BMI with CHD was ''J'' shaped, null with stroke (estimates not reported), and reverse ''J'' shaped with total mortality
Diet and reinfarction trial[16]	2033 men (age not reported) with a hospital discharge record for MI; BMI categorised into quartiles	1083 deaths comprising 739 CHD deaths after up to 17 years' surveillance	Reverse ''J'' shaped relation of BMI with total and CHD mortality
Group health cooperative[12]	691 women aged 66.2 years (mean) with a hospital discharge record for MI; BMI categorised into thin, normal weight, overweight, and obese	166 deaths and 127 reinfarctions (fatal and non-fatal) after up to 13 years' surveillance	BMI positively related to reinfarction; BMI–total mortality association ''U'' shaped
San Diego and Vancouver study[14]	1760 men and women (age and sex distribution not reported) with a hospital admission for acute MI; BMI categorised into normal weight, overweight, and underweight	Mortality and reinfarction after 12 months (numbers not reported)	Relation of BMI categories inverse for mortality and null for reinfarction

All studies used a cohort design; assessment of obesity and overweight was based on body mass index (BMI); follow up was at least one year after study recruitment.
CVD, cardiovascular disease; MI, myocardial infarction.

bronchitis, marital status, physical activity, unexplained weight loss in the preceding year, physician-diagnosed heart problems or high blood pressure, the use of drugs for high blood pressure, and family history of CHD (one third of participants only). Forced expiratory volume in one second (FEV_1) adjusted for height, fasting plasma cholesterol, post-challenge two hour blood glucose, and blood pressure were determined using standardised protocols.[19]

Ascertainment of obesity and overweight

Height was measured with the man wearing shoes and standing with his back to a measuring rod; readings were taken to the nearest half inch (approximately 12.7 mm) below.[18] Weight was recorded with the participant wearing shoes but with jacket removed; readings were taken to the nearest half pound (227 g).[18] After conversion from imperial to metric units, BMI (weight (kg) divided by height squared (m^2)) was computed. By using this index of adiposity, we defined normal weight (18.5 to < 25.0 kg/m^2), overweight (25.0–29.99 kg/m^2), and obesity (≥ 30.0 kg/m^2) according to criteria advanced by the World Health Organization.[20] We excluded three men with missing data for height and weight and a further 220 men in the underweight category (< 18.5 kg/m^2) because there were too few participants with CHD (n = 47) to facilitate meaningful analyses. By using these classifications, we[21] and others[22 23] have recently reported on the link between weight and organ-specific cancers.

Ascertainment of CHD

For these analyses, the presence of CHD was defined on the basis of a resting ECG or self report.[24] The ECG was regarded as positive for CHD if Q/QS items (codes 1.1–3), or ST/T items (codes 4.1–4 or 5.1–3), or left bundle branch block (code 7.1) was present. All traces were double coded by trained technicians according to the Minnesota system with adjudication by a physician if dispute arose.[25 26] Self reported CHD was defined as a positive response to the Rose angina questionnaire or a report of severe pain across the front of the chest lasting half an hour or more.[27] These various assessments of existing CHD, approved by the World Health Organization, have been shown to be strongly predictive of CHD mortality in the present cohort.[26 28 29] CHD status was unknown for 162 men, who were excluded from all analyses.

Ascertainment of death

The records of study participants were traced and flagged by using the procedures of the National Health Service Central Registry until 31 December 2002. Among decedents, 91.6% of death certificates were coded according to the eighth revision of the *International classification of diseases* (ICD),[30] 7.0% according to the ninth revision,[31] and 1.4% according to the 10th revision.[32] Deaths were classified as CHD (ICD-8/9 codes 410–414; ICD-10 codes I20–I25), stroke (ICD-8/9 codes 430–438; ICD-10 codes I60–I69), cardiovascular disease (ICD-8/9 codes 390–458; ICD-10 codes I00–I99), or non-cardiovascular disease (all other deaths with specified cause).

Data manipulation and statistical analyses

In the present study, existing disease at study entry was defined as a positive response to inquiries regarding a range of health conditions: intermittent claudication, physician diagnosed heart problems or high blood pressure (one question), dyspnoea, and bronchitis. Further, men with diabetes comprised those who gave a positive response to the questionnaire inquiry ''are you, or have you been, diabetic?'' or those who had blood glucose concentration two hours after the glucose load of ≥ 11.1 mmol/l (≥ 200 mg/100 ml). A blood glucose concentration of 5.4–11.0 mmol/l (96–199 mg/100 ml) was used to designate participants with impaired glucose tolerance, with all remaining men termed normoglycaemic.[19 33] Participants who, according to the questionnaire inquiry, had declared themselves to be diabetic did not undergo a blood glucose test. By using these data on diabetes, we created three covariates: one each to indicate the presence of diabetes or impaired glucose tolerance; and another (continuous) variable for blood glucose concentration in normoglycaemic participants, in which those with diabetes or impaired glucose tolerance were denoted zero. Smoking status was grouped into four categories (never smoker, former smoker, current pipe or cigar smoker, and current cigarette smoker) together with additional adjustment for the number of cigarettes smoked daily by current smokers. An indicator variable for whether the study participant had any first degree relatives (parents, siblings, or children) with heart disease was also created. Lastly, during the baseline study, the physical activity inquiries on the questionnaire were modified. Levels of this behaviour were therefore determined from either an item about travel activity (administered to

Table 2 Baseline characteristics* of men with and without prevalent CHD at baseline

	Without baseline CHD	With baseline CHD	p Value
Number	14400 (84.7%)	2596 (15.3%)	
Age (years)	51.2 (0.1)	53.2 (0.1)	<0.001
Plasma cholesterol (mmol/l)	5.10 (0.01)	5.19 (0.02)	<0.001
FEV_1 (l/s)	3.16 (0.01)	3.04 (0.01)	<0.001
Systolic BP (mm Hg)	135.5 (0.2)	139.7 (0.4)	<0.001
Diastolic BP (mm Hg)	84.1 (0.1)	86.9 (0.3)	<0.001
Blood glucose (mmol/l)†	4.06 (0.01)	4.06 (0.01)	0.98
Physically inactive (%)	15.8 (0.3)	17.3 (0.8)	0.03
Unintentional weight loss in previous year (%)	1.9 (0.1)	2.6 (0.3)	0.02
Current cigarette smoker (%)	40.5 (0.4)	42.6 (1.0)	0.02
Low work grade (%)	23.0 (0.3)	25.2 (0.8)	0.01
No partner (%)	11.5 (0.3)	13.0 (0.7)	0.06
Disease at study entry (%)‡	6.6 (0.2)	25.0 (0.8)	<0.001
BP lowering medication (%)	1.1 (0.1)	4.1 (0.4)	<0.001
Glucose intolerance (%)†	5.0 (0.2)	6.9 (0.5)	<0.001
Diabetes (%)§	1.3 (0.1)	1.5 (0.2)	0.43
Family history of CHD (%)¶	12.7 (0.5)	16.3 (1.3)	0.003

Data are number (%), mean (SE), or percentage (SE).
*Adjusted for age (age is unadjusted); †data available for normoglycaemic men only; ‡defined as a positive response to inquiries regarding a range of health conditions (intermittent claudication, physician diagnosed heart problems or high blood pressure (BP), dyspnoea, and bronchitis); §defined by a positive response to the questionnaire inquiry ''are you, or have you been, diabetic?'' or having blood glucose concentration two hours after glucose load of ⩾11.1 mmol/l); ¶assessed in a subset of 6287 men only.
FEV_1, forced expiratory volume in one second (adjusted for height).

about the first two thirds of study participants) or from leisure activities (administered to the remainder).[34 35] Analyses of the weight–mortality relation indicated that there was no confounding effect due to questionnaire type.

The vital status of 17 868 men (99% of those available for analysis) was ascertained; 16 996 (95.1%) of these had full baseline data. In analyses of baseline characteristics according to presence of CHD at study induction and the level of obesity and overweight, the prevalences of the baseline characteristics were adjusted for age (five year age groups) by the direct standardisation method. Differences and trends in proportions were tested for significance by using the Mantel-Haenszel test. For continuous variables, least squares means were used to present the age-adjusted means and tests for differences between the CHD groups and trends across obesity, overweight, and normal weight groups were computed by fitting a CHD group term and a linear trend term, respectively.

Hazard ratios and accompanying confidence intervals (CIs) were computed for the relation of obesity and overweight with each mortality outcome by using Cox's proportional hazards regression model with follow up period as the time scale.[36] These models were initially adjusted for age and then for other potential covariates. P values for trends in effect estimates across the weight categories were also calculated. For statistical adjustment, age, plasma cholesterol, height adjusted FEV_1, systolic and diastolic blood pressure, and blood glucose in normoglycaemic participants were fitted as continuous variables.[19] Unexplained weight loss in the previous year (two levels), employment grade (five), marital status (four), blood pressure lowering medication (two), physical activity (six), and disease at study entry (two) were fitted categorically. All statistical analyses were computed using SAS computer software (SAS Institute Inc, Cary, North Carolina, USA).

RESULTS

Table 2 presents the baseline characteristics of men with and without prevalent CHD at study induction. As expected, men with CHD had less favourable characteristics. Thus, they were older, had higher cholesterol concentration and blood pressure, and poorer lung function than their disease-free co-workers. Men with CHD were also more likely to be physically inactive, smoke cigarettes, be without a partner, and to report having experienced unintentional weight loss in the preceding year, although differences according to CHD status were not substantial. They were also more likely to carry a morbid load other than CHD as evidenced by the increased prevalence of blood pressure lowering medication use and impaired glucose tolerance.

In table 3 we present the relation (age-adjusted) of obesity and overweight with baseline characteristics in men with and without CHD. Men with obesity and overweight constituted 4.2% (n = 711 men) and 41.5% (n = 7048 men) of the analytical sample, respectively. In general, unfavourable levels of most characteristics were apparent in the higher weight categories in both men with and men without CHD at induction. The prevalence of morbidity of overweight and obese men—according to disease at entry, glucose intolerance, and diabetes—was generally raised in comparison with their normal weight colleagues. In comparison with the obese, leaner men were also younger, had lower plasma cholesterol concentration and blood pressure, were more active, and were less likely to be employed in a low grade job. By contrast, the prevalence of smokers was reduced in the overweight and obese groups.

Table 4 shows the relations of obesity and overweight to five mortality end points in men with and without baseline CHD. A total of 10 845 men (64%) had died (8886 without baseline CHD; 1959 with baseline CHD) during a maximum of 35 years' follow up. After age-adjustment in men with CHD, a modest raised risk in the overweight groups relative to the normal weight was apparent for all-cause (hazard ratio 1.10, 95% CI 1.00 to 1.20), cardiovascular disease (1.27, 95% CI 1.13 to 1.43), and CHD mortality (1.28, 95% CI 1.11 to 1.47) but not for non-cardiovascular disease (0.88, 95% CI 0.77 to 1.02) or stroke (1.01, 95% CI 0.73 to 1.40). The number of cases in the stroke analyses was low, however. In general, for men with CHD, the point estimates were similar in the obese and overweight groups. Hazard ratios for these outcomes were similar for men with obesity.

In men with no evidence of baseline CHD, weight was positively associated with each outcome in an age-adjusted analysis. The magnitude of these relations was typically higher than in analyses featuring men with baseline CHD. The raised risk was largely evident in obese men for all causes

Table 3 Obesity and overweight in relation to baseline characteristics*

	Without baseline CHD (n = 14400)				With baseline CHD (n = 2596)			
	Normal weight	Overweight	Obese	p Value for trend	Normal weight	Overweight	Obese	p Value for trend
Number	7901 (54.9%)	5916 (41.1%)	583 (4.0%)		1336 (51.5%)	1132 (43.6%)	128 (4.9%)	
Age (years)	50.8 (0.1)	51.7 (0.1)	52.1 (0.3)	<0.001	52.6 (0.2)	53.8 (0.2)	54.7 (0.5)	<0.001
Plasma cholesterol (mmol/l)	5.01 (0.01)	5.21 (0.02)	5.14 (0.05)	<0.001	5.14 (0.03)	5.24 (0.04)	5.25 (0.11)	0.06
FEV_1 (l/s)	3.15 (0.01)	3.17 (0.01)	3.10 (0.02)	0.19	3.00 (0.02)	3.08 (0.02)	3.09 (0.05)	<0.001
Systolic BP (mm Hg)	132.5 (0.2)	138.2 (0.3)	147.3 (0.8)	<0.001	136.1 (0.5)	142.3 (0.7)	155.6 (1.8)	<0.001
Diastolic BP (mm Hg)	81.3 (0.1)	87.0 (0.2)	93.1 (0.5)	<0.001	83.7 (0.4)	89.7 (0.4)	97.7 (1.2)	<0.001
Blood glucose (mmol/l)†	4.06 (0.01)	4.07 (0.02)	4.11 (0.0.02)	0.03	4.06 (0.02)	4.06 (0.02)	4.10 (0.05)	0.72
Physically inactive (%)	15.0 (0.4)	15.8 (0.5)	24.4 (1.8)	<0.001	16.4 (1.0)	17.8 (1.2)	19.2 (3.4)	0.18
Unintentional weight loss in previous year (%)	2.9 (0.2)	0.9 (0.1)	0.0	<0.001	3.9 (0.5)	1.2 (0.4)	1.7 (1.2)	<0.001
Current cigarette smoker (%)	43.5 (0.6)	37.2 (0.6)	36.7 (2.0)	<0.001	47.2 (37.7)	37.7 (1.5)	40.1 (5.4)	<0.001
Low work grade (%)	22.9 (0.5)	22.6 (0.5)	29.2 (1.8)	0.08	25.2 (1.1)	24.3 (1.3)	32.9 (3.8)	0.46
No partner (%)	12.2 (0.4)	10.4 (0.4)	14.1 (1.5)	0.09	13.5 (1.0)	12.0 (1.0)	13.7 (2.8)	0.73
Disease at study entry (%)	6.0 (0.3)	7.1 (0.3)	9.8 (1.2)	<0.001	24.4 (1.2)	25.1 (1.3)	28.7 (3.8)	0.31
BP lowering medication (%)	0.8 (0.1)	1.4 (0.2)	1.0 (0.4)	0.004	3.5 (0.5)	4.5 (0.6)	6.8 (2.1)	0.04
Glucose intolerance (%)†	4.4 (0.2)	5.5 (0.3)	7.1 (1.0)	<0.001	6.1 (0.7)	7.2 (0.8)	11.2 (2.6)	0.02
Diabetes (%)	1.2 (0.1)	1.2 (0.1)	1.6 (0.5)	0.83	1.1 (0.3)	1.5 (0.4)	4.0 (1.6)	0.01
Family history of CHD (%)‡	12.1 (0.6)	13.7 (0.8)	10.8 (1.9)	0.40	15.8 (1.7)	17.1 (2.1)	12.5 (4.2)	0.91

Data are number (%), mean (SE), or percentage (SE).
*Adjusted for age (age is unadjusted); †data available for normoglycaemic men only; ‡assessed in a subset of 6287 men only.

(hazard ratio for obese compared with normal weight: 1.53, 95% CI 1.39 to 1.69), stroke (1.64, 95% CI 1.17 to 2.28), and non-cardiovascular disease (1.24, 95% CI 1.08 to 1.44), whereas for cardiovascular disease and CHD an incremental effect was suggested across the weight categories. On comparing gradients across mortality outcomes according to baseline CHD status, these differences did not reach significance at conventional levels in any of the analyses (p value for interaction $\geqslant 0.24$). In both men with and men without CHD, with the exception of non-cardiovascular disease, the relation of each end point with weight was partially attenuated after adjustment for covariates. In general, control for potential mediating variables (for example, systolic and diastolic blood pressures and plasma cholesterol) rather than potential confounding variables (for example, employment grade and physical activity) was responsible for this attenuation.

Our definition of CHD comprised both positive responses to items on the Rose questionnaire and ECG measurement. That the Rose questionnaire is self reported raises concerns about validity. We therefore examined the effect on our results, if any, of confining our analyses to men with only positive ECG findings. A similar pattern of association was seen to that apparent when the all inclusive definition was used. Given that some men in the normal weight group may have experienced weight loss because of existing medical conditions other than CHD, we first re-computed our analyses after dropping deaths occurring within the first 10 years of mortality surveillance. In so doing we reasoned that men with serious illness would have died during this time frame. We hypothesised that this approach would have the effect of lowering the mortality in the normal weight group and therefore strengthen the overall positive relation between weight and mortality. In addition, we fitted interaction terms for the BMI categories with the logarithm of the follow up time, expecting the positive weight–mortality relation to increase in magnitude with follow up time. Both these hypotheses were supported in men with and without CHD at study induction, although the interaction terms were significant at conventional levels ($p \leqslant 0.05$) only for the overweight category in men without baseline CHD for all cause and non-cardiovascular disease mortality (data not shown).

DISCUSSION

The main finding of the present study of men with baseline CHD was a raised rate of all-cause, cardiovascular disease, and CHD mortality in the overweight and obese groups. There was, however, no apparent relation between weight and stroke risk, although the number of cases was low in this analysis. As expected, among men who were apparently CHD-free at study induction, obesity and overweight were positively related to each of these end points. While the gradients were somewhat steeper in this group, they were not significantly different from those apparent in men with baseline CHD.

Comparison with other studies

The raised rates of total mortality, CHD, and probably stroke in overweight or obese men without prevalent CHD are generally consistent across large scale prospective studies and accord with the findings herein.[4–6] By observing attenuation in these associations after adjustment for mediating variables but not confounding variables, we found support for the suggestion that some of the weight–mortality effect may be ascribed to the relation of increased weight with other risk indices for mortality such as raised blood pressure and plasma cholesterol concentrations.[5] We were, however, unable to examine the suggestion made recently that the

Table 4 Mortality rates and hazard ratios (HRs) (95% confidence intervals) for selected mortality outcomes in relation to obesity and overweight in men with and without prevalent CHD at baseline in the original Whitehall study

	Without baseline CHD (n = 14400)				With baseline CHD (n = 2596)				
Mortality outcome	Normal weight	Overweight	Obese	p Value for trend	Normal	Overweight	Obese	p Value for trend	p Value for interaction*
Numbers of subjects	7901	5916	583		1336	1132	128		
All causes									
Number of deaths	4639	3807	440		955	895	109		
Mortality rates (age adjusted)†	25.7	26.7	34.6		32.9	36.0	39.2		
Age adjusted HR	1.0 (ref)	1.06 (1.02 to 1.11)	1.53 (1.39 to 1.69)	<0.001	1.0 (ref)	1.10 (1.00 to 1.20)	1.28 (1.05 to 1.57)	0.005	0.95
Confounder adjusted HR‡	1.0	1.08 (1.03 to 1.13)	1.55 (1.41 to 1.71)	<0.001	1.0	1.16 (1.05 to 1.27)	1.32 (1.08 to 1.62)	<0.001	0.31
Multiply adjusted HR§	1.0	1.00 (0.96 to 1.04)	1.33 (1.20 to 1.47)	0.004	1.0	1.10 (1.00 to 1.21)	1.13 (0.92 to 1.39)	0.05	0.24
CVD									
Number of deaths	2032	1839	241		517	562	62		
Mortality rates (age adjusted)	11.3	12.9	19.4		17.9	22.5	22.2		
Age adjusted HR	1.0	1.17 (1.10 to 1.24)	1.91 (1.67 to 2.19)	<0.001	1.0	1.27 (1.13 to 1.43)	1.31 (1.01 to 1.71)	<0.001	0.78
Confounder adjusted HR	1.0	1.18 (1.11 to 1.26)	1.94 (1.70 to 2.22)	<0.001	1.0	1.32 (1.17 to 1.49)	1.35 (1.04 to 1.77)	<0.001	0.83
Multiply adjusted HR	1.0	1.03 (0.97 to 1.10)	1.52 (1.32 to 1.74)	<0.001	1.0	1.22 (1.08 to 1.38)	1.08 (0.82 to 1.42)	0.02	0.80
CHD									
Number of deaths	1279	1183	159		361	394	45		
Mortality rates (age adjusted)	7.0	8.3	10.2		12.4	15.7	16.3		
Age adjusted HR	1.0	1.20 (1.11 to 1.30)	1.98 (1.68 to 2.34)	<0.001	1.0	1.28 (1.11 to 1.47)	1.34 (0.99 to 1.84)	<0.001	0.67
Confounder adjusted HR	1.0	1.21 (1.12 to 1.31)	2.00 (1.70 to 2.36)	<0.001	1.0	1.34 (1.16 to 1.55)	1.40 (1.02 to 1.92)	<0.001	0.99
Multiply adjusted HR	1.0	1.07 (0.98 to 1.16)	1.61 (1.36 to 1.90)	<0.001	1.0	1.24 (1.07 to 1.44)	1.13 (0.82 to 1.56)	0.02	0.91
Stroke									
Number of deaths	381	336	38		79	68	7		
Mortality rates (age adjusted)	2.2	2.4	3.2		2.7	2.8	2.3		
Age adjusted HR	1.0	1.11 (0.96 to 1.29)	1.64 (1.17 to 2.28)	0.01	1.0	1.01 (0.73 to 1.40)	1.06 (0.49 to 2.31)	0.90	0.30
Confounder adjusted HR	1.0	1.13 (0.97 to 1.31)	1.70 (1.22 to 2.39)	0.005	1.0	0.98 (0.70 to 1.36)	1.06 (0.48 to 2.30)	0.98	0.36
Multiply adjusted HR	1.0	0.96 (0.83 to 1.12)	1.25 (0.89 to 1.76)	0.73	1.0	0.87 (0.62 to 1.22)	0.78 (0.35 to 1.73)	0.35	0.30
Non-CVD									
Number of deaths	2590	1957	197		434	327	46		
Mortality rates (age adjusted)	14.4	13.8	15.2		14.9	13.3	16.9		
Age adjusted HR	1.0	0.98 (0.92 to 1.04)	1.24 (1.08 to 1.44)	0.38	1.0	0.88 (0.77 to 1.02)	1.26 (0.93 to 1.70)	0.69	0.53
Confounder adjusted HR	1.0	1.00 (0.94 to 1.06)	1.27 (1.09 to 1.46)	0.12	1.0	0.95 (0.82 to 1.10)	1.29 (0.95 to 1.75)	0.68	0.85
Multiply adjusted HR	1.0	0.98 (0.92 to 1.04)	1.19 (1.02 to 1.38)	0.52	1.0	0.96 (0.82 to 1.11)	1.23 (0.90 to 1.69)	0.74	0.69

Forty one men with unknown cause of death have been excluded from the cause specific analyses.
*Compares differences, if any, in the BMI–mortality slopes according to baseline CHD status; †mortality rates expressed per 1000 person years; ‡confounder adjusted model adjusted for age, employment grade, physical activity, smoking habit, marital status, disease at entry, and weight loss in the previous year; §multiply adjusted model adjusted for all potential confounding variables (as above) and BP lowering medication, height adjusted FEV_1, systolic BP, diastolic BP, plasma cholesterol, blood glucose (in normoglycaemic patients), glucose intolerance, and diabetes status.
ref, reference value.

influence of obesity and overweight on mortality risk may also be partially mediated by other health indices such as hyperinsulinaemia and hyperleptinaemia.[37]

In people with a history of CHD, the findings of studies of the relation of weight and the mortality outcomes reported herein are, as discussed, rather discrepant (table 1). While we found a positive BMI-total mortality gradient, Ness *et al*[16] reported a reverse J shaped relation, which has been replicated elsewhere.[13] Similarly, a positive overweight– or obesity–CHD gradient has been observed in some,[12] but not all,[14] studies. The only study to examine the link between BMI and stroke in men with ischaemic heart disease reported little evidence of an effect, supporting the results of the present analyses.[15] That we found that obesity or overweight was a predictor of CHD but not stroke mortality in men with prevalent CHD may indicate differences in the functions of coronary and cerebral arteries.

Alternative explanations

Confounding, bias, and chance may plausibly explain the associations reported herein. We incorporated a wide range of social, behavioural, and physiological variables into our statistical models so minimising confounding as a likely explanation. The loss to follow up in this cohort study was low, so also reducing concerns regarding selection bias. In the present analyses we necessarily conducted a large number of statistical tests (a total of five mortality outcomes in men with and without prevalent CHD). It is therefore conceivable that some of the present results could have arisen by chance alone. While we explored the effect of reverse causality due to both measured and unmeasured disease, given that the weight–mortality gradients were all positive rather than inverse, this would not have accounted for such associations.

Study strengths and limitations

The strengths of the present study include its size, its prospective design, the measurement of a range of covariate data including socioeconomic position, and the definition of obesity and overweight according to World Health Organization criteria.[20] This study is not, however, without its weaknesses. The assessment of obesity and overweight was based on BMI, a widely used index of overall adiposity but one that does not provide an indication of fat distribution. Although skinfold thickness was measured in the Whitehall study participants, readings were taken only at the triceps, rendering the data of little practical use. The cardiovascular disease outcomes reported herein were based on mortality surveillance. Thus, our results reflect the combined effect of weight on survival and incidence. It is unclear whether a differential association by end point definition exists as we do not have data on non-fatal events with which to make such a comparison.

In conclusion, the present study found support for a raised risk of mortality from all-cause, cardiovascular disease, CHD, and stroke in obese and overweight men who were CHD-free at study induction. With the exception of stroke mortality, similar patterns of association were apparent in men with existing CHD. Middle aged men with or without CHD should avoid becoming overweight or obese.

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IMAGES IN CARDIOLOGY

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Absorbable metal stent in human coronary arteries: imaging with intravascular ultrasound

A 39 year old woman without history of prior cardiac disease presented with typical angina on exertion. Subsequent coronary angiography revealed high grade stenosis of the proximal right coronary artery (RCA). Within the scope of the first-in-human clinical trial, the patient was treated by implantation of a novel absorbable metal stent (Biotronik, Bülach, Switzerland). This novel stent consists of a magnesium-based alloy which provides mechanical properties comparable to conventional stainless steel stents. At the same time, the magnesium alloy allows controlled complete absorption within approximately two months. Thereby, the stent provides temporary vessel scaffolding to prevent elastic recoil of the vessel wall in the first weeks after angioplasty, without remaining in the vessel life long. This allows adaptive vascular remodelling processes in the long term.

Panel A shows the satisfactory angiographic result after stent implantation without residual stenosis. Complete expansion of the stent is well visualised by intravascular ultrasound (IVUS) cross sectional images as well as in the longitudinal reconstruction.

After 18 days the patient presented again with atypical, non-exercise induced chest pain. The control angiography showed a good result without restenosis in the treated vessel segment (panel B). Interestingly, IVUS showed that the stent was already mostly absorbed in the first three weeks after implantation.

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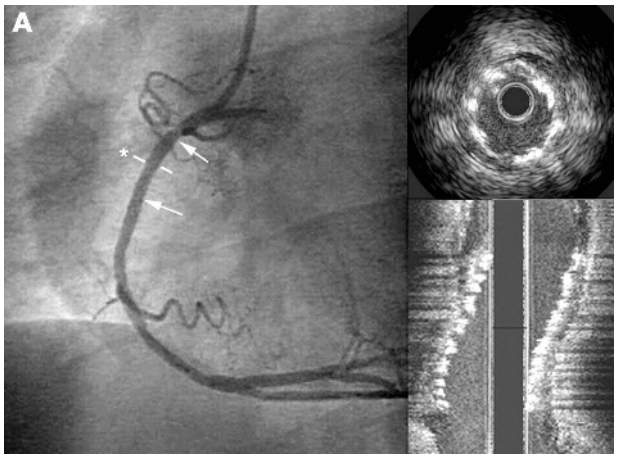
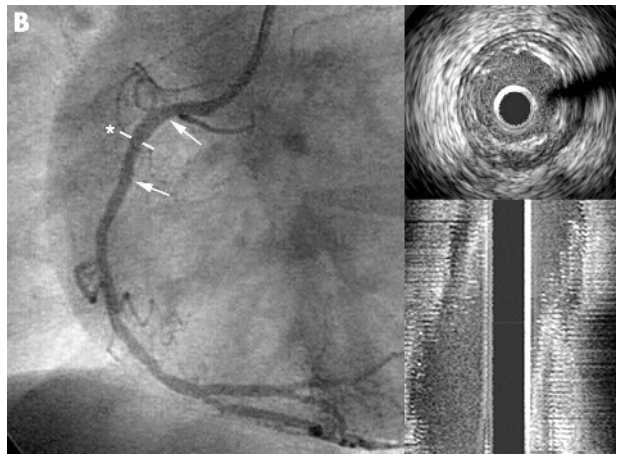


Left panel shows the angiographic result after stent implantation in the proximal part of the right coronary artery without residual stenosis (the position of the stent is indicated by the arrows). The intravascular ultrasound (IVUS) cross sectional image in the right upper panel shows a circular stent expansion with complete apposition of the stent struts to the vessel wall (asterisk indicates the site of the IVUS cross sectional image). The right lower panel shows a longitudinal reconstruction of the IVUS images in the stented segment with complete covering of the stenosis. The well apposed stent struts can be clearly identified in the longitudinal reconstruction.



Left panel shows the angiographic result three weeks after stent implantation without restenosis in the treated segment. The IVUS cross sectional image (upper right panel) and the longitudinal IVUS reconstruction (lower right panel) shows that the stent is mostly dissolved in the first three weeks without plaque progression.