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Anthropometric assessment of abdominal obesity and coronary heart disease risk in men: the PRIME study

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ABSTRACT

Objective: Waist-to-height ratio is an anthropometric indicator of abdominal obesity that accounts for stature. Earlier studies have reported marked associations between the waist-to-height ratio and cardiovascular risk factors. The goal of this study was to compare the associations of waist-to-height ratio, waist girth, waist-to-hip ratio or body mass index (BMI) with incidence of coronary events.

Design: Prospective study with 10 602 men, aged 50–59 years, recruited between 1991 and 1993 in three centres in France and one centre in Northern Ireland. Clinical and biological data were obtained at interview by trained staff. During the 10 years of follow-up 659 incident coronary events (CHD) were recorded. The relations between anthropometric markers and coronary events were estimated by Cox proportional hazards models.

Results: Waist circumference, waist-to-hip ratio, waist-to-height ratios and BMI were positively associated with blood pressure ($p<0.0001$), diabetes ($p<0.0001$), low-density lipoprotein (LDL)-cholesterol ($p<0.0001$), triglycerides ($p<0.0001$) and inversely correlated to high-density lipoprotein (HDL)-cholesterol ($p<0.0001$). There was a linear association between waist circumference, waist-to-hip ratio, waist-to-height ratio, BMI and CHD events. The age-adjusted and centre-adjusted relative risks (95% CI) for CHD were 1.57 (1.22 to 2.01), 1.75 (1.34 to 2.87), 2.3 (1.79 to 2.99) and 1.99 (1.54 to 2.56) in the 5th quintile vs the first quintile of waist circumference, waist-to-hip ratio, waist-to-height ratio and BMI distribution, respectively. After further adjustment for school duration, physical activity, tobacco and alcohol consumption, hypertension, diabetes, HDL-cholesterol and triglycerides, the relative risks for CHD were 0.99 (0.76 to 1.30) for waist circumference (p = 0.5), 1.22 (0.93 to 1.60) for waist-to-hip ratio (p = 0.1), 1.53 (1.16 to 2.01) for waist-to-height ratio (p = 0.03) and 1.30 (0.99 to 1.71) for BMI (p = 0.06).

Conclusion: In middle-aged European men, waist-to-height ratio identifies coronary risk more strongly than waist circumference, waist-to-hip ratio or BMI, though the difference is marginal.

Abdominal obesity is a risk factor of cardiovascular disease. Accumulation of visceral adipose tissue, which promotes insulin resistance, dyslipidaemia and hypertension, plays a major part in this process.[1] Computed tomography or magnetic resonance imaging is used to assess visceral adipose tissue depots.[2] However, owing to their cost, the need of radiological equipment and exposure to ionising radiation, the use of these methods is limited in clinical practice and epidemiological studies.

Anthropometric assessments of abdominal obesity are simple and inexpensive to obtain. Waist circumference is a common proxy measure of visceral adipose tissue that is highly correlated to radiological measurements.[3–6] Numerous studies have shown that waist circumference is strongly associated with cardiovascular risk factors and with the occurrence of coronary heart disease (CHD).[7–11] Waist circumference measurement is easy to use in daily clinical practice and thus has spread worldwide in recommendations for cardiovascular risk assessment.

Other indicators of visceral adipose tissue have been proposed for assessing the health consequences of abdominal obesity.[12] In a radiological study, the visceral fat was better correlated to waist-to-height ratio than waist circumference.[13] In a meta-analysis of published studies the waist-to-height ratio was better correlated to cardiovascular risk factors (hypertension, diabetes mellitus and dyslipidaemia) than other usual anthropometric indicators of visceral adiposity—that is, waist circumference and waist-to-hip ratio.[14] Altogether these observations provide support for the hypothesis that waist-to-height ratio is possibly a better marker of coronary risk than usual anthropometric markers of visceral adiposity. Therefore, the goal of the present study was to compare the association between waist-to-height ratio, waist circumference and waist-to-hip ratio and coronary risk. To this end, we assessed the relation between different markers of body adiposity and the occurrence of coronary events in a prospective study of heart disease.

METHODS

Population study

We analysed data from the Prospective Epidemiological Study of Myocardial Infarction (PRIME) cohort, whose recruitment, examination methods and diagnostic procedures for CHD cases at entry and during follow-up have been described previously.[15][16] Briefly, 10 602 men aged 50–59 were recruited in four centres in Belfast (Northern Ireland), Lille, Strasbourg and Toulouse (France) between 1991 and 1993. The sample was recruited in factories and in various working organisations, in occupational medicine, health-screening centres and general practice. Subjects were informed of the aim of the study and agreed to an annual follow-up.

Approval from the appropriate local ethics committee was obtained in each study centre.

Baseline measurements

Subjects who agreed to take part in the study were given a morning appointment and asked to fast for at least 12 hours. A full description of clinical[15 16] and laboratory[17] measurements has been published elsewhere. Briefly, after completing a self-administered health questionnaire at home, trained interviewers checked at the clinic a broad range of clinical information. Each subject completed self-administered questionnaires on demographic, socioeconomic factors, dietary habits and physical activity, which was then checked by specially trained medical staff. Additional questionnaires on family and personal clinical history, tobacco consumption and drug intake were administered at the clinic. Baseline investigations included a 12-lead electrocardiogram, standardised blood pressure measurements using an automatic sphygmomanometer. The anthropometric measurements included height (to the nearest cm), waist and hip circumferences (to the nearest 0.5 cm), body weight (to the nearest 200 g) with subjects in light clothing without shoes. Body mass index (BMI) was calculated by dividing weight by height[2]. Plasma lipid analyses included total cholesterol, triglycerides and high-density lipoprotein (HDL) cholesterol measurements were centralised (Serlia INSERM U325, Institut Pasteur de Lille, France). Low-density lipoprotein (LDL) cholesterol was calculating according to the Friedewald formula.

The waist-to-height ratio was computed as waist (cm) divided by height (cm). Subjects were classified into three categories for physical activity: regular physical activity (if they took intense physical activity more than 20 minutes, once a week or more); moderate physical activity (light physical activity with no increased heart rates most weeks); and no physical activity. Tobacco consumption was categorised as: no smokers, ex-smokers and current smokers if individuals currently smoking at least one cigarette per day. Alcohol consumption, expressed in millilitres of pure ethanol/day, was defined by three categories (0 ml/J; <40 ml/J or ≥40 ml/J). Hypertension was defined by systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg and/or current blood pressure-lowering treatment. Self-reported diabetes and current blood glucose-lowering therapy defined diabetes mellitus by dietary or pharmacological means. At inclusion, subjects were considered as having a history of coronary disease at entry if they had any one of: (1) myocardial infarction and/or angina pectoris diagnosed by a physician; (2) electrocardiographic evidence of myocardial infarction, defined as major or moderate Q waves coded using the Minnesota system; (3) a positive chest pain questionnaire.

Follow-up and ascertainment of cases

During the 10 years of follow-up, subjects were contacted annually by letter and asked to complete a clinical event questionnaire to be returned to the centre in a pre-paid envelope. A medical committee, comprising one member of each PRIME centre and three independent cardiologists was established in order to provide an independent validation of coronary events. All medical information related to any available event was examined and the committee decided a code for each, according to the protocol. Myocardial infarction (MI) was defined by one of the following sets of conditions: (1) new diagnostic Q wave or new other typical aspect of necrosis on electrocardiographs; (2) typical or atypical pain symptoms and new (or increased) ischaemia on electrocardiographs and a myocardial enzyme level higher than twice the upper limit; or (3) postmortem evidence of fresh MI or thrombosis. Angina pectoris was defined by the presence of chest pain at rest and/or on exertion and at least one of the following criteria: (1) angiographic stenosis over 50%; or (2) a positive scintigraphy (if no angiographic data); or (3) positive exercise stress test (if no angiographic or scintigraphic data were available); or (4) electrocardiographic changes at rest, (if no angiographic, scintigraphic or exercise stress data were available), but without any set of conditions for MI and no evidence of a non-coronary cause in the clinical history. Unstable angina was defined as a crescendo pain or chest pain at rest with either enzyme changes or electrical changes. In the absence of enzyme or electrical data, the diagnosis was not upheld. Coronary deaths were defined from death certification with supporting clinical or pathological information whenever possible. The total coronary heart disease outcome was a composite variable, defined by incident coronary death, non-fatal MI, angina pectoris and unstable angina.

Statistical analysis

All analyses were conducted using SAS v8.9, and statistical significance was assessed for $p<0.05$. Of the initial 10 602 subjects, 19 were excluded for missing anthropometric data and 823 for prevalent CHD, giving 9760 subjects for analyses. During 90 850 person-years of follow-up, 659 incident coronary events were documented. For the sake of presentation, subjects were categorised by quintiles of waist circumference, waist-to-hip ratio and waist-to-height ratio. Baseline characteristics were compared using ANOVA for the quantitative variables and χ^2 tests for the qualitative ones. Pearson correlation was used for correlation analyses of anthropometric variables. A Cox proportional hazards model was employed to compute the relative risks (RRs) of total coronary events associated with waist circumference, waist-to-hip ratio, waist-to-height ratio and BMI and their 95% confidence intervals (CIs) and to adjust for various confounding factors. The lowest quintile was used as the reference group. In a first model, the risks were adjusted for age at entry and centre. Adjustment variables were included in the second model: age, centre, school duration, physical activity, tobacco and alcohol consumption, hypertension, diabetes, HDL-cholesterol and triglycerides. To test for linear trend across the quintiles of anthropometric measurements, the quintiles (four dummy variables) of waist circumference, waist-to-hip ratio and waist-to-height ratio were replaced in the model by a linear term and the likelihood ratio test statistic thus obtained was compared to χ^2 distribution with 3 degrees of freedom. In order to compare the magnitude of risk estimates, we also calculated relative risks for every SD change in waist circumference, waist-to-hip ratio and waist-to-height ratio and compared the global fitness of the models by minimisation of the Bayes Information Criterion (BIC).

RESULTS

Table 1 presents the subjects' characteristics by quintile of waist-to-height ratio distribution. Mean age, as well as the proportion of former smokers, of alcohol consumers and of physically inactive subjects increased across quintiles. In contrast, educational level decreased across the same quintiles. The cardiovascular risk factors—that is, history of diabetes, systolic and diastolic blood pressure, LDL-cholesterol, triglycerides and HDL-cholesterol—worsened with increasing quintiles

Table 1 Baseline characteristics of the subjects according to quintiles of waist-to-height ratio

	Quintiles of waist-to-height ratio (WHtR)					p Value*
	<0.51	⩽0.51–<0.54	⩽0.54–<0.56	⩽0.56–<0.60	⩽0.60	
Number of subjects	2011	1889	1958	1952	1950	
Age (years)	54.3 (2.8)	54.7 (2.8)	54.8 (2.9)	55.1 (2.9)	55.4 (2.9)	<0.0001
Weight (kg)	70.4 (8.8)	75.4 (8.1)	78.5 (8.6)	82.0 (8.7)	90.4 (11.7)	<0.0001
WC (cm)	82 (5)	90 (3)	94 (4)	99 (4)	108 (7)	<0.0001
Height (cm)	175 (7)	173 (6)	173 (6)	172 (6)	171 (6)	<0.0001
BMI (kg/m²)	23.0 (2.0)	25.0 (1.7)	26.2 (1.7)	27.7 (1.8)	31.0 (3.1)	<0.0001
School duration (years)	12.2 (3.7)	11.8 (3.4)	11.5 (3.5)	11.0 (3.2)	10.4 (3.3)	<0.0001
Tobacco (n) (%)						<0.0001
Never smokers	683 (34)	579 (31)	577 (29)	555 (28)	488 (25)	
Ex-smokers	663 (33)	768 (41)	876 (44)	915 (47)	975 (50)	
Current Smokers	665 (33)	542 (29)	518 (26)	482 (25)	487 (25)	
Alcohol intake (n) (%)						<0.0001
Abstinent	474 (24)	361 (19)	304 (16)	262 (13)	241 (12)	
<40 ml/day	907 (45)	906 (48)	889 (45)	835 (43)	802 (41)	
⩾40 ml/day	630 (31)	622 (33)	765 (39)	855 (44)	907 (46)	
Physical activity (n (%)						<0.0001
No activity	219 (11)	216 (11)	234 (12)	255 (13)	383 (20)	
Moderate activity	1196 (59)	1091 (58)	1153 (59)	1182 (61)	1141 (58)	
Regular activity	596 (29)	579 (31)	570 (29)	514 (26)	425 (22)	
Diabetics (n (%)	39 (1.9)	39 (2.1)	53 (2.7)	80 (4.1)	113 (5.8)	<0.0001
Systolic BP (mm Hg)	126 (17)	131 (18)	133 (18)	136 (18)	142 (19)	<0.0001
Diastolic BP (mm Hg)	79 (11)	82 (10)	83 (11)	86 (11)	89 (12)	<0.0001
LDL-C (g/l)	1.40 (0.34)	1.46 (0.34)	1.45 (0.33)	1.46 (0.33)	1.44 (0.35)	<0.0001
HDL-C (g/l)	0.53 (0.14)	0.49 (0.13)	0.49 (0.13)	0.47 (0.12)	0.46 (0.12)	<0.0001
Triglycerides (g/l)	1.22 (0.74)	1.35 (0.78)	1.45 (0.90)	1.59 (1.16)	1.80 (1.23)	<0.0001

Values are means (SD) for continuous variables and number of subjects (%) for categorical variables.
*ANOVA or χ^2.
BMI, body mass; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; WC, waist circumference.

of the anthropometric variables' distribution. Similar associations were found for waist, waist-to-hip ratio and BMI. Waist-to-height ratio was strongly positively correlated with waist circumference and BMI, and to a lesser extent with waist-to-hip ratio (table 2).

Figure 1A shows the relative risks (RRs) (95% CI) of coronary events by quintile of waist circumference, waist-to-hip ratio and waist-to-height ratio. Compared to the first quintile of distribution, the age-adjusted and centre-adjusted RR for coronary events increased until 1.57 (1.22 to 2.01) in the fifth quintile of waist circumference, 1.75 (1.34 to 2.27) in the fifth quintile of waist-to-hip ratio, 2.31 (1.79 to 2.99) in the fifth quintile of waist-to-height ratio and 1.99 (1.54 to 2.56) in the fifth quintile of BMI distribution. Further adjustment for school duration, physical activity, tobacco and alcohol consumption, hypertension, diabetes, HDL-cholesterol and triglycerides attenuated the association (fig 1B). The latter was no longer statistically significant in the fifth quintile of waist circumference distribution 0.99 (0.76 to 1.30) (p = 0.50), waist-to-hip ratio distribution 1.22 (0.93 to 1.60) (p = 0.10) and BMI 1.30 (0.99 to 1.71) (p = 0.06), but remained statistically significant for in the fifth quintile of waist-to-height ratio distribution 1.53

(1.16 to 2.01) (p = 0.03). There was no evidence of departure from linearity.

In order to compare the strengths of the association of waist circumference, waist-to-hip ratio and waist-to-height ratio with coronary events, we calculated the RRs (95% CI) of coronary events for 1 SD increase of the anthropometric indicators. The global goodness-of-fit of the models was assessed using the BIC (table 3). The age-adjusted and centre-adjusted RR for coronary events was higher for waist-to-height ratio 1.28 (1.19 to 1.38) than for waist circumference 1.20 (1.11 to 1.30), waist-to-hip ratio 1.21 (1.12 to 1.31) and BMI 1.26 (1.17 to 1.35). The corresponding BIC values were lower for waist-to-height ratio and BMI than for waist circumference and waist-to-hip ratio. After further adjustment for confounders and cardiovascular risk factors (model 2), the RR was attenuated for waist-to-height ratio 1.11 (1.02 to 1.20) and was no longer statistically significant for waist circumference 1.03 (0.94 to 1.12) and waist-to-hip ratio 1.08 (0.99 to 1.18). The BIC was lower for the waist-to-height ratio model than for one that included waist circumference or BMI, and very slightly lower than that for waist-to-hip ratio.

DISCUSSION
Anthropometric indicators of visceral fat are useful tools for clinicians to identify patients at risk for coronary events. The results of the present study showed that waist-to-height ratio was positively associated with coronary risk and that this association was slightly more pronounced than waist circumference and waist-to-hip ratio. Adjustment for cardiovascular risk factors attenuated the relative risk associated with increased waist-to-height ratio to a lesser extent than the risk associated with increased waist, waist-to-hip ratio and BMI. These results

Table 2 Correlation matrix of anthropometric measures

	WC	WHR	BMI
WHtR	0.94	*0.68*	0.85
WC		0.66	0.84
WHR			0.50

All correlation at p<0.0001.
BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio.
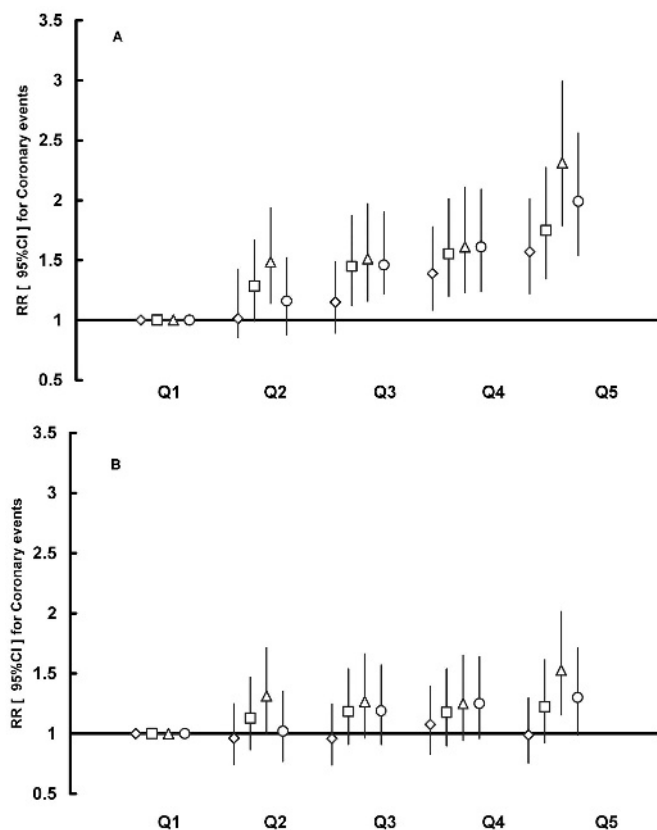
Figure 1 Relative risk (RR) (95% CI) for coronary heart disease events by quintiles of waist (diamonds), waist-to-hip ratio (squares), waist-to-height ratio (triangles) and body mass index (circles) by quintile (Q) of anthropometric indicator distribution. (A) Age-adjusted and centre-adjusted relative risks. (B) Age, centre, school duration, physical activity, tobacco and alcohol consumption, hypertension, diabetes, HDL-cholesterol and triglycerides adjusted relative risks.

suggest that waist-to-height ratio is a better indicator of coronary heart disease risk than waist circumference, waist-to-hip ratio and BMI. However, the magnitude of the differences between waist-to-height ratio and the other anthropometric measurements was small, probably not clinically important and, thus, given the ease of measurement, the standard indicators of adiposity remain the most useful measures for clinical practice.

In agreement with our own results, Gelber et al[18] showed, in American health professionals, that waist-to-height ratio presented the best model fit and the strongest association with incident cardiovascular disease including non-fatal myocardial infarction, non-fatal ischaemic stroke and cardiovascular death.

In a cohort of Chinese women Zhang et al[19] showed a similar threefold increase in myocardial infarction risk in the third tertile of waist-to-height ratio and waist circumference distributions. In the INTERHEART study, the odds ratios for myocardial infarction adjusted for age, gender and geographical area were also similar for waist-to-height ratio and waist circumference.[11] One might presume that differences in the definition of events, in study design (survivors vs incident events) or the subject's characteristics may explain most of contrasting findings in this area.

Although waist circumference, waist-to-hip ratio, waist-to-height ratio and BMI were associated with coronary risk, the association remained statistically significant for waist-to-height ratio after adjustment for history of diabetes, systolic and diastolic blood pressure, triglycerides and HDL-cholesterol, whereas it was no longer significant for waist-to-hip ratio, waist circumference and BMI. This suggests that the latter variables explain a large part of coronary risk related to excess visceral adipose tissue. Earlier studies have reported an independent association; however, most of them did not attempt to adjust for variables such as triglycerides and HDL-cholesterol, which might explain the differences with the present study.

Several hypotheses might explain the superiority of waist-to-height ratio in predicting coronary risk. First, waist-to-height ratio might be a better indicator of visceral adipose tissue than waist circumference. This hypothesis is supported by at least one radiological study of a small number of men and women, which showed better correlations between CT assessed visceral adipose tissue and waist-to-height ratio than with waist circumference.[13] However, these findings were not confirmed in other investigations,[20] suggesting that additional studies are necessary to assess the predictive value of waist-to-height ratio for visceral adipose tissue. Furthermore, in men, waist circumference and waist-to-height ratio agreed similarly with total body fat,[21] suggesting a similar relation with risk. Second, waist-to-height ratio was inversely correlated with height, although weakly ($r = -0.22$), and height was associated with a lower risk for CHD. A residual effect of height could possibly confound the relation between waist-to-height ratio and CHD risk.

The present study has several strengths and limitations. The follow-up rate was very satisfactory with less than a 5% loss. Anthropometric indices were measured following standard protocols, by trained examiners and standardised instruments. However, since waist circumference was not recorded during follow-up it was impractical to assess the possible influence of body weight or body fat distribution changes that might have occurred during follow-up. Furthermore, the study was conducted in white men only, aged 50–59 years. Owing to the morphological differences in fat distribution between men and

Table 3 Relative risks (RR) and 95% confidence intervals (CI) (p value) of total coronary events per 1 SD increase in waist circumference, waist-to-hip ratio and waist-to-height ratio

	Model 1 (n = 9760)			Model 2 (n = 9678)		
	RR*	95% CI (p value)	BIC	RR*	95% CI (p value)	BIC
WC	1.20	1.11 to 1.30 (<0.0001)	11955	1.03	0.94 to 1.12 (0.50)	11584
WHR	1.21	1.12 to 1.31 (<0.0001)	11954	1.08	0.99 to 1.18 (0.10)	11581
WHtR	1.28	1.19 to 1.38 (<0.0001)	11936	1.11	1.02 to 1.20 (0.03)	11579
BMI	1.26	1.17 to 1.35 (<0.0001)	11938	1.09	1.01 to 1.18 (0.61)	11585

Model 1: adjusted for age at entry and centre; model 2: adjusted for age, centre, school duration, physical activity, tobacco and alcohol consumption, hypertension, diabetes, HDL-C and triglycerides.
SD for WC = 9.92 cm; WHR = 0.061; WhtR = 0.058; BMI = 3.44 kg/m².
BIC, Bayes Information Criterion; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio.

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women and subjects from different ethnic backgrounds,[22] extrapolation of the results to other populations would be unwise. Participation in the study was voluntary and a "healthy worker effect" cannot be excluded. The study design allowed for many statistical adjustments but residual confounding due to unmeasured factors or measurement errors cannot be ruled out. Finally, although there were 659 well-defined CHD incident events this might still be insufficient to detect subtle relations between visceral adipose tissue and CHD risk or to assess the added value of anthropometric indicators of visceral adiposity when compared to BMI. Furthermore, because there is so much co-linearity among the anthropometric variables and BMI it was not possible to obtain reliable risk estimates combining visceral adiposity markers and BMI in the same model.

In conclusion, waist circumference, waist-to-hip ratio and waist-to-height ratio are anthropometric indicators of visceral adipose tissue that are associated with coronary events. From a risk assessment perspective, the waist-to-height ratio is a marginally better discriminator of coronary risk than waist circumference, waist-to-hip ratio and BMI. However, the magnitude of the differences is probably not clinically important, and thus the standard indicators of adiposity remain the most useful measures for clinical practice. The distribution of waist-to-height ratio values of the American population has been recently reported[21] and compared to those of body fat. These values may assist in refining the proportion of subjects at increased risk of coronary heart disease owing to excess visceral adiposity.

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