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Association of Body Mass Index with Reinfarction and Survival After First Myocardial Infarction in Women

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ABSTRACT

Few studies have reported the association between adiposity and prognosis after myocardial infarction (MI) or the gender differences in these associations for women and men. The purpose of this study was to examine the association between body mass index (BMI) and reinfarction and long-term survival after the first MI in women. We conducted a retrospective cohort study of 691 women (mean age 66.2 years) who survived the first MI to hospital discharge between January 1, 1980, and December 31, 1991, while enrolled at the Group Health Cooperative of Puget Sound. Reinfarctions (n = 127) and deaths (n = 166) through December 31, 1993, were then identified. Weight and height were ascertained from medical records, and BMI (weight in kilograms divided by square of height in meters) was calculated. Relative risks were determined using proportional hazards regression. For each 1-unit increase in BMI, the relative risk of reinfarction increased by 5% (relative risk 1.05, 95% confidence interval 1.02 to 1.08). This association was unaffected by smoking and was attenuated, but not eliminated, after adjustment for diabetes and hypertension (relative risk 1.03, 95% confidence interval 1.00 to 1.07). The association between risk of all-cause mortality and BMI had a U-shaped distribution. When the analysis was limited to women with no history of cancer or pulmonary disease who had survived for 1 year, there was no association between BMI and all-cause mortality. This study provides evidence that, in women, higher BMI scores are associated with increased risk of reinfarction after a first MI.

INTRODUCTION

OVERWEIGHT IS A MAJOR HEALTH PROBLEM in the United States. Data from the National Health and Nutrition Examination Surveys (NHANES) indicate that 52% of women aged 50–59 years and 42.5% of women aged 60–69 years are overweight.[1] The association between overweight and coronary heart disease risk factors, including hypertension, hyperlipidemia, and diabetes, is well established.[2] However, studies of the independent association between body weight and coronary heart disease have yielded inconsistent findings.[2–10] Few studies have reported the association between measures of adiposity and prognosis among individuals with established coronary heart disease, nor have the particular associations for women been addressed.[11–16] The purpose of this study was to examine the association be-

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tween body mass index (BMI) and reinfarction and long-term survival among women who survived a first myocardial infarction (MI) to hospital discharge.

MATERIALS AND METHODS

Cohort identification

This retrospective cohort study was conducted at Group Health Cooperative of Puget Sound (GHC), a health maintenance organization in western Washington state. Institutional review committee approval was granted by GHC, the University of Washington, and all participating hospitals. We attempted to identify all female enrollees hospitalized for incident acute MI between January 1, 1980, and December 31, 1991. Eligibility criteria included (1) enrollment at GHC for at least 12 months prior to hospitalization, (2) postmenopausal, (3) age less than 80 years, (4) survival to hospital discharge, (5) no prior MI, cardiac arrest, coronary artery bypass graft surgery, coronary angioplasty, or stroke, and (6) absence of diseases likely to be fatal within 6 months, including cancer, advanced renal failure, and severe pulmonary disease. Women with mild or moderate pulmonary disease or a distant history of cancer were included. This study was limited to postmenopausal women because the purpose of the original study on which these analyses are based was to evaluate the associations between hormone replacement therapy and prognosis. Menopause was defined as amenorrhea for at least 6 months, bilateral oophorectomy, and (in women with hysterectomy without bilateral oophorectomy before menopause) either age past 55 years or documented menopausal symptoms.

Potential cases were identified by searching four GHC automated databases for International Classification of Diseases (ICD-9CM) diagnosis codes indicative of hospitalization for acute MI. All records of hospitalizations with admission or discharge diagnosis codes of acute MI, ventricular fibrillation, or cardiac arrest (ICD-9CM 410, 427.4, 427.5, respectively) were selected. In addition, hospitalization records with diagnosis codes for acute ischemic heart disease (ICD-9CM 411), subacute ischemic heart disease (ICD-9CM 413), and chronic ischemic heart disease (ICD-9CM 414) were selected from the two databases that contained only admission diagnosis codes. Using this approach, 3714 women with possible MI were identified. Outpatient and inpatient records were then reviewed for eligibility. Only 105 records (2.8%) were not located. Potential cases were classified by one investigator (K.M.N.) without knowledge of the patients' prior or subsequent estrogen use as having definite, probable, or no MI based on chest pain, cardiac enzyme levels, and electrocardiographic (ECG) findings using the American Heart Association's Council on Epidemiology and Prevention criteria.[17,18] Women with perioperative MI were excluded. After outpatient and inpatient record review, 726 women (638 with definite MI, 88 with probable MI) comprised the study cohort. Exclusion of women with probable MI had no effect on the results; thus, the findings are presented for the entire cohort.

Ascertainment of weight and height

The most recent measurements for weight and height reported in the outpatient medical record before the first acute MI and the last height and weight measurements reported during hospitalization for the first acute MI were recorded in the same units found in the medical record and later converted to kilograms and centimeters. Height measurements were available in 423 hospital and 689 clinic records. Clinic height measurements were recorded at varying times before the first MI. Approximately 50% were within 10 years and 80% were within 20 years of first MI. Weight measurements were available in 630 hospital and 714 clinic records. BMI (weight in kilograms divided by square of height in meters) was used as the measure of overweight in this analysis because it is highly correlated with other, more direct measurements of body fatness, is minimally correlated with height, and is ethnicity independent in black and white adults after controlling for age.[19,20] BMI scores calculated from data in hospital and clinic records were highly correlated (Pearson's R =

0.94), and our results were similar regardless of whether BMI was calculated from clinic or hospital weight records. We wished to use data gathered as closely a possible to the date of MI and, therefore, used the following priority to select height and weight measurements to calculate BMI: hospital weight and height (n = 413); hospital weight, clinic height (n = 201); clinic weight and height (n = 91). BMI could not be calculated for 21 women because of missing data, and data for 14 women were deleted because their most recent available weight was recorded more than 2 years prior to MI. Thus, 691 women were included in the final analysis. BMI was classified into four groups: <20, "thin"; 20–24, "normal"; 25–29, "overweight"; and ≥30, "obese." We did not evaluate the effects of weight change after the first MI because of our inability to distinguish voluntary weight change for the purposes of risk reduction from involuntary weight change as a result of worsening clinical status.

Ascertainment of reinfarction and vital status

Reinfarction and vital status through December 31, 1993, were determined from (1) outpatient record review, (2) GHC's hospitalization databases, and (3) the GHC death file. The GHC hospitalization databases were searched for hospital readmissions for fatal and nonfatal MI and hospitalizations during which a woman died of any cause, using a strategy similar to that used for identifying the first MI. All records of hospitalizations with admission or discharge diagnosis codes of acute MI, ventricular fibrillation, or cardiac arrest (ICD-9CM 410, 427.4, 427.5) and of hospitalizations resulting in death were selected. In addition, hospitalization records with diagnosis codes for acute ischemic heart disease (ICD-9CM 411), subacute ischemic heart disease (ICD-9CM 413), and chronic ischemic heart disease (ICD-9CM 414) were selected from the two databases that contained only admission diagnosis codes. There were 357 readmissions identified among 266 women in the cohort. The discharge summary was used to classify the event when it contained sufficient information on chest pain and ECG and enzyme level changes for us to apply the myocardial infarction algorithm. In the remaining cases, data were collected at the admitting hospital. All records were searched for hospitalizations that occurred outside the stage during medical record review. As long as women remained actively enrolled at GHC, discharge records from such hospitalizations were available for review. The GHC death file is constructed annually from Washington State death certificates, hospitalization databases, and information provided by the Cancer Surveillance System of Western Washington. We relied on a death certificate ICD9-CM code of 410 (acute MI) as evidence of fatal MI for 20 cases. In the Framingham study,[21] silent reinfarction was rare, so we chose not to examine follow-up ECG for silent reinfarction. There were no perioperative reinfarctions.

To determine whether the patients were alive or dead, all deaths were first identified. Among the remaining women, if any prescription was filled after December 31, 1993, or if GHC enrollment was active on December 31, 1993, the woman was considered alive at the end of follow-up. Otherwise, follow-up was censored as of the end of the last quarter of GHC enrollment. Only 48 women (6.9%) had follow-up time truncated because of disenrollment.

Ascertainment of prognostic factors

Information on known or suspected prognostic factors abstracted from the medical records included age, race (white, nonwhite), marital status (married, single/widowed/divorced), height (centimeters), weight (kilograms), cigarette smoking at time of the first MI (current, never, former), history (yes/no) prior to the first MI of angina, high blood pressure, diabetes, congestive heart failure, or peripheral vascular disease, serum cholesterol ≤200 mg/dl, 201–240 mg/dl, or >240 mg/dl, and serum glucose levels prior to or at the first MI. The use of hormone replacement therapy (current, past, never) before and after the first MI was ascertained from computerized pharmacy records maintained at GHC since 1977. The chronic disease score,[22,23] a validated measure of comorbidity, was calculated for the year immediately before the first MI. This score, determined from computerized pharmacy records, is derived from a weighted sum of

medications reflecting the number and severity of major chronic illnesses during a 1-year period.

Data on measures of left ventricular function, such as ejection fraction, were seldom available, particularly for women from the earlier years of the cohort. However, we documented evidence in the hospital record of signs and symptoms of ventricular failure (yes/no), including rales, sinus tachycardia, and radiographic evidence of congestive heart failure, as well as the prescription of digitalis, diuretics, or beta-blockers at hospital discharge. Measures of left ventricular function after MI were inconsistently available and could not be addressed. Similarly, reliable information on the timing of smoking cessation after the first MI were seldom available, and the effects of smoking cessation could not be evaluated.

Statistical analysis

Follow-up time accrued from the date of hospital discharge for the first MI until the date of nonfatal or fatal reinfarction (for the reinfarction analyses), death, disenrollment from GHC, or December 31, 1993, whichever came first. Age-standardized incidence rates were calculated by the direct method, standardized to the age distribution of person-years for the entire cohort.[24] Cox proportional hazards models were used to estimate the relative risks associated with body weight measures, adjusting for age and other prognostic factors.[25] After controlling for age and diabetes, those covariates that continued to influence the associations between BMI and our outcomes of interest were included in the final models. Because reinfarction rates within levels of BMI were similar in white and nonwhite women and there were too few nonwhite women to analyze separately, these groups were analyzed together. The use of estrogen replacement therapy after MI was modeled as a time-dependent covariate, allowing the coding of estrogen use (current, past, never) to change over time.

RESULTS

Demographic characteristics and prognostic indicators stratified by BMI are presented in Table 1. Mean height was similar across the four categories of BMI. Women with BMI ≥30 were younger, less likely to be current smokers, more likely to have a history of diabetes, serum glucose ≥110 mg/dl, and hypertension, and more likely to have a chronic disease score of ≥7 than were women with BMI 20–24. Women with BMI <20 were more likely to have a history of chronic pulmonary disease before the first MI than women with BMI 20–24. History of serum cholesterol > 240 mg/dl was similar across the BMI categories, as was a history of cancer and use of estrogen replacement therapy either before or after the first MI. There were few differences in physical or x-ray findings from hospitalization for the first acute MI according to BMI. However, women in the highest BMI category were more likely to have cardiomegaly on x-ray than women with BMI 20–24. Women in the lowest BMI category were more likely to have sinus tachycardia than women with BMI 20–24.

There were 127 first reinfarctions (92 nonfatal, 35 fatal), and 165 women died during follow-up. Over half of the deaths ($n = 91$) were caused by coronary heart disease (MI, coronary artery disease, or cardiac arrest). Other causes of death included congestive heart failure and acute pulmonary edema ($n = 11$), stroke or cerebrovascular disease ($n = 11$), other cardiovascular disease ($n = 7$), cancer ($n = 23$), respiratory diseases ($n = 9$), and other causes ($n = 13$). Seven women died of lung cancer and two of breast cancer.

The age-standardized rate of reinfarction increased with increasing BMI, from 24.31/1000 person-years for women with BMI <20 to 51.03/1000 person-years for women with BMI ≥30 (Fig. 1). There was a U-shaped association between BMI and the age-standardized rate of all-cause mortality (Fig. 2). Women with BMI <20 had the highest mortality rate, followed by those with BMI ≥30, whereas the rate for women with intermediate BMI was lower than these two extremes.

The age-adjusted relative risk of reinfarction for women with BMI ≥30 was 2.6 times that of women with a BMI <20 (Table 2). Adjustment for smoking did not change this risk estimate. Adjustment for diabetes, hypertension, and the chronic disease score attenuated but did not

TABLE 1. CHARACTERISTICS OF WOMEN WHO SURVIVED FIRST MI TO HOSPITAL DISCHARGE, 1980–1991, BY LEVELS OF BMI, GROUP HEALTH COOPERATIVE OF PUGET SOUND

	Body mass index			
	<20 *n = 55 (8%)*	*20–24* *n = 184 (27%)*	*25–29* *n = 286 (43%)*	*≥30* *n = 145 (22%)*
Mean weight (kg)	49.1	58.2	69.8	90.2
Mean height (cm)	163.1	161.3	161.5	160.9
Age in years at first myocardial infarction (MI) (%)				
50–59	7.3	15.8	16.8	24.8
60–69	41.8	36.4	41.6	51.0
70–79	50.9	47.8	41.6	24.2*
Reference year (%)				
1980–1983	25.5	28.8	25.2	19.3
1984–1987	30.9	30.4	34.6	27.6
1988–1991	43.6	40.8	40.2	53.1**
Nonwhite (%)	3.8	5.5	5.7	8.5
Married (%)	49.1	51.1	58.9	52.1
Cigarette smoking before first MI (%)				
Never/nonsmoker	29.6	43.4	44.1	54.2
Former smoker	27.8	19.2	17.8	19.7
Current smoker	42.6	37.4	38.1	26.1**
Quit smoking after MI	55.5	44.9	47.7	48.6
Prior history of (%)				
Angina pectoris	34.6	28.3	32.6	39.6
Diabetes mellitus	10.9	10.9	19.0**	41.4*
Serum glucose ≥110 mg/dl	27.3	32.0	35.1	60.0*
Hypertension	43.6	59.2	62.5	69.7***
Cholesterol >240 mg/dl	62.2	61.4	65.5	62.8
Congestive heart failure	21.8	10.9	7.4	6.2
Peripheral vascular disease	9.1	9.2	7.7	4.1
Chronic pulmonary disease	29.1***	14.1	13.3	11.0
Cancer	16.4	12.0	15.8	16.6
Hysterectomy (%)	32.7	34.6	40.8	38.6
Estrogen replacement therapy (%)				
Never	52.7	54.9	57.4	62.1
Before first MI only	32.7	26.6	26.9	26.9
Used after first MI	14.6	18.5	15.7	11.0
Chronic disease score ≥7	30.9	23.1*	25.9	40.6*
Physical findings in hospital (%)				
Rales	20.0	24.7	25.5	24.8
Congestive heart failure	27.3	28.3	31.0	32.4
Sinus tachycardia	40.0	24.5	28.4	31.0
X-ray findings in hospital (%)				
Pulmonary congestion	8.2	12.0	15.3	16.1
Pulmonary edema	6.1	11.4	11.9	11.7
Congestive heart failure	18.4	19.4	21.1	19.7
Cardiomegaly	18.4	15.4	17.6	30.3**

*$p \leq 0.001$ compared with BMI 20-24, by Mantel-Haenzel chi square.
**$p \leq 0.01$ compared with BMI 20-24, by Mantel-Haenzel chi square.
***$p \leq 0.05$ compared with BMI 20-24, by Mantel-Haenzel chi square.

eliminate the relationship between BMI and reinfarction. Modeling BMI as a continuous variable and adjusting for age, a 1-unit increment in BMI was associated with a 5% increase in risk of reinfarction (relative risk 1.05, 95% confidence interval 1.02 to 1.08). Adjustment for diabetes, hypertension, and the chronic disease score attenuated but did not eliminate this association (relative risk 1.03, 95% confidence interval 1.00 to 1.07). Adjusting simultaneously for a large number of additional prognostic factors (cigarette smoking history at first MI, history of congestive heart failure, peripheral vascular disease, or chronic pulmonary disease

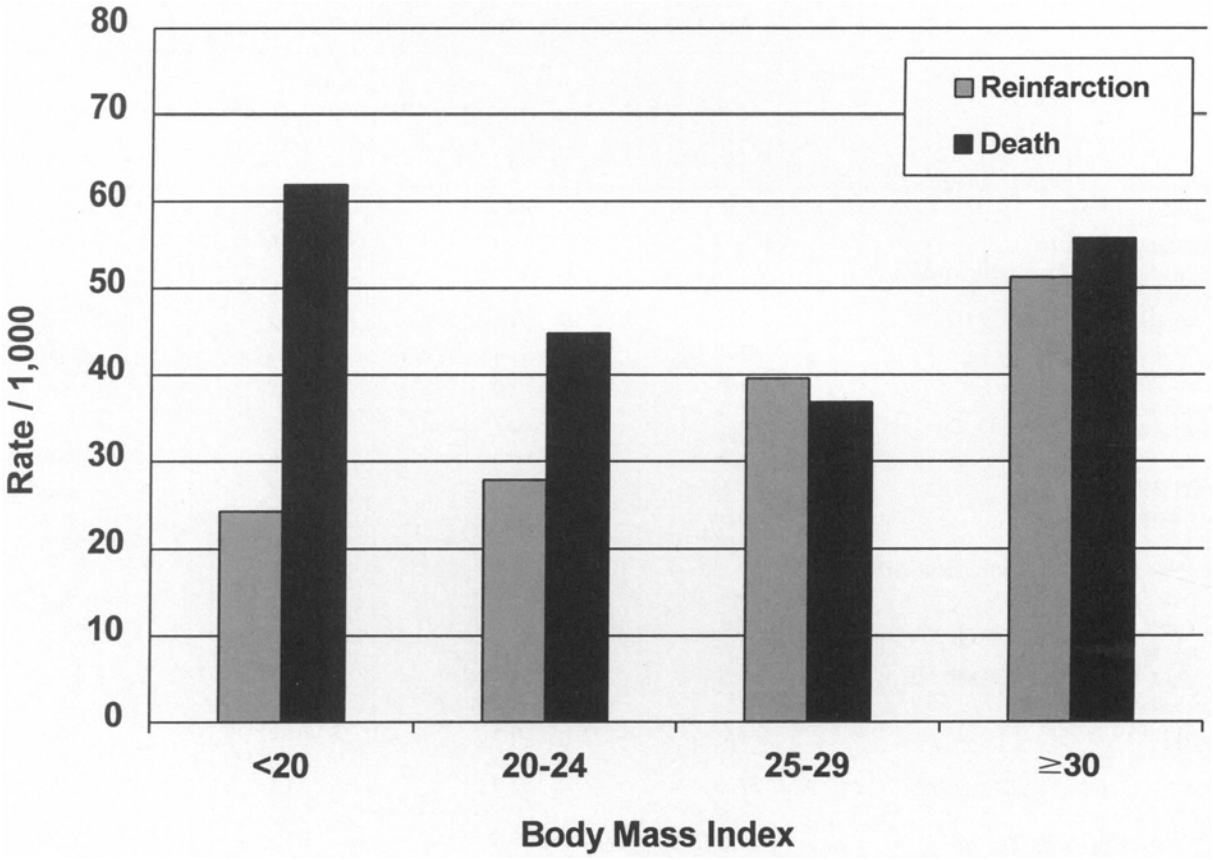

FIG. 1. Age-standardized rates of reinfarction and all-cause mortality per 1000 person-years, by body mass index (BMI).

before first MI, serum cholesterol >240 mg/dl, use of estrogen replacement therapy after myocardial infarction, and signs of ventricular dysfunction while hospitalized, including rales on physical examination, radiographic evidence of congestive heart failure or cardiomegaly, and prescription of digoxin, diuretics, or beta-blockers at hospital discharge) left this point estimate unchanged (relative risk 1.03, 95% confidence interval 0.99 to 1.08), although the confidence limits widened because of the added variance introduced by the large number of covariates. Because of concerns about the validity of the diagnosis of MI from death certificates, we repeated our analysis, including only those events confirmed by hospitalization data. The age-adjusted relative risk for confirmed reinfarction associated with BMI, adjusted for age, diabetes, hypertension, and the chronic disease score was 1.04 (95% confidence interval 1.00 to 1.08).

The relative risk for all-cause mortality was virtually the same in women with BMI <20 and those with BMI ≥30. As with reinfarction, smoking did not confound these estimates. However, adjustment for diabetes, hypertension, and the chronic disease score increased the difference in risk of all-cause mortality between women with BMI <20 compared with women of higher BMI. The risk of all-cause mortality for women with BMI 25–29 was half that of women with BMI <20. To explore the association between BMI and mortality further, we examined BMI in relation to causes of death. Cancer and respiratory deaths accounted for 45% of deaths in women with BMI <20 compared with 23% of deaths in women with BMI 20–24, 11% in women with BMI 25–29, and 16% in women with BMI ≥30 (Fig. 2). Restricting the analysis to those individuals who survived the first year after MI and to those without a history of cancer or pulmonary disease eliminated the association between BMI and all-cause mortality (Table 2). There were 99 car-

diovascular disease deaths, including 40 deaths attributed to MI. The number of fatal reinfarctions in the mortality analysis was larger than that in the reinfarction analysis because of women who had a fatal reinfarction after a nonfatal reinfarction. There was no association between cardiovascular disease death and BMI adjusted for age, diabetes, hypertension, and the chronic disease score (relative risk 0.98, 95% confidence interval 0.94 to 1.03).

DISCUSSION

In this retrospective cohort study of women who survived a first MI to hospital discharge, increasing BMI was associated with an increased risk for reinfarction. In women, 1 BMI unit is equivalent to approximately 2.6 kg.[20] For each 1-unit increase in BMI, there was a 5% increase in reinfarction risk. Women with BMI ≥30 were 2.6 times more likely to have a second infarction compared with women whose BMI was <20. These associations were independent of smoking and only partially attenuated by adjustment for hypertension, diabetes, and the chronic disease score. Additional adjustment for a large number of potentially confounding factors did not further attenuate this risk estimate.

Age-adjusted risk of all-cause mortality after the first MI was greatest for women in the high and low extremes of BMI. Women with BMI <20 had double the risk of mortality of women with BMI 25–29. We were unable to control for weight loss caused by subclinical disease, a strategy sometimes recommended in analyses of the association between measures of body weight and mortality.[26] However, we excluded women at high risk of death within 6 months

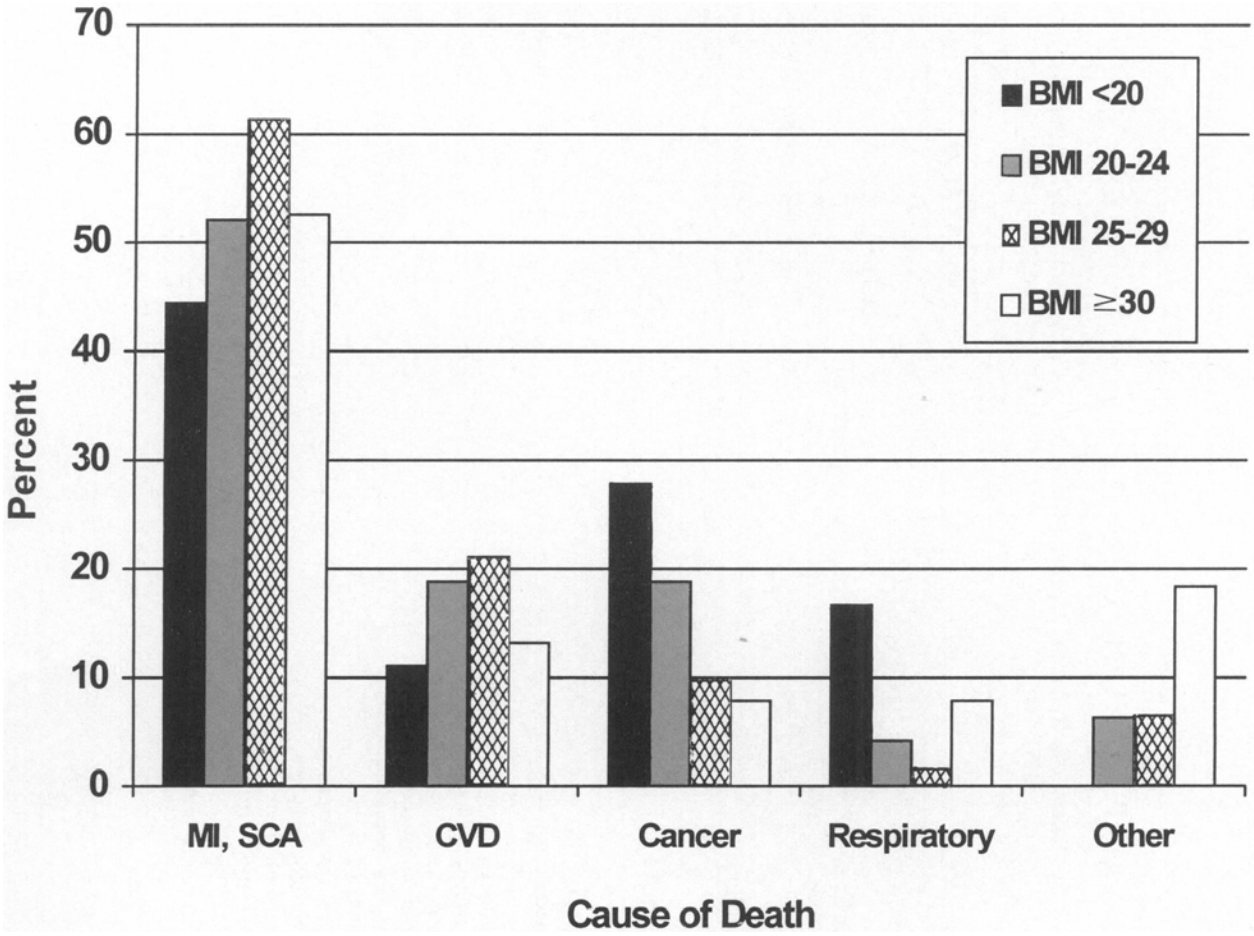

FIG. 2. Percent of causes of deaths within categories of body mass index (BMI). MI, reinfarction; SCA, sudden cardiac arrest; CVD, cardiovascular disease excluding MI and SCA.

TABLE 2. RATES AND RELATIVE RISKS FOR MI AND ALL-CAUSE MORTALITY ASSOCIATED WITH BMI, GROUP HEALTH COOPERATIVE OF PUGET SOUND, 1980–1991

	Reinfarction				*All-cause mortality*			
Body mass index	*<20*	*20–24*	*25–29*	*≥30*	*<20*	*20–24*	*25–29*	*≥30*
Age-standardized rates per 1000 person-years	24.31	27.99	39.62	51.03	61.86	44.79	36.87	55.70
Relative risks and 95% confidence interval limit adjusted for								
Age (5-year groups)	1.0	1.26 0.52, 3.04	2.02 0.87, 4.70	2.64 1.10, 6.36 *p* trend = 0.02	1.0	0.68 0.40, 1.18	0.60 0.35, 1.01	0.92 0.52, 1.62
Age, smoking	1.0	1.25 0.51, 3.04	2.01 0.86, 4.68	2.60 1.07, 6.30 *p* trend = 0.02	1.0	0.69 0.40, 1.19	0.61 0.36, 1.04	0.96 0.54, 1.72
Age, diabetes	1.0	1.28 0.53, 3.10	1.95 0.84, 4.54	2.29 0.94, 5.52 *p* trend = 0.08	1.0	0.71 0.41, 1.23	0.59 0.35, 0.99	0.78 0.44, 1.39
Age, diabetes, hypertension	1.0	1.26 0.52, 3.05	1.90 0.82, 4.44	2.21 0.91, 5.39 *p* trend = 0.09	1.0	0.66 0.38, 1.15	0.53 0.31, 0.91	0.69 0.39, 1.24
Age, diabetes, hypertension, chronic disease score	1.0	1.24 0.51, 3.03	1.89 0.81, 4.41	2.07 0.84, 5.08 *p* trend = 0.08	1.0	0.64 0.36, 1.11	0.48 0.28, 0.82	0.59 0.33, 1.08
Restricted: confirmed in hospital only; adjusted for age, diabetes, hypertension, chronic disease score	1.0	1.30 0.44, 3.84	2.39 0.86, 6.68	2.67 0.92, 7.80 *p* trend = 0.04				
Restricted: no prior diagnosis of cancer or pulmonary disease and survived at least 1 year after first MI; adjusted for age, diabetes, hypertension, chronic disease score					1.00	0.81 0.30, 2.18	1.00 0.39, 2.58	1.01 0.36, 2.83

after the first MI. We were able to examine this question further using restriction analysis. The association between BMI and all-cause mortality was partially explained by the increase in risk among women with a history of cancer or pulmonary disease and by higher early mortality in very thin women. When the analysis was restricted to those women without a history of cancer or pulmonary disease who survived the first year after MI, there was no association between BMI and all-cause mortality. Thus, associations between BMI and mortality appeared to reflect the relationship between body weight and other chronic illnesses, rather than an independent effect of either thinness or obesity. We also found no association between cardiovascular disease mortality and BMI. This finding seems at odds with that of an increase in risk for reinfarction. However, the majority of first reinfarctions were nonfatal, and it appears that by the time of end-stage cardiovascular disease in women who have already survived at least one MI, factors other than BMI at the time of the first infarction predominate in predicting mortality.

Few other studies have examined the association between measures of body weight and prognosis after MI,[11–16] and none have stratified or compared separately gender differences in the outcomes in women and men. Comparisons are, therefore, limited to prognostic studies that either combined women and men or looked exclusively at men and studies of the association between BMI and incident cardiovascular disease risk or mortality. Our findings differ from those of the Framingham study, in which a 20% increase in Metropolitan relative weight was associated with a 20% decrease in risk of reinfarction after the first MI in men and women.[11] However, in the Framingham analysis, the relative risk was adjusted for systolic blood pressure, serum cholesterol, and diabetes, all factors that may lie in the causal pathway between relative weight and coronary disease outcomes.[27] Findings from other studies have yielded mixed results regarding the association between measures of body weight and mortality after MI. Some have found no association between survival after MI and obesity in men and women, defined as weight more than 20% percent greater than ideal Metropolitan relative weight[13] or BMI.[14,15] On the other hand, Pardaens et al. found a modest (16%) increase in 3- to 9-year mortality among men and women who were overweight or underweight (these two groups combined) compared with normal weight subjects.[12] These results are similar to our own before restricting our mortality analysis to women without a history of cancer or pulmonary disease. In the control arm of the Coronary Drug Project, a study of risk in men who survived MI, the 5-year rate of coronary death and reinfarction was 19% higher for men with a Metropolitan relative weight over 1.14 than for men with lower relative body weight.[16]

Several large studies have found associations between measures of body weight and incident MI in women. In a random sample of middle-aged Swedish women, weight index (weight in kilograms times 100 divided by height in centimeters minus 100) was weakly associated with the 6-year incidence of MI, with excess risk limited to women in the highest weight quintiles.[6] In the NHANES I Epidemiologic Follow-up Study, women aged 65–74 with BMI $\geq$29 experienced a 50% increase in coronary heart disease risk compared to women with BMI $<$21.[4] In the Nurses' Health Study, increasing BMI was associated with increasing risk of fatal and nonfatal first MI, with more than a threefold increase in risk for those women with a BMI $\geq$29,[5] an association that was attenuated but not eliminated after controlling for history of hypertension, diabetes, and hypercholesterolemia. Furthermore, even within the range of weight considered normal, higher levels of body weight were associated with increased coronary heart disease risk.[3] Similar results have been documented in men. In the Health Professionals Follow-up Study, there was a threefold increase in coronary heart disease for men with BMI $>$32 compared with men with BMI $<$23.[10] Again, this association was attenuated (relative risk 2.3) after adjustment for diabetes and hypertension, and the association was stronger in men younger than 65. In older men, waist/hip ratio was a stronger predictor of risk than BMI. In the Copenhagen City Heart Study, the association between BMI and acute MI was similar in men and women;

the relative risk associated with a 1-unit increase in BMI was 1.03 ($p < 0.05$), a number similar to our own for reinfarction. However, unlike our findings, this association was eliminated after adjustment for diabetes, cholesterol, hypertension, and smoking.[9] Finally, in the Framingham Study, Metropolitan relative weight was independently associated with 26-year incidence of MI in both men and women.[7] Our findings indicate that the increase in risk for incident MI associated with increasing BMI continues among survivors of a first MI.

Studies of associations between body weight and mortality have yielded inconsistent results. In the Walnut Creek Contraceptive Drug Study, there was no association between BMI and all-cause mortality in postmenopausal women after controlling for other cardiovascular disease risk factors.[8] The Charleston Heart Study cohort reported a similar lack of association between BMI and mortality for white men aged 35 and older but found that increasing BMI was predictive of both coronary heart disease mortality and all-cause mortality in black men.[28] One study from the Established Populations for Epidemiologic Studies of the Elderly (EPESE) reported that overweight was, if anything, associated with a decrease in risk for all-cause mortality in both men and women aged 70 and older.[29] Conversely, among nonsmoking participants aged 65 and older in the Framingham Study, there was a 40% increase in mortality in men and a 60% increase in mortality in women who were in the 70th or greater percentile of BMI compared with those in the 10th–20th percentile.[30] In the Nurses' Health Study, among women who had never smoked, with recent stable weight, increasing BMI was directly associated with increased risk of both total mortality and cardiovascular disease death. Women in the lowest weight category were at lowest risk.[31]

There are numerous mechanisms whereby increased adiposity might increase the risk of MI. The metabolic correlates of obesity include adverse effects on lipid metabolism, blood pressure, carbohydrate metabolism, blood glucose, and insulin.[32–37] The distribution of body fat appears to contribute to these associations. Waist/hip ratio is positively associated with the incidence of MI, angina pectoris, stroke, and death in women.[32] Upper body obesity is associated with an increase in risk of glucose intolerance, diabetes, and hypertension, above and beyond the effects of obesity.[33] Waist/hip ratio is positively associated with serum cholesterol, triglycerides, apoplipoprotein B, plasma insulin, plasma viscosity, and the ratio of total/high-density lipoprotein cholesterol (HDL) and inversely associated with levels of HDL and HDL_2.[33–37] Furthermore, abdominal obesity is associated to a greater degree than peripheral obesity with significant disturbances in hemostatic variables, including elevations of fibrinogen, factor VII, and tissue plasminogen activator.[36] It has been suggested that differences in abdominal obesity may partially explain gender differences in MI risk.[37] Because our data were gathered through review of medical records, we were unable to evaluate body weight distributions, such as abdominal obesity. Finally, although we lacked more sophisticated measures of ventricular function and MI severity, those measures available to us (including rales on physical examination, radiographic evidence of congestive heart failure or cardiomegaly, and the prescription of digoxin, diuretics, or beta-blockers at hospital discharge) did not appear to explain our findings.

Despite findings that overweight increases both primary and secondary risk for MI, the efficacy of weight loss as a means to reduce risk of reinfarction remains to be determined. Observational studies of this question often are hampered by the inability to distinguish voluntary from involuntary weight loss. Thus, in the NHANES I Epidemiologic Follow-up Study, where intentional and unintentional loss could not be distinguished, in both men and women aged 47–74, weight loss was associated with an increase in cardiovascular disease mortality and all-cause mortality.[38] Similarly, in the EPESE study, men and women ≥70 years of age who lost more than 10% of their body weight between ages 50 and 70 had the greatest mortality.[29] Conversely, in the Cancer Prevention Study I, white women aged 40–64 with obesity-related conditions had a 20% decrease in all-cause mortality associated with any intentional weight loss, and those women without preexisting illness who lost more than

20 pounds within a 1-year interval had a 20% decrease in all-cause mortality, whereas women with slow intentional loss were at increased risk for all-cause mortality.[39] Therefore, the outcomes of weight loss appear related to intentionality, age, and the presence of preexisting illnesses.

Our findings of an increase in risk for mortality associated with either thinness or obesity appear to reflect the relationship between body weight and other chronic illnesses. Our findings for reinfarction suggest that for postmenopausal women who survive a first MI, a 1-unit increase in BMI is associated with a 5% increase in the risk for reinfarction. This effect appears to be mediated in part by diabetes, high blood pressure, and other comorbidities but is incompletely explained by these factors. Other factors that might explain the association between BMI and MI risk, such as differences in cardiac workload, physical activity, and lipid and carbohydrate metabolism, deserve further consideration.

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