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Research Article

Wrist Circumference in Relation to the Risk of Metabolic Syndrome in Middle-Aged and Elderly Chinese Patients with Type 2 Diabetes

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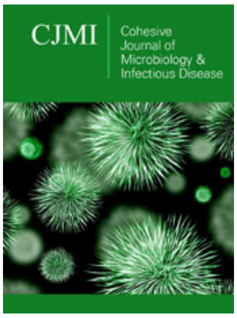

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Abstract

Objective: In this study, we aimed to determine whether wrist circumference is associated with increased with of metabolic syndrome (MetS) among middle-aged and elderly Chinese type 2 diabetes (T2DM) subjects.

Method: A total of 470 type 2 diabetes hospitalized patients were included in the study. Data on demographic characteristics, anthropometry and variables were collected. Serum lipid profile, HbA1c, and beta-cell function were detected in blood samples. The diagnosis of MetS was ascertained by the International Diabetes Federation (IDF) criteria. Results: The mean of wrist circumference in male and female patients were 15.5 and 17.0cm, respectively. Weight, body mass index, waist circumference, triglycerides and incident MetS gradually increased with the increment of wrist circumferenc etertiles and HDL gradually decreased with the increment of wrist circumference tertiles (all $P<0.05$) even after adjustment of onset age of diabetes and duration of T2DM in both gender. When adjusted for body mass index, and waist circumference, the association between wrist circumference and MetS remained significant only among the normal group women ($BMI<25kg/m^2$).

Conclusion: These results suggested that a higher wrist circumference was associated with higher risk for MetS in T2DM subjects, especially in the female T2DM with $BMI<25kg/m^2$.

Keywords: Wrist circumference; Type 2 diabetes; Metabolic syndrome

Introduction

The metabolic syndrome is the clustering of abdominal obesity, hypertension, hyperglycemia, elevated triglycerides, and/or decreased high-density lipoprotein cholesterol (HDL) levels [1]. The prevalence of metabolic syndrome has grown markedly worldwide during the past decades. The syndrome not only contributes to the risk of cardiovascular diseases and type 2 diabetes, but also cardiovascular morbidity and mortality [2-4]. The core manifestation of metabolic syndrome is insulin resistance, which is associated with each individual metabolic syndrome components [5,6]. Wrist circumference, an easy to measure anthropometric index of body frame and bone size, has recently been suggested to be associated with insulin resistance in both children and adults [7,8]. Furthermore, wrist circumference proved to be a significant predictor of diabetes in both genders of adult population, but its predictability was independent of body mass index or waist circumference only in females [9]. A result of a decade follow-up in a West Asian cohort showed that wrist circumference as a novel predictor of hypertension and cardiovascular disease [10], while it was in contrast with a media follow-up of nine years study showing a higher wrist circumference was a negative predictor for incident cardiovascular disease among adult men [11]. However, limited data was available on the association between wrist circumference and metabolic syndrome. Only one study stated that wrist circumference was significant association with incident metabolic syndrome (as pre-diabetes state) in both males and females [9]. Our objective is to assess the association between wrist circumference and metabolic syndrome among middle-aged and elderly type 2 diabetes patients requiring admission to a large urban hospital in China.

Method

Patients

A total of 193 female and 277 male patients with type 2 diabetes who were admitted to the Shanghai Tenth People's Hospital between January 2014 and December 2015 were recruited in our study. Exclusion criteria included 1) clinical symptoms with generalized edema; 2) hyperthyroidism; 3) hypothyroidism; 4) the presence or history of cancer; 5) moderate or severe liver and renal dysfunction. The diagnosed of type 2 diabetes was based on the American Diabetes Association definition. Metabolic syndrome was defined according to the International Diabetes Federation (IDF) definition (1). According to the IDF definition, a person was defined as having metabolic syndrome if he or she had central obesity (defined as waist circumference ≥90cm for men and ≥80cm for women) plus any two of the following four factors: 1) Raised triglyceride level: ≥150mg/dL (1.7mmol/L), or specific treatment for this lipid abnormality, 2) Reduced high-density lipoprotein cholesterol: <40mg/dL (1.03mmol/L) in males and<50 mg/dL (1.29mmol/L) in females, or specific treatment for this lipid abnormality, 3) Raised blood pressure: systolic blood pressure ≥130 or diastolic blood pressure≥85mm Hg, or treatment of previously diagnosed hypertension, 4) Raised fasting plasma glucose≥100mg/dL (5.6mmol/L), or previously diagnosed type 2 diabetes. The study protocol was approved by the Institutional Human Subjects Review Board of Shanghai Tenth People's Hospital, and all participants gave their informed consent.

Measurements

Age, age of onset, and duration of diabetes, family history, blood pressure, height, body weight and body mass index (BMI) were obtained. Wrist circumference was measured to the nearest 0.1cm using a tape measure. 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. Waist Circumference was measured against the skin at the natural waist (midpoint between the top of the iliac crest and the lower ribs) with a non-elastic flexible tape measure. After 12 hours of overnight fasting, laboratory test parameters were collected in the morning during the patients' admission, including Total Cholesterol (TC), Triglyceride (TG), High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), Free Fatty Acid (FFA), Uric Acid (UA), glycosylated hemoglobin A1c (HbA1c), fasting plasma glucose, and fasting C-peptide. The standard meal-load test (70g of instant noodles equivalent to an energy intake of 500 kilocalories) was performed [12], followed in 120 minutes by examination of plasma glucose, insulin, and C-peptide. AUC (Area Under the Curve) was calculated with the following equations (AUC for glucose, for example): AUC for glucose= (glucose 0min + glucose30min)×30/2+(glucose 30min+glucose120min) × 90/2+(glucose120 min + glucose180min) × 60/2 [13]; glucose 0 min denotes the glucose concentration tested just before the patient started the standard meal, and glucose 30 min the concentration tested 30 min after starting the meal, and so on.

Statistical Analysis

Data were expressed as mean ± standard deviation (SD) for normal distribution and expressed as median (upper and lower quartiles) for skewed distribution. Standard T test was used to compare the baseline morphometric measurements. Data of skewed deviations were compared by nonparametric test. Pearson's correlation analysis was used to investigate the relationship of two indices. Binary logistic analysis was performed to analyze the association between variables and incident MetS. Statistical Product and Service Solutions version 20 (SPSS 20) software were used for statistical analysis. A value of $P<0.05$ was considered statistically significant.

Result

General characteristics of patients with T2DM

Clinical characteristics of the patients (193 females and 277 males) are summarized in Table 1. Mean age of the baseline population was 63.4±12.9 years for females and 58.9±12.8 years for males; and the mean wrist circumference was 15.6±1.2 cm in females and 16.9±0.9 cm in males. Duration of diabetes in female group was longer than that of male group. Onset age of diabetes, family history of diabetes, BMI, hip circumference, TG, FFA, HbA1c, fasting glucose and postprandial glucose were not different between the female and male groups. Blood pressure, AUC for glucose, AUC for c-peptide, TC, LDL in female group were higher than that of male group, whereas uric acid and HDL in female group were lower than in male group. The prevalence of MetS was much higher in female that in male group.

Table 1: Baseline Characteristics of the Study Population.

Items	Total N=470	Females N=193	Males N=277	P- Values
Age (year)	60.7±13.0	63.4±12.9	58.9±12.81	<0.001
Onset Age of Diabetes (year)	49.6±11.9	50.2±12.5	49.2±11.6	0.502
Duration of T2DM (year)	12.20±7.94	13.6±8.6	11.1±7.3	<0.001
Family History of Diabetes (%)	37.9	40.9	35.8	0.154
Weight (kg)	70.3±13.2	64.3±12.0	74.4±12.3	<0.001
BMI (kg/m^2)	25.2±3.9	25.1±4.2	25.3±3.6	0.588
Wrist Circumference (cm)	16.4±1.3	15.6±1.2	16.9±0.9	<0.001
Waist Circumference (cm)	91.5±11.2	89.6±12.9	92.9±9.7	<0.001

Hip Circumference (cm)	96.2±7.4	96.4±8.4	96.1±6.7	0.583
SBP (mmHg)	136.2±19.5	140.0±23.2	134.2±15.5	<0.001
DBP (mmHg)	77.2±11.0	74.6±12.4	78.2±9.6	<0.001
HbA1C (% (mmol/mol))	9.1±4.6	8.9±2.2	9.2±2.3	0.126
Fasting Glucose (mmol/L)	8.9±3.6	9.2±3.8	8.7±3.4	0.13
Postprandial Glucose (mmol/L)	17.9±5.3	18.2±5.9	17.6±4.8	0.274
Fasting C-peptide (ng/ml)	2.0±1.7	2.2±1.9	1.9±1.2	0.157
Postprandial C-peptide (ng/ml)	4.6±3.0	4.9±3.3	4.5±2.7	0.202
AUC for Glucose	2784.0(2272.5-3304.5)	2910.0(2428.1-3529.1)	2718.0(2198.3-3124.5)	0.006
AUC for C-peptide	606.3(393.6-863.65)	622.9(438.2-945.5)	604.4(381.8-817.8)	0.046
TC (mmol/L)	4.7±1.4	4.9±1.3	4.6±1.4	0.019
TG (mmol/L)	1.9(1.0-2.1)	1.8(1.1-2.1)	2.0(1.0-2.1)	0.179
HDL (mmol/L)	1.1±0.3	1.1±0.4	1.2±0.4	0.036
LDL (mmol/L)	2.7±1.1	2.9±1.1	2.6±1.0	<0.001
UA (umol/L)	316.9±104.7	292.9±89.9	332.9±110.8	<0.001
FFA (mmol/L)	0.5±0.2	0.5±0.3	0.5±0.2	0.308
MetS (%)	71.1	78.2	66.4	0.007

Data are presented as mean ± SD or median (inter quartile range). P<0.05 (female vs male).

BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HbA1c: Glycosylated Hemoglobin A1c; AUC: Area Under the Curve; TC: Total Cholesterol; TG: Triglyceride; HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein; FFA: Free Fatty Acid; UA: Uric Acid; MetS: Metabolic Syndrome

Univariate correlations between wrist circumference and component of MetS

The results of all correlation analyses are reported in Table 2. Univariate correlations analysis in the entire cohort showed that wrist circumference was positively associated with weight, BMI, WC, SBP, TG, MetS, and negatively associated with HDL, AUC-glucose. In female, wrist circumference was correlated with weight, BMI, WC, TG, HDL, DBP, AUC for glucose and MetS. In male, wrist circumference was correlated with weight, BMI, WC, TG, HDL, and MetS. There was no significant association between wrist circumference and DBP among three groups. All data were adjusted for age, onset age of diabetes and duration of T2DM.

Table 2: Univariate correlations between wrist circumference and component of MetS.

Items	Total N=470		Females N=193		Males N=277	
	r	P*	r	P*	r	P*
Weight (Kg)	0.726	<0.001	0.668	<0.001	0.598	<0.001
BMI (kg/m^2)	0.512	<0.001	0.618	<0.001	0.692	<0.001
Waist Circumference(cm)	0.516	<0.001	0.43	<0.001	0.622	<0.001
TG (mmol/L)	0.12	0.012	0.226	0.003	0.132	0.034
HDL (mmol/L)	-0.208	<0.001	-0.28	<0.001	-0.166	0.025
AUC- glucose	-0.232	<0.001	-0.289	<0.001	-0.071	0.342
SBP (mmHg)	0.152	<0.001	-0.079	0.367	0.078	0.295
DBP (mmHg)	0.026	0.647	0.182	0.037	0.086	0.25
MetS (%)	0.223	<0.001	0.42	<0.001	0.364	<0.001

*All data were adjusted for age, onset age of diabetes and duration of T2DM.

BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; AUC: Area Under the Curve; TG: Triglyceride; HDL: High-Density Lipoprotein; MetS: Metabolic Syndrome

Association of wrist circumference tertiles with MetS

The patients were divided into three groups according to the cut-off points of the wrist circumference tertiles. From the lowest tertiles to the highest tertiles, the range of wrist circumference was<15.0, 15.0–15.9, and >15.9 cm for females; <16.6, 16.6–17.3, and >17.3 cm for male. Weight, BMI, WC, TG and incident MetS gradually increased with the increment of wrist circumference tertiles and HDL gradually decreased with the increment of wrist circumference tertiles (all P<0.05) even after adjustment of onset age of diabetes and duration of T2DM in both genders. Overall, as well as in both the genders, there was no significant association between wrist circumference and DBP (Table 3). In multivariable model, a significant association was shown between the increase of wrist circumference tertiles and MetS. Furthermore, compared with the participants in the first wrist circumference, those in the other two tertiles had successively a 7.61- and 22.71-fold risk of MetS in females and a 2.18- and 9.60-fold in males after adjustment for various risk factors (Table 4). In the normal women group (BMI<25kg/m^2), after adjusting for variable various characteristics plus BMI and waist circumference, increase in wrist circumference was independently associated with MetS (OR8.45 (1.12-43.61)). However, wrist circumference increase could not predict MetS among the overweight/obese women (BMI≥25 kg/m^2), the normal male or the overweight/obese male groups (Table 5).

Table 3: Component of MetS in patients according to wrist circumference tertiles.

Items	Female				Male			
	Tertile1	Tertile2	Tertile3	P Value	Tertile1	Tertile2	Tertile3	P Value
Weight (Kg)	57.9±10.7	62.9±7.0	72.0±13.5	<0.001	65.5±8.0	73.0±8.5	83.5±12.1	<0.001
BMI (kg/m^2)	22.8±3.6	25.0±3.1	27.5±4.7	<0.001	23.1±2.7	24.8±2.9	27.8±3.5	<0.001
Waist Circumference(cm)	84.5±10.6	90.2±8.9	93.4±16.5	<0.001	86.5±8.0	92.0±7.8	99.6±8.1	<0.001
TG (mmol/L)	1.3(1.0-1.8)	1.5(1.1-2.0)	1.7(1.3-2.3)	0.048	1.2(0.8 -1.9)	1.4(1.0-1.7)	1.7(1.3-2.4)	0.032
HDL (mmol/L)	1.3±0.4	1.2±0.4	1.0±0.2	0.003	1.2±0.3	1.1±0.3	1.0±0.4	0.039
AUC for glucose	3033.0 (2449.5-3592.5)	3003 (2443.1-3548.6)	2571 (2238.0-3145.5)	0.069	2780.3 (2228.6-3232.8)	2730 (2341.9-3291.0)	2677.5 (2178.8-3078.8)	0.598
SBP (mmHg)	136.8±25.8	138.0±19.7	140.1±23.6	0.35	128.6±15.9	131.6±16.1	133.8±14.8	0.346
DBP (mmHg)	74.8±13.7	75.8±10.8	76.2±12.5	0.228	78.0±10.9	78.9±9.5	80.0±8.4	0.365
MetS (%)	59.6	82.2	94.6	<0.001	39.7	70.3	87.4	<0.001

*All data were adjusted for age, onset age of diabetes and duration of T2DM.

BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; AUC: Area Under the Curve; TG: Triglyceride; HDL: High-Density Lipoprotein; MetS: Metabolic Syndrome

Table 4: Association of wrist circumference tertiles with metabolic syndrome.

Metabolism Syndrome	Female					Male		
	OR (95%CI)			P Values	OR (95%CI)			P Values
	Q1	Q2	Q3		Q1	Q2	Q3	
Model 1	1	3.46(1.45-8.24)	13.51(3.66-49.86)	0.001	1	3.60(1.89-6.82)	9.81(4.60 -20.66)	0.001
Model 2	1	4.24(1.68-10.69)	15.75(4.05-41.19)	0.001	1	3.19(3.47-16.24)	7.50(3.47-16.23)	0.001
Model 3	1	4.66(1.51-14.49)	16.20(2.99-53.72)	0.001	1	2.87(1.28-6.42)	7.08(2.78-17.99)	0.001
Model 4	1	7.61(1.83-31.59)	22.79(3.61-63.67)	0.001	1	2.18(1.18-5.20)	9.60(3.37-27.76)	0.001

Analyzed by binary logistic regression analysis; CI: Confidence Interval; OR: Odds Ratio; Model 1, adjusted for age. Model 2, adjusted for age, duration of diabetes and family history of diabetes. Model 3, adjusted for age, duration of diabetes, family history of diabetes, glycated hemoglobin, fasting C-peptide, Postprandial C-peptide. Model 4, adjusted for adjusted for age, duration of diabetes, family history of diabetes, glycated hemoglobin, fasting C-peptide, Postprandial C-peptide, total cholesterol, LDL: Low-Density Lipoprotein, free fatty acid, uric acid

Table 5: Odds Ratios of developing metabolic syndrome for 1 cm increase in wrist circumference beyond other fat distribution.

Metabolism Syndrome	Model	Female		Male	
		OR (95%CI)	P Values	OR (95%CI)	P Values
BMI<25kg/m^2	Model 1	4.23(1.73-10.38)	0.002	2.46(1.30-4.64)	0.005
	Model 2	7.89(1.18-32.63)	0.033	1.17(0.34-3.91)	0.805
	Model 3	8.45(1.12-43.61)	0.038	1.10(0.31-3.85)	0.881
BMI≥25kg/m^2	Model 1	1.86(0.54-2.35)	0.33	1.28(0.54-3.02)	0.581
	Model 2	0.88(0.17-4.44)	0.871	0.43(0.13-1.42)	0.166
	Model 3	0.87 (0.17-4.14)	0.868	0.39 (0.80-1.20)	0.09

Analyzed using binary logistic regression analysis; OR: odds ratio; CI: confidence interval; Model 1, adjusted for adjusted for age, duration of diabetes, family history of diabetes, glycated hemoglobin, fasting C-peptide, total cholesterol, LDL: Low-Density Lipoprotein; free fatty acid, uric acid; Model 2, Model1+Waist circumference; Model 3, Model 2+BMI

Discussion

The wrist circumference parameter is easily accessible and measurable by the doctor, which has been recently demonstrated that it was associated with insulin resistance, diabetes, cardiovascular risk [7-10]. However, limited data was available on the association between wrist circumference and metabolic syndrome. The present study provided the first evidence that wrist circumference was significantly associated with MetS in the middle-aged and elderly T2DM requiring admission requiring admission to a large urban hospital in China. Wrist circumference is considered as a measure of peripheral fat distribution, and it could be a good surrogate to assess bone metabolism in relation to hyperinsulinemia and diabetes [14,15]. Showed that this peripheral girth was related with insulin resistance and claimed that wrist circumference opens a new perspective in the prediction of cardiovascular risk [7]. Amini et al. [16] in a study of 3000 first-degree relatives of diabetic patients found a positive association between wrist circumference and cardio metabolic risk factors [16]. In addition, a recent prospective study demonstrated that wrist circumference was a significant predictor of development of diabetes and MetS as pre-diabetes state [9]. In the light of these findings, we wonder that whether wrist circumference was associated with MetS in patients with T2DM. In our study, after adjusting for age, onset age of diabetes and duration of T2DM, wrist circumference was positively associated with weight, BMI, WC, TG, and negatively associated with HDL, AUC-glucose in both genders. Our results were in generally in line with previous studies that wrist circumference was associated with components of MetS [9,10,16]. However, the results were not significant for SBP and DBP in both genders. This was supported by some studies [11,16], while it was in contradiction to those reached by others which demonstrated with wrist circumference as a novel predictor of hypertension [10].

In this cross-section analysis, wrist circumference was significant related with MetS in both genders as well. Most of hazard ratios for MetS could be explained by confounding effects of BMI and WC in both genders, respectively. However, after controlling for BMI or WC, the association remained significant only among females. Differences between the two genders regarding the association between wrist girth and metabolic risk factors have been reported by the other study, which demonstrated that wrist circumference could be a predictor of diabetes and MetS after controlling for BMI or waist circumference only among females [9]. The higher prevalence of MetS in female group than in male might contribute to find the association of wrist girth and MetS. These observations are generally in accordance with many other studies which reported that, female genders had higher hypertension, hyperglycemia and hyperlipidemia as compared to male counterparts, especially among the elder patients with diabetes [17-19]. The phenomena might be explained by estrogen deficiency, severe low-degree chronic inflammation in female patients [17,20]. Besides, it was reported that wrist circumference could be a good surrogate to assess bone metabolism in relation to hyperinsulinemia and diabetes [14,15]. Bones may also be involved as an endocrine organ in the regulation of whole-body glucose and energy metabolism [21,22]. Thus, the gender difference on bone metabolism might also attribute to the association of wrist girth and MetS in female patients [23,24]. However, when adjusted for BMI and WC, the association between wrist circumference and MetS remained significant only among the normal group women (BMI<25kg/m^2). The similar observation has been reported by Mohebi R et al, which demonstrate that wrist circumference was an independent predictor for incident hypertension and cardiovascular disease events among non-centrally obese women [10]. As we known, both of bone tissue and adipose could regulate energy hemostasis and impact metabolism [21,25-27]. Thus, compared with obesity or overweight patients, the association between wrist circumference and metabolism might be more prominent in patients with normal weight, which might attribute to reduce the effect of adipose on metabolism. Further studies are required to confirm our findings. Limitations of this cross-sectional study were listed as following: first, there was no age matched normal control in the study, and because of all patients from hospitals but not from out-patient, a selection bias might exist in our study that. Those factors will limit the using of wrist circumference as a marker of metabolic syndrome; Second, assessment of wrist circumference levels was based on single measurements, which might underestimate the true strength of the association; Third, the number of samples is relatively small, large number of samples should be recruited to confirm our findings.

Conclusion

According to our results, in the middle-aged and elderly type 2 diabetic patients requiring admission to a large urban hospital in China, wrist circumference was significantly associated with MetS among even after adjustment for various characteristics in both genders as well. However, after considering other fat measures, the association remained significant only among the normal group women (BMI<25kg/m^2).

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