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Original Contribution

Association of Hip Circumference With Incident Diabetes and Coronary Heart Disease

The Atherosclerosis Risk in Communities Study

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When waist circumference is taken into account, larger hip circumference is associated with reduced risk factors for diabetes and cardiovascular disease. The authors investigated the prospective association of hip circumference with type 2 diabetes and coronary heart disease (CHD) incidence in a biracial cohort of men and women in 4 US communities. A total of 10,767 participants from the Atherosclerosis Risk in Communities (ARIC) study were followed from 1987 to 1998. Hip and waist circumferences and body mass index (BMI) were modeled separately and mutually in association with incident diabetes and CHD by using proportional hazards regression. After adjustment for age, race, sex, and clinical center, hip circumference was positively associated with incident diabetes. However, after further controlling for waist circumference, BMI, and confounding variables, successive quintiles of hip circumference were associated with a statistically significant reduced hazard of incident diabetes (hazard ratios = 1.00, 0.79, 0.60, 0.44, 0.41). Similarly, successive quintiles of hip circumference were associated with a statistically significant reduced hazard of CHD after controlling for waist circumference, BMI, and confounding variables (hazard ratios = 1.00, 0.92, 0.75, 0.63, 0.50). Although excess adiposity is a general risk factor for diabetes and CHD, for a given BMI and waist circumference, greater hip circumference appears to lessen the risk of diabetes and CHD.

adiposity; anthropometry; coronary disease; diabetes mellitus

Abbreviations: ARIC, Atherosclerosis Risk in Communities; BMI, body mass index; CHD, coronary heart disease.

It is well established that obesity is associated with increased prevalence of metabolic syndrome components and subsequent increased risk of type 2 diabetes and coronary heart disease (CHD) (1, 2). Excess visceral fat is important in the etiology of these chronic diseases given its association with circulating free fatty acids, insulin resistance, hyperinsulinemia, dyslipidemia, and atherosclerotic inflammatory markers (3, 4).

Waist circumference and the waist-hip ratio are widely used as indicators of abdominal adiposity in epidemiologic studies. Compared with waist-hip ratio, waist circumference has been shown to be a better marker of visceral fat (5, 6) and correlates more strongly with cardiovascular disease risk factors (7–10). Waist-hip ratio has also been shown to be a good predictor of increased risk of diabetes (11, 12) and CHD (13, 14), which may be due to attributes related to small hip relative to waist circumference. Cross-sectional and prospective studies have found that when waist circumference is taken into account, a larger hip circumference is associated with reduced risk factors for diabetes (15–22) and cardiovascular disease (16, 18, 23–27). Both fat and lean tissue from the hip and thigh may contribute, and regional differences in lipolysis may be involved in reduced disease risk associated with relatively larger hip circumference.

Few prospective studies have looked at hip circumference as an independent predictor of diabetes mellitus and CHD (17, 24, 28). These studies had small sample sizes, which

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may be prone to instability because of multicollinearity of waist and hip circumferences, and investigated primarily white populations. The present study examined prospectively the association of hip circumference with diabetes and CHD in the Atherosclerosis Risk in Communities study (ARIC). We hypothesized that after adjustment for abdominal girth and body size, larger hip circumference is associated with reduced risk of incident diabetes and CHD.

MATERIALS AND METHODS

ARIC study overview

The prospective ARIC study comprises 15,792 persons sampled from 4 US communities in 1987–1989 (29). The cohort continues to be followed for morbidity and mortality, and this paper includes follow-up through 2003. At baseline, the ARIC study population, aged 45–64 years, consisted of members of samples of households in selected Minneapolis suburbs (Minnesota), Forsyth County (North Carolina), Washington County (Maryland), and Jackson (Mississippi); the latter sample included black residents. Details of the sampling procedures have been described elsewhere (29). There were 3 follow-up examinations in 1990–1992, 1993–1995, and 1996–1998. The ARIC study was approved by institutional review boards at each clinical center.

The baseline examination ascertained prevalent cardiovascular conditions and measured risk factors (29). Standardized questionnaires were used, and participants were interviewed regarding medical history, medication use, reproductive history, parental history of disease, smoking status and amount, and alcohol consumption. Participants also underwent a digitally recorded electrocardiogram. Sitting blood pressures were measured 3 times with a random zero sphygmomanometer, and the average of the final 2 measurements was considered the blood pressure measure. Blood samples were collected for lipids, and blood glucose and fasting status of the participant was recorded. Sport physical activities were assessed with a modified version of the Baecke physical activity questionnaire (30). Usual diet was assessed with an interviewer-administered, 66-item semiquantitative food frequency questionnaire. The questionnaire was a modified version of the 62-item instrument validated by Willet et al. (31). Keys' score was computed as a prediction of serum cholesterol from reported dietary saturated and polyunsaturated fatty acids (32).

Exposure measures

During the baseline examination, anthropometrics were taken by trained technicians following a standard protocol (33). Waist circumference was measured at the level of the umbilicus, and hip circumference was measured at the maximum protrusion of the gluteal region. Waist-hip ratio and waist and hip circumference measurements had intra- and intertechnician reliability coefficients of >0.91 (33). Height was measured to the nearest centimeter by using a metal rule attached to a wall and standard triangular headboard. Weight was measured in pounds (1 pound = 0.454 kg) using a beam balance scale with participants in scrubs and no shoes. Body mass index (BMI) was calculated as weight in kilograms divided by height in squared meters.

Ascertainment of incident events

At all follow-up examinations, diabetes status was reevaluated for each participant. ARIC study participants were classified as having diabetes if they 1) had a glucose level of $\geq$126 mg/dL after fasting for at least 8 hours, 2) had a nonfasting glucose level of $\geq$200 mg/dL, 3) reported having been told by a physician that they had diabetes, or 4) reported taking medications for diabetes.

The ARIC study ascertained CHD by several methods (34, 35). Interviewers contacted participants annually by telephone to identify all hospitalizations and deaths. ARIC study staff surveyed death certificates and discharge lists from local hospitals to detect additional cardiovascular events. For hospitalized patients, trained abstractors recorded the presenting signs and symptoms, including chest pain, cardiac enzymes, and related clinical information (36). Technicians visually coded as many as three 12-lead electrocardiograms for central reading. The ARIC study investigated out-of-hospital death by means of the death certificate and, in most cases, an interview with next of kin and questionnaires completed by the patient's physicians. Coroner reports and autopsy reports, when available, were obtained for use in validation.

A CHD event was defined as a validated definite or probable hospitalized myocardial infarction, a definite CHD death, an unrecognized myocardial infarction defined by ARIC electrocardiogram readings, or coronary revascularization. All potential CHD events were reviewed and adjudicated using published criteria by an ARIC Morbidity and Mortality Classification Committee (36). Unrecognized myocardial infarction was determined by the appearance between the first and subsequent ARIC study examinations of a major Q-wave or minor Q-wave with ischemic ST-T changes or a myocardial infarction by computerized NOVACODE (36) criteria, confirmed by side-by-side visual comparison of baseline and follow-up electrocardiograms.

Statistical analysis

Participants who self-reported races other than black or white ($n = 48$) and blacks in Minneapolis and Washington County ($n = 55$) were excluded from the study population because of small numbers. Persons were excluded because of baseline diabetes ($n = 1,863$), CHD ($n = 1,119$), stroke ($n = 127$), or cancer ($n = 676$); nonfasting status at baseline ($n = 209$); missing data on waist or hip measures ($n = 11$); or missing data for other covariates of interest ($n = 665$, mostly due to excluded dietary data). The study sample for these analyses was 10,767.

SAS 9.1 (37) software was used for all descriptive and prospective analyses. Pearson correlations of baseline anthropometrics were computed. Baseline descriptive characteristics were generated as follows: for continuous variables, means and standard deviations were computed; for binary variables, percentages were computed. Quintiles of anthropometrics were calculated by using race- and sex-specific cutpoints, so that each subgroup was equally distributed across quintiles. Selected baseline characteristics were stratified by BMI-adjusted hip circumference quintiles. BMI-adjusted hip circumference was generated by linear regression adjusted for BMI.

Cox proportional hazards regression (38) was used to compute hazard ratios and 95% confidence intervals for incident diabetes and CHD in relation to quintiles of hip circumference. Incident date of diabetes was estimated by date of diagnosis or linear interpolation (39) using glucose values at the diabetes ascertainment visit and the previous visit. Person-years of follow-up were calculated from baseline to the time of diabetes diagnosis or censoring. The median follow-up for diabetes analyses was 8.8 years, with an interquartile range of 2.3 years. For CHD analyses, time to event was calculated as the time from baseline to a CHD event, death, last contact, or through December 31, 2003, whichever occurred first. The median follow-up for CHD analyses was 15 years, with an interquartile range of 1.6 years. The null hypothesis that the hazard ratio for the exposure-disease association is the same at all follow-up time points was tested by modeling an interaction between hip circumference and follow-up time. We found no evidence that the proportional hazards assumption was violated.

A series of models were compared to assess confounding. The first model was minimal and was adjusted for age, race, sex, and clinical center (model 1); additionally, we added waist circumference and BMI to model 1 separately and simultaneously. Model 2 adjusted for potential confounding variables, including education attained (greater than high school, high school or less), current smoking status at baseline (yes, no) and pack-years of cigarette smoking (quartiles), alcohol consumption (none, any), menopausal status at baseline (yes, no), hormone use (women) at baseline (current yes, no), family history of diabetes or CHD (yes, no, unknown), dietary variables (Keys' score, cereal fiber, fruit and vegetables intake in quintiles), and physical activity (Baecke sport index in quartiles). Regarding the association of hip circumference with diabetes, a supplemental model including baseline glucose (mg/dL) was examined. For the association of hip circumference with CHD, we examined a supplemental model (model 3) (with systolic blood pressure (continuous), use of antihypertensive medications (yes, no), and plasma lipids (high density lipoprotein and low density lipoprotein cholesterol as continuous variables) to investigate potential mediation by these variables. In addition to models examining the associations of hip circumference with incident diabetes and CHD, we assessed the associations with waist-hip ratio adjusted for model 2 variables. Trends in hazard ratios across quintiles of anthropometric variables, designated by their median values, were tested by a χ^2 statistic.

Modeling hip circumference and other measures of body size simultaneously may impose a high degree of multicollinearity, thereby disturbing stability of models (40). As used elsewhere (15, 41–44), tolerance of ≤ 0.10 was set as a stringent criterion for an unacceptable level of multicollinearity in statistical models.

Effect modification by race and sex was tested in models in which all race and sex groups were combined. A statistically significant interaction was observed for sex with hip circumference ($P = 0.001$) and race with hip circumference ($P < 0.0001$) in the model for incident diabetes. We chose to stratify by race and sex in separate analyses, as indicated by statistically significant interactions of hip circumference with race and sex, thus allowing a sufficiently large sample to protect against multicollinearity. There was no effect modification by race or sex in the association of hip circumference with incident CHD. We found no strong evidence for effect modification by either waist circumference or BMI in the association of hip circumference with incident diabetes or CHD.

RESULTS

Baseline age and consumption of cereal fiber, fruits, and vegetables were similar across hip circumference quintiles (Tables 1 and 2). Compared with that in the lowest quintile of hip circumference, smoking and alcohol consumption were less prevalent in higher quintiles of hip circumference. Those in the higher quintiles of hip circumference reported less physical activity and were more likely to report use of cholesterol-lowering medication or antihypertensive medication. Compared with persons in the lowest quintile of hip circumference, those in the highest quintile had lower high density lipoprotein cholesterol and higher low density lipoprotein cholesterol and systolic blood pressure. Compared with persons in the lowest quintile of hip circumference, those in the highest quintiles of hip circumference had higher BMIs and higher waist-hip ratios. For comparison, selected baseline characteristics are shown stratified by BMI-adjusted hip circumference quintile (Table 2). Those in the higher categories of hip circumference were more educated, were less likely to smoke, had lower low density lipoprotein cholesterol and higher high density lipoprotein cholesterol concentrations, and had a lower prevalence of hypertension at baseline; there were no significant differences in alcohol consumption, Keys' score, cereal fiber, physical activity, or blood glucose. Hip circumference was highly correlated with waist circumference, BMI, and body weight; poorly correlated with height; and modestly correlated with waist-hip ratio (Table 3).

Adjusted for age, race, sex, and clinical center, hip circumference was positively associated with incident diabetes over follow-up (model 1, Table 4). The addition of BMI and waist circumference to the model yielded an inverse association of hip circumference with incident diabetes. After adjustment for potential confounders (model 2), the hazard ratios of incident diabetes were slightly attenuated. In a supplemental analysis, baseline blood glucose was added to the model; compared with those for model 3, hazard ratios for hip circumference quintiles were attenuated (1.00, 0.85, 0.74, 0.59, 0.55; *P* for trend = 0.0042), and confidence intervals included the null value for all but the highest quintile (data not shown).

The association of hip circumference with incident diabetes was stronger among whites compared with blacks after controlling for waist circumference, BMI, and confounding variables (Table 5). For whites, compared with

Table 1. Descriptive Characteristics at Baseline for a Biracial Cohort of Adults According to Race- and Sex-specific Quintiles of Hip Circumference, the Atherosclerosis Risk in Communities Study, 1987–1989

Variable	Quintile of Hip Circumference				
	1	2	3	4	5
Total no. of participants	2,126	2,170	2,256	2,028	2,187
Male, %	41	48	42	43	43
Black, %	25	23	24	24	24
Hip circumference, mean (SD), cm*	92.7 (3.7)	98.8 (2.2)	102.7 (2.4)	107.6 (3.4)	118.1 (9.3)
Black women, mean (SD)	95.4 (4.3)	103.0 (1.4)	108.0 (1.3)	114.2 (2.2)	128.2 (9.3)
Black women, range	79–100	101–105	106–110	111–118	119–179
Black men, mean (SD)	91.1 (4.1)	97.6 (1.2)	101.5 (1.1)	106.0 (1.3)	115.9 (10.2)
Black men, range	59–95	96–99	100–103	104–108	109–192
White women, mean (SD)	91.7 (3.1)	97.5 (1.1)	101.9 (1.4)	107.3 (1.7)	119.0 (7.9)
White women, range	56–95	96–99	100–104	105–110	111–158
White men, mean (SD)	93.3 (3.1)	98.6 (1.1)	102.0 (0.8)	105.4 (1.1)	113.0 (6.0)
White men, range	61–96	97–100	101–103	104–107	108–165
Waist circumference, mean (SD), cm*	82.5 (7.9)	89.7 (7.6)	93.5 (8.2)	99.5 (7.9)	112.2 (11.9)
Waist-hip ratio, mean (SD)*	0.89 (0.08)	0.91 (0.07)	0.91 (0.08)	0.93 (0.07)	0.95 (0.07)
BMI, mean (SD), kg/m^2*	22.3 (2.4)	24.8 (2.3)	26.3 (2.5)	28.7 (2.8)	33.9 (5.1)
Age, mean (SD), years	53.9 (5.9)	53.8 (5.5)	53.6 (5.7)	53.6 (5.6)	53.6 (5.7)
≥High school education, %*	77	81	82	80	78
Never drinker, %*	21	23	24	25	27
Alcohol consumption, mean (SD), g/day*	7.3 (15.3)	6.8 (13.7)	6.3 (13.2)	5.5 (11.7)	5.1 (11.9)
Current smoker, %*	38	27	22	21	17
Score of <2 on the Baecke sport index, %*	38	38	36	41	47
Energy intake, mean (SD), Kcal/day	1,613 (583)	1,599 (565)	1,585 (566)	1,601 (562)	1,626 (566)
Keys' score, mean (SD)*	41.6 (9.7)	41.8 (9.2)	42.3 (9.0)	42.4 (8.9)	43.3 (9.0)
Cereal fiber, mean (SD), g/day	3.5 (2.3)	3.5 (2.2)	3.6 (2.4)	3.5 (2.4)	3.5 (2.1)
Fruit and vegetables, mean (SD), servings/day	3.9 (2.2)	4.0 (2.2)	4.0 (2.1)	4.0 (2.2)	4.0 (2.2)
Fruit, mean (SD), servings/day	1.9 (1.5)	2.0 (1.5)	2.0 (1.4)	2.0 (1.5)	2.0 (1.5)
Vegetables, mean (SD), servings/day	2.1 (1.2)	2.0 (1.2)	2.0 (1.2)	2.0 (1.2)	2.0 (1.2)
LDL cholesterol, mean (SD), mg/dL*	131 (40)	137 (39)	138 (39)	138 (38)	139 (38)
HDL cholesterol, mean (SD), mg/dL*	59 (19)	54 (18)	54 (16)	51 (16)	48 (14)
Triglycerides, mean (SD), mg/dL*	105 (53)	116 (59)	117 (58)	126 (65)	133 (63)
Blood glucose, mean (SD), mg/dL*	96 (9)	98 (9)	98 (9)	99 (9)	101 (9)
Systolic blood pressure, mean (SD), mm Hg*	124 (20)	125 (19)	125 (18)	127 (19)	132 (19)
Hypertensive at baseline, %*	18	20	22	24	31
Menopausal at baseline,[a] %	59	56	56	56	56
Use of hormone replacement therapy,[a] %*	22	24	22	19	14
Use of antihypertensive medication, %*	15	18	19	21	28
Use of cholesterol-lowering medication, %	2	2	2	2	2
Family history of diabetes, %*	20	21	22	22	26
Family history of CHD, %	38	40	39	40	38

Abbreviations: BMI, body mass index; CHD, coronary heart disease; HDL, high density lipoprotein; LDL, low density lipoprotein; SD, standard deviation.

* $P < 0.05$.

[a] Among 6,083 women in the study population.

Table 2. Descriptive Characteristics at Baseline for a Biracial Cohort of Adults According to Race- and Sex-specific Quintiles of BMI-adjusted Hip Circumference, the Atherosclerosis Risk in Communities Study, 1987–1989

Variable	Quintile of Hip Circumference				
	1	2	3	4	5
Total no. of participants	2,151	2,154	2,155	2,154	2,153
Waist circumference, mean (SD), cm*	94.8 (13.3)	93.6 (12.4)	94.6 (12.2)	95.3 (12.9)	99.3 (15.2)
Waist-hip ratio, mean (SD)*	0.95 (0.08)	0.92 (0.07)	0.92 (0.07)	0.90 (0.08)	0.89 (0.08)
BMI, mean (SD), kg/m^2*	27.9 (5.54)	26.7 (4.7)	26.8 (4.6)	26.8 (4.8)	27.9 (5.7)
Age, mean (SD), years	53.6 (5.7)	53.4 (5.8)	54.0 (5.8)	53.7 (5.6)	53.8 (5.7)
≥High school education, %*	75	78	79	82	85
Never drinker, %*	23	24	23	25	26
Alcohol consumption, mean (SD), g/day	6.0 (12.7)	6.5 (14.1)	6.4 (13.5)	6.4 (13.4)	5.9 (12.4)
Current smoker, %*	29	29	23	25	20
Keys' score, mean (SD)	42.5 (9.3)	42.4 (9.3)	42.1 (9.3)	42.4 (9.0)	42.0 (9.0)
Cereal fiber, mean (SD), g/day	3.4 (2.3)	3.5 (2.3)	3.4 (2.1)	3.5 (2.4)	2.7 (2.4)
Score of <2 on the Baecke sport index, %	42	40	38	39	41
LDL cholesterol, mean (SD), mg/dL*	141 (41)	137 (38)	136 (38)	134 (39)	134 (38)
HDL cholesterol, mean (SD), mg/dL*	51 (16)	53 (17)	53 (17)	55 (18)	55 (17)
Triglycerides, mean (SD), mg/dL*	132 (66)	121 (61)	119 (61)	114 (57)	112 (55)
Blood glucose, mean (SD), mg/dL	97 (10)	98 (9)	98 (9)	98 (9)	98 (9)
Systolic blood pressure, mean (SD), mm Hg*	128 (20)	126 (126)	126 (19)	125 (19)	126 (19)
Hypertensive at baseline, %*	29	23	22	20	21

Abbreviations: BMI, body mass index; HDL, high density lipoprotein; LDL, low density lipoprotein; SD, standard deviation.

* $P < 0.05$.

those in the lowest quintile of hip circumference, those in the highest quintile had a 60% reduced risk of incident diabetes. The association of hip circumference with incident diabetes among blacks was also inverse, but less precise. Among women, larger hip circumferences were associated with significantly reduced risk of diabetes. There was no association of hip circumference with incident diabetes in men.

When we controlled for age, race, sex, and clinical center, we found no association of hip circumference with incident CHD (model 1, Table 6). After the addition of BMI and waist circumference, we observed an inverse association of hip circumference with incident CHD, where higher quintiles were associated with reduced risk of incident CHD. Adjustment for potential confounders (model 2) moderately attenuated the association; fruit and vegetable intakes as well as smoking status and amount were significant, and addition of these variables to the model resulted in attenuation of the association of hip circumference with CHD. In a supplemental analysis (model 3) that included potential mediating variables in the causal pathway between hip circumference and incident CHD (systolic blood pressure, use of antihypertensive medications, high density lipoprotein cholesterol, and low density lipoprotein cholesterol), the association of hip circumference with incident CHD was eliminated. In a sensitivity analysis of the association of hip circumference with CHD, in which individuals with diabetes at baseline were included in the study population and baseline diabetes status was adjusted for, the hazard ratios were faintly attenuated (hazard ratios = 1.00, 0.87 (95% confidence interval: 0.71, 1.05), 0.76 (95% confidence interval: 0.61, 0.94), 0.61 (95% confidence interval: 0.48, 0.77), and 0.47 (95% confidence interval: 0.35, 0.63)) compared with the hazard ratios in the primary analysis (Table 7). The types of CHD events were as follows: validated definite or probable hospitalized myocardial infarction

Table 3. Pearson Correlation of Hip Circumference With Anthropometrics at Baseline in a Biracial Cohort of Adults, the Atherosclerosis Risk in Communities Study, 1987–1989

	Black Men	Black Women	White Men	White Women
Waist circumference	0.92	0.85	0.86	0.83
Waist-hip ratio	0.38	0.29	0.29	0.29
BMI	0.90	0.92	0.84	0.91
Body weight	0.93	0.93	0.90	0.92
Height	0.26	0.10	0.31	0.16

Abbreviation: BMI, body mass index.

Table 4. Hazard Ratios and 95% Confidence Intervals for the Association of Hip Circumference With Incident Diabetes in a Biracial Cohort of Men and Women, the Atherosclerosis Risk in Communities Study, 1987–1998

	Quintile of Anthropometric Variable[a]									
	1	2		3		4		5		*P* trend
	Referent	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	
No. of participants	2,126	2,170		2,256		2,028		2,187		
Events	103	167		214		251		437		
Person-years	15,615	16,095		16,801		14,637		14,794		
Model 1[b]										
Hip	1.00	1.59	1.25, 2.04	1.96	1.55, 2.48	2.64	2.10, 3.32	4.50	3.63, 5.57	<0.0001
Model 1 + waist										
Hip	1.00	0.92	0.71, 1.20	0.77	0.59, 1.02	0.67	0.50, 0.90	0.72	0.53, 0.98	0.037
Model 1 + BMI										
Hip	1.00	0.92	0.70, 1.20	0.80	0.61, 1.06	0.69	0.51, 0.92	0.75	0.54, 1.02	0.074
Model 1 + waist and BMI										
Hip	1.00	0.75	0.57, 0.98	0.56	0.42, 0.75	0.41	0.30, 0.56	0.37	0.27, 0.52	<0.0001
Waist	1.00	1.73	1.24, 2.42	2.56	1.81, 3.61	4.13	2.87, 5.95	5.86	3.96, 8.69	<0.0001
BMI	1.00	1.73	1.23, 2.42	2.34	1.64, 3.33	3.09	2.12, 4.50	5.01	3.34, 7.53	<0.0001
Model 2[c]										
Hip	1.00	0.79	0.60, 1.04	0.60	0.45, 0.80	0.44	0.32, 0.61	0.41	0.29, 0.58	<0.0001
Waist	1.00	1.63	1.16, 2.29	2.38	1.68, 3.38	3.72	2.57, 5.37	5.08	3.41, 7.57	<0.0001
BMI	1.00	1.77	1.25, 2.50	2.42	1.69, 3.47	3.22	2.19, 4.73	5.21	3.44, 7.89	<0.0001

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio.
[a] Quintiles of hip circumference were created by using race- and sex-specific cutpoints.
[b] Model 1 was adjusted for age, race, sex, and clinical center.
[c] Model 2 was adjusted for model 1 variables plus level of education (≤high school graduate, >high school graduate), current smoking status at baseline (yes, no) and pack-years of cigarette smoking (quartiles), alcohol consumption (none vs. any), family history of diabetes (yes, no, unknown), baseline menopausal status (yes, no) and baseline hormone use by women (current yes, no), Keys' score (quintiles), cereal fiber (grams per day in quintiles), fruit and vegetable intake (servings per day in quintiles), and physical activity (Baecke sport index score in quartiles).

(n = 39), a definite CHD death (n = 114), an unrecognized myocardial infarction defined by ARIC electrocardiogram readings (n = 80), or coronary revascularization (n = 505).

For comparison, the number of events, person-years, and hazard ratios and 95% confidence intervals for the associations of waist-hip ratio in quintiles with incident diabetes and CHD are shown in Table 7. There was a graded increased risk of incident diabetes and CHD with successively increasing quintiles of waist-hip ratio.

DISCUSSION

This prospective study of a biracial cohort demonstrated that in models not adjusted for BMI and waist circumference, hip circumference was positively associated with incident diabetes but not associated with CHD. However, after controlling for waist circumference and BMI, hip circumference was strongly and inversely associated with incident diabetes and CHD. The inverse association of adjusted hip circumference with diabetes was stronger among women compared with men and appeared somewhat stronger for whites compared with blacks.

Other evidence exists for a possible inverse association between hip circumference and risk of diabetes once overall adiposity is controlled for (15–17, 19–21). Although most studies were cross-sectional (15, 16, 19–21), they consistently found inverse associations of hip circumference with diabetes prevalence after adjusting for BMI and waist circumference. In one prospective study, when hip circumference was modeled alone, there was no significant association with diabetes for men or women; after adjustment for age, BMI, and waist circumference, greater hip circumference was associated with a reduced odds of developing diabetes (17).

In several studies, after adjustment for waist circumference and BMI, hip circumference was inversely associated with risk factors for CHD (22) and for cardiovascular disease morbidity and mortality (24, 27, 28, 41). Most of the studies that have specifically examined associations of hip circumference with risk factors for CHD events were cross-sectional (15, 16, 18, 20–23, 44). In cross-sectional studies, after control for waist circumference and BMI, larger hip circumference was associated with lower total serum cholesterol and triglycerides (22). Yusuf et al. (25), in a large case-control study, observed a strong inverse association between hip circumference and occurrence of myocardial infarction for those in the highest versus lowest quintile of hip circumference after adjusting for age, sex, smoking, BMI, and waist circumference (25). The few prospective

Table 5. Stratified Results for the Association of Hip Circumference With Incident Type 2 Diabetes Over 12 Years of Follow-up, the Atherosclerosis Risk in Communities Study, 1987–1998[a]

	Quintile of Anthropometric Variable[b]									*P* trend
	1	2		3		4		5		
	Referent	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	
Stratified by race										
Black										
No.	435	447		490		442		477		
Events	35	63		80		92		136		
Person-years	3,356	3,109		3,465		2,938		3,044		
Hip	1.00	0.93	0.57, 1.53	0.71	0.42, 1.21	0.58	0.33, 1.04	0.60	0.32, 1.12	0.22
Waist	1.00	2.03	1.15, 3.59	2.90	1.60, 5.27	5.88	3.16, 10.94	6.39	3.23, 12.64	<0.0001
BMI	1.00	1.28	0.63, 2.63	1.52	0.71, 3.25	1.82	0.82, 4.06	2.17	0.92, 5.14	0.38
White										
No.	1,526	1,622		1,665		1,481		1,574		
Events	68	104		134		159		301		
Person-years	12,259	12,986		13,337		11,698		11,750		
Hip	1.00	0.74	0.53, 1.05	0.61	0.43, 0.88	0.46	0.31, 0.68	0.40	0.26, 0.61	0.0003
Waist	1.00	1.60	1.04, 2.45	2.45	1.58, 3.81	3.50	2.19, 5.61	5.39	3.25, 8.93	<0.0001
BMI	1.00	1.77	1.18, 2.64	2.30	1.49, 3.54	2.98	1.87, 4.77	5.37	3.24, 8.91	<0.0001
Stratified by sex										
Women										
No.	1,176	1,078		1,245		1,086		1,179		
Events	61	82		109		127		233		
Person-years	9,303	8,417		9,824		8,325		8,556		
Hip	1.00	0.75	0.50, 1.11	0.42	0.27, 0.64	0.28	0.18, 0.45	0.26	0.15, 0.43	<0.0001
Waist	1.00	1.17	0.72, 1.91	1.93	1.19, 3.11	3.23	1.95, 5.35	4.81	2.76, 8.39	<0.0001
BMI	1.00	2.43	1.49, 3.97	4.06	2.43, 6.78	4.85	2.77, 8.48	9.20	4.97, 17.03	<0.0001
Men										
No.	805	991		910		837		872		
Events	42	85		105		124		204		
Person-years	6,312	7,678		6,977		6,312		6,238		
Hip	1.00	1.01	0.66, 1.55	0.96	0.60, 1.51	0.81	0.49, 1.32	0.81	0.48, 1.39	0.72
Waist	1.00	2.55	1.49, 4.36	2.99	1.66, 5.38	4.15	2.22, 7.74	5.62	2.89, 10.96	<0.0001
BMI	1.00	0.85	0.49, 1.47	1.01	0.57, 1.81	1.36	0.73, 2.52	1.88	0.97, 3.66	0.008

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio.

[a] Models were adjusted for age, race (except were stratified by race), sex (except where stratified by sex), clinical center, level of education (≤high school graduate, >high school graduate), current smoking status at baseline (yes, no) and pack-years of cigarette smoking (quartiles), alcohol consumption (none vs. any), family history of diabetes (yes, no, unknown), baseline menopausal status (yes, no) and baseline hormone use by women (current yes, no), Keys' score (quintiles), cereal fiber (grams per day in quintiles), fruit and vegetable intake (servings per day in quintiles), and physical activity (score of ≥2 or <2 on the Baecke sport index).

[b] Quintiles of hip circumference were created by using race- and sex-specific cutpoints.

studies of incident CHD had small sample sizes and/or short follow-up times (17, 24, 28). A prospective study from the DANISH MONICA project reported that larger hip circumference, adjusted for BMI and waist circumference, predicted lower incidence of cardiovascular disease over 10 years of follow-up for men and women and, for women only, lower total mortality rates over 13 years (24). The Nurses' Health Study reported a strong inverse and graded association between hip circumference and cardiovascular mortality after adjusting for waist circumference and BMI (27). The literature on this topic is consistent with our findings.

Of course, larger body fat mass, regardless of location, is a risk factor for diabetes and CHD. However, a number of studies have observed that more peripheral fat accumulation in the hips and thighs, for a given amount of abdominal fat, may be associated with a more favorable metabolic profile (44–48). Larger hips may reflect proportionally greater lean mass in addition to and/or independent of greater

Table 6. Hazard Ratios and 95% Confidence Intervals for the Association of Hip Circumference With Incident Coronary Heart Disease in a Biracial Cohort of Men and Women, the Atherosclerosis Risk in Communities Study, 1987–2003

	Quintile of Anthropometric Variable[a]									*P* trend
	1	2		3		4		5		
	Referent	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	
No. of participants	2,126	2,170		2,256		2,028		2,187		
Events	198	243		219		208		240		
Person-years	29,758	30,645		32,150		28,827		30,785		
Model 1[b]										
Hip	1.00	1.12	0.93, 1.35	1.02	0.84, 1.24	1.06	0.88, 1.29	1.18	0.98, 1.43	0.3916
Model 1 + waist										
Hip	1.00	0.91	0.74, 1.11	0.71	0.57, 0.900	0.61	0.47, 0.79	0.51	0.38, 0.69	<0.0001
Model 1 + BMI										
Hip	1.00	0.89	0.72, 1.09	0.68	0.54, 0.86	0.51	0.44, 0.74	0.48	0.36, 0.64	<0.0001
Model 1 + waist and BMI										
Hip	1.00	0.83	0.67, 1.03	0.62	0.48, 0.79	0.49	0.37, 0.64	0.37	0.26, 0.51	<0.0001
Waist	1.00	1.29	1.02, 1.64	1.36	1.05, 1.77	1.49	1.11, 2.00	1.98	1.40, 2.80	0.0039
BMI	1.00	1.14	0.89, 1.45	1.47	1.12, 1.920	1.78	1.31, 2.41	2.32	1.62, 3.32	<0.0001
Model 2[c]										
Hip	1.00	0.92	0.74, 1.14	0.75	0.59, 0.97	0.63	0.48, 0.84	0.50	0.35, 0.70	0.0002
Waist	1.00	1.21	0.95, 1.53	1.19	0.91, 1.55	1.17	0.87, 1.58	1.44	1.01, 2.05	0.2274
BMI	1.00	1.18	0.92, 1.51	1.57	1.19, 2.06	1.96	1.43, 2.67	2.61	1.81, 3.76	<0.0001
Model 3[d]										
Hip	1.00	0.94	0.75, 1.17	0.81	0.63, 1.05	0.74	0.55, 0.99	0.58	0.41, 0.82	0.0298
Waist	1.00	1.07	0.84, 1.36	1.00	0.76, 1.31	0.87	0.64, 1.19	1.07	0.75, 1.17	0.2784
BMI	1.00	0.97	0.75, 1.24	1.19	0.90, 1.57	1.41	1.02, 1.94	1.61	1.10, 2.35	0.0303

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio.
[a] Quintiles of hip circumference were created by using race- and sex-specific cutpoints.
[b] Model 1 was adjusted for age, race, sex, and clinical center.
[c] Model 2 was adjusted for model 1 variables plus waist circumference (quintiles) and BMI (quintiles).
[d] Model 3 was adjusted for model 2 variables plus level of education (≤high school graduate, >high school graduate), current smoking status at baseline (yes, no) and pack-years of cigarette smoking (quartiles), alcohol consumption (none vs. any), family history of diabetes (yes, no, unknown), baseline menopausal status (yes, no) and baseline hormone use by women (current yes, no), Keys' score (quintiles), cereal fiber (grams per day in quintiles), fruit and vegetable intake (servings per day in quintiles), and physical activity (Baecke sport index score in quartiles).

subcutaneous fat mass in the lower body (45, 49). Furthermore, muscle mass is important because of known benefits with respect to insulin resistance (44, 50, 51). The reduced risk of diabetes may be attributed to greater lean mass indicated by larger hip circumference. Alternatively, narrow hips may indicate changes in body fat distribution and sarcopenia (52, 53), particularly among older adults. The observed inverse associations of hip circumference after adjusting for waist and/or BMI with chronic disease risk underscore the clinical and public health importance of understanding the disease risk conferred by different body shapes.

Waist-hip ratio has been found to be a good predictor of diabetes (11, 12) and CHD (13, 14). Including waist-hip ratio in statistical models is not without limitations. When waist and hip measurements are combined into a waist-hip ratio, properties unique to adipose and lean compartments cannot be independently evaluated, a potentially important limitation in the literature regarding body composition/body fat distribution and diabetes and cardiovascular disease etiology. Additionally, a ratio prohibits examination of nonlinear associations between the numerator (waist) and denominator (hip).

Different fat depots have different metabolic properties. Compared with visceral fat, subcutaneous fat has low levels of basal lypolysis and lipolytic stimulation, thus potentially lowering release of free fatty acids into the bloodstream (54). By contrast, there is free fatty acid flux directly from visceral fat into hepatic circulation, a likely mechanism for increased gluconeogenesis and dyslipidemia associated with large visceral fat depots (54, 55). It remains unclear whether disease risk differs by site of subcutaneous fat accumulation. A number of studies have observed that more peripheral fat in the legs, for a given amount of abdominal fat, may be associated with a more favorable metabolic profile (44, 48, 56–58). It has been suggested that femoral-gluteal fat accumulation may play a protective role by acting as a sink for circulating free fatty acids (55). In addition,

Table 7. Hazard Ratios and 95% Confidence Intervals for the Association of Waist-Hip Ratio With Incident Diabetes and Coronary Heart Disease in a Biracial Cohort of Men and Women, the Atherosclerosis Risk in Communities Study[a]

	Quintile of Waist-Hip Ratio									*P* trend
	1	2		3		4		5		
	Referent	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	
Incident diabetes, 1987–1998										
No. of participants	2,042	2,057		2,043		2,022		2,015		
Events	63	139		213		307		450		
Person-years	16,504	16,227		15,769		15,268		14,176		
Waist-hip ratio	1.00	2.21	1.64, 2.98	3.34	2.52, 4.43	4.87	3.70, 6.40	7.65	5.85, 10.00	<0.0001
Incident coronary heart disease, 1987–2003										
No. of participants	2,145	2,169		2,156		2,142		2,155		
Events	143	185		229		254		297		
Person-years	30,874	31,026		30,505		30,129		29,631		
Waist-hip ratio	1.00	1.22	98, 1.52	1.47	1.19, 1.81	1.54	1.25, 1.90	1.73	1.41, 2.13	<0.0001

Abbreviations: CI, confidence interval; HR, hazard ratio.

[a] Adjusted for age, race, sex, clinical center, level of education (≤high school graduate, >high school graduate), current smoking status at baseline (yes, no) and pack-years of cigarette smoking (quartiles), alcohol consumption (none vs. any), family history of diabetes (yes, no, unknown), baseline menopausal status (yes, no) and baseline hormone use by women (current yes, no), Keys' score (quintiles), cereal fiber (grams per day in quintiles), fruit and vegetable intake (servings per day in quintiles), physical activity (score of ≥2 or < 2 on the Baecke sport index).

subcutaneous fat may consist of smaller adipocytes that are relatively more sensitive to insulin (59). The reduced risk of CHD associated with larger hips relative to waist may be attributed to properties of subcutaneous fat that may be beneficial, such as reduced insulin resistance and reduced free fatty acid circulation. By accounting for the effects of visceral fat by including waist circumference in models, our results may support this hypothesis.

There are possible explanations for why associations of anthropometrics with disease differ by race and sex. It has been observed that compared with whites, blacks have less visceral fat for the same BMI and waist measurements (60). These differences in visceral fat would result in differing risk profiles whereby less visceral fat would confer a reduced risk compared with greater visceral fat for a given waist measurement. Sex-related differences in our findings may be due to variation in body fat distribution and body composition between men and women. For example, for a given BMI, women are likely to have more body fat compared with men (61). In addition, it is hypothesized that compared with those in men, peripheral fat depots in women have high lipoprotein lipase activity and low rates of lipolysis (59), which in turn may reduce exposure to free fatty acids.

Strengths and limitations

The large cohort of adult men and women blacks and whites and relatively long follow-up time are major strengths. Careful assessment of diabetes and CHD outcomes as well as standardized data collection methods for covariates are assets of the study. In particular, anthropometric variables collected by using direct measurement by trained staff rather than self-report is a strength.

This study is not without limitations. The ARIC cohort was selected from 4 US communities but is not representative of the US population in general; whites were recruited from 3 different regions (North Carolina, Minnesota, and Maryland) of the United States and blacks from 2 regions (North Carolina and Mississippi); thus, ethnicity and geographic area were confounded by sampling. Body fat distribution was measured only anthropometrically and there was no direct measure of visceral fat, nor were there direct measures of lean mass. Nevertheless, this study appears to be one of the largest examining the association of hip circumference with metabolic disease prospectively in a biracial cohort.

Conclusions

After adjustment for BMI and waist circumference, hip circumference was inversely associated with the incidence of diabetes and CHD. Without these adjustments, there was a positive association between hip circumference and diabetes and no association between hip circumference and CHD. More studies of adipose tissue are needed to expand our understanding of the metabolism and function of adipocytes located at different sites of the body. It is important to know how having relatively more fat and/or muscle mass deposited in the femoral-gluteal area could decrease risk of diabetes and CHD. Further etiology of differences in body shapes needs to be better elucidated and the influences of body shape on other chronic diseases evaluated. In addition, to better understand race and sex differences in the associations of hip circumference with incident diabetes and CHD, future research should investigate large and more diverse samples of multiethnic populations of men and women.

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