Endocrine Research

Wrist Circumference as a Novel Predictor of Diabetes and Prediabetes: Results of Cross-Sectional and 8.8-Year Follow-up Studies

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Objective: Our objective was to examine whether wrist circumference is associated with incident type 2 diabetes mellitus, independently of general (body mass index [BMI]) or central (waist circumference [WC]) adiposity measures in a cohort of an Iranian adult population.

Research Design and Methods: A total of 9330 subjects ≥20 years of age were included in the cross-sectional study. For prospective analysis, subjects with prevalent diabetes were excluded, leaving 6393 subjects (2716 males and 3677 females). The standard 2-hour postchallenge plasma glucose test was performed at baseline and during follow-up. Cox regression analysis was used to estimate the hazard ratio of diabetes for wrist circumference.

Results: During a mean follow-up of 8.8 years, 649 new cases of diabetes occurred. At baseline, using linear regression models, we showed significant linear associations between wrist circumference and diabetes risk factors in both genders, and this association remained significant after controlling for BMI or WC among females. In prospective evaluation, wrist circumference was significantly associated with incident diabetes (multivariable-adjusted hazard ratio = 1.17 [1.03–1.32] and 1.31 [1.18–1.45] for males and females, respectively). After controlling for the subjects' BMI or WC, wrist circumference was an independent predictor of diabetes only among females. Wrist circumference was an independent predictor of metabolic syndrome only among women even after adjustment for BMI, WC, or both.

Conclusions: Wrist circumference is a significant predictor of diabetes in both genders of adult population. However, its predictability is independent of BMI or WC only among females. Because of its simple and easy-to-detect nature, wrist circumference could be considered as a new anthropometric assessment for prediction of type 2 diabetes and metabolic syndrome. (*J Clin Endocrinol Metab* 98: 777–784, 2013)

The prevalence of diabetes and obesity is growing rapidly in both developed and developing communities (1–5). Obesity has already been proved to be a cause of type 2 diabetes mellitus (hereafter, diabetes) (6). Vague et al (7) described characteristics of body fat distribution patterns leading to diabetes and atherosclerosis; since then, multiple general and central obesity measures have

been studied as diabetes predictors. Wrist circumference is a simple anthropometric measure of the skeletal frame size (8), and it has recently been suggested to be associated with insulin resistance in obese children and adolescents in a cross-sectional study (9). No study has yet prospectively examined the predictive ability of this anthropometric measure for diabetes in a study of an adult population.

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Abbreviations: BMI, Body mass index; BP, blood pressure; CI, confidence interval; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; 2h-PLG, 2-hour post-challenge plasma glucose; IGT, impaired glucose tolerance; MetS, metabolic syndrome; OR, odds ratio; SBP, systolic BP; TG, triglyceride; TLGS, Tehran Lipid and Glucose Study; WC, waist circumference.

Our objective is to determine whether wrist circumference predicts diabetes incidence in adults of a prospective population-based study, the Tehran Lipid and Glucose Study (TLGS).

Subjects and Methods

Study subjects

The study design of the TLGS has been described in detail previously (10). Briefly, from February 1999 to August 2001, a total of 15 005 residents of District 13 of Tehran aged over 3 years were enrolled in the ongoing prospective TLGS study; subjects were categorized into the cohort and intervention groups at baseline, the latter to be educated for implementation of lifestyle changes. This study was designed for and aimed at determining the risk factors and outcomes for noncommunicable diseases, performing regular assessments at 3-year intervals. Until October 2011, 4 follow-up visits were done for all cases.

From a total of 15 005 subjects, we excluded subjects aged <20 years (n = 4637), those with missing data on their diabetes status (using glucose-lowering drugs or high fasting plasma or 2-hour postload glucose levels) or wrist circumference measurement (n = 1038) at baseline, leaving 9330 cases (3934 males and 5396 females). For prospective survival analysis regarding subjects' future diabetes status, we also excluded subjects with a prevalent diabetes at their baseline visit (n = 1135) or those with missing data on their diabetes event at all visits (n = 1802) leaving 6393 subjects (2716 males and 3677 females).

The protocol for the selection of the subjects is shown in detail in a flowchart (Figure 1).

Secondarily, we also examined the predictability of wrist circumference for future incidence of impaired glucose tolerance (IGT) as well as metabolic syndrome (MetS) as prediabetes states. For these analyses, we excluded baseline prevalent cases of IGT and MetS, respectively, leaving 5532 (2381 males and 3151 females) and 4079 (1730 males and 2349 females) subjects for IGT and MetS studies, respectively.

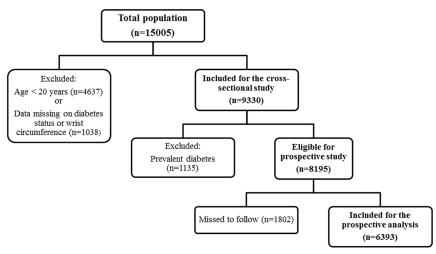


Figure 1. Flowchart showing study population selection method; subjects were selected from the population of the TLGS.

Clinical and laboratory measurements

At the beginning of the cross-sectional phase, all participants provided written informed consent, which was approved by the institutional ethics committees (Research Institute for Endocrine Sciences) and was conducted in accordance with the principles of the Declaration of Helsinki (11). Thereafter, collection of demographic data and anthropometric examinations were undertaken by trained general physicians (10).

A trained interviewer collected information using a pretested questionnaire. The information obtained included demographic data, family history of diabetes, and their medication use. Wrist circumference was measured to the nearest 0.1 cm using a tape meter. Subjects were asked to hold their wrist anterior surface up; the superior border of the tape measure was placed just distal to the prominences of radial and ulnar bones. The wrist circumference was measured without any tape pressure over it. Details of anthropometric measurements including height, body mass index (BMI), waist circumference (WC), and blood pressure (BP) measurements reported elsewhere (12). Digit preference score was 9.32 for all anthropometric measurements including wrist circumference.

After 12 to 14 hours overnight fasting, a blood sample was taken from the participants between 7:00 and 9:00 AM. Blood samples were taken in a sitting position according to the standard protocol and were then centrifuged within 45 minutes of collection. The standard oral glucose tolerance test was performed for all participants not on glucose-lowering drugs. Clinical and laboratory measurements methodology has been explained in detail elsewhere (10).

Definition of terms and outcomes

According to the American Diabetes Association definition, participants with fasting plasma glucose (FPG) \geq 7 mmol/L or 2-hour postchallenge plasma glucose (2h-PLG) \geq 11.1 mmol/L or those who used antidiabetic drugs were defined as having diabetes; and IGT also was described as 2h-PLG being \geq 7.8 mmol/L or <11.1 mmol/L (13).

MetS was defined according to the 2009 scientific consensus (14) but using appropriate cutoff points of WC for prediction of incident cardiovascular disease in Iranian men and women (15).

A positive family history of diabetes was considered as having at least 1 parent or sibling with diabetes mellitus; and the event date for any of the positive events (type 2 diabetes, MetS, or IGT) was defined as the midtime between the date of follow-up visit at which the diabetes was diagnosed for the first time (based on the use of glucose-lowering drugs and FPG and 2h-PLG tests results) and the most recent visit prior to the diagnosis of diabetes; and for those with negative event (censor subjects), the time was the interval between the first and the last observation dates. A similar method was applied for the calculation of event date for other events (IGT or MetS).

Statistical analysis

We split the population data based on subjects' sex for all analyses. Age-adjusted partial correlation coefficients were calculated between wrist circumference and continuous diabetes risk factors.

We also designed regression models for cross-sectional as well as prospective studies. Wrist circumference, BMI, and WC were standardized to a mean of 0 and SD of 1 to facilitate comparisons of the regression coefficients across different models; and all other numerical risk factors were natural logarithm-transformed to improve normality of their distributions.

In all regression models, model 1 was adjusted for the subjects' age (years) and their participation in the lifestyle change program (intervention) (yes, no), and model 2 was adjusted additionally for family history of diabetes (yes, no), FPG (mmol/L), 2h-PLG (mmol/L), triglyceride (TG) to high-density lipoprotein cholesterol (HDL-C) ratio, and systolic BP (SBP) (mm Hg). Each model was subsequently further adjusted for the subjects' BMI as well as their WC to examine the confounder effect of these obesity measures on wrist circumference.

Age- and intervention-adjusted linear regression models were applied to investigate any linear association between wrist circumference and that of numerical risk factors of diabetes (3, 16), and a binary logistic model was applied to examine the association between wrist circumference and family history of diabetes. We also constructed a binary logistic model to assess whether wrist circumference is significantly associated with the subjects' baseline status regarding diabetes (diabetes = 1, no diabetes = 0), IGT (IGT = 1, no IGT = 0), and MetS (MetS = 1, no MetS = 0).

To prospectively investigate whether subjects' baseline wrist circumference was associated with the development of IGT, MetS, or diabetes mellitus, we constructed Cox proportional hazard models.

With above-mentioned outcomes, model 1 included the subjects' age and wrist circumference and model 2 was further adjusted for family history of diabetes, intervention participation, and natural logarithm of baseline FPG, 2h-PLG, SBP, and TG/HDL-C levels. In all models containing MetS as outcome, model 2 was further adjusted for previous history of cardiovascular disease (yes, no).

The proportionality of the multivariable Cox model was assessed both visually (considering tertiles of wrist circumference as the strata variable) and using Schoenfeld's global test of residuals (17). Acquired hazard ratios of a 1-SD increase in wrist circumference were compared against that of BMI or WC using Wald χ^2 test when wrist circumference was entered in a multivariable-adjusted model simultaneously with any of these measures (18).

To determine an appropriate cutoff point of wrist circumference to predict incidence of diabetes over a subpopulation of above-mentioned subjects with valid data upon their diabetes status on phase 4 assessment (1965 men and 2689 women), we performed a receiver-operator curve analysis regarding the subjects' phase 4 diabetes status as the outcome variable and wrist circumference as the exposure. The appropriate cutoff of wrist circumference was defined by calculating Youden's J statistics (sensitivity + specificity - 1) for each cutoff measure of wrist circumference and a cutoff wrist circumference measure with the maximum value of Youden's index was taken as the appropriate cutoff value. The cutoff points were determined both in overall and separately for tertiles of body height of both genders.

Table 1. Baseline Characteristics of the Study Population^a

Baseline Measures	Males (n = 3934)	Females (n = 5396)
Age, y	44.8 ± 15.2	42.4 ± 13.9
Wrist circumference, cm	17.7 ± 0.9	16.1 ± 1.1
BMI, kg/m ²	25.9 ± 4.1	27.7 ± 5.0
WC, cm	88.9 ± 11.3	88.3 ± 12.7
FPG, mmol/L	5.49 ± 1.72	5.50 ± 2.02
2h-PLG, mmol/L	6.35 ± 3.24	6.67 ± 2.93
SBP, mm Hg	121.4 ± 19.0	119.7 ± 20.0
TG/HDL-C	2.38 ± 2.33	1.80 ± 1.59
Positive family history of diabetes, n (%)	1053 (26.8)	1583 (29.3)
Intervention participation, n (%)	1494 (38.0)	2060 (38.2)

^a Results are shown as mean \pm SD unless indicated otherwise.

We performed all analyses using IBM SPSS for Windows version 20 and STATA version 12 SE. A two-tailed P value < .05 was considered significant in all analyses.

Results

Cross-sectional perspective

Mean age of the baseline population was 44.8 ± 15.2 years for males and 42.4 ± 13.9 years for females; and the mean wrist circumference was 17.7 ± 0.9 cm in males and 16.1 ± 1.1 cm in females. Family history of diabetes was positive in 26.8% of men and 29.3% of women.

Baseline characteristics of the study population are presented in Table 1.

Wrist circumference was significantly correlated to simultaneous measurements of numerical risk factors of diabetes in the studied population. Age-adjusted correlation coefficient for FPG was 0.09 in males and 0.12 in females (P < .0001 for both analyses) and for 2h-PLG it was 0.05 in males and 0.09 in females (P = .002 and P < .0001, respectively). When adjusted for age, wrist circumference among males was 62% correlated with both BMI and WC; these values were 62% and 57%, respectively, among female subjects (P < .0001 for all analyses) (Supplemental Table 1, published on The Endocrine Society's Journals Online web site at http://jcem.endojournals.org).

The results of regression analyses on the associations between wrist circumference and diabetes risk factors have been also presented in detail in Table 2. From among diabetes risk factors, only SBP and TG/HDL-C among females preserved their positive association with the wrist circumference after adjusting for BMI or WC in cross-sectional association analysis.

Table 2. Results of Linear Regression Analysis Demonstrating Associations Between Wrist Circumference and the Subjects' Baseline Diabetes Risk Factors

	Males		Females		
	B (SE)	Adjusted R ²	B (SE)	Adjusted R ²	
Fasting plasma glucose, mmol/L Model 1	0.020 (0.004) P < .0001	0.101	0.022 (0.003) P < .0001	0.139	
Model 1 + BMI	0.002 (0.004) P = .652	0.111	0.016 (0.004) P < .0001	0.138	
Model 1 + WC	<0.0001 (0.004) P = .945	0.114	0.001 (0.005) P = .786	0.149	
2h-PGL, mmol/L					
Model 1	0.018 (0.006) P = .003	0.132	0.036 (0.005) P < .0001	0.161	
Model 1 + BMI	-0.047 (0.008) P < .0001	0.173	-0.002 (0.006) P = .784	0.179	
Model 1 + WC	-0.050 (0.008) P < .0001	0.179	-0.010 (0.006) P = .083	0.194	
SBP, mm Hg					
Model 1	0.020 (0.002) P < .0001	0.190	0.025 (0.002) P < .0001	0.329	
Model 1 + BMI	-0.003 (0.003) P = .348	0.227	0.013 (0.002) P < .0001	0.337	
Model 1 + WC	-0.001 (0.003) $P = .618$	0.225	0.013 (0.002) P < .0001	0.338	
TG/HDL-C	7 .010		. 4.0001		
Model 1	0.144 (0.011) P < .0001	0.048	0.156 (0.10) P < .0001	0.160	
Model 1 + BMI	-0.018 (0.014) P = .204	0.127	0.063 (0.012) P < .0001	0.186	
Model 1 + WC	-0.034 (0.014) $P = .012$	0.148	0.055 (0.011) P < .0001	0.199	
Family history of diabetes ^a	7 - 1012		7 (1000)		
Model 1	1.136 (1.056-1.223) ^b P = .001	0.011 ^c	1.045 (0.980-1.114) ^b P = .179	0.008 ^c	
Model 1 + BMI	$0.961 (0.875-1.056)^{b}$ P = .413	0.023 ^c	0.938 (0.866–1.017) ^b P = .124	0.013 ^c	
Model 1 + WC	0.969 (0.883–1.063) ^b P = .502	0.022 ^c	$0.946 (0.875-1.022)^{b}$ P = .158	0.013 ^c	

Model 1 was adjusted for the subjects' age and their intervention participation; all numerical risk factors were Ln-transformed, and wrist circumference, BMI, and WC were transformed to a mean of zero and SD of 1. Statistically significant associations are shown in bold. R², coefficient of determination; B, regression coefficient.

Association of wrist circumference with diabetes and prediabetic states

Table 3 demonstrates the results of the analyses of association between wrist circumference and diabetes and prediabetic states IGT and MetS both in cross-sectional and prospective settings.

In cross-sectional analysis, in model 1, wrist circumference was significantly associated with the subjects' simultaneous diabetes status in both genders. After controlling for the subjects' BMI or WC, the association was no longer statistically significant in either gender. Although the results were similar for IGT, wrist circumference was significantly associated with the subjects' MetS status even after controlling for BMI in both genders (odds ratio

[OR] = 1.99 and 1.88 for males and females, respectively, P < .0001 for both genders) and WC among females (OR = 1.17, P = .013).

Prospective study setting

Of the eligible population (n = 8195), 6393 cases (2716 males, 3677 females) completed their follow-up for their diabetes status for a mean period of 8.77 ± 2.49 years (participation rate, 78%). During this period, a total of 649 new cases of diabetes occurred (269 males and 380 females). The incidence rate of diabetes was 11.3 per 1000 person-years (95% confidence interval [CI], 10.0–12.7) among males and 11.8 per 1000 person-year (95% CI, 10.7–13.1) among females. The baseline characteristics of

^a Binary logistic regression was applied.

^b Standardized ORs (95% CI) were reported.

^c Nagelkerke R².

Table 3. Results of Cross-Sectional Association (Binary Logistic Regression) and Prospective Predictability (Cox Proportional Hazard Regression) of a Baseline Measurement of Wrist Circumference for Simultaneous and Future IGT, MetS, and Type 2 Diabetes Mellitus Among Males and Females^a

	IGT		MetS		Diabetes	
	Males	Females	Males	Females	Males	Females
Cross-sectional association						
Model 1 ^b	1.19 (1.07–1.33) P = .001	1.23 (1.13-1.34) P < .0001	2.16 (2.00-2.34) P < .0001	2.21 (2.05-2.39) P < .0001	1.25 (1.13–1.39) P < .0001	1.22 (1.12–1.33) P < .0001
Model 2 ^c	0.82 (N/A) P = .994	1.38 (N/A) P = .990	1.99 (1.78-2.22) P < .0001	1.88 (1.70-2.09) P < .0001	0.85 (0.64–1.11) P = .233	1.00 (0.75-1.32) P = .991
Model 2 + BMI			1.12 (0.98-1.28) P = .095	1.17 (1.03–1.33) P = .013		
Model 2 + WC			1.01 (0.88-1.15) P = .912	1.06 (0.93-1.20) P = .367		
Prospective predictability						
Model 1 ^b	1.07 (0.97–1.18) P = .199	1.11 (1.02–1.21) P = .018	1.35 (1.25-1.45) P < .0001	1.45 (1.36-1.55) P < .0001	1.41 (1.25–1.59) P < .0001	1.50 (1.35-1.65) P < .0001
Model 2 ^c		0.99 (0.90-1.09) P = .890	1.32 (1.22-1.42) P < .0001	1.40 (1.30-1.50) P < .0001	1.17 (1.03–1.32) P = .012	1.31 (1.18-1.45) P < .0001
Model 2 + BMI			1.06 (0.97-1.16) P = .188	1.15 (1.06-1.25) P = .001	1.03 (0.89-1.20) P = .685	1.17 (1.04-1.33) P = .012
Model 2 + WC			1.03 (0.94–1.13) P = .480	1.14 (1.05–1.24) P = .002	1.04 (0.89–1.20) P = .640	1.16 (1.03–1.30) P = .018
Model 2 + BMI + WC			r = .480	P = .002 1.10 (1.01–1.20) P = .023	r = .640	1.15 (1.02–1.31) P = .025

Abbreviation: N/A, not available.

this followed population have been compared with those of the missed-to-follow-up population in Supplemental Table 2.

After allocating the subjects into tertiles of baseline wrist circumference in male and female populations, overall incidence of diabetes during an average of 8.8 years was 6.0%, 9.6%, and 14.8% in subsequent tertiles of baseline wrist measures, respectively, among males; and 4.6%, 10.8%, and 18.5% among the female population (*P* for trend <0.0001 in both genders) (Figure 2).

When considering a prospective setting with diabetes as the outcome variable in Cox proportional hazard models, wrist circumference was associated significantly with the incidence of diabetes in the age- and intervention participation-adjusted model in both genders.

The incidence of diabetes increased 41% in males and 50% in females for each 1-SD increase in wrist circumference (0.9 cm for males and 1.0 cm for females) in model 1; after controlling for multiple diabetes risk factors (model 2), a 1-SD increase in the subjects' wrist circumference was associated with a 17% increase in diabetes incidence in males (P = .012) and a 31% increase of diabetes incidence among females (P < .0001).

After considering BMI or WC as a confounder, the hazard ratios attributable to wrist circumference dropped to nonsignificant levels in males. Among females, however,

after considering BMI or WC or both as confounder variables, a 1-SD increase in the wrist circumference was associated with a 17%, 16%, and 15% increase in diabetes incidence, respectively (all P < .05).

When comparing predictive values of wrist circumference with that of BMI or WC for diabetes, there was no statistically significant difference between acquired hazard ratios of wrist circumference and BMI or WC when the measures were entered simultaneously in the multivariable-adjusted model either in males or in females (Supplemental Table 3).

On proportionality assessment of the multivariable Cox model, no significant interaction was seen between the model variables and time in Schoenfeld's global test of the residuals ($\chi^2 = 11.80$, df = 8, P = .160). In visual assessment also, considering tertiles of wrist circumference as the strata, no cross was seen among different categories of wrist circumference regarding log-log graph in either of the genders (Supplemental Figure 1).

Baseline measure of wrist circumference was a strong predictor of MetS during follow-up in the multivariable model and after adjustment for BMI, WC, or both among females (hazard ratio = 1.40, 1.15, 1.14, and 1.10, respectively; P < .05 for all analyses). However, among males, although it was a significant predictor of MetS in the multivariable model, wrist circumference lost its pre-

^a Figures show ORs for logistic regression and hazard ratios for Cox proportional hazard regression analyses for a 1-SD increase of wrist circumference; 1 SD means 0.9 cm for all outcomes in males and 1.0 cm for IGT and diabetes and 0.9 cm for MetS in females. Statistically significant associations are shown in bold.

b Adjusted for subjects' natural logarithm of age (years) and their participation in the lifestyle change program (intervention) (yes, no).

^c Adjusted for variables in model 1 and family history of diabetes (yes, no), and natural logarithm of fasting plasma glucose (mmol/L), 2h-PGL (mmol/L), serum TG/HDL-C ratio, and SBP (mm Hg).

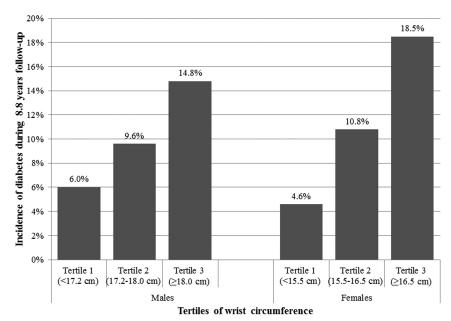


Figure 2. Incidence of diabetes during 8.8 years of follow-up in different tertiles of baseline wrist circumference among male and female populations (P for trend < .0001 in both genders)

dictability after taking into account the subjects' BMI or WC. Baseline wrist measure was not a statistically significant predictor of future IGT in the multivariable model (model 2) in either of genders, although it was of statistically significant predictability only in age- and intervention participation-adjusted model (model 1) among females (hazard ratio = 1.11, P = .018).

Appropriate cutoff points of wrist circumference to predict the incidence of diabetes after an average of 8.8 years were, respectively, 15.7, 16.0, and 16.4 cm in 3 consecutive tertiles of body height among females (Supplemental Table 4). When ignoring the subjects' body height, the overall cutoff wrist circumference was 15.7 cm (sensitivity = 80.6%, specificity = 53.0%, Youden's J statistic = 0.277) (Supplemental Figure 2).

Discussion

According to our results, in a population aged ≥ 20 years, wrist circumference was significantly associated with diabetes and its well-known risk factors in a cross-sectional setting and was a significant predictor of future development of diabetes and MetS (as prediabetes state) in both genders as well. Wrist circumference could be a predictor of diabetes and MetS even after controlling for BMI or WC only among females.

Various skinfold and circumference measurements have already been studied as predictors of diabetes. However, there are few studies regarding wrist circumference. Freedman and Rimm (19) studied the cross-sectional as-

sociation between 6 different girth measurements and prevalent diabetes in a population of U.S. and Canadian women, and they reported a statistically significant positive association between the highest tertile of wrist circumference and diabetes (OR = 1.3, P = .006); in their study, after controlling for the subjects' age and BMI (Quetelet index), diabetic women had larger neck, bust, and wrist circumferences. Later, a pilot study of nondiabetic Italian adolescent athletes demonstrated statistically significant higher wrist circumference measures in those with a positive family history of diabetes in comparison with those with a negative family history, a difference seen only among male subjects rather than females (20).

In our study of an Iranian adult population with large sample size, wrist cir-

cumference was significantly associated with the FPG, SBP, and TG/HDL-C values in both genders in the crosssectional analysis; BMI and WC explained most of the associations seen with all of the measures in males. However, among females, the associations were mostly independent of general (BMI) and central (WC) obesity measures. Wrist circumference was associated with the family history of diabetes in males rather than females, a finding reported previously among adolescents (20); however, inclusion of BMI or WC in the regression model reduced the association to a statistically nonsignificant level.

In this prospective analysis, wrist circumference showed a significant association with incident diabetes as well as incident MetS (as prediabetes state) in both males and females. Among males, the association was no longer statistically significant after the inclusion of central or general obesity measures as confounders, concordant with the cross-sectional analysis results. In fact, it was demonstrated that among males, about 82.3% {[(17 - 3)/17] $\times 100$ } and 76.5% {[(17 - 4)/17] $\times 100$ } of the observed hazard ratios with the wrist circumference could be explained by cofounding effects of BMI and WC, respectively. However, among females, wrist circumference was a strong predictor of both diabetes and MetS despite these obesity measures. In fact, $45.2\% \{[(31 - 17)/31] \times 100\}$ and 51.6% {[(31 - 15)/31] ×100} of hazard ratios for diabetes could be explained by confounding effects of BMI and WC, respectively.

Although Vague et al (7) emphasized the upper body obesity (android obesity) as a predictor of metabolic and cardiovascular risk among women rather than men, wrist girth has already been only weakly correlated with total body fat in women (21); other studies suggest that this peripheral girth may partly reflect regional fat deposition (19). In the present study, the independence of wrist circumference from general and central obesity measures in women in the prediction of diabetes and MetS is in line with previous cross-sectional studies (9, 19), although no previous study has shown the results in male and female populations separately.

Differences between the two genders regarding the association between wrist girth and diabetes occurrence could be explained by the effects of sex steroid hormones and their interaction with bone metabolism and glucose homeostasis (22, 23). Recently, it has been shown that in addition to the pancreatic β -cells and the hepatocytes, bones surprisingly may also be involved as an endocrine organ in the regulation of whole-body glucose metabolism (24, 25).

Wrist circumference is a simple, easy-to-detect anthropometric measure, and it is not subject to measurement problems involved in assessment of other anthropometrics like WC and hip circumference; clothing is one major perturbing factor complicating the measurement of waist and hip circumferences (26) as compared with measurement of wrist circumference.

Our study presents a new finding that is worth further assessment using data from larger cohorts that regard diabetes as their outcome measure. On the other hand, basic and experimental studies are needed to elucidate the basic mechanisms involved in the associations between wrist circumference and diabetes or its risk factors as well as the effects of sex hormones.

As strengths, we examined our hypothesis on a large cohort of an adult population with 8.8 years follow-up, which in the best way could determine the predictive value of wrist circumference for the incidence of future diabetes compared with cross-sectional study. In addition, we put the cross-sectional and prospective analyses results together to show whether the prospective analysis of the cohort data would confirm the significant associations of wrist circumference with the main risk factors of diabetes seen in the cross-sectional study. On the other hand, we performed the diagnosis of diabetes using 2h-PLG measures in addition to the subjects' FPG measurements.

As for limitations, just one measurement of FPG or 2h-PLG for the diagnosis of diabetes in our study, which is popular in epidemiological studies, may lead to an over-diagnosis of diabetes. On the other hand, higher measures of some diabetes risk factors in male participants compared with missed-to-follow-up counterparts may cause higher incidence of diabetes in the prospective analysis

among the male population; both these limitations cause an underestimation rather than an overestimation of the actual associations between wrist circumference and the incidence of diabetes. Also, our study population was from Tehran, the capital city of Iran. Therefore, we may not be able to generalize our findings to other populations; we suggest that our results be assessed in different cohorts of other countries or those that include different ethnic groups in their study population.

To conclude, wrist circumference is a significant predictor of diabetes and MetS in an adult population. However, its predictability is independent of general and central obesity measures only among females. Being a simple and easy-to-detect measure, it could be regarded as a new anthropometric assessment for prediction of type 2 diabetes and MetS.

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References

- 1. Danaei G, Finucane MM, Lu Y, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. *Lancet.* 2011;378:31–40.
- Finucane MM, Stevens GA, Cowan MJ, et al. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet*. 2011;377:557– 567.
- 3. Harati H, Hadaegh F, Saadat N, Azizi F. Population-based incidence of Type 2 diabetes and its associated risk factors: results from a six-year cohort study in Iran. *BMC Public Health*. 2009;9:186.
- 4. Hosseinpanah F, Barzin M, Eskandary PS, Mirmiran P, Azizi F. Trends of obesity and abdominal obesity in Tehranian adults: a cohort study. *BMC Public Health*. 20099:426.
- Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract. 2011;94:311–321.
- 6. Eckel RH, Kahn SE, Ferrannini E, et al. Obesity and type 2 diabetes: what can be unified and what needs to be individualized? *J Clin Endocrinol Metab*. 2011;96:1654–1663.

- Vague J, Vague P, Tramoni M, Vialettes B. Clinical features of diabetogenic and atherogenic obesity. *Tohoku J Exp Med*. 1983; 141(Suppl):147–159.
- 8. Grant JP, Custer PB, Thurlow J. Current techniques of nutritional assessment. Surg Clin North Am. 1981;61:437–463.
- Capizzi M, Leto G, Petrone A, et al. Wrist circumference is a clinical marker of insulin resistance in overweight and obese children and adolescents. *Circulation*. 2011;123:1757–1762.
- Azizi F, Ghanbarian A, Momenan AA, et al. Prevention of noncommunicable disease in a population in nutrition transition: Tehran Lipid and Glucose Study phase II. *Trials*. 2009;10:5.
- World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. *J Indian Med Assoc.* 2009;107:403–405.
- Azizi F, Rahmani M, Emami H, Madjid M. Tehran Lipid and Glucose Study: rationale and design. CVD Prev. 2000;3:242–247.
- American Diabetes Association Standards of medical care in diabetes–2011. *Diabetes Care*. 2011;34(Suppl 1):S11–S61.
- 14. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120:1640–1645.
- Hadaegh F, Zabetian A, Sarbakhsh P, Khalili D, James WP, Azizi F. Appropriate cutoff values of anthropometric variables to predict cardiovascular outcomes: 7.6 years follow-up in an Iranian population. *Int J Obes (Lond)*. 2009;33:1437–1445.
- 16. Bozorgmanesh M, Hadaegh F, Ghaffari S, Harati H, Azizi F. A simple risk score effectively predicted type 2 diabetes in Iranian adult

- population: population-based cohort study. Eur J Public Health. 2011;21:554-559.
- 17. **Schoenfeld D.** Partial residuals for the proportional hazards regression model. *Biometrika*. 1982;69:239–241.
- Stiger TR, Barnhart HX, Williamson JM. Testing proportionality in the proportional odds model fitted with GEE. Stat Med. 1999;18: 1419–1433.
- Freedman DS, Rimm AA. The relation of body fat distribution, as assessed by six girth measurements, to diabetes mellitus in women. Am J Public Health 1989;79:715–720.
- Pomara F, Grosso F, Basile D, et al. [A pilot study on adolescents of both sexes. Correlation between phenotype, athletic performances and family history to type 2 diabetes]. *Minerva Pediatr*. 2010;62: 425–430. (Italian)
- 21. Steinkamp RC, Cohen NL, Gaffey WR, et al. Measures of body fat and related factors in normal adults. II. A simple clinical method to estimate body fat and lean body mass. *J Chronic Dis.* 1965;18: 1291–1307.
- 22. Blaak E. Sex differences in the control of glucose homeostasis. *Curr Opin Clin Nutr Metab Care*. 2008;11:500–504.
- Callewaert F, Sinnesael M, Gielen E, Boonen S, Vanderschueren D. Skeletal sexual dimorphism: relative contribution of sex steroids, GH-IGF1, and mechanical loading. *J Endocrinol*. 2010;207:127– 134.
- Fukumoto S, Martin TJ. Bone as an endocrine organ. Trends Endocrinol Metab. 2009;20:230–236.
- 25. Lee NK, Sowa H, Hinoi E, et al. Endocrine regulation of energy metabolism by the skeleton. *Cell*. 2007;130:456–469.
- Wills SD, Bhopal RS. The challenges of accurate waist and hip measurement over clothing: Pilot data. Obes Res Clin Pract. 2010;4:e239-e244.





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