

Body Mass Index and the Risk of Recurrent Coronary Events Following Acute Myocardial Infarction

Thomas D. Rea, MD, Susan R. Heckbert, MD, PhD, Robert C. Kaplan, PhD, Bruce M. Psaty, MD, PhD, Nicholas L. Smith, MPH, PhD, Rozenn N. Lemaitre, PhD, MPH, and Danyu Lin, PhD

Although excess adiposity appears to increase the risk of coronary heart disease in the general population, its importance in patients with established coronary disease is less defined. We evaluated a population-based inception cohort of survivors to hospital discharge following first acute myocardial infarction (AMI) ($n = 2,541$) to assess the association between body mass index (BMI) and the risk of recurrent coronary events and to explore the mechanisms for this relation. Using Cox proportional-hazards regression, we assessed the risk of recurrent coronary events associated with levels of adiposity as defined by BMI and then investigated potential mechanisms through which adiposity conferred risk by examining how adjustment for diabetes mellitus, systemic hypertension, and dyslipidemia affected the association. Forty-one percent of the cohort were overweight (BMI 25 to 29.9), and 27.8% were obese (BMI ≥ 30). After adjustment for other risk factors,

the risk of recurrent coronary events ($n = 418$) increased as BMI increased, especially among those who were obese. Using a BMI of 16 to 24.9 as the reference group, for mildly overweight patients (BMI 25 to 27.4), the relative risk (RR) was 0.93 (95% confidence interval [CI] 0.70 to 1.24); it was 1.16 for more severe overweight patients (BMI 27.5 to 29.9; 95% CI 0.87 to 1.55). For patients with class I obesity (BMI 30 to 34.9), the RR was 1.49 (95% CI 1.12 to 1.98), and for class II to III obesity (BMI ≥ 35), the RR was 1.80 (95% CI 1.30 to 2.48). We estimated that clinical measurements of diabetes, hypertension, and dyslipidemia explained approximately 43% of this risk. Thus, excess adiposity as measured by BMI was associated with an increased risk of recurrent coronary events following AMI, particularly among those who were obese. ©2001 by Excerpta Medica, Inc.

(Am J Cardiol 2001;88:467-472)

The prevalence of obesity has climbed sharply over the last 20 years in the United States and other parts of the industrialized world.¹⁻³ It is estimated that in the United States >50% of adults are overweight or obese.¹ This increase in obesity is a considerable public health concern given the association between excess adiposity and increased morbidity and mortality.^{4,5} Overweight persons appear to be at especially high risk for the development of coronary heart disease, due in part to obesity-related conditions, such as diabetes mellitus, systemic hypertension, and dyslipidemia.^{4,6} The American Heart Association has identified obesity as an independent cardiac risk factor⁷ and the National Institutes of Health has issued guidelines to identify overweight persons for potential treatment aimed primarily at preventing coronary heart disease.⁸ Although excess adiposity appears to increase the risk

of coronary heart disease in the general population, its importance in patients with established coronary disease is less clearly defined. Existing studies of acute myocardial infarction (AMI) survivors have had limited information about clinical or medication variables, examined only a portion of the original AMI cohort, or did not explore specific disease mechanisms through which adiposity might confer risk.⁹⁻¹⁵ We examined the association between body mass index (BMI) and the risk of recurrent coronary events and explored the disease mechanisms (diabetes, hypertension, and dyslipidemia) that may potentially produce this relation in a population-based inception cohort of persons who survived incident AMI.

METHODS

Study population: The study setting was Group Health Cooperative, a health maintenance organization with >400,000 enrollees based in Washington state. Eligible patients included all enrollees who survived to hospital discharge following a first AMI during the period from July 1986 (women) or July 1989 (men) through December 1996. A potential incident AMI was identified by the International Classification of Disease 9th revision codes from the computerized discharge abstracts of the 2 Group Health Cooperative hospitals, the bills for out-of-plan services, and Washington state death records. Research assistants were trained to identify events that were and

From the Cardiovascular Health Research Unit, Departments of Medicine, Epidemiology, Pharmacy, Health Services, and Biostatistics, University of Washington, Seattle, Washington; and the Department of Epidemiology and Social Medicine, Albert Einstein College of Medicine, Bronx, New York. This study was supported by grants HL53375, HL40628, and HL43201 from the National Heart, Lung, and Blood Institute, Bethesda, Maryland. Manuscript received December 8, 2000; revised manuscript received and accepted March 30, 2001.

Address for reprints: Thomas D. Rea, MD, University of Washington, Cardiovascular Health Research Unit, Metropolitan Park, East Tower, 1730 Minor Avenue, Suite 1360, Seattle, Washington 98101. E-mail: rea123@u.washington.edu.

TABLE 1 Demographic, Clinical, and Medication Characteristics by Body Mass Index (BMI) Group

	BMI Group				
	Healthy Weight	Overweight		Class I Obesity	Class II–III Obesity
	16–24.9 kg/m ² (n = 798)	25–27.4 kg/m ² (n = 577)	27.5–29.9 kg/m ² (n = 460)	30–34.9 kg/m ² (n = 461)	35–48 kg/m ² (n = 245)
Demographic characteristics					
Age (mean ± SD)*	67.6 ± 9.2	64.5 ± 10.5	63.5 ± 10.4	61.4 ± 10.4	58.6 ± 10.0
Women	372 (46.5%)	177 (30.7%)	152 (32.8%)	144 (31.2%)	123 (50.2%)
Clinical characteristics					
BMI (mean ± SD)	22.5 ± 1.9	26.2 ± 0.7	28.7 ± 0.7	32.0 ± 1.4	38.9 ± 3.1
Congestive heart failure	223 (27.9%)	123 (21.3%)	99 (21.5%)	98 (21.3%)	60 (24.5%)
Smoking					
Nonsmoker	652 (81.7%)	491 (85.1%)	400 (87.0%)	388 (84.2%)	210 (85.7%)
Current smoker	146 (18.3%)	86 (14.9%)	60 (13.0%)	73 (15.8%)	35 (14.3%)
Physical activity [†]					
Sedentary	214 (26.8%)	113 (19.6%)	109 (23.7%)	94 (20.4%)	86 (35.1%)
Moderate	524 (65.7%)	424 (73.5%)	318 (69.1%)	326 (70.7%)	144 (58.8%)
Strenuous	60 (7.5%)	40 (6.8%)	33 (7.2%)	41 (8.9%)	15 (6.1%)
Diabetes mellitus*	108 (13.5%)	81 (14.0%)	89 (19.4%)	104 (22.6%)	96 (39.2%)
Systemic hypertension*	310 (38.9%)	246 (42.6%)	193 (42.1%)	220 (47.7%)	145 (59.2%)
Total cholesterol/HDL cholesterol ratio (mean ± SD)*	5.2 ± 1.7	5.7 ± 1.5	6.1 ± 2.8	6.3 ± 1.8	6.4 ± 1.7
Medication prescribed at hospital discharge					
Aspirin*	710 (89.0%)	538 (93.2%)	427 (92.8%)	438 (95.0%)	233 (95.1%)
β blockers*	334 (41.9%)	302 (52.3%)	237 (51.5%)	255 (55.3%)	144 (58.8%)
Lipid-lowering therapy	33 (4.1%)	46 (8.0%)	37 (8.0%)	36 (7.8%)	16 (6.5%)

*p <0.05 for linear trend across BMI groups.
[†]Moderate activity was defined as those persons who performed regular activity such as gardening or walking for exercise.
Strenuous activity was defined as regular activity in vigorous physical activity such as running or cycling.
HDL = high-density lipoprotein.

were not clearly AMIs. Questionable events were reviewed by study physicians (SRH, BMP). In a blinded validation study, the completeness of case ascertainment was 95%, and 97% of eligible cases met standard criteria for definite or probable AMI.¹⁶

Subjects were excluded if they: (1) were <30 or >79 years of age, (2) had <4 visits to Group Health Cooperative or were enrolled in Group Health Cooperative for <1 year before the first AMI, (3) had sustained a prior AMI, (4) experienced an AMI as a result of surgery or a procedure, or (5) died before hospital discharge. Of the 2,677 subjects who were initially eligible, 112 persons were excluded because they were missing information about height and 24 persons were excluded a priori because their values for BMI were within the lowest and highest 0.5% of the study population. These exclusions left 2,541 subjects for analysis.

Study end point: Information on recurrent AMI or coronary heart disease death during follow-up was obtained from the ambulatory medical record, available inpatient records, and the results of a match between the Washington state death records and the Group Health Cooperative enrollment records. Subjects who unenrolled from Group Health Cooperative before a recurrent event were considered lost to follow-up, and the date of loss to follow-up was the date of unenrollment from Group Health Cooperative.

Body mass index: BMI (weight in kilograms divided by the square of the height in meters) was used as a measure of adiposity and was derived from

weight and height information available in the ambulatory care record. The first weight recorded after hospital discharge was used in the analysis, provided the weight was measured not only before an outcome event but also within 6 months of the hospital discharge date. For the 2,397 subjects who met these requirements, the median time until the weight measurement was 13 days after discharge. Of the remaining 144 subjects, 92 had a weight recorded >6 months after hospital discharge (and before censoring) and 52 had no weight recorded before censoring. For these subjects, representing 5.7% of the study cohort, a postdischarge weight was imputed based on the individual's weight before the incident AMI, age, sex, and length of hospital stay.

Clinical and medication covariates: Trained research assistants reviewed the ambulatory care and available inpatient medical records to collect information about coronary disease risk factors, such as smoking status, physical activity, use of health services, marital status, and medical conditions such as hypertension, diabetes, and congestive heart failure. Congestive heart failure was based on the notes of the primary care physician and consultants and the results of diagnostic tests. Hypertension and diabetes required pharmacologic treatment with appropriate medication. In addition, physical examination measurements of blood pressure and pulse and laboratory values for random serum glucose, total cholesterol, high-density lipoprotein cholesterol, and creatinine were recorded. Lipid status

TABLE 2 Risk of Recurrent Coronary Events in Relation to Demographic, Clinical, and Medication Characteristics

	Rate*	RR	95% CI
Demographic Characteristics			
Age group (yrs)			
40–49	41.8	1	—
50–59	32.4	0.77	0.59–1.01
60–69	47.6	1.14	0.95–1.36
70–79	57.1	1.37	1.18–1.58
80–89	67.0	1.60	1.13–2.26
Gender			
Women	48.7	1	—
Men	48.7	0.99	0.82–1.20
Clinical characteristics			
Congestive heart failure (n)			
No	33.9	1	—
Yes	96.5	2.85	2.33–3.48
Smoking			
Nonsmoker	47.3	1	—
Current smoker	56.3	1.19	0.91–1.56
Physical activity			
Sedentary	101.2	1	—
Moderate	33.4	0.33	0.27–0.41
Strenuous	18.2	0.18	0.10–0.31
Diabetes			
No	37.1	1	—
Yes	99.0	2.67	2.17–3.28
Hypertension			
No	37.4	1	—
Yes	63.2	1.69	1.39–2.06
Total/HDL cholesterol ratio <6			
No	44.6	1	—
Yes	54.9	1.23	1.01–1.50
Medications prescribed at hospital discharge			
Aspirin			
No	100.8	1	—
Yes	44.4	0.44	0.33–0.59
β blocker			
No	52.9	1	—
Yes	44.5	0.84	0.69–1.03
Lipid-lowering therapy			
No	49.2	1	—
Yes	41.8	0.85	0.53–1.36

*The rate is per 1,000 person-years, directly standardized to the age distribution of the entire study population.

(dyslipidemia) was defined as the ratio of total cholesterol to high-density lipoprotein cholesterol. The status of the clinical and physical examination variables was determined at the time of the weight measurement, or for those whose weight was imputed, at the date of hospital discharge. Laboratory information was taken from the period before the incident AMI. Medication use was assessed at the time of hospital discharge following the incident AMI using information from the discharge summary, supplemented with information from the first outpatient visit in the medical record and the Group Health Cooperative computerized pharmacy database.

Statistical analysis: BMI was modeled as a categorical variable based on clinical guidelines¹⁷: <18.5 kg/m² (underweight), 18.5 to 24.9 kg/m² (healthy weight), 25 to 29.9 kg/m² (overweight), 30 to 34.9 kg/m² (class I obesity), and \geq 35 kg/m² (class II and III obesity combined). In our cohort, this included subjects up to 48 kg/m². In addition, the overweight

group was divided into 2 subgroups: 25 to 27.4 kg/m² and 27.5 to 29.9 kg/m². Because the underweight group was comprised of relatively few subjects (n = 32), and because the analysis revealed that the risks associated with this category were similar to those of the healthy weight group, these 2 groups were combined and served as the referent group for comparison. In the analyses examining mechanism, BMI was also modeled as a continuous term.

We calculated the age-adjusted rate of recurrent coronary events for each category of BMI and standardized these rates to the age distribution of the entire study population. We used Cox proportional-hazards regression to compute hazard ratios, thereby estimating the relative risk (RR), of recurrent coronary events associated with BMI after adjusting for potential confounding factors.¹⁸ Variables included in the multivariate Cox models in addition to BMI included age at hospital discharge (years), sex, tobacco use (current or nonsmoker), level of physical activity (sedentary, moderate activity such as walking, or strenuous activity such as running), presence of congestive heart failure, and the use of aspirin. Potential interactions were modeled using cross-product terms between the covariates of interest and the continuous BMI term. In models assessing the prognostic importance of BMI, we did not adjust for diabetes mellitus, hypertension, or dyslipidemia because these diseases represent mechanisms through

which adiposity may confer risk.¹⁹ However, when exploring the relative contribution of the disease-specific mechanism, we adjusted for these variables separately and together. One may estimate the relative contribution of a specific disease mechanism by first computing the β -coefficient value for the BMI term in the model unadjusted for diabetes, hypertension, or lipid status (β_{baseline}), and then by calculating the β coefficient value for the BMI term in the model adjusted for a specific disease mechanism (β_{adjusted}).²⁰ The relative contribution of the disease mechanism is then calculated using the expression: $1 - [\beta_{\text{adjusted}}/\beta_{\text{baseline}}]$. For these estimates, a continuous linear BMI term was used after determining that the fit of the model was not improved with the addition of a quadratic, square root, or spline (originating at the various categorical cut points) BMI term. There was no evidence that the proportional hazards assumption was violated.

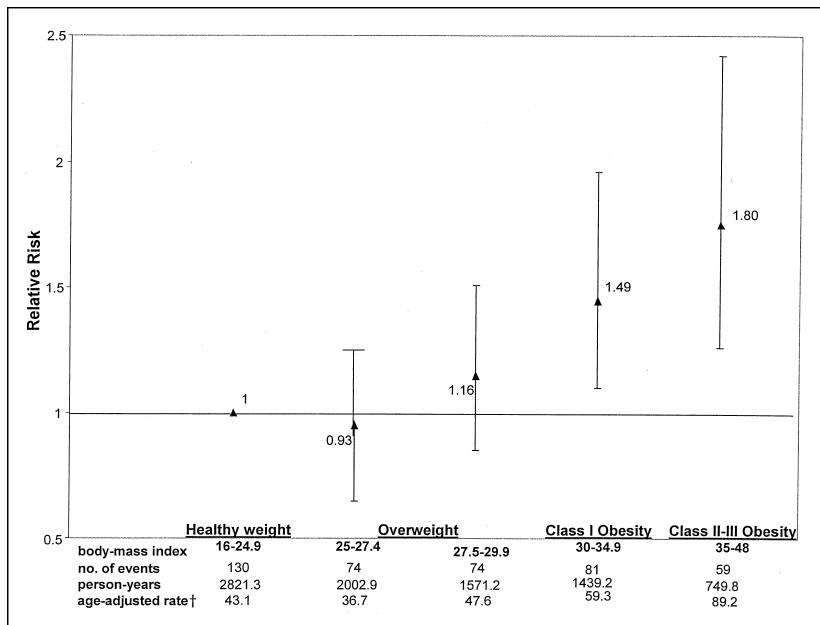


FIGURE 1. RR of recurrent events according to BMI group, adjusted for age, sex, tobacco use, physical activity, congestive heart failure, and aspirin use. †The rate is per 1,000 person-years, directly standardized to the age distribution of the entire study population. Test for linear trend across BMI groups ($p < 0.001$).

TABLE 3 Mechanism of Risk Associated With Body Mass Index (BMI)*

Model†	RR for BMI‡	β for BMI‡	Portion of Disease Attributable to Specific Mechanism (%)§
Baseline model	1.040	0.0393	—
Diabetes (categorical)	1.031	0.0305	22.4
Diabetes + random serum glucose level (continuous)	1.029	0.0287	27.0
Hypertension (categorical)	1.037	0.0363	7.6
Hypertension + systolic and diastolic blood pressure (quartiles)	1.035	0.0348	11.5
Ratio of total cholesterol/HDL cholesterol (continuous)	1.037	0.0365	7.1
Combined (adjusted for all of the above covariates)	1.023	0.0225	42.7

*Baseline model includes adjustment for age, sex, tobacco use, physical activity, congestive heart failure, and aspirin use.
 †Each model adds the named covariate(s) to the baseline model.
 ‡For a 1-unit increase in BMI, BMI was modeled as a continuous variable.
 §Percent calculated from the equation $\{1 - (\beta_{\text{adjusted}}/\beta_{\text{baseline}})\} \times 100$.

RESULTS

In the cohort of 2,541 patients who survived to hospital discharge following first AMI, 2/3 were either overweight (40.8%) with a BMI of 25 to 29.9, or obese (27.8%) with a BMI ≥ 30 . Patients with greater BMIs tended to be younger, have a greater prevalence of diabetes, hypertension, or dyslipidemia, and were more frequently taking aspirin and β blockers (Table 1). During the 8,584 person-years of follow-up on the 2,541 subjects (median years of follow-up 3.0), there were 418 recurrent coronary events: 264 nonfatal AMIs, 89 fatal AMIs, and 65 other coronary heart disease deaths. A total of 224 subjects (8.8%) were censored because they were lost to follow-up. Estab-

lished risk factors for coronary heart disease were evident in this cohort (Table 2).

Except for those patients who were mildly overweight (BMI 25 to 27.4), the risk of recurrent coronary events increased as the BMI group increased after adjustment for age, gender, congestive heart failure, smoking, physical activity, and the use of aspirin (Figure 1). Further adjustment for marital status, education level, race, family history of coronary heart disease, history of cancer, alcohol consumption, cardiac revascularization, menopausal status in women, pulse, creatinine level, and the use of β blockers, angiotensin-converting enzyme inhibitors, loop diuretics, or lipid-lowering therapy only slightly changed the risk estimates associated with BMI.

The association between BMI and the risk of recurrent coronary events did not differ across subgroups defined by gender, smoking status, physical activity, hypertension, diabetes, or the use of aspirin, although there was a suggestion that the association was attenuated with increasing age ($p = 0.1$). For example, among those < 65 years old, the RR of recurrent coronary events for obese patients (BMI ≥ 30) compared with patients of healthy weight (BMI 16 to 24.9) was 2.29 (95% confidence intervals [CI] 1.35 to 3.88), whereas among those ≥ 65 years old, the RR for obese patients compared with patients of healthy weight was 1.51 (95% CI 1.12 to 2.05). Although the RR was attenuated with increasing age, the absolute risk attributable to obesity (rate of recurrent events in obese patients - rate of recurrent events in healthy-weight patients) was similar between the 2

age groups: 24.7 excess recurrent events per 1,000 patient-years for obese patients < 65 years old compared with 29.4 excess recurrent events per 1,000 patient-years for obese patients ≥ 65 years old.

There was also a suggestion that the risk associated with elevated BMI was attenuated among those with congestive heart failure, especially among those with more severe congestive heart failure as indicated by the use of loop diuretics ($p = 0.1$). Among those with congestive heart failure treated with loop diuretics ($n = 373$), the RR of recurrent events for obese patients compared with patients of healthy weight was 1.13 (95% CI 0.72 to 1.77), whereas among those without congestive heart failure, the RR for obese

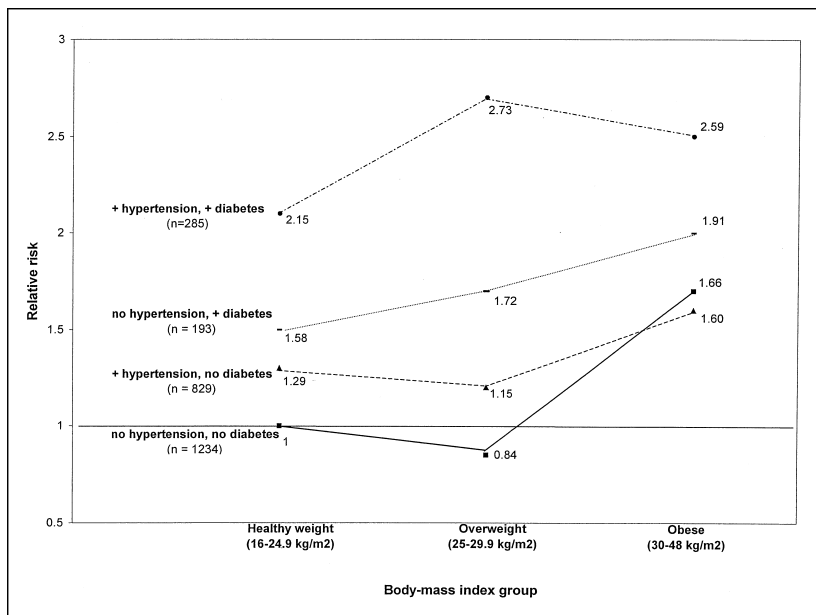


FIGURE 2. RR of recurrent coronary events for clinical risk groups according to BMI, adjusted for age, sex, tobacco use, physical activity, congestive heart failure, total to high-density lipoprotein cholesterol ratio, and aspirin use.

patients compared with patients of healthy weight was 1.80 (95% CI 1.28 to 2.52).

Adding measurements of diabetes, hypertension, or dyslipidemia to the baseline multivariate model attenuated the association between BMI and risk of recurrent coronary events. The addition of diabetes attenuated the association the most, with less attenuation following the addition of hypertension or dyslipidemia (Table 3). These models suggest that approximately 43% of the risk of recurrent coronary events associated with increasing BMI could be explained by adjusting for measurements of diabetes, hypertension, and dyslipidemia. Moreover, in an analysis stratified by hypertension and diabetes and adjusted for total cholesterol to high-density lipoprotein cholesterol ratio, obesity was associated with an increased risk of recurrent coronary events in the subgroup with neither hypertension nor diabetes, in subgroups with either hypertension or diabetes but not both, and in the subgroup with both conditions (Figure 2).

DISCUSSION

In this inception cohort of persons who survived incident AMI, excess adiposity as estimated by BMI was associated with an increased risk of recurrent coronary events after adjustment for other clinical risk factors. This risk was especially evident among obese patients (BMI ≥ 30), whose risk appeared to increase with higher levels of obesity. The increased RR in the obese subgroup is of significant public health importance because these persons comprise over 1/4 of the cohort, a proportion similar to other post-AMI populations.^{21,22} In contrast, our results suggest that there is little change in risk associated with being mildly overweight (BMI of 25 to 27.4) compared with healthy

weight individuals; however, the risk may begin to increase among those more severely overweight (BMI 27.5 to 29.9).

The shape of the risk profile associated with BMI may represent a combination of factors. BMI has been strongly associated with incident cardiovascular disease compared with other disease outcomes (e.g., all-cause death or cancer).²³ However, our cohort was relatively old, and the association between obesity and coronary heart disease has been reported to be attenuated as age increases.²⁴ Finally, this post-AMI cohort represents a specific clinical group whose BMI risk profile may be distinct.

The increased risk posed by elevated BMI was apparent in most clinical subgroups. Similar to other studies,²⁴ the association between adiposity and the risk of coronary events in our cohort was attenuated as age increased, although this difference did not attain statistical significance. Im-

portantly, however, because of the increased absolute risk among older persons, the risk of recurrent coronary events attributable to obesity was still considerable in older subjects. The risk associated with elevated BMI was also attenuated among those with congestive heart failure, especially among patients with more severe disease as reflected by the need for loop diuretics. Although obesity may be a risk factor for development of congestive heart failure,²⁵ among those with prevalent disease, low or normal BMI may represent cardiac cachexia, a state associated with advanced heart failure and a poor prognosis.²⁶

In this cohort, the risk associated with excess adiposity was explained in part, but not completely, by the established mechanisms: diabetes, hypertension, and dyslipidemia. It is possible that the markers we used to assess the mechanism were inadequate to completely capture the disease process; with use of more sensitive markers such as insulin sensitivity,^{6,27} a more exact and possibly greater contribution of these established disease mechanisms might be discernible. In contrast, obesity may confer excess risk by producing an inflammatory state, promoting thrombosis, or activating the sympathetic nervous system,^{6,28,29} mechanisms that may in part be separate from the traditional pathways.

Our study has several limitations. Because of sample size, we had limited ability to detect differences in the relative importance of BMI for specific subgroups, such as race (>90% of the cohort was Caucasian) in which BMI may function differently.⁴ Second, we were unable to adequately explore the significance of being underweight. However, in this and other similar cohorts,^{21,22} the prevalence of being underweight was very low. Finally, we used BMI to assess adiposity.

Other measurements provide additional, although not necessarily superior, measures of adiposity.¹⁷ In this respect, heights and weights in our study were measured rather than self-reported, a method of assessment that may more accurately classify the risk associated with the clinical levels of excess adiposity.³⁰

In conclusion, excess adiposity was associated with an increased risk of recurrent coronary events among survivors of a first AMI, especially among patients who were clinically obese. Readily measured markers of diabetes, hypertension, and dyslipidemia explained some, but not all, of the risk conferred by obesity. Following AMI, obese persons should be particularly targeted for proved preventive therapies. Whether weight loss should be included in these treatments is an important but unsettled question.

1. Flegal KM, Carroll MD, Kuczmarski RJ, Johnson CL. Overweight and obesity in the United States: prevalence and trends, 1960–1994. *Int J Obes Relat Metab Disord* 1998;22:39–47.
2. Seidell JC. Obesity in Europe. Scaling an epidemic. *Int J Obes Relat Metab Disord* 1995;19:1–4.
3. Obesity. Preventing and managing the global epidemic: report of a WHO Consultation on Obesity, Geneva, June 3–5, 1997. World Health Organization, 1988.
4. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW. Body mass index and mortality in a prospective cohort of U. S. adults. *N Engl J Med* 1999;341:1097–1105.
5. Allison DB, Fontaine KR, Manson JE, Stevens J, VanItallie TB. Annual deaths attributable to obesity in the United States. *JAMA* 1999;282:1530–1538.
6. Shehan MT, Jensen MD. Metabolic complications of obesity: pathological considerations. *Med Clin N Am* 2000;84:363–385.
7. Eckel RH, Krauss RM. American Heart Association call to action: obesity as a major risk factor for coronary heart disease. *Circulation* 1998;97:2099–2100.
8. Expert Panel. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. Bethesda, MD: National Institutes of Health, National Heart, Lung, and Blood Institute, U. S. Department of Health and Human Services, Public Health Service, 1998.
9. Newton KM, LaCroix AZ. Association of body mass index with reinfarction and survival after first myocardial infarction in women. *J Womens Health* 1996;5:433–444.
10. Wong ND, Cupples LA, Ostfeld AM, Levy D, Kannel WB. Risk factors for long-term coronary prognosis after initial myocardial infarction: The Framingham Study. *Am J Epidemiol* 1989;130:469–480.
11. Pardaens J, Lesaffre E, Willems JL, De Geest H. Multivariate survival analysis for the assessment of prognostic factors and risk categories after recovery

from acute myocardial infarction: the Belgian situation. *Am J Epidemiol* 1985; 122:805–819.

12. Howland JS, Vaillant HW. Long-term survival of 224 patients with myocardial infarction treated at a community hospital. *J Fam Pract* 1980;10:979–983.
13. Martin CA, Thompson PL, Armstrong BK, Hobbs MS, de Klerk N. Long-term prognosis after recovery from myocardial infarction: a nine year follow-up of the Perth Coronary Register. *Circulation* 1983;68:961–969.
14. Hoit BD, Gilpin EA, Maisel AA, Henning H, Carlisle J, Ross J. Influence of obesity after myocardial infarction. *Am Heart J* 1987;114:1334–1341.
15. Schlant RC, Forman S, Stamler J, Canner PL. The natural history of coronary heart disease: Prognostic factors after recovery from myocardial infarction in 2789 men, the 5-year findings of the Coronary Drug Project. *Circulation* 1982; 66:401–409.
16. Psaty BM, Heckbert SR, Atkins D, Lemaitre T, Koepsell TD, Wahl PW, Siscovick DS, Wagner EH. The risk of myocardial infarction associated with the combined use of estrogens and progestins in post-menopausal women. *Arch Intern Med* 1994;154:1333–1339.
17. Willett WC, Dietz WH, Colditz GA. Primary care: guidelines for a healthy weight. *N Engl J Med* 1999;341:427–434.
18. Cox DR. Regression models and life-tables. *J R Stat Soc [B]* 1972;34:187–220.
19. Manson JE, Stampfer MJ, Hennekens CH, Willett WC. Body weight and longevity: a reassessment. *JAMA* 1987;257:353–358.
20. Lin DY, Fleming TR, De Gruttola V. Estimating the proportion of treatment effect explained by a surrogate marker. *Statist Med* 1997;16:1515–1527.
21. Montaye M, De Bacquer D, De Backer G, Amouyel P. Overweight and obesity: a major challenge for coronary heart disease secondary prevention in Europe. *Eur Heart J* 2000;21:808–813.
22. Campbell NC, Thain J, Deans HG, Ritchie LD, Rawles JM. Secondary prevention in coronary heart disease: baseline survey of provision in general practice. *BMJ* 1998;316:1430–1434.
23. Manson JE, Willett WC, Stampfer MJ, Colditz GA, Hunter DJ, Hankinson SE, Hennekens CH, Speizer FE. Body weight and mortality among women. *N Engl J Med* 1995;333:677–685.
24. Stevens J, Cai J, Pamuk ER, Williamson DF, Thun MJ, Wood JL. The effect of age on the association between body-mass index and mortality. *N Engl J Med* 1998;338:1–7.
25. Chen YT, Vaccarino V, Williams CS, Butler J, Berkman LF, Krumboltz HM. Risk factors for heart failure in the elderly: a prospective community-based study. *Am J Med* 1999;106:605–612.
26. Anker SD, Rauchhaus M. Insights into the pathogenesis of chronic heart failure: immune activation and cachexia. *Curr Opin Cardiol* 1999;14:211–216.
27. Ferrannini E, Natali A, Capaldo B, Lehtovirta M. Insulin resistance, hyperinsulinemia, and blood pressure: role of age and obesity. *Hypertension* 1997;30: 1144–1149.
28. Samad F, Uysal KT, Wiesbrock SM, Pandey M, Hotamisligil GS, Loskutoff DJ. Tumor necrosis factor alpha is a key component in the obesity-linked elevation of plasminogen activator inhibitor 1. *Proc Natl Acad Sci USA* 1999; 96:6902–6907.
29. Karoson K, Wallentin I, Larsson B, Sjostrom L. Effects of obesity and weight loss on left ventricular mass and relative wall thickness: survey and intervention study. *BMJ* 1997;315:912–916.
30. Flood V, Webb K, Lazarus R, Pang G. Use of self-report to monitor overweight and obesity in populations: some issues for consideration. *Aust NZ J Public Health* 2000;24:96–99.