

Does Waist Circumference Predict Diabetes and Cardiovascular Disease Beyond Commonly Evaluated Cardiometabolic Risk Factors?

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OBJECTIVE — While the measurement of waist circumference (WC) is recommended in current clinical guidelines, its clinical utility was questioned in a recent consensus statement. In response, we sought to determine whether WC predicts diabetes and cardiovascular disease (CVD) beyond that explained by BMI and commonly obtained cardiometabolic risk factors including blood pressure, lipoproteins, and glucose.

RESEARCH DESIGN AND METHODS — Subjects consisted of 5,882 adults from the 1999–2004 National Health and Nutrition Examination Survey, which is nationally representative and cross-sectional. Subjects were grouped into sex-specific WC and BMI tertiles. Blood pressure, triglycerides, LDL and HDL cholesterol, and glucose were categorized using standard clinical thresholds. Logistic regression analyses were used to calculate the odds for diabetes and CVD according to WC tertiles.

RESULTS — After controlling for basic confounders, the medium and high WC tertiles were more likely to have diabetes and CVD compared with the low WC tertile ($P < 0.05$). After inclusion of BMI and cardiometabolic risk factors in the regression models, the magnitude of the odds ratios were attenuated (i.e., for diabetes the magnitude decreased from 6.54 to 5.03 for the high WC group) but remained significant in the medium and high WC tertiles for the prediction of diabetes, though not for CVD.

CONCLUSIONS — WC predicted diabetes, but not CVD, beyond that explained by traditional cardiometabolic risk factors and BMI. The findings lend critical support for the recommendation that WC be a routine measure for identification of the high-risk, abdominally obese patient.

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It is established that waist circumference (WC) predicts increased risk of morbidity (1–4) and mortality (5) beyond that explained by BMI alone. Several organizations, including the National Institutes of Health (6), currently advocate for the measurement of WC in clinical

practice. However, a recent consensus statement from the American Diabetes Association (ADA), the Obesity Society, and the American Society for Nutrition questioned the clinical utility of WC measurement (7). Opposition to the inclusion of WC measurement in clinical practice is

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Abbreviations: ADA, American Diabetes Association; CVD, cardiovascular disease; NHANES, National Health and Nutrition Examination Survey; WC, waist circumference.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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hinged on the observation that it is unclear whether WC predicts health risk beyond that explained by BMI and commonly evaluated cardiometabolic risk factors (7). It is reasoned that clinicians would be unnecessarily burdened by the measurement of WC if this measure failed to explain health risk beyond the risk factors routinely obtained in clinical practice.

Limited evidence suggests that WC predicts risk of cardiovascular disease (CVD) after control for hypertension (1,2), hypercholesterolemia (2), and the apolipoprotein B-to-A ratio (1). Absent from the literature is a clear demonstration that WC predicts the risk of diabetes and CVD in men and women beyond that explained by the commonly evaluated cardiometabolic risk factors (blood pressure, triglyceride, LDL and HDL cholesterol, and glucose levels) and BMI. We addressed this issue using data from the most recent National Health and Nutrition Survey (NHANES).

RESEARCH DESIGN AND METHODS

The study sample was obtained from the 1999–2000, 2001–2002, and 2003–2004 NHANES. NHANES was designed to be a nationally representative cross-sectional survey, which allows for two or three survey rounds to be combined, as done here. NHANES was conducted by the U.S. National Center for Health Statistics to estimate the prevalence of major diseases, nutritional disorders, and risk factors for these diseases. The sampling plan used a stratified, multistage, probability cluster design. Full details of the study design and procedures are available elsewhere (8). Informed consent was obtained from all participants and the protocol approved by the National Center for Health Statistics.

Participants who were aged <18 years, pregnant women, or missing waist circumference, BMI, outcome measures, or covariates required for the analyses were excluded from this study. This left a

total of 5,882 subjects (3,001 men and 2,881 women).

Measurement and classification of anthropometric variables

WC was measured during minimal respiration to the nearest 0.1 cm at the level of the iliac crest (8). Height was measured to the nearest 0.1 cm and body mass to the nearest 0.1 kg (8). BMI was calculated as weight in kilograms divided by the square of height in meters. Subjects were divided into sex-specific tertiles for WC and BMI. We divided the subjects into WC and BMI tertiles instead of using commonly employed clinical thresholds to match the groups for size both within (i.e., three equally sized WC groups) and across (i.e., with high WC group the same size as high BMI group) anthropometric measures. In men, WC tertiles were defined by the following thresholds: <90.9, 90.9–102.9, and >102.9 cm. The corresponding values in women were <85.5, 85.5–98.7, and >98.7 cm. In men, BMI tertiles were defined by the following thresholds: <24.8, 24.8–28.8, and >28.8 kg/m². The corresponding values in women were <24.6, 24.6–29.9, and >29.9 kg/m².

Measurement and classification of cardiometabolic risk factors

Blood pressure. Three blood pressure measurements were obtained with the subject in a seated position using a standard manual mercury sphygmomanometer (8). The average of the three readings was utilized. Blood pressure was classified according to established guidelines (9): normal (systolic <120 and diastolic <80 mmHg), prehypertension (systolic 120–139 or diastolic 80–89 mmHg), or hypertension (systolic ≥140 or diastolic ≥90 mmHg). When systolic and diastolic blood pressures fell into different categories, the higher category was selected for classification. Participants who reported taking blood pressure medication were considered to have hypertension regardless of their blood pressure measurements.

Lipids and lipoproteins. Blood samples were obtained after an overnight fast for the measurement of serum LDL cholesterol, HDL cholesterol, triglycerides, and glucose as described in detail elsewhere (8,10). Briefly, cholesterol and triglyceride levels were measured enzymatically in a series of coupled reactions hydrolyzing cholesterol ester and triglyceride to cholesterol and glycerol, respectively. LDL cholesterol, HDL cholesterol, and triglyceride levels were classified according to

Table 1—Descriptive characteristics of study participants

Variable	Total	Men	Women
n	5,882	3,001	2,881
Age (years)	44.2 ± 0.5	43.3 ± 0.5	45.1 ± 0.5
Waist circumference (cm)	95.3 ± 0.4	98.5 ± 0.4	92.1 ± 0.5
BMI (kg/m ²)	27.7 ± 0.1	27.6 ± 0.1	27.8 ± 0.2
Impaired fasting glucose	24.6 (1.1)	30.3 (1.4)	19.0 (1.1)
Diabetes	8.1 (0.5)	9.2 (0.7)	7.1 (0.5)
Cardiovascular disease	7.0 (0.5)	8.0 (0.7)	6.0 (0.6)
Hypertension	27.3 (0.9)	26.6 (1.2)	28.1 (1.0)
High LDL cholesterol	21.6 (0.8)	22.8 (0.9)	20.4 (0.1)
Low HDL cholesterol	19.9 (0.8)	27.8 (1.0)	12.0 (0.9)
High triglycerides	14.7 (0.6)	17.0 (1.0)	12.4 (0.6)

Data are means ± SE for continuous variables or prevalence [SE] (%) for dichotomous variables.

the National Cholesterol Education Program guidelines (11). LDL cholesterol was categorized as optimal (<100 mg/dl), near optimal (100–129 mg/dl), borderline high (130–159 mg/dl), or high (≥160 mg/dl). Participants who reported taking a cholesterol-lowering medication were placed into the high LDL cholesterol category regardless of their LDL cholesterol level. HDL cholesterol was categorized as low (<40 mg/dl), normal (40–59 mg/dl), or high (≥60 mg/dl). Triglycerides were categorized as normal (<150 mg/dl), borderline high (150–199 mg/dl), or high (≥200 mg/dl).

Glucose and diabetes. Fasting plasma glucose samples were assayed using a hexokinase enzymatic method (8,12). Subjects were classified as having normal glucose (<100 mg/dl), impaired fasting glucose (100–125 mg/dl), or diabetes (≥126 mg/dl) in accordance with ADA guidelines (13). All participants with physician-diagnosed diabetes (outside of pregnancy) were coded positive for diabetes, as were those who reported using insulin or blood glucose-lowering medications.

CVD. Participants who reported that a physician had ever told them they had a heart attack, stroke, angina, congestive heart failure, or coronary heart disease were coded positive for CVD. All other participants were coded negative for CVD.

Confounding variables

Confounding variables included age, race/ethnicity, sex, and smoking status. Age was included in the analysis as a continuous variable. Race was categorized as non-Hispanic white, non-Hispanic black, Hispanic, and other. Subjects were considered current smokers if they smoked cigarettes at the time of the interview, previous smokers if they were not current

smokers but had smoked 100 cigarettes in their entire life, and nonsmokers if they smoked less than this amount.

Statistical analysis

The Intercooled Stata program (version 7; Stata, College Station, TX) was used to properly weight the sample to be representative of the U.S. population and to take into account the complex sampling strategy of the NHANES design. Initially, logistic regression tests were used to examine associations among WC or BMI categories, CVD, and diabetes. Three models were run for each disease outcome. The first model controlled for the basic confounding variables (age, sex, race, and smoking). The second model controlled for the basic confounding variables and the risk factor categories for the cardiometabolic variables (glucose categories were not controlled for in the diabetes analysis). The third model controlled for the basic confounding variables, the cardiometabolic risk factor categories, and BMI (or WC) categories. Next, subjects were cross-classified according to WC (low, moderate, or high) and the number of metabolic risk factors (0, 1, 2, or ≥3), creating 12 different categories. Odds ratios (ORs) for CVD and diabetes were then computed for these 12 groups. *P* for trend values were calculated to determine whether the WC and metabolic risk factor groups had independent effects on CVD and diabetes.

To further explore the added value of WC, we determined the discriminatory ability of the diabetes and CVD models (e.g., ability to correctly separate those who did and did not have disease) using the *c* statistic. For each disease outcome, the *c* statistic was calculated for three separate models that included the following

Table 2—ORs for diabetes and CVD according to WC

Covariates included in regression model	Waist circumference tertile		
	Low	Medium	High
Diabetes			
Age, sex, race, and smoking	1.00	2.44 (1.53–3.89)*	6.54 (4.43–9.67)*
Age, sex, race, smoking, and metabolic risk factors†	1.00	1.98 (1.26–3.11)*	4.62 (3.16–6.75)*
Age, sex, race, smoking, metabolic risk factors, and BMI‡	1.00	2.32 (1.30–4.12)*	5.03 (2.87–8.83)*
Cardiovascular disease			
Age, sex, race, and smoking	1.00	1.41 (1.01–1.98)*	1.73 (1.22–2.44)*
Age, sex, race, smoking, and metabolic risk factors‡	1.00	1.14 (0.79–1.64)	1.16 (0.79–1.70)
Age, sex, race, smoking, metabolic risk factors, and BMI‡	1.00	0.97 (0.62–1.50)	0.80 (0.43–1.52)

Data are OR (95% CI). The low waist circumference group was used as the referent. *Significantly greater than low waist circumference group ($P < 0.05$). †Metabolic risk factors include blood pressure, LDL cholesterol, HDL cholesterol, and triglyceride risk factor categories. ‡Metabolic risk factors include blood pressure, LDL cholesterol, HDL cholesterol, triglyceride, and fasting glucose risk factor categories.

variables: 1) demographics (age, race, sex, and smoking), 2) demographics plus traditional risk factors (blood pressure, LDL and HDL cholesterol, and triglyceride categories), and 3) demographics, traditional risk factors, and WC categories. The c statistic is identical to the area under the receiver operating characteristic curve, with values ranging from 0.5 (no better than chance alone) to 1.0 (perfect).

RESULTS— The descriptive characteristics of the study sample are contained within Table 1. Table 2 presents the results of the logistic regression models in which WC groups were used to predict the likelihood of having diabetes and CVD. After controlling for age, sex, race, and smoking, participants in the medium and high WC groups were more likely to have diabetes and CVD compared with participants in the low WC group ($P <$

0.05). After inclusion of the cardiometabolic risk factor categories in the logistic regression models, the magnitude of the ORs were attenuated but remained significant in the medium and high WC groups for the prediction of diabetes (OR 1.98 [95% CI 1.26–3.11] and 4.62 [3.16–6.75], respectively) but not for CVD. A final set of logistic regression models included BMI categories among the covariates. After controlling for demographic characteristics, smoking, cardiometabolic risk factors categories, and BMI categories, the moderate and high WC categories remained predictive of a higher likelihood of diabetes (2.32 [1.30–4.12] and 5.03 [2.87–8.83], respectively) but not CVD ($P > 0.1$) (Table 2).

Table 3 presents the results of the logistic regression models in which BMI groups were used to predict the likelihood of having diabetes and CVD. After

controlling for age, sex, race, and smoking, participants in the medium and high BMI groups were more likely to have diabetes and CVD compared with participants in the low BMI group ($P < 0.05$). After the inclusion of cardiometabolic risk factor categories in the logistic regression models, ORs for the medium and high BMI categories were attenuated for both diabetes and CVD, with only the high BMI category remaining associated with a greater risk of diabetes (OR 2.92 [95% CI 1.95–4.37]). Lastly, after inclusion of WC in addition to demographic characteristics, smoking, and cardiometabolic risk factors, neither the moderate nor the high BMI categories remained predictive of a higher likelihood of diabetes or CVD ($P > 0.1$) (Table 3).

To further illustrate the effect of WC, we divided the study participants into groups based on their number of high-risk metabolic variables. We then cross-tabulated the WC and cardiometabolic risk factor groups to form 12 WC \times metabolic risk factor groups. As illustrated in Fig. 1A, both WC and cardiometabolic risk factor groups were independent predictors of diabetes ($P_{trend} < 0.001$); i.e., for a given number of cardiometabolic risk factors, the likelihood of having diabetes increased when moving from the low to high WC groups. Conversely, within a given WC group, the likelihood of having diabetes increased when moving from the group with no cardiometabolic risk factors to the group with three or more. As illustrated in Fig. 1B, cardiometabolic risk factor groups, but not WC groups, significantly predicted CVD. Thus, for a given number of cardiometabolic risk factors, the likelihood of having CVD was not different across WC groups ($P_{trend} = 0.415$).

Table 3—ORs for diabetes and CVD according to BMI

Covariates included in regression model	BMI tertile		
	Low	Medium	High
Diabetes			
Age, sex, race, and smoking	1.00	1.71 (1.15–2.55)*	4.12 (2.72–6.24)*
Age, sex, race, smoking, and metabolic risk factors†	1.00	1.38 (0.93–2.05)	2.92 (1.95–4.37)*
Age, sex, race, smoking, metabolic risk factors, and WC†	1.00	0.73 (0.42–1.25)	0.91 (0.49–1.68)
Cardiovascular disease			
Age, sex, race, and smoking	1.00	1.41 (1.01–1.97)*	1.84 (1.38–2.44)*
Age, sex, race, smoking, and metabolic risk factors‡	1.00	1.19 (0.82–1.72)	1.32 (0.95–1.85)
Age, sex, race, smoking, metabolic risk factors, and WC‡	1.00	1.26 (0.81–1.99)	1.58 (0.88–2.23)

Data are OR (95% CI). The normal-weight BMI group was used as the referent. *Significantly greater than low BMI ($P < 0.05$). †Metabolic risk factors include blood pressure, LDL cholesterol, HDL cholesterol, and triglyceride risk factor categories. ‡Metabolic risk factors include blood pressure, LDL cholesterol, HDL cholesterol, triglyceride, and fasting glucose risk factor categories.

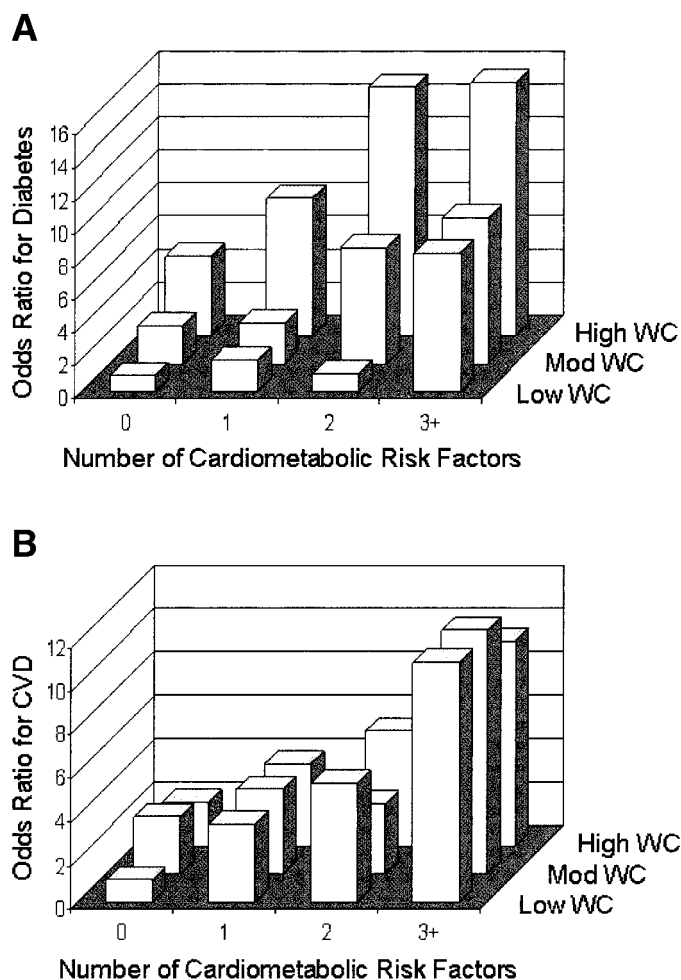


Figure 1—ORs for diabetes (A) and CVD (B) according to WC × metabolic risk factor groups. Both WC and metabolic risk factor groups were independent predictors of diabetes ($P_{trend} < 0.001$). The metabolic risk factor groups were independent predictors of CVD ($P_{trend} < 0.001$), whereas the WC groups were not ($P_{trend} = 0.415$). Mod, moderate.

Finally, the *c* statistic was calculated to determine the discriminatory ability of diabetes and CVD models. For diabetes, the *c* statistic increased from 0.77 to 0.80 to 0.82 across modes that included basic demographic characteristics; demographics plus traditional risk factor categories; and demographics, traditional risk factors, and waist circumference categories, respectively. The corresponding *c* statistic values for the CVD models were 0.83, 0.85, and 0.85.

CONCLUSIONS— The primary finding of this study is that WC predicts the likelihood of diabetes beyond that explained by commonly evaluated cardiometabolic risk factors and BMI. Conversely, BMI did not predict diabetes after consideration of common cardiometabolic risk factors and WC. Although both elevated WC and BMI were associated with greater CVD risk, these effects were eliminated

after control for cardiometabolic risk factors.

Clinical guidelines for the assessment and/or management of obesity in the U.S. (14) and Canada (15) recommend that measurement of WC be used to identify the need for further assessment including measurement of cardiometabolic risk factors. The recent consensus statement of the ADA, the Obesity Society, and the American Society for Nutrition questions the sequence of these clinical measures and, more importantly, the relevance of WC measurement in clinical practice (7). Our finding that WC predicts the risk of diabetes beyond that explained by cardiometabolic risk factors and BMI extends previous observations that document an approximately fivefold greater risk of diabetes in the highest relative to the lowest category of WC in multivariate analysis controlling for lifestyle factors and BMI (3,4). Combined with the fact that the

sex-specific WC cut points used in the current study approximate those advocated in the guidelines (≥ 102 and 88 cm in men and women, respectively), these observations reinforce the utility of WC as a first step in the identification of the high-risk, abdominally obese patient. Indeed, although an elevated WC per se alerts the clinician to the need for further clinical assessment, we (16) and others (17) have shown that only patients with an elevated WC in combination with elevations in one or more cardiometabolic risk factors represent those who are at substantially increased health risk and thus require aggressive treatment.

The mechanistic link that explains the association between WC and diabetes risk independent of cardiometabolic risk factors and BMI is unclear and remains the focus of ongoing investigation (18). Although the portal theory originally proposed a substrate-driven mechanism (19), recent evidence suggests that the pathophysiology of abdominal adiposity may result from the augmented secretion of various prothrombotic and proinflammatory cytokines from an expanded abdominal fat depot (20).

Although WC was associated with CVD, such that individuals with a high WC were 73% more likely to have CVD than those with a low WC, the association did not remain significant after control for the cardiometabolic risk factors. This finding was not unexpected given that WC is a strong correlate of dyslipidemia, hypertension, and the metabolic syndrome (21), themselves established antecedents for CVD. Accordingly, this finding does not indicate that a high WC is not a risk factor for CVD but, rather, that WC predicts CVD via its influence on cardiometabolic risk factors. Indeed, the utility of WC to predict CVD risk will always be attenuated when metabolic risk factors that lie in the causal pathway between WC and risk of CVD are included in the prediction model. This observation agrees with the findings of the INTERHEART study, wherein the strong association between WC and myocardial infarction was substantially attenuated after control for hypertension and the apolipoprotein B-to-A ratio (1).

From a clinical perspective, it is noteworthy that in addition to the utility of WC measurement to identify the high-risk, abdominally obese patient, WC is the single best anthropometric measure for detecting changes in abdominal obesity in response to treatment. It has re-

peatedly been demonstrated that although WC is reduced consequent to weight loss, WC can also be reduced in response to treatment in obese individuals who are resistant to weight loss or changes in BMI (22). The implication is that when considering the efficacy of treatment strategies designed to manage abdominal obesity, practitioners are encouraged to look beyond body weight as the measure of benefit and measure WC.

The analyses presented here are based on a large and representative dataset and are therefore generalizable to the U.S. adult population. However, the cross-sectional nature of this study precludes definitive causal inferences about the association between WC and BMI with diabetes and CVD. Numerous studies, however, have shown that high WC and BMI precede the onset of morbidity (1–4) and mortality (5). The assessment of CVD presence in the current study relied on participant recall of previous diagnosis and thus may have been a source of error. Additionally, as our assessment of diabetes was based on fasting plasma glucose values, a limited number of new diabetes cases may have been misclassified as non-diabetes. Lastly, due to the limited sample size, we were not able to perform ethnicity- and/or sex-specific analyses.

The demonstration that WC predicts risk of diabetes beyond that explained by cardiometabolic risk factors routinely acquired in clinical practice responds to prior criticism (7) and lends critical support for the recommendation that WC be a routine measure for identification and management of the high-risk, abdominally obese patient (14,15). Indeed, combined with the observation that WC is associated with changes in abdominal obesity in response to treatment with or without weight loss (22), it is difficult to imagine a cogent argument against inclusion of WC in clinical practice.

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