International Journal of Obesity (2001) 25, 1047–1056

0307–0565/01 $15.00
www.nature.com/ijo

PAPER

Abdominal and total adiposity and risk of coronary heart disease in men

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BACKGROUND: Waist circumference is a simpler measure of abdominal adiposity than waist/hip ratio (WHR), but few studies have directly compared the two measures as predictors of coronary heart disease (CHD) in men. In addition, whether the association of abdominal adiposity is independent of total adiposity as measured by body mass index (BMI) in men remains uncertain.

OBJECTIVE: To compare waist circumference and WHR as predictors of CHD in men, and to determine whether the association is independent of BMI.

DESIGN: Prospective cohort study.

METHODS: We compared WHR, waist circumference and BMI with risk of CHD (myocardial infarction or coronary revascularization) among men in the Physicians' Health Study, a randomized trial of aspirin and beta-carotene among 22 071 apparently healthy US male physicians, aged 40–84 y at baseline in 1982. Men reported height at baseline, and weight, waist and hip measurements on the 9 y follow-up questionnaire.

RESULTS: Among the 16 164 men who reported anthropometric measurements and were free from prior CHD, stroke or cancer, a total of 552 subsequent CHD events occurred during an average follow-up of 3.9 y. After adjusting for age, randomized study agent, smoking, physical activity, parental history of myocardial infarction, alcohol intake, multivitamin and aspirin use, men in the highest WHR quintile (≥ 0.99) had a relative risk (RR) for CHD of 1.50 (95% CI 1.14–1.98) compared with those in the lowest quintile (< 0.90). Men in the highest waist circumference quintile (≥ 103.6 cm) had a RR of 1.60 (CI, 1.21–2.11) for CHD compared with men in the lowest quintile (< 88.4 cm). Further adjustment for BMI substantially attenuated these associations: men in the highest WHR and waist circumference quintiles had relative risks for CHD of 1.23 (CI, 0.92–1.66) and 1.06 (CI, 0.74–1.53), respectively. Men in the highest BMI quintile (≥ 27.6 kg/m^2) had a multivariate RR of CHD of 1.73 (CI, 1.29–2.32), after adjustment for WHR. No significant effect modification by age of the relationship between either measure of abdominal adiposity and risk of CHD was observed.

CONCLUSIONS: These data support a modest relationship between abdominal adiposity, as measured by either WHR or waist circumference, and risk of CHD both in middle-aged and older men. However, abdominal adiposity did not remain an independent predictor of CHD after adjustment for BMI.

International Journal of Obesity (2001) **25**, 1047–1056

Keywords: obesity; coronary heart disease; fat distribution; anthropometry; epidemiology

Background

Abdominal adiposity has been associated with significant metabolic abnormalities including insulin resistance, hyperinsulinemia and elevated triglycerides, as well as increased incidence of hypertension,[1] glucose intolerance[2] and diabetes mellitus.[3] Several studies suggest that abdominal adiposity, as measured by waist/hip ratio (WHR), is a risk factor for coronary heart disease (CHD) in men[4–6] and in women.[7–9] In men, however, the risk has not always remained significant after adjusting for total adiposity, as measured by BMI.[4] Waist circumference, another measure of abdominal adiposity, has also been associated with increased risk of CHD,[4,8,10] and has been advocated by some as a simpler measure to calculate.[11] The National Heart, Lung and Blood Institute recently issued a report using waist circumference >102 cm in men, as an additional means of

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Received 18 July 2000; revised 30 November 2000; accepted 8 January 2001

classifying high risk obesity.[12] Few studies have directly compared WHR and waist circumference as predictors of CHD in middle-aged and older men. In addition, abdominal adiposity may be a better marker of adiposity than body mass index (BMI) in the elderly as lean muscle mass decreases and abdominal girth increases. One study suggested that abdominal adiposity was a stronger predictor of CHD in older than middle-aged men;[4] however, no other studies have directly examined this finding in men.

The purpose of this study was to determine the association of abdominal adiposity and CHD (myocardial infarction or coronary revascularization) in men, and to assess whether the relationship was independent of total obesity. In addition, we wished to compare WHR and waist circumference, as measures of abdominal adiposity, to see if these were equivalent predictors of CHD in men. To minimize potential diagnostic and procedural bias associated with coronary revascularization we also examined myocardial infarction separately. Furthermore, we wanted to determine whether the relationship between abdominal adiposity and risk of CHD is modified by age.

Methods

The design and methods of the Physicians' Health Study (PHS) are described in detail elsewhere.[13] Briefly, 22 071 male physicians, without prior history of heart disease, cancer or other major medical illnesses, were randomly assigned, in a two-by-two factorial design, to one of four treatment groups: active aspirin (325 mg on alternate days) and active beta carotene (50 mg on alternate days), active aspirin and beta carotene placebo, aspirin placebo and active beta carotene, and both placebos. In January 1988, the randomized aspirin arm of the study was terminated by recommendation of the Data Safety Monitoring Board, when a statistically extreme reduction (44%) was seen in the risk of myocardial infarction among those allocated to active aspirin. After the unblinding of aspirin status and the presentation of the results, participants were free to choose whether or not they wanted to continue taking aspirin. Information on self-selected aspirin use was collected on annual questionnaires. The randomized beta carotene component continued until the regularly scheduled end of the trial in December, 1995.

Exposure information

Every 6 months for the first year, and annually thereafter, participants were sent brief follow-up questionnaires regarding their health behaviors and the occurrence of any relevant medical events. On the 9 y questionnaire, participants were asked to measure their waist at the level of the umbilicus and to record the measurement to the nearest quarter inch. A paper tape measure was enclosed for their use. They were also asked to record their hip measurement, defined as the largest measurement between the umbilicus and the thigh. WHR was calculated by dividing the waist circumference by the hip circumference. A low WHR represents a 'pear' shape while a high WHR corresponds with an 'apple' shape. BMI was calculated by dividing weight (kg) by the square of height (m). Waist circumference, WHR and BMI were divided into quintiles and tertiles, based on their distribution in the total population.

A validation study in a similar population of men in the Health Professionals' Follow-up Study, which compared the average of two technician measures to those recorded by participants in the prior year on a mailed questionnaire, found a correlation of 0.95 for waist circumference, 0.88 for hip circumference, 0.69 for WHR, and 0.97 for weight.[14] Other studies have found similar correlations.[15]

Covariate information

Data on weight, smoking, physical activity, history of diabetes, as well as aspirin and multivitamin use, were obtained from the 9 y questionnaire. Since not all covariates were ascertained on every questionnaire, for covariates that were not available on the 9 y questionnaire the data were taken from the most recently available questionnaire on which the information was available. Alcohol consumption, history of hypertension and elevated cholesterol were obtained from the 7 y questionnaire. Data on height and family history of myocardial infarction were obtained from the baseline questionnaire.

Endpoints

When a cardiovascular event or other outcome was reported, written permission to review medical records was obtained from the participant or next of kin. Coronary revascularizations (coronary artery bypass surgery and percutaneous transluminal coronary angioplasty) were confirmed based on the self-report by the physician. Confirmation of all other cardiovascular endpoints required review of available records by an endpoints committee of physicians who used standardized criteria for disease confirmation and were blinded to study agent assignment as well as exposure and covariate information. Myocardial infarctions were confirmed according to the criteria of the World Health Organization[16] which require symptoms and either elevated plasma levels of cardiac enzymes or characteristic EKG changes. Deaths due to myocardial infarction were confirmed on the basis of autopsy reports, symptoms, circumstances of death and a history of CHD. Reports of death or myocardial infarction without relevant records were not considered confirmed. Silent myocardial infarctions were also not confirmed since they could not be accurately dated. Only confirmed events were considered for these analyses. Morbidity follow-up of this cohort has been $>99\%$ complete and mortality follow-up nearly 100%. For these analyses, the first confirmed CHD event (myocardial infarction or coronary revascularization) was the primary endpoint, and all confirmed myocardial infarctions were also considered separately.

Statistical analyses

Among the 22 071 participants in the PHS, 16 164 reported weight, waist and hip information on the 9 y questionnaire and were free from prior cancer or cardiovascular disease. Person-years of follow-up were calculated from the return of the 9 y questionnaire until the end of the trial in December 1995 or the diagnosis of CHD, whichever came first. The average follow-up was 3.9 y. Incidence rates were calculated by dividing the number of new cases by the number of person-years of follow-up for each category. Rates were adjusted for age in 5 y categories. Relative risks were calculated as the number of events per person-year of observation in each quintile, divided by the number in the lowest quintile, after adjustment for age and randomized treatment assignment. Cox proportional hazards analysis was performed to adjust for age (5 y categories) and other potential confounders: BMI quintiles, smoking (past, never, current: <15, 15–24, 25+ cigarettes/day), self-selected aspirin use (≥ 3 pills/week), parental history of myocardial infarction before age 60, alcohol consumption (never/rarely, daily, weekly, monthly), physical activity (never, $<$once/week, 1–2 times/week, ≥ 3 times/week), and multivitamin use (daily, nondaily). For each RR, the two-sided *P*-value and 95% confidence intervals were calculated.

Results

Table 1 presents the baseline characteristics of the population according to WHR quintiles. Men with higher WHR were older, had higher mean BMI, were more likely to be current smokers, to consume alcohol daily, and to be sedentary. Men in the highest WHR quintile were nearly twice as likely to have a history of hypertension or diabetes than men in the lowest WHR quintile. Table 2 presents baseline characteristics of participants according to waist circumference quintiles. Men in the highest waist circumference quintile had higher BMI, and were more likely to be current smokers, and to be sedentary. Prevalence of hypertension and diabetes were again twice as high among men in the highest waist circumference quintile as those in the lowest waist quintile. Waist circumference was weakly correlated with height ($r=0.23$) and strongly correlated with weight ($r=0.79$) and BMI ($r=0.72$), while WHR was not correlated with height ($r=-0.01$) and only weakly associated with weight ($r=0.29$) and BMI ($r=0.30$).

During an average follow-up of 3.9 y and 62 293 person-years of follow-up, there were 552 confirmed first CHD events, including 209 myocardial infarctions. Relative risks (RR) adjusted for age and randomized treatment assignment were significantly elevated for men with a WHR ≥ 0.95 (Table 3). Men in the highest WHR quintile (≥ 0.99) had a RR of 1.58 (1.20–2.08) for all CHD and a RR of 1.45 (0.54–2.24) for myocardial infarction, compared to those in the lowest WHR quintile (*P* trend $=0.0001$ and 0.03, respectively). Multivariate adjustment for other cardiac risk factors,

Table 1 Characteristics according to waist/hip ratio quintiles among 16 164 men in the Physicians' Health Study

	Waist–hip ratio quintiles				
	1	*2*	*3*	*4*	*5*
	<0.90 (n=3215)	*0.90–<0.93 (n=3249)*	*0.93–<0.95 (n=3134)*	*0.95–<0.99 (n=3328)*	*≥0.99 (n=3238)*
Age (mean)	58.7	59.8	61.1	62.0	62.8
BMI (kg/m^2; mean)	23.8	24.7	25.2	26.1	27.0
Smoking (%)					
Never	57.1	54.0	49.7	47.5	44.6
Past	38.5	40.8	43.7	44.7	46.3
Current	4.4	5.2	6.6	7.7	9.1
Parental history MI (%)	13.6	13.6	13.0	12.5	12.6
Alcohol intake (%)					
Never	20.6	19.9	19.5	20.0	20.7
Monthly	12.6	13.6	12.5	13.9	14.0
Weekly	51.7	50.5	49.0	47.0	45.2
Daily	15.1	16.0	18.9	19.2	20.1
Physical activity (%)					
Rarely/never	28.7	33.5	36.5	42.3	49.0
1–2/week	19.2	20.4	19.5	18.3	18.5
3+/week	52.1	46.1	44.0	38.9	32.5
Aspirin ≥3/week (%)	71.6	73.6	73.4	73.0	72.8
Daily multivitamin (%)	34.5	32.4	33.6	33.1	34.8
History of hypertension (%)	14.2	18.0	20.6	24.2	27.8
History of high cholesterol (%)	13.0	14.4	15.4	16.3	15.4
History of diabetes mellitus (%)	2.4	2.8	2.8	4.8	6.9

Table 2 Characteristics according to waist circumference quintiles among 16 164 men in the Physicians' Health Study

	Waist circumference quintiles (cm)				
	1	*2*	*3*	*4*	*5*
	< 88.4 (n = 3105)	*88.4–< 92.7 (n = 3169)*	*92.7–< 97.3 (n = 3343)*	*97.3–< 103.6 (n = 3271)*	*≥ 103.6 (n = 3276)*
Age (mean)	59.7	60.3	61.1	61.7	61.6
BMI (kg/m^2; mean)	22.5	24.0	25.0	26.2	29.0
Smoking (%)					
Never	56.2	54.6	50.6	47.5	44.4
Past	38.8	40.1	43.5	44.7	46.7
Current	5.0	5.3	5.9	7.7	8.9
Parental history of MI (%)	13.6	12.6	12.7	12.8	13.5
Alcohol intake (%)					
Never	22.1	20.0	18.6	19.1	20.9
Monthly	12.8	11.5	13.2	13.6	15.5
Weekly	48.2	50.3	50.3	48.3	46.2
Daily	16.8	18.2	17.8	19.0	17.4
Physical activity (%)					
Rarely/never	27.5	32.1	37.0	41.5	52.0
1–2/week	16.0	19.8	20.3	19.9	19.5
3 + /week	56.5	48.0	42.6	38.6	28.5
Aspirin ≥ 3/week (%)	71.7	73.0	73.3	72.6	73.7
Daily multivitamin (%)	35.2	34.9	32.3	33.2	32.9
History of hypertension (%)	14.1	17.1	20.0	23.2	30.1
History of high cholesterol (%)	13.4	13.9	17.2	15.6	14.1
History of diabetes mellitus (%)	2.7	2.6	3.5	4.0	6.8

Table 3 Age-adjusted and multivariate relative risks for coronary heart disease (CHD) and myocardial infarction (MI) according to waist–hip ratio quintiles, among 16 166 men in the Physicians' Health Study

	Waist–hip ratio quintiles					
	1	*2*	*3*	*4*	*5*	
	< 0.90	*0.90–< 0.92*	*0.92–< 0.95*	*0.95–< 0.99*	*≥ 0.99*	*P-trend*
All CHD (n = 552)						
Person years	12 564	12 623	12 113	12 732	12 260	
Cases	78	94	91	138	147	
Age/agent-adjusted[a]	1.00 (referent)	1.06 (0.78–1.43)	1.12 (0.83–1.50)	1.45 (1.10–1.92)	1.58 (1.20–2.08)	0.0001
Multivariate model 1[b]	1.00 (referent)	1.03 (0.26–1.39)	1.09 (0.81–1.47)	1.39 (1.05–1.84)	1.50 (1.14–1.98)	0.0003
Multivariate model 2[c]	1.00 (referent)	0.97 (0.72–1.31)	0.99 (0.73–1.34)	1.20 (0.90–1.60)	1.23 (0.92–1.66)	0.05
MI only (n = 209)						
Person years	12 645	12 731	12 238	12 910	12 435	
Cases	33	37	28	52	60	
Age/agent-adjusted	1.00 (referent)	1.05 (0.66–1.68)	0.77 (0.46–1.27)	1.29 (0.83–2.00)	1.45 (0.94–2.24)	0.03
Multivariate model 1	1.00 (referent)	1.02 (0.64–1.63)	0.75 (0.45–1.24)	1.23 (0.79–1.91)	1.36 (0.88–2.10)	0.07
Multivariate model 2	1.00 (referent)	0.93 (0.58–1.50)	0.64 (0.39–1.08)	0.97 (0.61–1.53)	0.99 (0.62–1.56)	0.78

[a]Adjusted for age (5 y categories) and randomized beta-carotene treatment assignment.
[b]Adjusted for age, randomized beta-carotene assignment, aspirin use, smoking, parental history of MI, physical activity, alcohol consumption and multivitamin use.
[c]Adjusted for all of the variables in model 1, as well as BMI quintiles.

including smoking, physical activity, alcohol consumption, family history of myocardial infarction, multivitamin and aspirin use, resulted in only a modest change in the RRs. However, further adjustment for BMI quintiles (model 2) significantly attenuated the associations: the relative risks for CHD and myocardial infarction were 1.23 (0.92–1.66) and 0.99 (0.62–1.56), respectively.

Age-adjusted and multivariate RR for CHD according to waist circumference quintiles are presented in Table 4. Age and randomized agent-adjusted RR were significantly elevated for men with a waist circumference of 92.7 cm or higher. Men in the highest waist circumference quintile ($\geq$103.6 cm) had a RR of 1.70 (1.29–2.23) for CHD and a RR of 1.94 (1.25–3.02) for myocardial infarction (*P*-trend = 0.001 and 0.001, respectively), compared with men in the lowest quintile. Little change in the risk estimates was observed after multivariate adjustment for other cardiac risk factors. However, further adjustment for BMI quintiles (model 2) resulted in an association that was not statistically significant, with an RR for CHD of 1.06 (0.74–1.53) and an RR for myocardial infarction of 1.10 (0.61–2.00) for men in the highest waist quintile (*P*-trend = 0.69 and 0.37, respectively).

BMI was strongly associated with increased risk of CHD and myocardial infarction (Table 5). Among men in the highest BMI quintile ($\geq$27.6 kg/m^2), the age-adjusted RR for CHD was 2.00 (1.52–2.64) and the RR for myocardial infarction was 2.52 (1.59–3.94; *P*-trends both 0.0001). Even after adjusting for WHR and other cardiac risk factors, the association between BMI and CHD remained statistically significant: men in the highest BMI quintile had a RR of 1.73 (1.29–2.32) for CHD and 2.48 (1.54–4.01) for myocardial infarction.

Measurements of both central and total obesity were generally associated with increased risk of CHD. As shown in Figure 1, larger waist circumference was associated with increased incidence of CHD within the upper two tertiles of BMI, although the gradient was absent among men in the lowest BMI tertile. Within each waist circumference tertile, higher BMI was associated with increased incidence of CHD. Men with both a large waist circumference and high BMI had the highest age-adjusted incidence rate of CHD. As shown in Figure 2, within each WHR tertile, higher BMI was associated with increased risk, but higher WHR was not associated with a stepwise increase within each BMI tertile.

We also examined possible effect modification of the association of abdominal adiposity and CHD by age (Table 6). For both those aged 65 and older, and those younger than 65 y, the multivariate associations of the highest quintile of both WHR and waist circumference were similar in magnitude, and were attenuated by the inclusion of BMI. Specifically, among men aged 65 y or older in the highest WHR quintile, the multivariate RR for CHD was 1.59 (1.03–2.46) while for men younger than age 65 the RR was 1.41

Table 4 Age-adjusted and multivariate relative risks for coronary heart disease (CHD) and myocardial infarction (MI) according to waist circumference quintiles, among 16 166 men in the Physicians' Health Study

	Waist circumference quintiles (cm)					
	1	*2*	*3*	*4*	*5*	
	<88.4	*88.4–<92.7*	*92.7–<97.3*	*97.3–<103.6*	*≥103.6*	P-*trend*
All CHD (n = 552)						
Person years	12 114	12 322	12 839	12 598	12 421	
Cases						
Age/agent-adjusted[a]	76	84	122	116	151	
1.00	1.00	1.35	1.28	1.70	0.0001	
	(referent)	(0.74–1.36)	(1.02–1.80)	(0.96–1.70)	(1.30–2.23)	
Multivariate model 1[b]	1.00	1.01	1.34	1.26	1.60	0.001
	(referent)	(0.74–1.37)	(1.01–1.78)	(0.94–1.68)	(1.21–2.11)	
Multivariate model 2[c]	1.00	0.90	1.10	0.94	1.06	0.69
	(referent)	(0.65–1.24)	(0.80–1.51)	(0.66–1.32)	(0.74–1.53)	
MI only (n = 209)						
Person years	12 209	12 433	13 010	12 722	12 586	
Cases	29	24	38	54	64	
Age/agent-adjusted	1.00	0.78	1.13	1.60	1.94	0.0001
	(referent)	(0.45–1.34)	(0.70–1.84)	(1.02–2.52)	(1.25–3.02)	
Multivariate model 1	1.00	0.80	1.13	1.60	1.83	0.0001
	(referent)	(0.46–1.37)	(0.70–1.84)	(1.01–2.52)	(1.17–2.87)	
Multivariate model 2	1.00	0.71	0.92	1.15	1.10	0.37
	(referent)	(0.40–1.24)	(0.54–1.59)	(0.66–2.03)	(0.61–2.00)	

[a]Adjusted for age (5 y categories) and randomized beta-carotene treatment assignment.
[b]Adjusted for age, randomized beta-carotene assignment, aspirin use, smoking, parental history of MI, physical activity, alcohol consumption and multivitamin use.
[c]Adjusted for all of the variables in model 1, as well as BMI quintiles.

Table 5 Age-adjusted and multivariate relative risks for coronary heart disease (CHD) and myocardial infarction (MI) according to body mass index quintiles, among 16 166 men in the Physicians' Health Study

	Body mass index quintiles (kg/m²)					
	1	*2*	*3*	*4*	*5*	
	< 22.8	*22.8–< 24.3*	*24.3–< 25.7*	*25.7–< 27.6*	*≥ 27.6*	P-*trend*
All CHD (n = *552)*						
Person years	12 463	12 460	12 614	12 413	12 335	
Cases	77	101	97	131	142	
Age/agent-adjusted[a]	1.00 (referent)	1.31 (0.98–1.76)	1.29 (0.96–1.74)	1.77 (1.34–2.34)	2.00 (1.52–2.64)	0.0001
Multivariate model 1[b]	1.00 (referent)	1.33 (0.99–1.79)	1.28 (0.95–1.73)	1.74 (1.31–2.30)	1.89 (1.43–2.51)	0.0001
Multivariate model 2[c]	1.00 (referent)	1.31 (0.97–1.75)	1.23 (0.91–1.67)	1.62 (1.21–2.16)	1.73 (1.29–2.32)	0.0001
MI only (n = *209)*						
Person years	12 563	12 588	12 747	12 562	12 490	
Cases	29	34	34	49	63	
Age/agent adjusted	1.00 (referent)	1.28 (0.78–2.11)	1.32 (0.80–2.17)	1.96 (1.23–3.17)	2.65 (1.69–4.15)	0.0001
Multivariate model 1	1.00 (referent)	1.33 (0.81–2.19)	1.33 (0.81–2.19)	1.94 (1.22–3.09)	2.52 (1.60–3.96)	0.0001
Multivariate model 2	1.00 (referent)	1.34 (0.81–2.21)	1.34 (0.81–2.19)	1.93 (1.19–3.13)	2.48 (1.54–4.01)	0.0001

[a]Age and agent adjusted model is adjusted for age (5 y categories) and randomized beta-carotene assignment.
[b]Adjusted for age, randomized beta-carotene treatment assignment, aspirin use, smoking, parental history of MI, physical activity, alcohol consumption, and multivitamin use.
[c]Adjusted for all of the variables in model 1, as well as WHR quintiles.

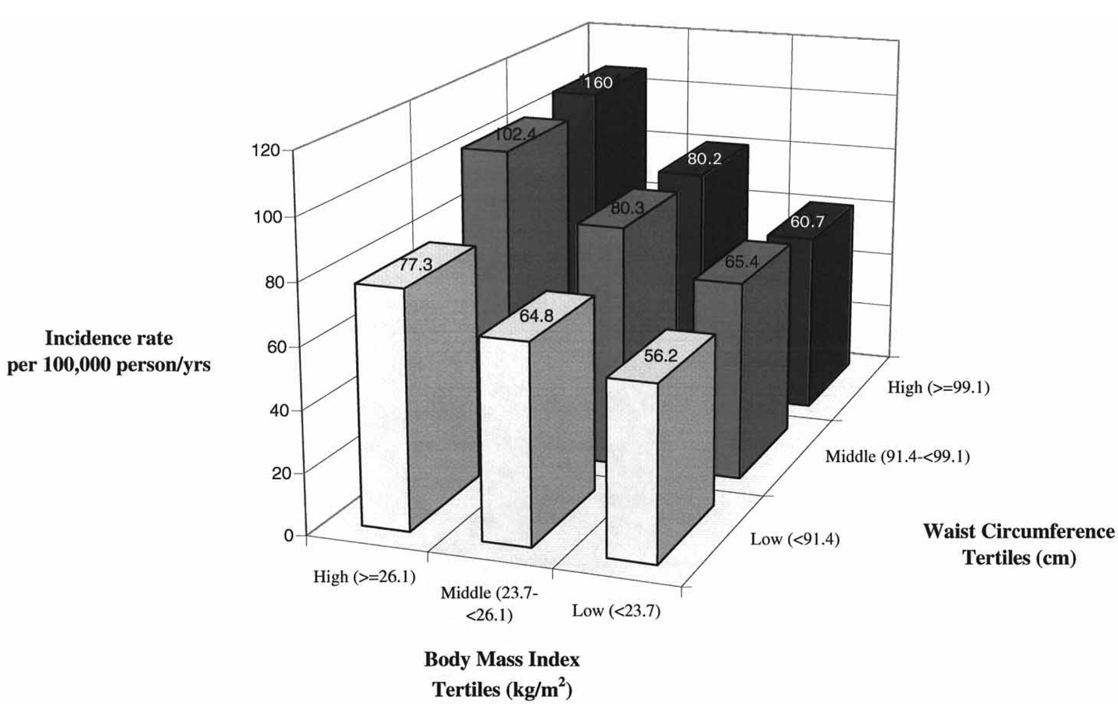

Figure 1 Age-adjusted incidence rates for coronary heart disease according to body mass index and waist circumference tertiles.

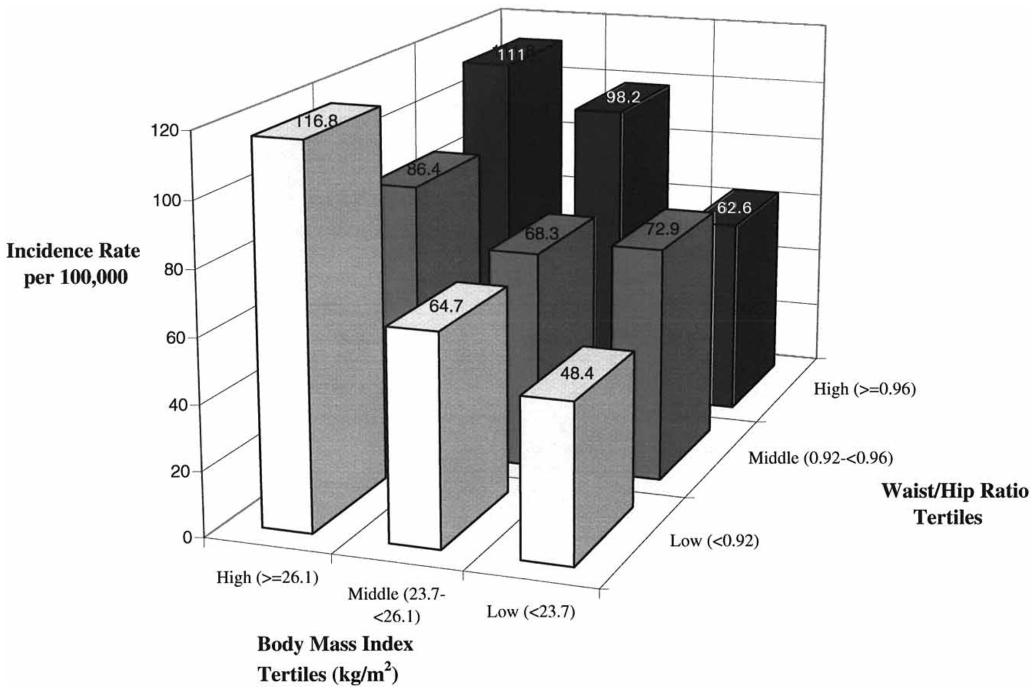

Figure 2 Age-adjusted incidence rates for coronary heart disease according to body mass index and waist/hip ratio tertiles.

(0.98–2.03), compared with men of the same age in the lowest quintile. For waist circumference, men in the highest quintile had a RR for CHD of 1.56 (1.03–2.37) if aged 65 y or older and 1.63 (1.12–2.36) if younger than age 65 y. Adjustment for BMI resulted in substantial attenuations of the RR for both the younger as well as the older men and eliminated an independent association for both age groups and measures. When BMI quintiles were examined, BMI was more strongly associated with risk of CHD in the younger than the older men. Men in the highest BMI quintile had a RR for CHD of 2.23 (1.48–3.45) if they were younger than age 65, while those age 65 and older had a RR for CHD of 1.47 (0.97–2.21). Even after adjustment for WHR, BMI remained significantly associated with CHD among the younger men (RR = 2.05 (1.34–3.14)), while among the older men, the association was further weakened by adjustment for WHR.

Discussion

We found that measures of regional fat distribution were associated with risk of CHD in men, although to a weaker extent than has been reported in women.[8] In this cohort of middle-aged and older men, those with a WHR $\geq$ 0.95 or a waist circumference $\geq$ 36.8 inches had a significantly elevated age-adjusted risk for CHD. After adjustment for cardiac risk factors, men in the highest WHR quintile ($\geq$ 0.99) had a 50% increased risk of CHD, while those in the highest waist circumference quintile ($\geq$ 103.6 cm) had a 60% increased risk of CHD. Adjustment for BMI weakened these associations, eliminating an independent association for abdominal adiposity measures. In our cohort of middle-aged and older men, BMI was more strongly associated with risk of CHD than either measure of regional adiposity. Men in the highest BMI quintile had a multivariate RR of CHD of 1.89. Although WHR and waist circumference are both imperfect proxies for visceral fat accumulation, several studies have suggested that waist circumference is more closely correlated with visceral adipose tissue mass.[17] However, we found that both waist circumference and WHR were similarly associated with risk of CHD, and both were nonsignificant after adjustment for BMI.

Previous subgroup analyses in men have suggested that abdominal adiposity was a stronger predictor of CHD in men age 65 and older than men younger than age 65. In the Health Professionals' Follow-up Study, men age 65 or older with a WHR of $\geq$ 0.98 had an RR of 2.76 (1.22–6.23) for CHD, after adjustment for BMI and other cardiac risk factors.[4] In contrast, we found that the risks of CHD associated with increased WHR and waist circumference were similar for older and middle-aged men. Men aged 65 or older with a WHR of $\geq$ 0.99 had an RR of 1.37 (0.87–2.17), after adjustment for BMI and other cardiac risk factors. Total adiposity, as measured by BMI, was more strongly associated with risk of CHD in the younger than the older men. For men younger than age 65, the risk of CHD among men in the highest BMI quintile was increased 2.2-fold, while for those aged 65 and older there was a nonsignificant 47% increased risk.

Table 6 Multivariate relative risks of coronary heart disease (CHD) according to waist/hip ratio, waist circumference and body mass index quintiles, stratified by age

		Waist–hip ratio quintiles					
		1	*2*	*3*	*4*	*5*	
Age strata	Model	*<0.90*	*0.90–<0.92*	*0.92–<0.95*	*0.95–<0.99*	*≥0.99*	*P-trend*
Age <65 (n=296)	Model 1[a]	1.00 (referent)	1.01 (0.69–1.49)	0.90 (0.60–1.34)	1.58 (1.11–2.25)	1.41 (0.98–2.03)	0.01
	Model 2[b]	1.00 (referent)	0.95 (0.64–1.39)	0.80 (0.53–1.21)	1.33 (0.92–1.92)	1.13 (0.76–1.66)	0.21
Age ≥65 (n=256)	Model 1	1.00 (referent)	1.06 (0.65–1.73)	1.33 (0.84–2.11)	1.22 (0.78–1.93)	1.59 (1.03–2.46)	0.02
	Model 2	1.00 (referent)	1.00 (0.61–1.64)	1.25 (0.79–1.99)	1.09 (0.68–1.73)	1.37 (0.87–2.17)	0.13
		Waist circumference quintiles (cm)					
		1	*2*	*3*	*4*	*5*	
		<88.4	*88.4–<92.7*	*92.7–<97.3*	*97.3–<103.6*	*≥103.6*	
Age <65 (n=296)	Model 1	1.00 (referent)	1.03 (0.68–1.55)	1.27 (0.87–1.88)	1.22 (0.82–1.80)	1.63 (1.12–2.36)	0.005
	Model 2	1.00 (referent)	0.88 (0.57–1.35)	0.99 (0.64–1.53)	0.82 (0.51–1.32)	0.93 (0.56–1.53)	0.83
Age ≥65 (n=256)	Model 1	1.00 (referent)	1.00 (0.63–1.59)	1.42 (0.93–2.17)	1.30 (0.85–1.99)	1.56 (1.03–2.37)	0.02
	Model 2	1.00 (referent)	0.93 (0.58–1.51)	1.23 (0.77–1.97)	1.05 (0.64–1.74)	1.24 (0.72–2.25)	0.43
		Body mass index quintiles (kg/m²)					
		1	*2*	*3*	*4*	*5*	
		<22.8	*22.8–<24.3*	*24.3–<25.7*	*25.7–<27.6*	*≥27.6*	
Age <65 (n=296)	Model 1	1.00 (referent)	1.36 (0.87–2.14)	1.45 (0.94–2.23)	1.65 (1.08–2.53)	2.23 (1.48–3.35)	0.0001
	Model 3[c]	1.00 (referent)	1.36 (0.87–2.14)	1.42 (0.91–2.20)	1.56 (1.01–2.42)	2.05 (1.34–3.14)	0.005
Age ≥65 (n=256)	Model 1	1.00 (referent)	1.31 (0.89–1.94)	1.13 (0.75–1.72)	1.88 (1.29–2.73)	1.47 (0.97–2.21)	0.02
	Model 3	1.00 (referent)	1.28 (0.87–1.90)	1.07 (0.70–1.63)	1.75 (1.18–2.58)	1.33 (0.86–2.04)	0.10

[a]Adjusted for age within stratum, randomized beta carotene assignment, aspirin use, smoking, parental history of MI, physical activity, consumption and multivitamin use.
[b]Adjusted for all of the factors in models 1, as well as body mass index quintiles.
[c]Adjusted for all of the factors in model 1, as well as for WHR quintiles.

This study has several strengths. Follow-up rates in this study have been very high and endpoints have been carefully reviewed. Although all of the anthropometric measures were self-reported, the validity of self-reported weight, waist and hip measures has been high in other health professional cohorts.[14] There are also several limitations of our analyses. Because WHR involves the ratio of two separate measurements, each measured with error, there is more measurement error associated with WHR than waist circumference. Thus, the weakness of the association with WHR in this study may possibly be due to measurement error, but these errors would likely be similar if WHR were measured in clinical practice. The men in the PHS are somewhat healthier than the general population, and have lower rates of obesity. Obese men were also somewhat less likely to provide waist and hip circumferences; thus, our results may not apply to more obese populations. Additionally, the PHS is a cohort of predominantly white, middle-aged and older men. It is possible that abdominal adiposity measures might be more strongly associated with CHD risk in other ethnic populations or in other age groups.

Our results are fairly similar to the other studies that have assessed regional fat distribution and risk of CHD in men. In studies that have adjusted for BMI, abdominal adiposity has not remained an independent predictor of CHD in men. In the Health Professionals' Follow-up Study, men with a WHR > 0.98 had an RR of 1.42 (0.99–2.04) after adjustment for BMI and other cardiac risk factors. Men in the highest waist circumference quintile ($\geq$ 40 inches) had an RR of 1.44 (0.95–2.17), compared with the lowest quintile, during 3 y of follow-up.[4] In the Atherosclerosis Risk in Communities (ARIC) Study, men in the highest quartile of WHR (> 1.00) had a multivariate RR of 1.8 (1.2–2.6) for CHD without adjustment for BMI, during six years of follow-up.[6] In the Gothenburg Study, WHR was significantly higher among men who developed ischemic heart disease than among those who did not. In contrast to our study, the highest probability of heart disease was observed among men who were in the lowest BMI tertile and highest WHR tertile, although results were not adjusted for age.[5] In the Framingham Study, men in the highest quintile of waist circumference had an age-adjusted RR of 2.0 (1.6–2.7) for CHD during 28 y of follow-up.[10] In the Charleston Heart Study, waist circumference was associated with a nonsignificant two-fold increased risk in CHD mortality among black but not white men during 28 y of follow-up.[18] Several other studies in men have found increased risk of CHD among men with larger upper body skin fold thicknesses.[19,20]

The risk relationships observed in our analyses, as well as those reported in other studies of men, are generally lower than those reported for women. In the Nurses' Health Study, women in the highest quintile of WHR had a multivariate RR of 2.58 for CHD after adjustment for BMI, compared with those in the lowest quintile. In contrast to the data in men, abdominal adiposity was a stronger predictor in younger than older women.[8] In the Iowa Women's Health Study women in the highest WHR tertile had a multivariate RR for CHD mortality of 2.8 after adjusting for BMI, compared with those in the lowest tertile.[9] In another small cohort in Sweden, women in the highest quintile of WHR had an age-adjusted RR of 8.2 for myocardial infarction, compared with those in the lowest WHR quintile.[7] The causes of these observed gender differences in the strength of the association between abdominal adiposity and CHD remain unknown. Higher RRs in women may be due in part to lower baseline risks. Alternatively, abdominal adiposity may be associated with higher androgen levels in women, which may be associated with higher CHD risk in women.[21]

Our data suggest that abdominal adiposity, whether measured by WHR or waist circumference, is associated with a modest elevation in the risk of CHD in middle-aged and older men. However, BMI is more strongly associated with risk of CHD than either measure of abdominal adiposity. When BMI was taken into account, neither WHR or waist circumference independently predicted risk of CHD. We found no significant effect modification by age for the association between abdominal adiposity and CHD, while BMI was more strongly associated with risk of CHD among the middle-aged men than the older men. In contrast to previous findings in women,[8] abdominal adiposity was not independently associated with risk of CHD after adjustment for total obesity.

Acknowledgments

We are indebted to the participants of the Physicians' Health Study for their outstanding commitment and cooperation and to the Physicians' Health Study staff and Bill McCullen for their expert and unfailing assistance. This work was supported by NIH grants CA-40360, CA-34994, HL-26490 and HL-34595.

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