Body fat distribution and risk of type 2 diabetes in the general population: are there differences between men and women? The MONICA/KORA Augsburg Cohort Study[1–3]

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ABSTRACT

Background: It remains controversial whether body mass index (BMI), waist circumference (WC), or waist-hip ratio (WHR) is a better risk predictor of type 2 diabetes.

Objective: The objective was to examine the sex-specific relevance of WC, WHR, and BMI to the development of type 2 diabetes.

Design: The prospective population-based cohort study was based on 3055 men and 2957 women aged 35–74 y who participated in the second (1989–1990) or third (1994–1995) MONICA (Monitoring Trends and Determinants on Cardiovascular Diseases) Augsburg survey. The subjects were free of diabetes at baseline. Hazard ratios (HRs) were estimated from Cox proportional hazards models.

Results: During a mean follow-up of 9.2 y, 243 cases of incident type 2 diabetes occurred in men and 158 occurred in women. Multivariable-adjusted HRs across quartiles of BMI were 1.0, 1.37, 2.08, and 4.15 in men and 1.0, 3.77, 4.95, and 10.58 in women; those of WC were 1.0, 1.15, 1.57, and 3.40 in men and 1.0, 3.21, 3.98, and 10.70 in women; those of WHR were 1.0, 1.14, 1.80, and 2.84 in men and 1.0, 0.82, 2.06, and 3.51 in women. In joint analyses, the highest risk was observed in men and women with a high BMI in combination with a high WC and a high WHR.

Conclusions: Both overall and abdominal adiposity were strongly related to the development of type 2 diabetes. Because there was an additive effect of overall and abdominal obesity on risk prediction, WC should be measured in addition to BMI to assess the risk of type 2 diabetes in both sexes. *Am J Clin Nutr* 2006;84:483–9.

KEY WORDS Type 2 diabetes, risk factors, cohort study, body mass index, abdominal obesity

INTRODUCTION

The number of people diagnosed with diabetes has exploded in the past several decades. In 2000, it was estimated that 151 million persons worldwide had diabetes. At the current rate of increase, it has been projected that 221 million persons will be affected by 2010 and 324 million by 2025; most of these cases will be type 2 diabetes (1). It is well known that type 2 diabetes is a polygenetic disease (2) and that environmental factors such as sedentary lifestyle, a high calorie intake, and consequent obesity play a major role in disease development (3). Moreover, the term "diabesity" has been created to express that type 2 diabetes is obesity dependent and that obesity is the main etiologic cause of type 2 diabetes (4). Many epidemiologic studies have shown that body mass index (BMI), a general measure of obesity, is a powerful predictor of type 2 diabetes (5–9). However, a growing body of evidence indicates that waist circumference (WC) and waist-hip ratio (WHR)—measures of central obesity—also provide information on the risk of type 2 diabetes (10–15). Only a few studies have investigated the joint association of BMI, WC, and WHR with diabetes risk (16, 17). Furthermore, it remains controversial whether WC or WHR is a better risk predictor and whether these measures have the same predictive effect in men and women. It is of great interest whether different measures of body fat distribution are similar predictors of risk in men and women within the same population. Therefore, the aim of this study was to analyze the sex-specific relevance of measures of body fat distribution in comparison with BMI on the development of type 2 diabetes in a prospective population-based cohort study. Furthermore, we examined the combined relation of overall obesity and abdominal adiposity with type 2 diabetes in men and women.

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[2] The KORA research platform and the MONICA Augsburg studies were initiated and financed by the GSF National Research Center for Environment and Health, which is funded by the German Federal Ministry of Education, Science, Research and Technology and by the State of Bavaria. The morbidity and mortality follow-ups in 1997–1998 and 2002–2003 were supported by grants from the Federal Ministry of Education, Science, Research and Technology (01 ER 9701/4) and the German Research Foundation (TH 784/2-1), respectively.

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Received December 29, 2005.

Accepted for publication April 12, 2006.

SUBJECTS AND METHODS

The data were derived from the second and third population-based MONICA (Monitoring Trends and Determinants on Cardiovascular Diseases) Augsburg (Southern Germany) surveys conducted in 1989–1990 and 1994–1995. The MONICA Augsburg project was part of the multinational WHO MONICA project, and the design of both projects was described in detail elsewhere (18, 19). The independent cross-sectional surveys were carried out in the city of Augsburg and the counties Augsburg and Aichach-Friedberg to estimate the prevalence and distribution of cardiovascular disease risk factors in men and women. A total of 9658 persons (4828 men, 4830 women; response rate: 75%) aged 25–74 y participated in ≥1 of the 2 cross-sectional studies. All subjects were prospectively followed within the framework of the Cooperative Health Research in the Region of Augsburg (KORA). Mortality was ascertained by regularly checking the vital status of all sampled persons of the MONICA surveys through the population registries. In 1997–1998 and 2002–2003 the health status of all living persons was assessed with the use of follow-up questionnaires.

The present analysis was restricted to all men and women aged 35–74 y at baseline, because the incidence of type 2 diabetes is low in younger subjects. A total of 7814 subjects (3916 men, 3898 women) in this age-range participated in at least one of the surveys. Of this total, 1082 persons (486 men, 596 women) were lost to follow-up and were therefore excluded from analysis. Thus, follow-up information was available for 6732 persons. Up until 31 December 2002, 973 participants (650 men, 323 women) aged 35–74 y had died. All subjects who had died between baseline and follow-up were also included in the analyses if follow-up information could be ascertained.

We excluded from the analysis all persons with prevalent type 2 diabetes at baseline ($n = 488$) and persons with types of diabetes other than type 2 diabetes ($n = 14$). Furthermore, we excluded subjects from whom no information about diabetes status at follow-up was available and all subjects with incomplete data for any of the covariables ($n = 218$). Finally, the prospective analyses included 6012 nondiabetic study participants (3055 men, 2957 women) aged 35–74 y at baseline. Written informed consent was obtained from each study participant, and the study was approved by the local ethics committee.

Data collection

Baseline information on sociodemographic variables, physical activity level, medication use, parental history of diabetes, and alcohol consumption was gathered by trained medical staff during a standardized interview. In addition, all participants underwent an extensive standardized medical examination that included the collection of a nonfasting blood sample. All measurement procedures were described elsewhere in detail (8, 18). Anthropometric measurements were taken after the participants had removed their shoes, heavy clothing, and belts. Body weight was measured to the nearest 0.1 kg and height to the nearest 0.5 cm while the subjects were wearing light clothing. WC was measured at the level midway between the lower rib margin and the iliac crest while the participants breathed out gently. Hip circumference was taken at the level of maximal gluteal protrusion (20, 21). BMI was calculated as weight (kg)/height^2 (m). WHR was calculated by dividing WC by hip circumference. Actual hypertension was defined as blood pressure values ≥140/90 mm Hg or the use of antihypertensive medication. Dyslipidemia was defined as a ratio of total cholesterol to HDL cholesterol ≥5.0. A regular smoker was defined as a subject who currently smoked at least one cigarette per day. Participants were classified as active during leisure time if they regularly participated in sports in the summer and winter and if they were active for ≥1 h/wk in either season.

A nonfasting venous blood sample was obtained from all study participants while they were sitting. Total serum cholesterol analyses were carried out with an autoanalyzer by using an enzymatic method (CHOD-PAP; Boehringer Mannheim, Mannheim, Germany). HDL cholesterol was also measured enzymatically after precipitation of the apoprotein B–containing lipoproteins with phosphotungstate/Mg^{2+} (Boehringer Mannheim).

Ascertainment of diabetes

In the 1997–1998 and 2002–2003 follow-up questionnaires, we inquired about the diagnosis of diabetes. All incident cases of type 2 diabetes that had been diagnosed up to 31 December 2002 were included. Self-reported incident cases of diabetes mellitus and the date of diagnosis were validated by hospital records or by contacting the probands treating physician. Furthermore, the hospital records of those deceased during the follow-up period without a diagnosis of type 2 diabetes at baseline were also examined and their last treating physicians were contacted. The records were searched for or the physicians were asked for a history of diabetes; if a person had diabetes, the type of diabetes and the date of diagnosis were ascertained. Thus, only clinically diagnosed type 2 diabetes cases were included in the analysis.

Statistical analyses

The duration of the follow-up was calculated as the interval between the baseline examination and the diagnosis of type 2 diabetes mellitus, death, or the date when the 1997–1998 or 2002–2003 follow-up questionnaire was completed. Follow-up times were censored for men and women at death, the date when they filled out the follow-up questionnaire, or on 31 December 2002. All analyses were performed separately for men and women. Means or proportions for baseline demographic and clinical characteristics were computed for quartiles of WC. The chi-square test was used to test the differences in prevalences. The general linear model was used to compare means (F test). The study population was stratified into sex-specific quartiles of BMI, WC, and WHR. The relative risks of incident type 2 diabetes were computed for quartiles 2, 3, and 4 as compared with the lowest quartile in different Cox proportional hazards models for each measure of body fat distribution. The first model included the respective measure of body fat distribution and in addition age (4 categories: 35–44, 45–54, 55–64, and 65–74 y), coded as dummy variables, and survey. The second model included all previous factors plus years of education (< or ≥12 y), actual hypertension (yes or no), dyslipidemia (yes or no), physical activity (active or inactive), regular smoking (yes or no), alcohol intake (men: 0, 0.1–39.9, or ≥40 g/d; women: 0, 0.1–19.9, or ≥20 g/d), and parental history of diabetes (yes, no, or unknown). When BMI was the main exposure of interest, WC and WHR were included as additional covariates in a third and fourth model, respectively. Tests for linear trend across increasing categories of body fat measures were conducted by assigning the median value within each category to the respective category

TABLE 1
Crude means and prevalences of baseline characteristics according to waist circumference quartiles in men and women

	Waist circumference quartiles (cm)									
	Men (n = 3055)					Women (n = 2957)				
Characteristic	1: <90.0 (n = 697)	2: 90.0 to <96.0 (n = 759)	3: 96.0 to <102.0 (n = 776)	4: ≥102.0 (n = 823)	P	1: <75.0 (n = 713)	2: 75.0 to <82.0 (n = 721)	3: 82.0 to <90.5 (n = 780)	4: ≥90.5 (n = 743)	P
Age (y)	50.1 ± 11.2[1]	53.1 ± 11.2	55.2 ± 10.9	57.3 ± 10.2	<0.0001	46.2 ± 9.2	51.6 ± 10.7	55.8 ± 10.3	57.8 ± 10.1	<0.0001
BMI (kg/m^2)	24.0 ± 2.1	26.1 ± 1.7	27.9 ± 1.8	31.3 ± 3.2	<0.0001	22.1 ± 1.9	24.8 ± 2.0	27.5 ± 2.5	32.3 ± 4.2	<0.0001
Hip circumference (cm)	97.2 ± 4.7	101.2 ± 3.7	104.3 ± 4.0	110.0 ± 6.5	<0.0001	93.6 ± 5.3	99.1 ± 5.0	104.6 ± 5.5	114.2 ± 8.9	<0.0001
Waist-hip ratio	0.87 ± 0.04	0.92 ± 0.03	0.95 ± 0.04	0.99 ± 0.05	<0.0001	0.75 ± 0.04	0.79 ± 0.04	0.82 ± 0.04	0.87 ± 0.05	<0.0001
Regular smoking (%)	29.7	24.2	21.8	21.8	0.0008	22.4	15.4	15.4	11.3	<0.0001
Dyslipidemia (%)	30.3	44.8	52.8	61.4	<0.0001	6.5	12.3	24.7	37.3	<0.0001
Physically active (%)	52.7	46.9	36.0	33.9	<0.0001	49.8	42.7	34.7	24.8	<0.0001
Alcohol intake (%)										
0 g/d	20.5	15.7	17.7	17.3	0.1560	35.6	42.0	46.7	50.5	<0.0001
0.1–39.9 g/d (M), 0.1–19.9 g/d (F)	51.7	52.4	49.4	52.1		40.7	37.3	39.1	35.7	
≥40 g/d (M), ≥20 g/d (F)	27.8	31.9	33.0	30.6		23.7	20.7	14.2	13.9	
Hypertension (%)	35.9	47.6	51.4	64.0	<0.0001	16.8	31.1	43.0	61.0	<0.0001
Parental history of diabetes (%)	18.2	17.8	20.0	18.6	0.7159	20.8	21.9	22.8	21.9	0.8179
Education <12 y (%)	56.7	62.6	66.9	70.2	<0.0001	74.3	81.0	87.6	90.7	<0.0001
Living in an urban area (%)	46.9	46.4	43.4	41.2	0.0815	45.0	45.1	42.7	43.5	0.7376

[1] $\bar{x}$ ± SD (all such values).

and by treating the categories as a continuous variable. To examine the joint effects of BMI and WC and of BMI and WHR on the development of type 2 diabetes, combined variables were created. For this purpose the upper quartile values of the different measurements were used as cutoffs. High BMI was defined as ≥29.4 in men and ≥29.5 in women; high WC was defined as ≥102.0 cm in men and ≥90.5 cm in women, and high WHR was defined as ≥0.97 in men and ≥0.85 in women. We plotted the [-log(survival)] curves for each risk factor to assess the proportional hazards assumptions. This assumption was met for all variables. We tested for possible interactions of anthropometric measurements with sex, age, smoking, living environment (urban or rural area), parental history of diabetes, hypertension, physical activity, dyslipidemia, and education. The results are presented as hazard ratios (HRs) and 95% CIs. Significance tests were 2-tailed, and P values <0.05 were considered statistically significant. All analyses were performed by using Statistical Analysis System software (version 8.2; SAS Institute Inc, Cary, NC).

RESULTS

During follow-up, 243 incident cases of type 2 diabetes were identified in the 3055 men and 158 cases in the 2957 women. Sex-specific baseline characteristics of the study sample according to quartiles of WC are shown in **Table 1**. Men and women with higher WCs were older, had higher mean BMIs and hip circumferences, were more likely to have had a history of hypertension and dyslipidemia, were less physically active, and were less likely to be regular smokers. In both sexes, participants with a higher WC were more often less educated, whereas the percentage with a positive family history of diabetes did not differ significantly between the categories.

The observed crude incidence rates of diabetes mellitus by categories of WC, WHR, and BMI are shown in **Table 2** and **Table 3**. In general, in all categories of WC, WHR, and BMI, the incidence of diabetes was higher in men than in women, but the incidence increased with increasing BMI, WC, and WHR in both sexes. Elevated BMI at baseline was significantly associated with type 2 diabetes in men (Table 2) and women (Table 3). The positive association between BMI and type 2 diabetes remained significant after adjustment for age, survey, education, parental history of diabetes, actual hypertension, dyslipidemia, smoking status, alcohol intake, and physical activity level. The multivariable-adjusted HRs across quartiles of BMI were 1.0, 1.37, 2.08, and 4.15 (P for trend < 0.0001) in men; the corresponding HRs in women were 1.0, 3.77, 4.95, and 10.58 (P for trend < 0.0001). The

TABLE 2
Age-adjusted and multivariable-adjusted hazard ratios (HRs) and 95% CIs for type 2 diabetes according to different measures of body fat distribution in men[1]

	No. of person-years	No. of cases	Crude incidence rate/10 000 person-years	Age- and survey-adjusted HRs	Multivariable-adjusted HRs[2]	Multivariable-adjusted[2] + BMI-adjusted HRs	Multivariable-adjusted[2] + WC-adjusted HRs	Multivariable-adjusted[2] + WHR-adjusted HRs
BMI quartiles (kg/m^2)								
1: <25.1	6711	21/727	31.3	1.0	1.0	—	1.0	1.0
2: 25.1 to <27.2	7297	37/800	50.7	1.49 (0.87, 2.54)	1.37 (0.80, 2.34)	—	1.11 (0.64, 1.91)	1.21 (0.70, 2.08)
3: 27.2 to <29.4	6631	59/739	89.0	2.46 (1.49, 4.05)	2.08 (1.25, 3.45)	—	1.43 (0.84, 2.44)	1.70 (1.01, 2.86)
4: ≥29.4	6598	126/789	191.0	5.17 (3.25, 8.22)	4.15 (2.58, 6.66)	—	2.07 (1.16, 3.69)	3.01 (1.81, 5.02)
P for trend	—	—	—	<0.0001	<0.0001	—	0.0021	<0.0001
WC quartiles (cm)								
1: <90.0	6703	23/697	34.3	1.0	1.0	1.0	—	—
2: 90.0 to <96.0	6872	34/759	49.5	1.28 (0.75, 2.18)	1.15 (0.68, 1.96)	0.93 (0.54, 1.59)	—	—
3: 96.0 to <102.0	6988	55/776	78.7	1.91 (1.17, 3.13)	1.57 (0.96, 2.58)	1.04 (0.62, 1.74)	—	—
4: ≥102.0	6674	131/823	196.3	4.48 (2.85, 7.03)	3.40 (2.15, 5.37)	1.48 (0.85, 2.60)	—	—
P for trend	—	—	—	<0.0001	<0.0001	0.0535	—	—
WHR quartiles								
1: <0.89	7408	26/763	35.1	1.0	1.0	1.0	—	—
2: 0.89 to <0.93	7215	38/784	52.7	1.31 (0.80, 2.17)	1.14 (0.69, 1.88)	0.88 (0.53, 1.46)	—	—
3: 0.93 to <0.97	6265	63/731	100.6	2.32 (1.46, 3.68)	1.80 (1.13, 2.86)	1.21 (0.75, 1.95)	—	—
4: ≥0.97	6350	116/777	182.7	3.99 (2.58, 6.16)	2.84 (1.82, 4.42)	1.51 (0.94, 2.44)	—	—
P for trend	—	—	—	<0.0001	<0.0001	0.0099	—	—

[1] WC, waist circumference; WHR, waist-hip ratio.
[2] Adjusted for age, survey, education, parental history of diabetes, hypertension, dyslipidemia, smoking, alcohol intake, and physical activity.

positive association between BMI and the risk of type 2 diabetes remained strong even after adjustment for WHR in both men and women (*P* for trend < 0.0001 for both sexes). However, the relation remained independent after further adjustment for WC in men only (*P* for trend 0.0021).

Increased WC at baseline also predicted type 2 diabetes in both sexes (Tables 2 and 3). The association was somewhat weaker than for BMI in men, whereas in women the association was almost equal in comparison with BMI. The multivariable-adjusted HRs across quartiles of WC were 1.0, 1.15, 1.57, and 3.40 (*P* for trend < 0.0001) in men and 1.0, 3.21, 3.98, and 10.70 (*P* for trend < 0.0001) in women. Further adjustment for BMI considerably attenuated the association; the HR for men in the highest quartile compared with the lowest quartile was 1.48 (NS), whereas the corresponding value for women was 5.60, which was significant.

The risk of type 2 diabetes increased with increasing WHR (Table 2 and Table 3). The association was clearly weaker than that for BMI in men and women. After multivariable adjustment, the HRs across WHR quartiles were 1.0, 1.14, 1.80, and 2.84, respectively (*P* for trend < 0.0001), in men and 1.0, 0.82, 2.06, and 3.51, respectively (*P* for trend < 0.0001), in women. Further adjustment for BMI considerably attenuated the relation, and the HR for the highest versus the lowest quartile was 1.51 (95% CI: 0.94, 2.44) in men and 2.25 (95% CI: 1.19, 4.27) in women.

TABLE 3
Age-adjusted and multivariable-adjusted hazard ratios (HRs) and 95% CIs for type 2 diabetes according to different measures of body fat distribution in women[1]

	No. of person-years	No. of cases	Crude incidence rate/10 000 person-years	Age- and survey-adjusted HRs	Multivariable-adjusted HRs[2]	Multivariable-adjusted[2] + BMI-adjusted HRs	Multivariable-adjusted[2] + WC-adjusted HRs	Multivariable-adjusted[2] + WHR-adjusted HRs
BMI quartiles (kg/m^2)								
1: <23.4	7279	4/734	5.5	1.0	1.0	—	1.0	1.0
2: 23.4 to <26.1	7255	21/739	28.9	4.25 (1.46, 12.42)	3.77 (1.29, 11.03)	—	2.79 (0.95, 8.20)	3.29 (1.12, 9.61)
3: 26.1 to <29.5	6955	39/737	56.1	7.01 (2.49, 19.73)	4.95 (1.75, 14.02)	—	2.66 (0.92, 7.68)	3.69 (1.30, 10.49)
4: ≥29.5	6550	94/747	143.5	17.92 (6.54, 49.12)	10.58 (3.81, 29.33)	—	3.28 (1.09, 9.86)	6.73 (2.40, 18.89)
P for trend	—	—	—	<0.0001	<0.0001	—	0.0974	<0.0001
WC quartiles (cm)								
1: <75.0	7130	4/713	5.6	1.0	1.0	1.0	—	—
2: 75.0 to <82.0	7227	19/721	26.3	3.72 (1.26, 11.0)	3.21 (1.08, 9.49)	2.73 (0.92, 8.11)	—	—
3: 82.0 to <90.5	7317	35/780	47.8	5.90 (2.07, 16.78)	3.98 (1.39, 11.38)	2.84 (0.98, 8.29)	—	—
4: ≥90.5	6366	100/743	157.1	18.75 (6.80, 51.68)	10.70 (3.84, 29.80)	5.60 (1.86, 16.86)	—	—
P for trend	—	—	—	<0.0001	<0.0001	0.0002	—	—
WHR quartiles								
1: <0.77	7233	12/737	16.6	1.0	1.0	1.0	—	—
2: 0.77 to <0.80	7253	14/736	19.3	0.99 (0.46, 2.14)	0.82 (0.38, 1.79)	0.67 (0.30, 1.45)	—	—
3: 0.80 to <0.85	6891	43/732	62.4	2.91 (1.52, 5.57)	2.06 (1.07, 3.96)	1.50 (0.78, 2.91)	—	—
4: ≥0.85	6663	89/752	133.6	5.76 (3.11, 10.69)	3.51 (1.88, 6.57)	2.25 (1.19, 4.27)	—	—
P for trend	—	—	—	<0.0001	<0.0001	<0.0001	—	—

[1] WC, waist circumference; WHR, waist-hip ratio.
[2] Adjusted for age, survey, education, parental history of diabetes, hypertension, dyslipidemia, smoking, alcohol intake, and physical activity.

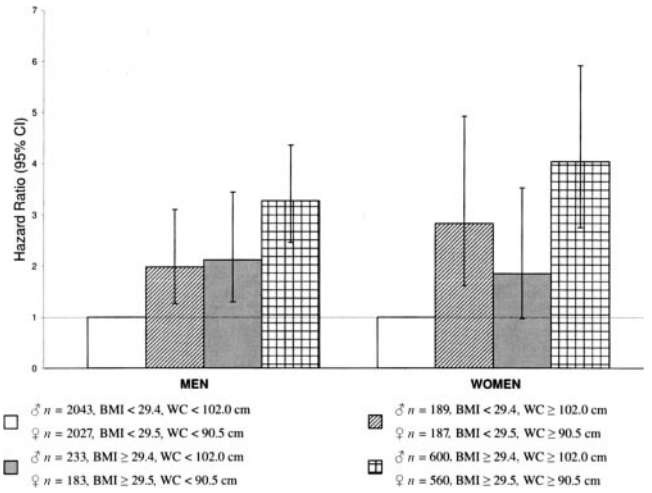

FIGURE 1. Joint effect of BMI (in kg/m^2) and waist circumference (WC) in predicting the risk of type 2 diabetes in men and women (adjusted for age, survey, education, parental history of diabetes, hypertension, dyslipidemia, smoking, alcohol intake, and physical activity).

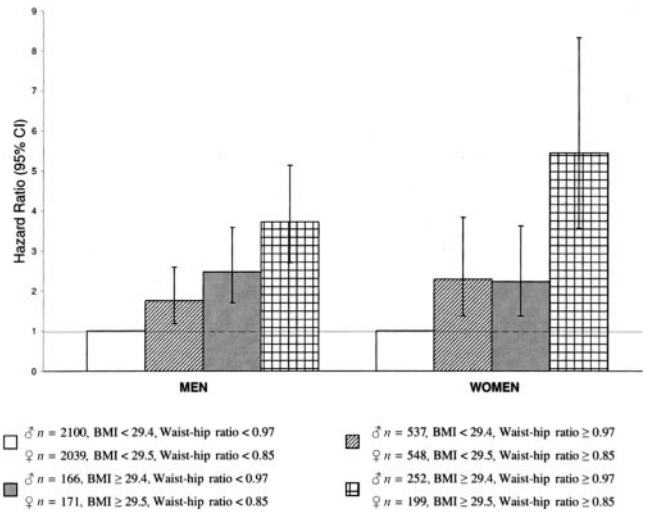

FIGURE 2. Joint effect of BMI (in kg/m^2) and waist-hip ratio in predicting the risk of type 2 diabetes in men and women (adjusted for age, survey, education, parental history of diabetes, hypertension, dyslipidemia, smoking, alcohol intake, and physical activity).

The *P* values for interactions between sex and quartiles of BMI, WC, and WHR were 0.1, 0.08, and 0.02, respectively. No significant interactions were found between smoking, parental history of diabetes, physical activity level, living environment, and dyslipidemia with anthropometric measurements as predictors of type 2 diabetes. However, for hypertension, a significant interaction with BMI ($P = 0.03$) and WC ($P = 0.02$) was found. Furthermore, there was a significant interaction between BMI, WC, and WHR and age (<55 y compared with ≥55 y at baseline; *P* for interaction < 0.01 for all). In stratified analyses, associations between measures of obesity and incident type 2 diabetes were stronger in younger men (<55 y). However, in women, the association of WC with type 2 diabetes was stronger in older women (≥55 y), whereas the association between BMI and incident type 2 diabetes was stronger in younger women. In a comparison of the highest and lowest quartiles of BMI, WC, and WHR, the multivariable-adjusted HRs were 9.83, 15.07, and 5.10 in men <55 y; the corresponding HRs in men aged ≥55 y were 2.69, 1.60, and 1.96. In contrast, in a comparison of the highest and lowest quartiles of BMI, WC, and WHR, the HRs were 13.14, 9.90, and 3.28 in women younger than 55 y; the corresponding HRs in women aged ≥55 y were 8.97, 12.40, and 3.87 (data not shown).

The joint relations between BMI and measures of abdominal adiposity in men and women are shown in **Figure 1** (BMI and WC) and **Figure 2** (BMI and WHR). For these analyses, for the definition of high BMI, WC, and WHR, the upper-quartile cutoff was used. The subjects were classified into 4 categories. Those with a low BMI and a low WC and WHR were the reference group. After multivariable adjustment, the risk of type 2 diabetes increased across the categories and was highest in men who had a high BMI and a high WC (HR: 3.27), compared with men who had a low BMI and low WC (Figure 1). Similar patterns were observed for BMI in combination with WHR in men (Figure 2). In women, the joint association of BMI and WHR also showed an increasing risk of type 2 diabetes across the 4 categories, ie, an HR of 5.44 in women with a high BMI and a high WHR compared with women with a low BMI and a low WHR (Figure 2). Those women with a high WC and a high BMI also had the highest risk of type 2 diabetes (HR: 4.03) in comparison with the reference category. In contrast with men, women with a low WC and a high BMI had no significantly increased risk of disease development after adjustment for potential confounders (Figure 1).

DISCUSSION

In this large cohort of men and women, drawn from the general population, in separate analysis, each of the anthropometric measures (BMI, WC, and WHR) was strongly and independently related to the development of incident type 2 diabetes in both sexes, even after control for a variety of potential confounders. In general, the crude incidence rates were higher in men than in women in each category of BMI, WC, and WHR. WC displayed the greatest relative risks in older women, whereas BMI showed the strongest association with type 2 diabetes in younger women. However, BMI, WC, and WHR were stronger predictors of diabetes in younger men. Finally, the present study showed an additive effect of BMI and WC or BMI and WHR on risk prediction. In joint analyses, the highest risk was observed in men and women with a high BMI in combination with a high WC and a high WHR, respectively. Interestingly, women in the low BMI category had a markedly elevated diabetes risk if they had a high WC, whereas women in the high BMI category with a low WC had no significantly increased risk of type 2 diabetes.

Many previous prospective studies have shown that BMI is a powerful predictor of type 2 diabetes in both sexes (5–9). For example, Field et al (7) reported that both men and women with a BMI of ≥35.0 were ≈20 times as likely to develop diabetes than were their same-sex peers with a BMI between 18.5 and 24.9. In another investigation from the Nurses' Health Study, overweight and obesity was the single most important predictor of type 2 diabetes in 30–55-y-old women (6). Because growing evidence suggests that the accumulation of visceral fat may play an important role in the etiology of type 2 diabetes, many additional studies examined whether WHR and WC—both measures

of abdominal adiposity—are stronger predictors of disease development than is BMI. However, the findings were inconsistent; therefore it remains controversial which anthropometric measures should be used for risk assessment (21, 22). Furthermore, only a few studies investigated whether different measures of body fat distribution are similar in predicting risk in men and women within the same population (11–13, 22–24). Most of these studies were smaller than the present study (12, 22–24). Chan et al (15) reported that WC is a better indicator than is WHR of the relation between abdominal adiposity and the risk of type 2 diabetes. However, in this study BMI was also the dominant risk factor for type 2 diabetes A Swedish study showed that WHR was positively and significantly associated with the risk of type 2 diabetes in men, even when the confounding effect of BMI was accounted for (10). In 12 814 African American and white participants of the ARIC cohort (ages 45–64 y), WC tended to have the highest receiver operating characteristic statistic in all groups, but the differences were small (11). Also, in the San Antonio Heart Study, WC was the best predictor of type 2 diabetes compared with BMI, WHR, and other measurements in 25–64-y-old Mexican Americans. In this study the predictive power of a single measurement of WC was at least equal to that of WHR and BMI combined (12). In contrast, in a study of Pima Indians older than 18 y, BMI and WHR were the best predictors of diabetes in men, whereas BMI, waist-height ratio, WC, and the waist-thigh ratio were the best predictors in women. The predictive abilities of models containing BMI were not significantly improved by other measures of obesity (24). Limited data are available that show the joint association of BMI, WC, and WHR with diabetes risk (16, 17). In accordance with the present study, the Iowa Women's Health Study found that, of the 3 anthropometric variables, WC showed the greatest relative risks. Women in the highest quintiles of BMI and WHR had a relative risk of 29 compared with women in the lowest combined quintiles (16). The Health Professionals Follow-Up Study reported that men who had a high BMI ($\geq$25) and a high WC ($\geq$102 cm) had the highest relative risk (8.7) compared with those who had a low BMI and a low WC (17). The results of our study are consistent with those studies that emphasized the role of abdominal and general obesity in causing type 2 diabetes. In addition, the joint analyses in the present study extend the understanding of the relative influence of anthropometric measurements on the development of type 2 diabetes. The analyses suggested that there are differences in the sex-specific relevance of measures of body fat distribution in predicting the risk of type 2 diabetes. Although all 3 investigated anthropometric variables had almost the same predictive power in men, the present data support that abdominal fat localization is more important than is the total amount of body fat in predicting the risk of type 2 diabetes in women. However, the relative risk for any of the indexes was very strong, confirming once again that obesity bears a powerful relation to future diabetes risk. It is possible that WC might be more closely correlated with the level of abdominal visceral adipose tissue than is WHR. Prior studies have shown that central (intraabdominal) depots of fat are more strongly linked to insulin resistance, and thus type 2 diabetes, than are peripheral (gluteal and subcutaneous) fat depots (25). It has been postulated that expanded intraabdominal fat stores affects insulin metabolism by releasing free fatty acids (26). Free fatty acids reduce the hepatic clearance of insulin, which may lead to insulin resistance and hyperinsulinemia (27, 28). In contrast, a larger hip circumference (ie, gluteal subcutaneous fat depots) is associated with high lipoprotein lipase activity and relatively low rates of basal and stimulated lipolysis (29). This fat distribution pattern may protect the liver from high exposure to free fatty acids through uptake and storage. Furthermore, adrenal and sex steroid concentrations and growth hormone concentrations may play a role in visceral fat accumulation and in the development of insulin resistance (30, 31). In addition, fat cells secrete a number of signaling factors, which may be involved in the development of insulin resistance (32), eg, leptin, adiponectin, interleukin 6, and tumor necrosis factor α. It is possible that regional differences in the biochemical characteristics of fat and in the secretion of these adipokines between abdominal fat depots and gluteal-femoral fat depots contribute to the different associations of these fat depots with glucose metabolism. More research is needed to elucidate what role genetic and environmental factors play in the individuals' body fat distribution. In particular, it remains to be investigated whether there are sex-specific mechanisms with regard to body fat distribution and the development of insulin resistance and type 2 diabetes.

The MONICA/KORA Augsburg Study has several limitations that need to be considered. The follow-up was not complete for all participants in the original study who were still alive in 1998 and in 2002, which might have introduced a selection bias. Furthermore, response bias cannot be excluded in the present study. Because, the study was limited to men and women of German nationality, caution should be used in generalizing these results to people of other ethnicities. Finally, only self-reported information on the diabetes status of the subjects or the use of antidiabetic medication was available. Although this information was validated with medical records, it is likely that the group of nondiabetic persons may have included some subjects who were unaware that they had diabetes. Some of the strengths of the MONICA/KORA Augsburg Cohort Study include its prospective design, the population-representativeness of the cohort, and the availability of data on lifestyle and multiple cardiovascular disease risk factors. In addition, in contrast with most other prospective studies of this kind in which the diagnosis of diabetes was based on self-report, the diabetes diagnosis in the present study was based on a physician-validated diagnosis of type 2 diabetes.

In conclusion, the present study showed that both overall and abdominal adiposity play an important role in the development of type 2 diabetes in men and women from the general population. Although BMI, WC, and WHR were almost equally good predictors of diabetes in men, WC and BMI displayed the greatest relative risks in women. In joint analyses there was an additive effect of BMI and WC and of BMI and WHR on risk prediction. Because WC is easy to interpret, it should be measured in addition to BMI to assess the risk of type 2 diabetes in men and women. This would entail an improvement in risk stratification, particularly in women, and may help to prevent type 2 diabetes.

We thank all of the study participants, all members of the GSF Institute of Epidemiology, and the field staff in Augsburg who helped plan and conduct the study.

CM analyzed the data and wrote the drafts and the final article. AD, BT, MH, and HL critically revised the manuscript for important intellectual content. None of the authors had a conflict of interest.

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