Abdominal Adiposity and Coronary Heart Disease in Women

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Context.—Obesity is a well-established risk factor for coronary heart disease (CHD), but whether regional fat distribution contributes independently to risk remains unclear.

Objective.—To compare waist-hip ratio (WHR) and waist circumference in determining risk of CHD in women.

Design and Setting.—Prospective cohort study among US female registered nurses participating in the Nurses' Health Study conducted between 1986, when the nurses completed a questionnaire, and follow-up in June 1994.

Participants.—A total of 44 702 women aged 40 to 65 years who provided waist and hip circumferences and were free of prior CHD, stroke, or cancer in 1986.

Main Outcome Measures.—Incidence of CHD (nonfatal myocardial infarction or CHD death).

Results.—During 8 years of follow-up 320 CHD events (251 myocardial infarctions and 69 CHD deaths) were documented. Higher WHR and greater waist circumference were independently associated with a significantly increased age-adjusted risk of CHD. After adjusting for body mass index (BMI) (defined as weight in kilograms divided by the square of height in meters) and other cardiac risk factors, women with a WHR of 0.88 or higher had a relative risk (RR) of 3.25 (95% confidence interval [CI], 1.78-5.95) for CHD compared with women with a WHR of less than 0.72. A waist circumference of 96.5 cm (38 in) or more was associated with an RR of 3.06 (95% CI, 1.54-6.10). The WHR and waist circumference were independently strongly associated with increased risk of CHD also among women with a BMI of 25 kg/m^2 or less. After adjustment for reported hypertension, diabetes, and high cholesterol level, a WHR of 0.76 or higher or waist circumference of 76.2 cm (30 in) or more was associated with more than a 2-fold higher risk of CHD.

Conclusions.—The WHR and waist circumference are independently associated with risk of CHD in women.

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OBESITY is well recognized as a major risk factor for coronary heart disease (CHD) in men and women.[1-3] However, since Vague's[4] description of the association between upper body obesity and cardiovascular disease, the relative importance of total and regional obesity has been debated. Abdominal adiposity has been linked to significant metabolic abnormalities, including insulin resistance, hyperinsulinemia, and elevated triglyceride levels, as well as increased incidence of hypertension,[5] glucose intolerance,[6] and diabetes mellitus.[7] Several studies suggest that abdominal adiposity, as measured by waist-hip ratio (WHR), is an independent risk factor for CHD in men[8,9] and perhaps also in women.[10,11] Waist circumference has also been associated with increased risk of CHD[9,12] and has been advocated by some as a simpler measure of abdominal obesity.[13] However, whether regional obesity remains a risk factor after taking total adiposity into account remains controversial. The purpose of this study was to determine the risk of CHD associated with abdominal adiposity in women and to compare the effects of WHR and waist circumference.

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METHODS

The Nurses' Health Study (NHS) cohort was formed in 1976 when 121 701 female registered nurses, aged 30 to 55 years and living in 11 US states, returned a mailed questionnaire. These women have answered questionnaires every 2 years, reporting information about exposures, risk factors, and health outcomes, including the diagnosis of myocardial infarction (MI).

All covariates for these analyses were obtained from the 1986 questionnaire with the exception of height (collected in 1976), aspirin intake (collected in 1984), family history of MI (collected in 1976 and 1980), and oral contraceptive use (collected biennially from 1976 to 1984). In 1986, women were instructed to measure their waist at the level of the umbilicus and their hips at the largest circumference with a tape measure while standing relaxed and to report values to the nearest quarter inch (reported herein in centimeters [inches]).

Documentation of CHD

The primary end point for this analysis was CHD, defined as incidence of nonfatal MI or fatal CHD. Myocardial infarction was classified by medical record review using the World Health Organization criteria of symptoms and either diagnostic electrocardiographic changes or elevated cardiac enzyme levels.[14] Silent MI was excluded. Fatal CHD was considered confirmed if hospital or autopsy records confirmed fatal MI or the death certificate listed CHD as the primary cause of death and available evidence from next of kin, hospital records, or prior participant report indicated a previous diagnosis of CHD. If the cause of death on the death certificate could not be confirmed by supplemental confirmatory data, the death was not included as an end point. Deaths of nonrespondents to the biennial questionnaire were ascertained by surveillance of the National Death Index and vital records of the states. There were 251 nonfatal MIs and 69 confirmed CHD deaths.

Validation Studies

In 1987, we assessed the validity of self-reported waist and hip measures in a random sample of 140 participants in the greater Boston, Mass, area. The average of 2 technician measurements spaced 6 months apart was compared with the waist and hip circumference values reported on the most recent questionnaire. Women reliably reported waist circum-

Table 1.—Baseline Characteristics of Women in the Nurses' Health Study, According to Waist-Hip Ratio Category and Waist Circumference in 1986

	Waist-Hip Ratio Category					
Characteristic	**<0.72**	**0.72-<0.76**	**0.76-<0.80**	**0.80-<0.84**	**0.84-<0.88**	**≥0.88**
No. of women	7213	11 479	10 427	8003	4299	3281
Age, mean ± SD, y	50.8 ± 6.9	52.1 ± 7.0	53.4 ± 7.0	54.3 ± 6.9	55.3 ± 6.9	55.4 ± 6.9
BMI, mean ± SD, kg/m^2	22.6 ± 3.2	23.0 ± 3.3	24.4 ± 4.0	25.6 ± 4.4	26.9 ± 4.6	28.2 ± 5.0
Height, mean ± SD, cm	163.9 ± 6.1	163.9 ± 6.1	164.0 ± 6.2	163.9 ± 6.2	163.7 ± 6.2	163.5 ± 6.1
Alcohol intake, mean ± SD, g/d	5.6 ± 8.9	6.5 ± 10.4	6.7 ± 11.1	6.9 ± 12.1	6.9 ± 12.7	6.9 ± 13.3
Physical activity, mean ± SD, METs*	17.6 ± 23.6	16.6 ± 23.0	14.7 ± 20.4	13.3 ± 18.9	12.3 ± 18.9	11.8 ± 19.7
Current smoker, %	16.6	19.8	20.8	22.3	22.8	24.5
Postmenopausal, %	45.4	52.7	58.6	64.3	68.9	69.8
Hormone use, %†						
Current	35	33	28	25	22	17
Former	19	22	23	24	26	25
Hypertension, %‡	11.8	15.3	21.5	27.7	34.1	41.6
Diabetes, %‡	1.2	1.4	2.1	3.3	5.3	9.9
High cholesterol level, %‡	7.2	8.7	11.1	14.1	17.7	20.5

	Waist Circumference Category, cm						
Characteristic	**<71.1**	**71.1-<76.2**	**76.2-<81.3**	**81.3-<86.4**	**86.4-<91.4**	**91.4-<96.5**	**≥96.5**
No. of women	9663	10 134	8226	6357	4131	2649	3542
Age, mean ± SD, y	50.8 ± 7.0	52.4 ± 7.1	53.6 ± 7.0	54.6 ± 6.9	54.8 ± 6.8	54.9 ± 6.9	54.7 ± 6.9
BMI, mean ± SD, kg/m^2	20.9 ± 1.9	22.5 ± 1.9	23.9 ± 2.2	25.6 ± 2.5	27.3 ± 2.9	29.1 ± 3.3	33.1 ± 4.7
Height, mean ± SD, cm	162.1 ± 5.9	163.7 ± 6.0	164.4 ± 6.2	164.6 ± 6.2	164.6 ± 6.3	164.7 ± 6.3	165.1 ± 6.3
Alcohol intake, mean ± SD, g/d	6.6 ± 10.3	7.1 ± 11.2	7.1 ± 11.6	6.7 ± 11.7	5.9 ± 11.1	5.6 ± 11.1	4.7 ± 11.2
Physical activity, mean ± SD, METs*	19.1 ± 25.0	16.1 ± 22.0	14.5 ± 20.1	13.5 ± 18.9	12.1 ± 18.5	11.3 ± 17.8	9.9 ± 17.6
Current smoker, %	23.2	21.6	20.1	20.0	19.1	17.3	17.2
Postmenopausal, %	45.4	54.3	60.3	65.1	66.0	66.6	66.4
Hormone use, %†							
Current	35	32	31	26	22	20	17
Former	20	22	23	25	26	25	23
Hypertension, %‡	11.5	14.5	19.7	26.6	32.3	37.5	47.4
Diabetes, %‡	1.3	1.3	1.6	3.0	4.3	5.7	10.9
High cholesterol level, %‡	7.4	9.7	10.9	13.7	16.0	16.6	18.8

*Physical activity scores were calculated from the self-reports of 8 activities and are recorded in metabolic equivalent units (METs).
†Hormone use refers to current use of postmenopausal hormone replacement therapy. The percentage is expressed as the percentage of postmenopausal women who were current users.
‡Hypertension, diabetes, and hypercholesterolemia are by participant's self-report of physician-diagnosed condition.

ference, but underestimated hip circumference by an average of 1.4 cm (0.54 in). Thus, reported WHR was slightly higher than that obtained from directly measured values. Crude Pearson correlation coefficients for reported and measured circumferences for waist and hip and the WHR were 0.89, 0.84, and 0.70, respectively. After adjusting for age and body mass index (BMI) and correcting for random within-person variability, the correlations were 0.64, 0.60, and 0.62, respectively.[15]

The BMI was calculated by dividing weight (in kilograms) in 1986 by the square of height (in meters) reported in 1976. In women, BMI is strongly correlated with absolute fat mass as determined by hydrostatic underwater weighing (r=0.84-0.92)[16] and is minimally correlated with height (r= −0.06 in this cohort). Heavier women were somewhat less likely to report waist and hip measurements.

In a separate validation study of weight in a subsample of 184 study participants, the Spearman correlation between self-reported and measured weight was 0.96, although self-report averaged 1.5 kg less than directly measured weight.[17] This difference corresponds to an average difference in BMI of 0.5 kg/m^2. Participants in the NHS are similar to the national average BMI (26.1 kg/m^2 among white women in 1988-1991),[18] with a mean BMI of 25.4 kg/m^2 for the entire NHS cohort. Since heavier women were somewhat less likely to report circumference measurements, the average BMI for the population used in our analyses was 23.6 kg/m^2 (in 1986).

Data Analysis

Of the 102 252 women who responded to the 1986 questionnaire, 89 921 were free of prior history of heart disease, stroke, or cancer. Of these, 98 failed to provide height in 1976, 18 013 did not report weight in 1986, and 27 012 failed to provide waist or hip circumference measurements. Of the remaining 44 798 women, outlier detection procedures[19] identified 137 individuals who were determined to have implausible values of waist, hip, or BMI in 1986 (see below). This resulted in 44 702 individuals with relevant anthropometric measures and outcomes. Covariate information was incomplete for 3401 women who were therefore excluded from multivariate analyses. The most frequently missing (nonexclusive) covariates were lack of information about aspirin use (2046 women), dietary information (942 women), and physical activity (111 women). The women with missing covariate information appeared similar in all other regards to the other women who had complete data. Multivariate analyses that include all relevant covariates were performed on the 41 301 women with complete data.

A generalized extreme studentized deviate outlier detection procedure[19] was used to identify outlying values of BMI, leading to exclusion of all BMI values higher than 48.9 kg/m^2. Clinical judgment led to the exclusion of waist measures greater than 139.7 cm (55 in) or less than 38.1 cm (15 in) and hip measures greater than 165.1 cm (65 in) or less than 50.8 cm (20 in). Pearson correlations among the anthropometric variables were calculated. Person-years of follow-up were calculated as the time from completion of the 1986 questionnaire to June 1994 or the diagnosis of an end point, whichever came first. 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 age-adjusted in 5-

Table 2.—Age-Adjusted and Multivariate Relative Risks (95% Confidence Intervals) for Coronary Heart Disease,* According to Waist-Hip Ratio and Waist Circumference

	Waist-Hip Ratio Category						
	<0.72	0.72-<0.76	0.76-<0.80	0.80-<0.84	0.84-<0.88	≥0.88	*P* Trend
Person-years†	55 542	88 349	80 005	61 073	32 830	24 642	. . .
No. of cases	17	49	72	73	53	56	. . .
Age adjusted	1.00 (Referent)	1.59 (0.91-2.76)	2.32 (1.36-3.93)	2.85 (1.68-4.84)	3.57 (2.06-6.19)	5.04 (2.92-8.71)	<.001
Model 1‡	1.00 (Referent)	1.51 (0.84-2.71)	2.10 (1.20-3.70)	2.18 (1.23-3.87)	2.59 (1.43-4.71)	3.25 (1.78-5.95)	<.001
Model 2§	1.00 (Referent)	1.54 (0.86-2.77)	2.26 (1.29-3.95)	2.45 (1.39-4.31)	3.10 (1.73-5.55)	4.08 (2.27-7.31)	<.001
Model 3, adjusted for biological mediators¶	1.00 (Referent)	1.50 (0.84-2.70)	2.02 (1.15-3.55)	2.02 (1.14-3.59)	2.28 (1.25-4.15)	2.43 (1.32-4.48)	.003

	Waist Circumference Category, cm							
	<71.1	71.1-<76.2	76.2-<81.3	81.3-<86.4	86.4-<91.4	91.4-<96.5	≥96.5	*P* Trend
Person-years	74 197	77 835	63 052	48 651	31 639	20 213	26 854	. . .
No. of cases	33	42	66	58	38	28	55	. . .
Age adjusted	1.00 (Referent)	1.03 (0.65-1.63)	1.81 (1.19-2.76)	1.90 (1.24-2.93)	1.89 (1.18-3.02)	2.17 (1.31-3.60)	3.24 (2.10-5.01)	<.001
Model 1‡	1.00 (Referent)	1.25 (0.75-2.07)	2.29 (1.37-3.81)	2.42 (1.39-4.21)	2.13 (1.14-3.97)	2.25 (1.13-4.48)	3.06 (1.54-6.10)	.002
Model 2§	1.00 (Referent)	1.15 (0.71-1.88)	2.09 (1.33-3.28)	2.27 (1.44-3.59)	2.08 (1.26-3.43)	2.32 (1.35-4.01)	3.51 (2.19-5.62)	<.001
Model 3, adjusted for biological mediators¶	1.00 (Referent)	1.24 (0.75-2.07)	2.21 (1.33-3.69)	2.20 (1.26-3.85)	1.80 (0.97-3.36)	1.86 (0.93-3.69)	2.32 (1.16-4.63)	.03

*Coronary heart disease includes nonfatal myocardial infarction and fatal coronary heart disease.
†Person-years and cases are for age-adjusted models.
‡Model 1 is adjusted for body mass index (<21, 21-<23, 23-<25, 25-<27, 27-<29, 29-<31, ≥31 kg/m^2), age (continuous), age^2, smoking, parental history of myocardial infarction, alcohol consumption (g/d), physical activity (metabolic equivalent units), menopausal status, hormone replacement therapy, oral contraceptive use, aspirin intake, saturated fat intake (g/d), and antioxidant score.
§Model 2 is adjusted for all of the variables in model 1, except body mass index.
¶Model 3 is adjusted for all of the factors in model 1, with additional adjustment for biological mediators, including self-reported hypertension, diabetes, and elevated cholesterol level.

year age intervals. Cox proportional hazards models were used to estimate the relative risk of CHD outcomes across each anthropometric category. Models were fit controlling simultaneously for age and available relevant confounders.

RESULTS

Table 1 shows the relationship of WHR and waist circumference to baseline characteristics in 1986. The prevalence of current smokers increased with higher WHR but declined with larger waist circumference. Waist circumference was weakly correlated with height (r=0.14) and strongly correlated with weight (r=0.82) and BMI (r=0.81), while WHR was not correlated with height (r=−0.01) and was more weakly associated with weight (r=0.31) and BMI (r=0.34).

During 342 441 person-years of follow-up we documented 320 CHD end points (251 nonfatal MIs and 69 CHD deaths). Age-adjusted risk of CHD was positively associated with WHR and waist circumference (Table 2). In categorical models adjusted for age alone, WHR showed a stronger gradient than waist circumference for risk of CHD. Women with a WHR of 0.88 or higher had a relative risk (RR) of 5.04 (95% confidence interval [CI], 2.92-8.71) for CHD compared with women with a WHR of less than 0.72. Waist circumference was also directly associated with risk, with an RR of 3.24 (95% CI, 2.10-5.01) for women with a waist circumference of 96.5 cm (38 in) compared with women with waist circumference of less than 71.1 cm (28 in).

Measurements of both central and total obesity were independently associated with increased risk of CHD in stratified analyses. As shown in Figure 1, higher WHR was associated with increased age-adjusted risk of CHD, regardless of BMI tertile. Within any BMI tertile, women in the highest WHR tertile had a 2-fold higher incidence of CHD than those in the lowest WHR tertile. Within each WHR tertile, higher BMI also was generally associated with increased risk. As shown in Figure 2, within each tertile of BMI, larger waist circumference was also associated with increased risk of CHD.

Multivariate models were fit to adjust simultaneously for regional and total adiposity measures as well as for other cardiac risk factors, including smoking, alcohol, physical activity, menopausal status, parental history of MI, hormone replacement therapy use, oral contraceptive use, saturated fat consumption, antioxidant vitamin score, and aspirin use (Table 2). After adjustment for BMI and other cardiac risk factors, women with a WHR of 0.88 or higher had an RR of 3.25 (95% CI, 1.78-5.95) compared with those with a WHR of less than 0.72. The BMI also remained significant in these models. As a continuous variable, each 0.02 of WHR was associated with an RR of 1.04 (95% CI, 1.02-1.06). Multivariate models were also performed including terms for both waist circumference and BMI. In multivariate models women with a waist circumference of 96.5 cm (38 in) or greater had an RR of 3.06 (95% CI, 1.54-6.10) compared with women with waist measurements of less than 71.1 cm (28 in). The BMI was not significant in these models. As a continuous variable, each additional 2.54 cm (1 in) of waist circumference was associated with an RR of 1.07 (95% CI, 1.03-1.12). Omitting BMI from the models modestly strengthened the association.

To compare directly WHR and waist circumference, we also performed multivariate models using quintiles of WHR and waist circumference for the cohort (Table 3). After adjustment for BMI and other cardiac risk factors, women in the highest WHR quintile had an RR of 2.58 (95% CI, 1.58, 4.22) for CHD compared with women in the lowest quintile. Women in the highest waist circumference quintile had an RR of 2.44 (95% CI, 1.34-4.44) for CHD compared with those in the lowest quintile. Hip circumference had a weak inverse but not significant association with CHD in models that included height and waist and hip circumferences as separate terms.

We also examined whether the associations of WHR and waist circumference were modified by age, BMI, and use

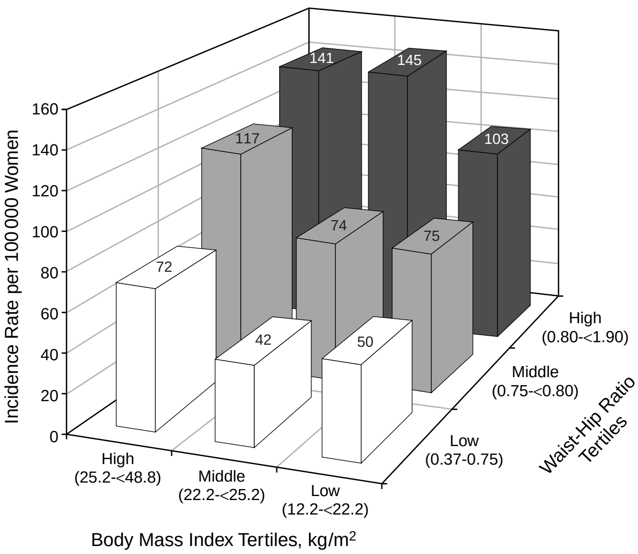

Figure 1.—Age-adjusted incidence rates for coronary heart disease according to body mass index and waist-hip ratio tertiles. Numbers at the top of each bar indicate incidence.

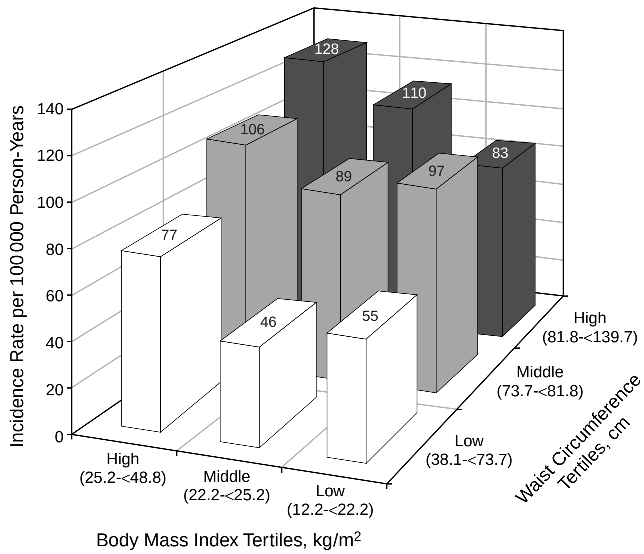

Figure 2.—Age-adjusted incidence rates for coronary heart disease according to body mass index and waist circumference tertiles.

of hormone replacement therapy (Table 4). The WHR was more strongly associated with risk of CHD in women younger than 60 years than in those aged 60 years or older (for WHR ≥0.88, RR, 4.47 [95% CI, 2.04-9.80] among the younger women, and RR, 1.86 [95% CI, 0.72-4.77] among the older women). Waist circumference was also a stronger predictor of CHD risk for younger than older women. There were no significant differences in the strength of association with CHD for premenopausal or postmenopausal women, after adjustment for age, with regard to WHR and waist circumference (data not presented).

When we stratified the sample according to current US Department of Agriculture desirable weight guidelines of BMI of less than 25 kg/m^2 or of 25 kg/m^2 or higher, WHR was strongly associated with increased risk of CHD in both groups (Table 4). Waist circumference was strongly associated with increased CHD risk among women with a BMI of less than 25 kg/m^2 but was not significantly predictive for women with a BMI of 25 kg/m^2 or higher. However, few women with large waist circumferences had a BMI of less than 25 kg/m^2. Because current hormone replacement therapy users had lower WHR and waist circumference values than past and never users, we examined the relationship between abdominal adiposity and CHD stratified by hormone replacement therapy use (Table 4). The association with CHD was significant for WHR and waist circumference only among women who had never used hormone replacement therapy, although the number of cases among past and current users was small. Formal interaction terms between hormone replacement therapy and measures of abdominal adiposity were nonsignificant.

To assess further the independent effects of waist circumference and WHR, we obtained a measure of waist circumference independent of BMI, by fitting a simple linear regression model for waist-hip ratio or waist circumference given BMI and entering the residuals into the model. The use of BMI-adjusted waist circumference residuals did not affect overall model fit, but the RR for each additional 2.54 cm (1 in) of waist was 1.28, compared with an RR of 1.07 in the linear model. For BMI-adjusted WHR residuals the RR for each 0.02 unit of WHR was 1.37, compared with an RR of 1.02 in the linear model that included both BMI and WHR. We also performed analyses correcting for measurement error. Correcting for the within-person variation noted in the validation study[15] increased the RR for CHD from 1.02 to 1.12 (95% CI, 1.06-1.14) for each 0.02 increase in WHR. Correcting for measurement error increased the RR for each inch of waist from 1.07 (95% CI, 1.04-1.13) to 1.15 (95% CI, 1.06-1.25).

Because hypertension, high cholesterol level, and diabetes are direct effects of central and total adiposity, we deliberately did not control for these factors in primary analyses. However, to assess residual effects we added these biological mediators stepwise into multivariate models (Table 4). After adjustment for BMI and reported hypertension, diabetes, high cholesterol level, and other cardiac risk factors, women with a WHR of 0.88 or higher had an RR of 2.43 (95% CI, 1.32-4.48) for CHD compared with women with a WHR of less than 0.72 (Table 2). Waist circumference was also strongly associated with CHD, even after controlling for these biological mediators. Women with a waist circumference of 96.5 cm (38 in) or greater had an RR of 2.32 (95% CI, 1.16-4.63) for CHD, compared with those women with a waist circumference of less than 71.1 cm (28 in).

COMMENT

We found that measures of regional fat distribution are independently associated with risk of CHD in women. In this cohort, both WHR and waist circumference were significantly associated with increased risk of CHD, even after controlling for BMI. In analyses stratified by BMI, higher WHR or waist circumference tertile was associated with higher risk of CHD, regardless of BMI tertile (Figures 1 and 2). After controlling for BMI and other cardiac risk factors, women with a WHR of 0.76 or greater were more than twice as likely to develop CHD during follow-up, while women with a WHR higher than 0.88 were more than 3 times as likely to develop CHD. Women in the highest quintile of WHR or waist circumference were nearly 2.5 times more likely to develop CHD than women in the lowest quintile.

Subgroup analyses in men have suggested that WHR may be a better predictor of cardiovascular risk than BMI among men older than 65 years.[9] Although our population was slightly younger, we found that WHR and waist circumference were more strongly associated with risk of CHD in women younger than 60 years than in those aged 60 years or older. The WHR was associated with increased risk of CHD, regardless of menopausal status and whether women were of "normal" weight or were overweight. In subgroup analyses, the relationship between abdominal adiposity appeared stronger in women who had never used hormone replacement therapy, although the numbers of cases were small among past and current users. Formal interaction terms were nonsignificant. Further studies of the potential interactions between weight, fat distribution, and hormone replacement therapy are necessary.

While direct effects of obesity, such as hypertension, diabetes mellitus, and high cholesterol level, appear to mediate the effects of obesity, more than a 2-fold residual risk of CHD was seen among women in the highest WHR category (≥0.88), even after controlling for these biological mediators. Since our measurement of these self-reported variables was imperfect, residual confounding by these factors is one explanation. However, other biological mechanisms, including lower high-density lipoprotein cholesterol level, higher serum triglyceride, insulin, and androgen levels, and increased insulin resistance, may also mediate the effects of abdominal adiposity.[6,20,21]

This study has several strengths. Follow-up rates in this large prospective cohort are high, end points have been care-

Table 3.—Multivariate Relative Risks (95% Confidence Intervals) for Coronary Heart Disease, According to Quintiles of Waist-Hip Ratio and Waist Circumference

	Waist-Hip Ratio Quintile					
	1 (0.37-<0.73)	**2 (0.73-<0.76)**	**3 (0.76-<0.79)**	**4 (0.79-<0.83)**	**5 (0.83-<1.90)**	***P* Trend**
Model 1*	1.00 (Referent)	1.34 (0.78-2.72)	1.63 (0.97-2.71)	2.04 (1.24-3.34)	2.58 (1.58-4.22)	<.001
Model 2†	1.00 (Referent)	1.38 (0.80-2.38)	1.74 (1.04-2.90)	2.25 (1.38-3.67)	3.09 (1.93-4.96)	<.001
	Waist Circumference Quintile (cm)					
	1 (38.1-<69.8)	**2 (69.8-<74.2)**	**3 (74.2-<79.2)**	**4 (79.2-<86.3)**	**5 (86.3-<139.7)**	***P* Trend**
Model 1*	1.00 (Referent)	1.27 (0.74-2.18)	2.08 (1.23-3.54)	2.31 (1.31-4.06)	2.44 (1.34-4.44)	.007
Model 2†	1.00 (Referent)	1.19 (0.71-2.00)	1.96 (1.22-3.17)	2.27 (1.42-3.64)	2.69 (1.72-4.22)	<.001

*Model 1 is adjusted for body mass index (<21, 21-<23, 23-<25, 25-<27, 27-<29, 29-<31, ≥31 kg/m^2), age, age^2, smoking (status and amount), parental history of myocardial infarction, alcohol consumption (g/d), physical activity (metabolic equivalent units), menopausal status, hormone replacement therapy, oral contraceptive use, aspirin intake, saturated fat intake (g/d), and antioxidant score.

†Model 2 is adjusted for all of the variables in model 1 except body mass index.

Table 4.—Multivariate Relative Risks* (95% Confidence Intervals) for Coronary Heart Disease,† According to Waist-Hip Ratio Category, Stratified by Age, Body Mass Index, and Use of Hormone Replacement Therapy‡

	No. of Cases	Waist-Hip Ratio Category						
		<0.72	**0.72-<0.76**	**0.76-0.80**	**0.80-<0.84**	**0.80-<0.88**	**≥0.88**	***P* Trend**
Age, y								
<60	176	1.00 (Referent)	1.70 (0.80-3.60)	2.51 (1.21-5.19)	2.98 (1.43-6.21)	2.92 (1.32-6.43)	4.47 (2.04-9.80)	<.001
≥60	119	1.00 (Referent)	1.17 (0.46-2.97)	1.46 (0.60-3.57)	1.23 (0.49-3.06)	1.88 (0.75-4.69)	1.86 (0.72-4.77)	.09
Body mass index, kg/m^2								
<25	151	1.00 (Referent)	1.33 (0.68-2.60)	1.97 (1.03-3.78)	2.21 (1.13-4.32)	2.18 (1.01-4.69)	3.54 (1.61-7.78)	<.001
≥25	144	1.00 (Referent)	2.11 (0.61-7.36)	2.41 (0.73-7.93)	2.26 (0.69-7.41)	3.11 (0.95-10.20)	3.53 (1.08-11.55)	.008
Hormone replacement therapy								
Current	47	1.00 (Referent)	0.76 (0.27-2.13)	0.87 (0.31-2.44)	0.61 (0.19-1.91)	0.89 (0.26-3.04)	1.72 (0.57-5.81)	.44
Past	66	1.00 (Referent)	1.12 (0.35-3.53)	1.33 (0.44-4.04)	1.16 (0.37-3.66)	1.88 (0.59-5.94)	1.26 (0.36-4.43)	.43
Never	135	1.00 (Referent)	1.38 (0.50-3.84)	2.24 (0.86-5.85)	2.85 (1.10-7.38)	3.06 (1.15-8.17)	3.79 (1.41-10.17)	<.001

	No. of Cases	Waist Circumference Category, cm							
		71.1	**71.1-<76.2**	**76.2-<81.3**	**81.3-<86.4**	**86.4-<91.4**	**91.4-<96.5**	**≥96.5**	***P* Trend**
Age, y									
<60	176	1.00 (Referent)	1.30 (0.70-2.40)	2.20 (1.17-4.15)	2.80 (1.41-5.55)	2.17 (0.98-4.81)	2.59 (1.08-6.22)	4.17 (1.73-10.02)	.001
≥60	119	1.00 (Referent)	1.23 (0.49-3.05)	2.49 (1.03-6.03)	2.02 (0.77-5.32)	2.03 (0.72-5.73)	1.93 (0.63-5.95)	1.98 (0.64-6.18)	.40
Body mass index, kg/m^2									
<25	151	1.00 (Referent)	1.33 (0.80-2.23)	2.34 (1.37-3.99)	1.81 (0.94-3.48)	3.21 (1.52-6.76)	2.91 (0.84-10.07)	2.64 (0.35-20.22)	.001
≥25	144	1.00 (Referent)	0.23 (0.01-3.65)	1.03 (0.13-7.90)	1.42 (0.19-10.43)	0.84 0.11-6.26)	1.04 (0.14-7.82)	1.47 (0.20-11.02)	.17
Hormone replacement therapy									
Current	47	1.00 (Referent)	0.45 (0.25-0.78)	0.95 (0.55-1.65)	1.09 (0.60-2.00)	0.56 (0.29-1.10)	0.44 (0.20-0.93)	1.05 (0.50-2.20)	.99
Past	66	1.00 (Referent)	1.74 (0.58-5.20)	2.60 (0.85-7.97)	1.84 (0.52-6.48)	3.07 0.84-11.20)	2.10 (0.47-9.42)	2.60 (0.58-11.69)	.22
Never	135	1.00 (Referent)	1.21 (0.49-2.96)	2.88 (1.23-6.73)	3.51 (1.43-8.63)	3.20 (1.20-8.50)	2.88 (0.99-8.38)	4.33 (1.49-12.60)	.01

*Adjusted for body mass index category (<21, 21-<23, 23-<25, 25-<27, 27-<29, 29-<31, ≥31 kg/m^2), age (continuous), age^2, smoking (status and amount), parental history of myocardial infarction, alcohol consumption (g/d), physical activity (metabolic equivalent units), menopausal status, hormone replacement therapy, oral contraceptive use, aspirin intake, saturated fat intake (g/d), and antioxidant score.

†Coronary heart disease includes cases of nonfatal myocardial infarction and fatal coronary heart disease.

‡Analysis restricted to postmenopausal women who reported information about hormone use. Person-years for each category were as follows: current, 6771; past, 5498; and never, 11 661.

fully documented, and reliability of self-reported risk factor information has been high.[22] Among a random sample of women in this cohort, all of the self-reports of hypertension, 87.5% of reports of elevated cholesterol level,[23] and 98.4% of reported cases of diabetes mellitus[24] were confirmed by medical record review. Although all of our anthropometric measures are by self-report, the validity of self-reported weight, as well as waist and hip circumference measurements, is fairly high in this population of female health professionals.[15] Correction for the error in these measurements[15] strengthened the associations between WHR or waist circumference and CHD. The range of WHR and waist circumference in our population may be somewhat narrower than that of the general population, since heavier women were somewhat less likely to report waist and hip circumferences. However, WHR was associated with increased risk even among heavier women.

Our results are similar to those of the few previous studies that have examined regional fat distribution and risk of CHD in women. The WHR was a stronger predictor of CHD mortality than was BMI among women aged 55 to 69 years of age in the Iowa Women's Health Study.[11] Women in the highest WHR tertile had a multivariate RR of 2.8 compared with those in the lowest tertile; WHR remained a significant predictor even after controlling for hypertension and diabetes. In a smaller population-based cohort in Sweden, women in the highest quintile of WHR had an age-adjusted RR of 8.2 for MI compared with those in the lowest WHR quintile.[10] High WHR has also been associated with increased mortality in women.[25] Several studies have observed increased risks associated with abdominal adiposity as measured by skinfold thickness ratios in women.[26-28]

In men, several studies support significant risk associated with abdominal adiposity. In the Health Professionals' Follow-up Study, men older than 65 years who were in the highest WHR quintile had a nearly 3-fold increased risk of CHD compared with those in the lowest quintile.[9] In 2 other studies, the WHR was associated with increased risk of MI[8] and cardiovascular mortality[29] in men. Additionally, abdominal adiposity as assessed by skinfold measurements was a risk factor for CHD among men in several studies.[12,30,31]

Although WHR and waist circumference are imperfect proxies for visceral adipose tissue accumulation, these measures are relatively easy to obtain and appear to impart clinically useful information regarding risk of CHD. Although WHR is somewhat more cumbersome to measure and calculate than waist circumference, in our study WHR appeared to be a slightly better measure than waist circumference of cardiac risk in multivariate models including BMI. The WHR is less strongly correlated with BMI and therefore may reflect more independent information about regional fat deposition. Waist circumference is simple to measure and has been advocated by some as a single measure to assess the need for weight loss, since it reflects both total adiposity and central fat deposition. A threshold of 80 cm (31.5 in) has been associated with a high sensitivity and specificity (>96.5%) for correctly identifying women with either a BMI higher than 25 kg/m^2 or a WHR greater than 0.80.[13] In our study, waist circumference greater than 76.2 cm (30 in) was associated with significantly increased risk of CHD.

Our data suggest that measures of abdominal adiposity are associated with risk of CHD in middle-aged women. In our cohort, both WHR and waist circumference were independently associated with risk of CHD, even after controlling for BMI. Prevention of obesity is the most effective means of reducing risk of abdominal adiposity, and interventions that effectively reduce total adiposity will also reduce WHR and waist circumference.[32,33] In addition, WHR and waist circumference may be modified by behavioral factors, such as increased physical activity,[34] smoking cessation, and changes in dietary intake. Because of the strong relationship of both central and total obesity with CHD, continued efforts at primary prevention of obesity and further research on modification of abdominal adiposity are necessary.

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