Interest of the waist-to-height ratio to predict metabolic syndrome in type 2 diabetic patients

Intérêt du rapport tour de taille/taille dans la prédiction du syndrome métabolique chez les patients diabétiques de type 2

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ABSTRACT

Introduction : Metabolic syndrome (MetS) is defined as a cluster of risk factors for cardiovascular disease.

Aim: To determine the optimal cut-off point of the waist-to-height ratio (WHtR) at which MetS can be identified with maximum sensitivity and specificity in a sample of Tunisian type 2 diabetic patients.

Methods: We enrolled 457 type 2 diabetic patients in a cross-sectional study. Blood pressure, anthropometric indices, fasting glucose, and lipid profile were measured. WHtR was calculated. MetS was defined according to the IDF criteria. Receiver operating characteristic (ROC) curve analysis was used to identify the optimal cut-off value of WHtR in MetS screening with maximum sensitivity and specificity.

Results: The overall prevalence of MetS was 79.8%, it was higher in women than in men (85.5% vs 61.4%; $p<10-3$). Macrovascular complications were significantly higher among patients with MetS. WHtR was more powerful for predicting MetS in men than in women (Area under ROC curve was 0.913 and 0.761 respectively). The optimal WHtR cut-off value to identify subjects with MetS was 0.55 in men and 0.63 in women.

Conclusion: MetS is a common finding in patients with type 2 diabetes mellitus. WHtR was an ideal tool to predict MetS in men but not in women. Prospective studies with larger cohorts may be required to determine the validity of our results.

Keywords: Type 2 Diabetes mellitus; metabolic syndrome; insulin resistance; anthropometric parameters; Waist to height ratio.

RÉSUMÉ

Introduction: Le syndrome métabolique (SM) est défini comme un groupe de facteurs de risque de maladies cardiovasculaires.

Objectif : Déterminer le seuil optimal du rapport tour de taille / taille (RTT) permettant d'identifier le SM chez le diabétique de type 2 (DT2) avec une sensibilité et une spécificité maximales.

Méthodes: Il s'agit d'une étude transversale ayant inclus 457 patients DT2. La pression artérielle, les paramètres anthropométriques, la glycémie à jeun et le profil lipidique ont été mesurés. Le RTT a été calculé. Le SM a été défini selon les critères de l'IDF. La courbe ROC a été utilisée pour identifier la valeur optimale du RTT dans le dépistage du SM avec une sensibilité et une spécificité maximales.

Résultats: La prévalence du SM était de 79,8%, elle était plus élevée chez les femmes que chez les hommes (85,5% vs 61,4%; p <10-3). Les complications macrovasculaires étaient significativement plus élevées chez les patients atteints de SM. Le RTT était plus performant pour prédire le SM chez les hommes que chez les femmes (l'aire sous la courbe ROC était respectivement de 0,913 et 0,761). La valeur seuil optimale du RTT pour identifier les patients avec SM était de 0,55 chez les hommes et de 0,63 chez les femmes.

Conclusion: Le SM est fréquent chez les patients DT2. Le RTT est un outil idéal pour prédire le SM chez les hommes mais pas chez les femmes. Cependant, des études prospectives avec des cohortes plus importantes sont nécessaires pour confirmer nos résultats.

Mots-clés : Diabète de type 2 ; syndrome métabolique ; insulinorésistance ; paramètres anthropométriques, rapport tour de taille/taille.

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INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a complex metabolic disorder affecting 8.8% of the adult population in the world [1, 2]. It is an increasing worldwide problem which is associated with an increased incidence of cardiovascular diseases [3]. Cardiovascular risk factors are very common in diabetic patients [4]. Moreover, their clustering is a characteristic phenomenon of T2DM [5]. The combination of risk factors is collectively called metabolic syndrome (MetS)[6]. It includes central obesity, impaired glucose tolerance or diabetes, hyperinsulinemia, insulin resistance, hypertension, and dyslipidemia [7]. The worldwide prevalence of MetS ranges from <10% to as much as 80%, depending on the region, sex, age, race, ethnicity, and the definition used. MetS is a highly prevalent clinical entity that can precede or accompany T2DM [8].

Several simplified anthropometric parameters have been proposed to identify diabetic patients who are at risk of MetS. One of these anthropometric measures is the waist-to-height ratio (WHtR) which has been recently shown to outperform the other measures in different ethnic groups [9, 10]. However, rigorous analysis using the WHtR to identify MetS has not been performed on Tunisian patients with T2DM.

The aims of our study were to determine the prevalence of MetS among patients with T2DM and to determine the WHtR cut-off value for MetS screening among Tunisian diabetic populations.

METHODS

Study design

We conducted a cross-sectional study among T2DM patients who attended the Endocrinology department at the Rabta University Hospital in Tunis and the department of External Consultations at the National Institute of Nutrition in Tunis between January and March 2016. The study was approved by the Ethics Committee and informed consent was obtained from all patients for participation in this study. Individuals, men and women, aged 35 years or older with a known and treated T2DM were included. The excluded patients were the ones who did not meet the inclusion criteria or who had type 1 diabetes mellitus, pregnancy, chronic renal failure, hepatic failure, malignancy, and congestive heart failure.

The prevalence of T2DM was 15.5% according to data from the 2016 Tunisian Health Survey whose results are not yet published. Considering a degree of error of 5% and a confidence interval of 95%, the estimated sample size was at least 201 individuals.

Clinical and biochemical Analysis

Demographic characteristics, diabetes mellitus history, diabetes complications, comorbidities (arterial hypertension, dyslipidemia…), physical activity, and smoking habits were determined. Anthropometric parameters were conducted following standardized procedures with patients wearing light clothes and without shoes. Height, measured to the nearest 0.1 cm, and weight, measured to the nearest 0.1 kg, were obtained using a mechanical column scale (Detecto). Body mass index, BMI (kg/m2) was calculated as weight (kilograms) divided by height (meters) squared. Obesity was defined as a BMI of ≥ 30 kg/m2[11]. Waist circumference (WC) was measured midway between the lowest border of the rib cage and the upper border of the iliac crest, at the end of normal expiration. WHtR was calculated as WC (cm) divided by height (cm). Blood pressure was recorded after approximately 15 minutes in a sitting position using an adapted adult mercury sphygmomanometer. High blood pressure was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or use of blood pressure-lowering medication during the previous 2 weeks [12].

Blood samples were drawn after an overnight fast of at least 12 hours. Fasting blood glucose and HbA1c were measured using the glucose oxidase method and high-performance liquid chromatography (HPLC) method respectively. Total cholesterol (TC), triglycerides (TG), and HDL-cholesterol (HDLc) were measured using enzymatic colorimetric methods.

We had defined dyslipidemia according to the guidelines of the European Society of Cardiology ESC 2016 [13]. The metabolic syndrome was defined according to the IDF definition for the Eastern Mediterranean populations [14]. MetS was retained if the patient had central obesity defined as waist circumference ≥ 94 cm in males or ≥80 cm in females plus any two of the following four factors:

- Triglycerides ≥1.5 g/ l or specific treatment for dyslipidemia;
- HDL cholesterol < 0.4 g/L in men and < 0.5 g/L in women.
- Systolic blood pressure (SBP) ≥130 mmHg or diastolic blood pressure (DBP) ≥85 mmHg or treatment for previously diagnosed hypertension;
- Fasting plasma glucose ≥100 mg/dl or previously diagnosed type 2 diabetes

Statistical analysis

The data were analyzed using the Statistical Program for Social Sciences, SPSS version 22.0 (SPSS Inc., Chicago, IL). All results were expressed as mean±standard deviation (SD) for quantitative variables and as percentages for qualitative variables. For independent groups, we used the parametric Student's T-test for the comparison of means and the Pearson's Chi-square test to compare proportions. Receiver operating characteristics (ROC) analysis was used to identify optimal cut-off values for WHtR. The area under the ROC curve (AUC) and the 95% confidence interval (95% CI) were used as a measure of the discriminative power of the WHtR. AUC value above 0.80

was considered excellent. We considered that a cut-off point was optimal for diagnosing MetS if it has the best sensitivity and specificity. It was selected using the Youden index (J) method [15]. Linear regressions were performed to assess correlations between WHtR and clinical characteristics of diabetic patients. We calculated quartiles of WHtR to analyze the association between WHtR and MetS. Relative risk analyses were performed using univariate regression analysis. A level of significance of 5% (p <0.05) was established to reject the null hypothesis.

RESULTS

A total of 457 T2DM patients (255 women and 202 men) were included. Their average age was 56.5±9.2 years. The mean duration of diabetes was 8.62±6.52 years. Only a fifth of the population had good glycemic control. Tables 1 and 2 summarize basic characteristics of study subjects stratified by gender and MetS status respectively. Abdominal obesity was the most frequent criterion among patients with type 2 DM (83.2%) followed by low HDLc (62.4%) and hypertension (61.1%). The prevalence of the MetS was 74.8% (Table 1). This prevalence was significantly higher among women than among men (85.5% vs 61.4%; p<10-3). Women were more likely to be suffered from raised blood pressure (67.8% vs 52.5%, p=0.030), raised triglyceride (40% vs 33.7%, p=NS), and reduced HDL (69.6% vs 60%, p<0.001) when compared with men.

Table1. Prevalence of metabolic syndrome and its components by gender.

	Total	Men	Women	P*
Patients, n (%)	475 (100)	202 (44.2)	255 (55.8)	
Metabolic Syndrome (%)	74.8	61.4	85.5	< 10-3
Central Obesity (%)	83.2	65.8	96.9	< 10-3
Hypertension (%)	61.1	52.5	67.8	0.001
Dyslipidemia (%)	67.1	63.1	69.7	NS
Low HDL cholesterol (%)	62.4	60	69.6	0.030
High triglycerides (%)	37.2	33.7	40	NS
High triglycerides (%)	37.2	33.7	40	NS

*: calculated between men and women. NS: non-significant.

Table 2 illustrates that both patients with MetS and those without MetS were age-matched and had similar duration of diabetes. Anthropometric parameters (BMI, WC, and WHtR) were significantly different between individuals with MetS and those without MetS (p<10-3). Diabetic patients who presented MetS had significantly lower HDLc and higher SBP, DBP, and TG. The mean CT was identical between the two groups. MetS was associated with a 1.6 fold increased presence of macrovascular complications.

Table 2. Descriptive data for patients with and without metabolic syndrome (MetS).

	Total	With MetS		Without MetS		P*
Patients, n (%)	457(100%)	342 (74.8%)		115 (25.2%)		
Age (years)	**56.5±9.2**	**56.5**	**± 9.1**	**56.4**	**± 9.2**	NS
Sex (M/F), n	202/255	124/218		78/37		< 10-3
Current Smoking (%)	27.8	21.9		44.3		< 10-3
BMI (Kg/m^2)	31±7.2	32.7 ± 7.2		26 ± 4.6		< 10-3
Obesity (%)	49.2	60.5		15,7		< 10-3
WC(cm)	103±15.7	107.2 ± 14.9		90±10.3		< 10-3
WtHR	0.64±0.1	0.66	± 0.1	0.55	± 0.1	< 10-3
Diabetes duration (years)	8.62±6.52	8.62	± 6.1	8.61	± 7.6	NS
Insulin treatment (%)	37.4	40.9		36.2		NS
HbA1c ≤ 7% (%)	19.4	19		20.5		NS
SBP(mmHg)	130.9 ± 19.1	132.9 ± 19.4		125.2	± 16.8	< 10-3
DBP(mmHg)	77.2 ± 10.9	78 ± 11.1		74.4	± 9.9	0.002
Total cholesterol (g/L)	1.83 ± 0.39	1.84	± 0.4	1.8 ± 0.35		NS
Triglyceride (g/L)	1.48 ± 0.87	1.62	± 0,9	1.1±0.5		**< 10-3**
HDL cholesterol (g/L)	0.42 ± 0.1	0.41	± 0,1	0.44	± 0.1	**0.002**
Macroangiopathy (%)	21.7	24.1		14.8		**0.036**

MetS: metabolic syndrome; M: male; F: female; BMI: body mass index; WC: waist circumference; WtHR: Waist to Height ratio; SBP: systolic blood pressure; DBP: diastolic blood pressure;*: calculated between patients with and without metabolic syndrome.

Table 3 showed that the association between WHtR and clinical characteristics of diabetic patients was influenced by gender. A positive significant correlation was observed between WHtR and blood pressure in diabetic women but not in diabetic men.

Linear regression analysis showed a significant association between WHtR and TG levels in both genders. No significant relationship was found between WHtR and HDL cholesterol levels neither in men nor in women. WHtR was significantly correlated with HbA1c measures only in men. The median WHtR was 0.59±0.1 in men and 0.67±0.1 in women. As it was shown in Table 4, the prevalence of MetS was higher among diabetic patients with a higher WHtR in both men and women showing a continuous increase with increasing WHtR. Compared to the first three quartiles of WHtR, the risk ratios of the fourth quartile for MetS were 10.9 and 4.4 in men and women respectively.

Based on the ROC analysis (Table 5), the AUC for identifying MetS was 0.913 (95% CI (0.867, 0.959)) in diabetic men and 0.761 (95% CI (0.670, 0.852)) in diabetic women.

The WHtR cut-off yielding maximal sensitivity plus specificity for representing Met S was 0.55 in men and 0.63 in women. The WHtR had a better discriminatory power to identify

MetS among diabetic patients than to predict the presence of one of its criteria separately.

Table 3. Linear regression analysis of baseline characteristics on the waist-to-height ratio (WHtR).

	Men			Women		
	Beta Coefficient	r^2	p	Beta Coefficient	r^2	p
Age	0.065	-0.001	0.358	-0.098	0.006	0.119
Diabetes duration	0.041	-0.003	0.564	0.142	0.016	0.029
BMI	0.665	0.440	$<10^{-3}$	0.842	0.710	$<10^{-3}$
SBP	0.073	0.000	0.304	0.245	0.056	$<10^{-3}$
DBP	0.106	0.006	0.137	0.130	0.013	0.045
HbA1c	-0.184	0.029	0.011	-0.043	-0.002	0.514
Total cholesterol	0.004	-0.005	0.950	0.142	0.016	0.023
Triglycerides	0.221	0.044	0.002	0.252	0.060	$<10^{-3}$
HDL-cholesterol	-0.125	0.011	0.079	-0.065	0.00	0.320

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure.

Table 4. Prevalence of metabolic syndrome according to the WHtR values.

	Men				Women		
Quartiles	n (%)	OR (95% CI)	p	Quartiles	n (%)	OR (95% CI)	p
Q1 (n=50) WHtR<0.54	4 (8%)	0.02 (0.01 –0.1)	$<10^{-3}$	Q1 (n=64) WHtR < 0.61	44 (69%)	1.02 (0.5 – 2.3)	$<10^{-3}$
Q2 (n=51) 0.54≤WHtR <0.58	27 (53%)	0.6 (0.34 –1.2)	NS	Q2 (n=63) 0.61≤ WHtR < 0.66	54 (84%)	0.22 (0.1 – 0.4)	NS
Q3 (n=51) 0.58≤WHtR <0.63	47 (92%)	11.3 (3.9 –32.9)	$<10^{-3}$	Q3 (n=64) 0.66≤ WHtR < 0.71	59 (92%)	2.4 (0.9 – 6.4)	NS
Q4 (n=50) WHtR ≥0.63	46 (92%)	10.9 (3.7 –31.8)	$<10^{-3}$	Q4 (n=64) WHtR ≥0.71	61 (95%)	4.4 (1.3 –14.9)	0.01

Q: quartile; OR: odds Ratio; 95% CI:95% Confidence Interval.

Based on the ROC analysis (Table 5), the AUC for identifying MetS was 0.913 (95% CI (0.867, 0.959)) in diabetic men and 0.761 (95% CI (0.670, 0.852)) in diabetic women.

The WHtR cut-off yielding maximal sensitivity plus specificity for representing Met S was 0.55 in men and 0.63 in women. The WHtR had a better discriminatory power to identify MetS among diabetic patients than to predict the presence of one of its criteria separately.

Table 5. Sensitivity and specificity for WHR cut-off points for screening metabolic syndrome in patients with type 2 diabetes mellitus.

Cut-off points	Men Sensitivity	Specificity	Cut-off points	Women Sensitivity	Specificity
0.52	98	50	0.59	88	46
0.53	97	58	0.60	86	49
0.54	95	70	0.61	78	57
0.55*	91	86	0.62	75	62
0.56	85	86	0.63*	72	70
0.57	79	88	0.64	65	76
0.58	71	90	0.65	64	76
0.59	62	90	0.66	57	78
AUC (95% CI)	0.913 (0.867–0.959)		AUC (95% CI)	0.761 (0.670–0.852)	
P	$<10^{-3}$		P	$<10^{-3}$	

95% CI: 95% Confidence Interval, *: optimal cut-off; AUC: area under curve.

DISCUSSION

Much controversy surrounds the utility of diagnosing MetS in diabetic patients. However, there are many reasons to believe that the identification of this clinical entity is useful [16]. In our study, MetS was common in diabetic patients (74.8%). The prevalence of MetS in patients with type 2 diabetes mellitus ranged from 43% to 84% depending on the diagnostic criteria [17-19]. Diabetic adults were about twice and a half as likely as were non-diabetic adults to have MetS (30%) [20, 21]. Chronic hyperglycemia was a fixed diagnostic criterion among our population, which could explain this higher prevalence of MetS among diabetic people. Besides, over half of the included patients had hypertension and dyslipidemia, which is similar to previous studies [22]. Likewise, as shown by several studies, MetS and its different components were more common in diabetic women than in diabetic men [16, 23].

Many factors had been revealed to be associated with an increased risk of MetS among women such as lower educational status, unemployment, higher prevalence of obesity, sedentary lifestyle, and menopausal status. Moreover, we found that macrovascular complications were significantly more frequent among diabetic patients with MetS than among those without MetS. Bonora et al. reported that MetS was associated independently with incident cardiovascular disease which led some authors to suggest the utility of the diagnosis of MetS in diabetic patients [24]. The molecular mechanisms underlying the MetS-induced vascular disease remain poorly understood because of the complicated of the syndrome itself. Recent work suggests the role of adipose-derived cytokines as molecular links between MetS and vascular disease [25]. Thus, screening MetS in patients with type 2 diabetes mellitus is a simple measure to identify people at increased risk of cardiovascular disease. Since central obesity is the key factor of this syndrome and its macrovascular complications, central obesity recognition itself is the first step to identify diabetic patients at increased risk [8].

Recent data show that anthropometric parameters such as BMI, WC, and WHtR were significantly associated with abdominal obesity. The waist-to-height ratio was the better anthropometric predictor for MetS [26]. BMI cannot represent fat distribution and WC cannot differentiate between visceral fat and subcutaneous fat. In addition, those two parameters may be affected by many factors, such as gender, height, age, and race. However, WHtR, which comprehensively considers the impact of height and WC, varies little as a function of race, age, and gender [16, 27].

In our Tunisian population, WHtR was more appropriate to detect MetS than to detect one of its components apart. It was a strong predictor of MetS among men with T2DM but not among women. This result is likely due to higher waist circumference in women than in men for the same amount of the visceral fat because of the subcutaneous fat which is often higher in women. This finding was similar to that found by Obirikorang et al. who reported that WHtR was a better predictor for MetS in men than in women [9]. Theirs AUC were similar to ours (0.99 in man and 0.8 in women). In addition, we observed that the optimal WHtR cut-off point for MetS was found to be 0.55 in men and 0.63 in women. The range of WHtR cut-offs for measuring central obesity varies from 0.51 to 0.58 in several studies[16]. But it is usually recommended the same WHtR cut-off in both men and women in each population [27].

In contrast, in our diabetic population, the cut-off value of WHtR predictive of MetS was higher in women compared to that in men. Women developed metabolic disorders at a higher WHtR in comparison with men. Other studies have shown that the correlation between anthropometric measures and visceral fat depends on gender and it is weaker in women [28]. Thus, WHtR seems to be not appropriate for identifying MetS in our diabetic women which suggests using gender-specific reference values in our clinical practice. Moreover, the high prevalence of MetS at low WHtR values in diabetic men suggests the need for higher cut-off points among them.

In summary, our study provides evidence showing a high prevalence of MetS in adults with T2DM in Tunisia. This syndrome was significantly associated with macrovascular diseases. We also reported that WHtR was a strong predictor of MetS, particularly among men. Our cut-off values seem to be higher compared to the reference values of other diabetic populations. However, as a cross-sectional study, our work is limited in its ability to elucidate a causal relationship between MetS and macroangiopathy. Additionally, the use of a non-randomized sampling approach may have affected the statistical power and introduced sampling bias. More studies should be conducted to assess the validity of our results.

CONCLUSION

The identification of metabolic syndrome is helpful to distinguish patients with a clustering of cardiovascular risk factors that put them at increased risk of cardiovascular disease. Such individuals need more intensive lifestyle interventions at an early stage to delay the cardiovascular disease progression. Our findings show that WHtR was an ideal tool to predict MetS in diabetic men with a cut-off value of 0.55 but not in women. Since body fat patterns show ethnic differences, identification of WHtR has to be undertaken in our Tunisian population via prospective studies with larger cohorts.

Conflict of interest

The authors declare that they have no conflict of interest

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