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CAN OBESITY INDICES PREDICT METABOLIC SYNDROME AND DIABETES? IMPACT OF INTENSIVE DIET, PHYSICAL EXERCISE AND LIFESTYLE INTERVENTION

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ABSTRACT
Aim: The aim of study was to evaluate different obesity indices [body mass index (BMI), waist circumference (WC), waist hip ratio (WHR), waist height ratio (WHtR)] to identify one that best predicts metabolic syndrome (MetS) among Turkish population. **Design**: Cross sectional study. **Setting**: Primary health care (PHC) Centres and Hospital. **Subjects and methods**: The survey was conducted from February to November 2016 among Turkish citizens above 25 years of age. Data was collected using pre-tested questionnaire from 1,811 subjects approached; 1,393 gave consent via interviews, followed by blood sampling for laboratory investigations. MetS was defined according to the National Cholesterol Education Program – Third Adult Treatment Panel (ATP III) as well as International Diabetes Federation (IDF) guidelines. Receiver operating characteristics (ROC) curve analysis was used to determine the obesity index with corresponding gender specific cut-off value that better predicts MetS among Turkish population. **Results :** MetS was 25.9% in relation to ATP III and 38.2% according to IDF. Levels of education, consumption of fast food and physical activity revealed significant differences between groups with and without MetS. Subjects with MetS were older, predominantly female and were either retired/not working or housewives as compared to those without MetS using ATPIII criteria. Among men, WC followed by both WHR and WHtR yielded the highest area under the curve (AUC) (0.83; 95%CI 0.74-0.86; 0.78 95%CI 0.73-0.82 and 0.80; 95%CI 0.71-0.84 respectively). Unlike men, among women WC followed by WHtR yielded highest AUC (0.81; 95%CI 0.78-0.85; 0.79; 95%CI 0.76-0.83 and 0.75; 95%CI 0.72-0.79). Among men, WC at a cut-off value of 99.0 cm resulted in highest Youden index with corresponding sensitivity of 81.6% and 63.9% specificity. In a similar way, among women, WC at a cut-off point of 90 cm resulted in highest Youden index with the corresponding sensitivity and specificity of 93.0% and 82.6% respectively. Among both men and women, the BMI at a cut-off value of 28 kg/m^2 and the traditional cut-off value of 30kg/m^2 was found to be having the lowest Youden index and corresponding sensitivity and specificity. **Conclusion**: The prevalence of MetS was found to be high in Turkey according to both ATP III and IDF criteria. The waist circumference at a cut-off point of 99cm among men and 92cm among women observed to be the best predictor of metabolic syndrome in the Turkish population. ATP III criteria for the Turkish population might result in underestimation of MetS among men and overestimation among women.

KEYWORDS: Obesity, Metabolic syndrome, Waist-hip-ratio, Weight-height-ratio, Waist circumference, Turkey.

INTRODUCTION
Metabolic syndrome (MetS) is a combination of interrelated risk factors such as glucose metabolism disturbances, dyslipidemia, blood pressures, obesity, atherosclerotic cardiovascular diseases and type 2 diabetes mellitus (T2DM)[1-5]. Obesity or body fat might be the predominant underlying risk factor not only in the development of MetS but also other cardiovascular risk factors.[6-9] The most widely accepted definition of MetS is WHO definition and alternatives proposed by the US National Cholesterol Education Program Adult Treatment Panel III (NCEA-ATPIII) and the latest definition is the one of the International Diabetes Federation (IDF)[4-5]

Several studies from various geographic and ethnic populations arrived at different conclusions regarding the superiority of one or the other obesity index and related cut-off points to diagnose obesity and MetS.[10-13] In fact, different cut-off points to diagnose obesity and MetS might be necessary for racial variation among population from different countries.[13-15]

The objective of the present study was to conduct a comparative validation of WC, BMI, WHR and WHtR for defining MetS study and determine the prevalence MetS and its components according to Adult Treatment Panel III (ATP III) and IDF criteria and the risk factors affecting MetS.

SUBJECTS AND METHODS

This is a cross sectional study which was performed among the diabetic patients registered in diabetic clinics of outpatient clinics of the hospitals during the study period from February 2016 to November 2016 among Turkish citizens above 25 years of age. IRB ethical approval for this study was obtained from the Medipol International School of Medicine, Istanbul Medipol University.

Sampling Procedure

The sample size calculation was based on previous studies that determined the prevalence of MetS in Turkey[17] to be between 25%-35%, with the 99% confidence interval and with 2.5% error of estimation. The minimum sample size for the current study was 1,811. Subjects were recruited by the systematic 1-in-2 sampling procedure. During the study period, 1,811 subjects were approached and 1,393 (77.31%) subjects gave consent and participated in the study.

Two different international criteria as given below were used to diagnose MetS among the participants: According to ATPIII criteria[1,3], presence of at least three of these risk factors diagnose the MetS; (1) high fasting plasma glucose FPG≥100mg/dl (5.6 mmol/L) or presence of diagnosis of type 2 diabetes mellitus (T2DM), (2) blood pressure ≥130/85 mmHg, (3) triglyceride ≥150mg/dl (1.7 mmol/L), (4) HDL cholesterol : men <40mg/dl (1.03 mmol/L); women < 50mg/dl (1.29 mmol/L), (5) males with waist circumference >102 cm and females with waist circumference >88cm. Secondly, according to IDF[4-5], a participant has the MetS if she/he has a waist circumference (≥94cm in men and ≥80 cm in women) plus any two of these risk factors; 1) FPG≥100 mg/dl (5.6 mmol/L) or previously diagnosed impaired fasting glucose, (2) blood pressure ≥130/85 mmHg or treatment for hypertension, (3) triglyceride ≥150mg/dl (1.7 mmol/L) (4) HDL cholesterol: men <40mg/dl (1.03 mmol/L); women < 50mg/dl (1.29 mmol/L) or treatment for low HDL.

The study included socio-demographic and anthropometric characteristics including age, sex, marital status, education level, occupation, BMI, waist and hip circumference, waist to hip ratio (WHR), waist to height ratio (WHtR) physical activity, fast food consumption and smoking habits, clinical data, such as systolic and diastolic blood pressures. Regarding to WHO criteria[16], obesity and overweight were classified if BMI >30 kg/m^2 as obese and if BMI 25-30kg/m^2, as overweight.

The systolic (SBP) and diastolic (DBP) blood pressure were measured from the subject’s left arm while seated and his/her arm at heart level, using a standard zero mercury sphygmomanometer after at least 12-16 minutes of rest and the average of the two readings was obtained.

A blood sample of 10 ml was collected through venepuncture from each participant after fasting for 10 hours, into vacutainer tubes containing EDTA. The samples were kept at room temperature and transported within 2 hrs to a central certified laboratory at Medipol Hospital, Medipol International School of Medicine. Serum triglyceride, total cholesterol, high-density lipoprotein (HDL) cholestrol, low density lipoprotein (LDL) cholestrol, Hemoglobin A1c (HbA1c), and fasting plasma glucose levels (FPG) were measured by an auto-analyser (ROCHE COBAS 6000 auto-analyzer, Roche Diagnostics, Germany)**.**

Data Analysis

The significance of differences between mean values of two continuous variables was determined by Student-t test. Chi-square and Fisher exact test (two-tailed) were used to test for differences in proportions of categorical variables between two or more groups. The receiver operating characteristic (ROC) curve was generated to obtain the values of area under the curve (AUC) with 95% CI, and also sensitivity and specificity for each obesity index as a predictor of MetS and the Youden index (sensitivity+specificity-1) was calculated. The cut-off value for significance was determined as p<0.05.

RESULTS

The current study revealed the prevalence of MetS was 25.9% according to ATP III and 38.2% according to IDF. Table 1 shows comparison of socio-demographic and lifestyle characteristics between participants with and without MetS in Turkey. The age groups, gender, level of education, gender, consumption of fast food, and physical activity were significantly different between groups with and without MetS using both the diagnostic criteria.

Majority of the subjects with MetS were obese (BMI≥30) as compared to slightly higher than one third of the metabolically healthy obese individuals (44.6% vs. 24.7% using ATPIII criteria & 35.1% vs. 26.6% using IDF criteria; p<0.001 respectively). Average WC, WHR, WHtR, BMI, FPG, haemoglobin, triglycerides, SBP, and DBP were significantly higher among the participants with MetS as compared to those without MetS irrespective of the diagnostic criteria (Table 2).

Obesity indices and metabolic syndrome using ROC curves

Table 3 and figure 1 show gender specific area under ROC curve and optimal cut-off points with corresponding validity parameters for different obesity indices in predicting MetS. Subjects with MetS were older, predominantly female and were either retired/not working or housewives in comparison to those without MetS using ATP III criteria. Among men; WC followed by both WHR and WHtR yielded the highest area under the curve (AUC) (0.83; 95% CI 0.74-0.86; 0.78 95% CI 0.73-0.82 and 0.80; 95%CI 0.71-0.84 respectively). Unlike men, among women WC followed by WHtR yielded highest AUC (0.81; 95% CI 0.78-0.85; 0.79; 95% CI 0.76-0.83 and 0.75; 95% CI 0.72-0.79). Among both men and women, the BMI at a cut-off value of 28 kg/m^2 and the traditional cut-off value of 30kg/m^2 was found to be having the lowest Youden index and corresponding sensitivity and specificity. WC at a cut-off point of 99cm among men and 92cm among women happened to be the best predictor of metabolic syndrome in the Turkish population.

Table: 1 Demographic and lifestyle habits of the study sample in Turkey (N=1393)

Variables	Total N=1,393	ATPIII MetS(+) n = 361	ATPIII MetS(-) n = 1,032	P value	IDF MetS(+) n = 533	IDF MetS(-) n = 860	P value
	N(%)	n(%)	n(%)		n(%)	n(%)	
Age (mean±SD)	42.66±11.1	45.93±10.03	41.50±11.30	<0.001	42.89±10.73	42.52±11.41	0.534
Age groups (years)							
<35	433(31.1)	53(14.7	380(36.8)		149(28.0)	284(33)	
35-44.9	390(28.0)	109(30.2)	281(27.2)		153(28.7)	237(27.6)	
45-54.9	404(29.0)	125(34.6)	279(27.0)	<0.001	167(313)	237(27.6)	0.141
55-64.9	139(10.0)	66(18.3)	73(7.1)		50(9.4)	89(10.3)	
65 and above	277(1.9)	8(2.2)	19(1.8)		14(2.6)	13(1.5)	
Gender							
Male	599(43.0)	129(35.7)	470(45.5)	<0.001	235(44.1)	364(42.3)	0.518
Female	794(57.0)	232(64.9.9)	562(54.5)		298(55.9)	496(57.7)	
Education level							
Primary	355(25.5)	88(24.3)	267(25.8)		126(23.6)	229(26.7)	
Secondary	369(26.8)	75(36.2)	294(28.5)	0.010	143(26.8)	226(26.3)	0.793
High school	379(27.2)	116(32.1)	263(25.5)		149(28.0)	230(26.7)	
University	290(20.8)	82(22.7)	208(20.2)		115(21.8)	175(20.3)	
Occupation							
Housewife	332(23.8)	98(27.1)	234(22.7)		106(27.1)	226(22.7)	
Clerical	410(29.4)	100(29.9)	306(29.3)		169(29.9)	241(29.3)	
Professional	353(25.3)	77(21.3)	276(26.7)	0.285	141(21.3)	212(26.7)	0.071
Manual worker	207(14.9)	51(14.1)	156(15.1)		79(14.1)	128(15.1)	
Businessman	91(6.5)	27(7.5)	64(6.2)		38(7.5)	53(6.2)	
Income							
High	504(36.2)	142(39.3)	362(35.1)		200(37.5)	304(35.3)	
Medium	624(44.8)	150(41.6)	474(45.9)	0.288	245(46.0)	379(44.1)	0.169
Low	265(19.0)	69(19.1)	196(19.0)		88(16.5)	177(20.6)	
Marital status							
Single	276(19.8)	71(19.7)	205(19.9)		93(17.4)	183(21.3)	
Married	992(71.2)	255(70.6)	737(71.4)	0.856	383(73.7)	599(69.7)	0.199
Widow/divorce	125(9.0)	35(9.7)	90(8.7)		47(8.7)	78(9.0)	
Smoking status							
Yes	268(19.2)	69(19.1)	199(19.3)	0.337	103(19.3)	165(19.2)	0.745
No	1125(80.8)	292(19.1)	833(80.7)		430(80.7)	695(80.8)	
Sleeping Hours							
= <7 Hours	716 (51.4)	219 (60.7)	497(48.2)	<0.001	275 (51.6)	441(51.3)	0.909
>7 Hours	677 (48.6)	142(39.3)	535(51.8)		258 (48.4)	419(48.7)	
Avg. No. of years smoked	13.25±9.53	13.28±11.60	13.24±8.86	0.984	12.99±8.70	13.71±10.89	0.624
Smoking cigarettes /day	19.63±13.01	22.44±12.71	18.81±13.02	0.099	18.93±13.38	20.03±12.83	0.567
Sheesha smoking	281(20.2)	67(18.6)	214(20.7)	0.375	118(22.1)	163(19.0)	0.150
Fast food consumption	457(32.8)	140(38.84)	317(30.7)	0.005	200(37.5)	257(29.9)	0.003
Physical activity	390(28.0)	75(20.8)	315(30.5)	0.001	128(24.0)	262(30.5)	0.009

Table: 2. Anthropometric measurements and clinical parameters of the study sample in Turkey (N=1,393)

Variables	ATPIII		P value	IDF		P value
	MetS(+) n = 361	**MetS(-) n = 1,032**		**MetS(+) n = 533**	**MetS(-) n = 860**	
	n(%)	**n(%)**		**n(%)**	**n(%)**	
Waist circumference(cm)	106.94±10.17	94.97±11.3	<0.001	99.80±13.27	96.28±11.50	<0.001
Hip circumference (cm)	114.08±10.32	108.81±9.50	<0.001	110.62±10.72	109.73±9.35	0.043
Height (Cm)	162.06±10.24	162.82±9.28	0.164	162.84±9.65	162.37±9.57	0.335
Weight (Kg)	84.65±17.02	75.73±15.20	0.004	78.92±18.10	76.69±14.52	0.033
Waist Hip Ratio (WHR)	0.93±0.09	0.85±0.07	<0.001	0.88±0.10	0.87±0.11	0.004
Waist Height Ratio	0.68±0.07	0.60±0.08	<0.001	0.63±0.09	0.61±0.08	0.030
Body Mass index (Kg/m^2)	32.30±7.19	28.61±5.45	<0.001	30.23±7.40	29.18±5.23	0.002
Body Mass Index: n(%) Normal <25 Overweight 25-29.9 Obese >30	 79(21.9) 121(33.5) 161(44.6)	 306(29.7) 471(45.6) 255(24.7)	<0.001	 178(33.4) 168(31.5) 187(35.1)	 207(24.1) 424(49.3) 229(26.6)	<0.001
Fasting glucose (mmol/L)	8.14±3.53	5.54±1.62	<0.001	6.82±3.04	5.87±1.32	<0.001
Haemoglobin A1c (%)	7.15±1.84	5.67±1.18	<0.001	6.58±1.79	5.44±1.20	<0.001
Total cholesterol (mmol/L)	4.90±0.79	4.81±0.82	<0.001	4.90±0.82	4.801±0.79	0.028
HDL cholesterol (mmol/L)	1.31±0.25	1.42±0.34	<0.001	1.35±0.30	1.62±0.36	0.182
LDL cholesterol (mmol/L)	2.85±0.67	2.79±0.70	0.032	2.82±0.70	2.77±0.69	0.205
Triglycerides (mmol/L)	1.62±0.80	1.34±0.79	<0.001	1.46±0.76	1.37±0.77	<0.001
Systolic blood pressure (mmHg)	131.73±15.64	125.28±15.79	<0.001	128.40±16.31	126.64±15.64	0.007
Diastolic blood pressure mmHg)	81.90±9.42	78.01±9.80	<0.001	80.07±10.16	78.37±9.61	0.002

Table: 3 Areas under the ROC curve, optimal cut-off value, 95% confidence interval, sensitivity, specificity, and Youden Index of BMI, waist circumference, waist-to-height ratio and waist-to-hip ratio associated with different obesity indices in predicting MetS (N=1,393)

	AUC(95%CI)	Cut-off value	Sensitivity	Specificity	Youden index
Men					
Body Mass Index(BMI)	0.56(0.51-0.62)	27.5 kg/m^2	58.0%	52.9%	0.102
		30 kg/m^2	38.5%	66.7%	0.188
Waist Circumference (WC)	0.83(0.74-0.86)	99.0 cm	81.6%	63.9%	0.455
		101 cm	75.9%	67.3%	0.432
Waist Height Ratio (WHtR)	0.78(0.73-0.82)	0.57	88.3%	64.8%	0.399
		0.64	87.6%	25.1%	0.211
Waist Hip Ratio (WHR)	0.80(0.71-0.84)	0.91	78.2%	69.9%	0.400
Women					
Body Mass Index(BMI)	0.70(0.66-0.73)	28.0 kg/m^2	76.3%	65.1%	0.345
		30 kg/m^2	67.4%	83.9%	0.209
Waist Circumference(WC)	0.81(0.78-0.85)	92.0 cm	80.4%	74.2%	0.543
		90.0 cm	93.0%	82.8%	0.167
Waist Height Ratio(WHtR)	0.79(0.76-0.83)	0.63	78.5%	70.4%	0.489
		0.65	95.1%	24.3%	0.190
Waist Hip Ratio (WHR)	0.75(0.72-0.79)	0.88	75.4%	71.5%	0.409

AUC=Area under the curve, ROC=Receiver Operating Characteristics, CI=Confidence Interval

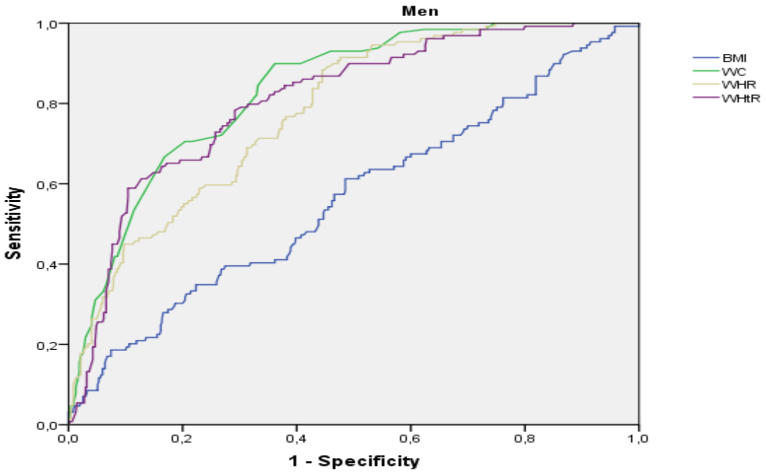

Fig: 1 Receiver Operating Characteristics Curve (ROC) for men.

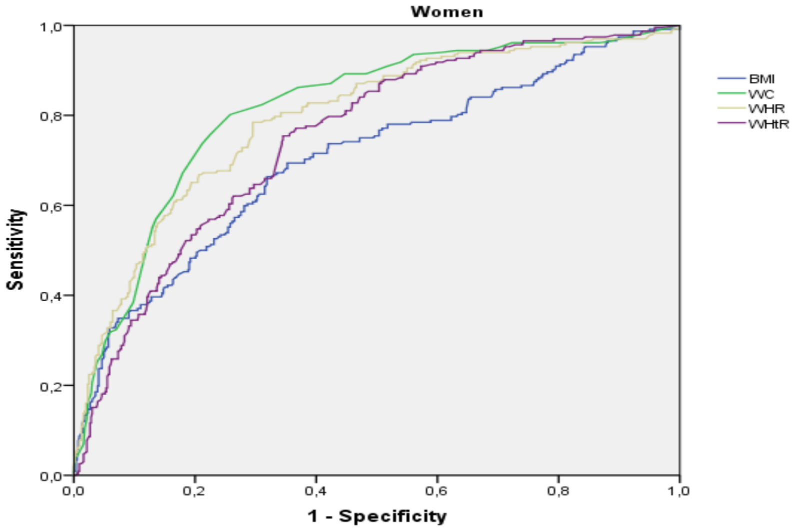

Fig: 2. Receiver Operating Characteristics Curve (ROC) for women.

DISCUSSION

In this cross-sectional survey of Turkish nationals aged 25 years and above, the overall prevalence of MetS was found to be 25.9% in accordance with the ATPIII and 38.2% with the IDF criteria. It was consistent with the previous study conducted among Turkish adult population.[17] The optimal cut-off values of WC to predict MetS were 99cm and 92cm in men and women. Those of WHR, WHtR and BMI were 0.91 and 0.88, 0.57 and 0.63, 27.5 kg/m^2 and 28.0 kg/m^2 in men and women, respectively. These results are consistent with the previous reported studies.[8-10,15]

MetS prevalence are increasing dramatically worldwide. Lifestyle factors such as physical inactivity, obesity, abdominal adiposity, alcohol, smoking and dietary factors such as fatty food and red meat consumption can be the main risk factors. Measurement of obesity for predicting MetS is a widely contradictive issue. It was pointed out in adult Iranian population that WC was superior than BMI and WHR in discriminating MetS among healthy subjects.[15] However, WC, WHR and BMI were considered as equally useful indicators to discriminate between those with and without MetS in the Chinese adult population.[8,18] Also, BMI was determined as a better predictor of hypertension in comparison to other obesity measurements.[19] According to this study, WC is stated as a better predictor of MetS in both the Turkish male and female population.

The WC is most widespread recommendation for calculation of cardiovascular risk factors and used in the definition of MetS.[1,3-4,20-21] Additionally, WC can be adjusted for height as WHtR is a better surrogate for measuring abdominal obesity[22,23] and adiposity in both men and women to determine metabolic risk factors.[24,25]

Present study revealed that WC at a cut-off value of 99cm for men and 92cm for women has the highest sensitivity and specificity for prediction of the MetS development. When the cut-off value of WC as 101 cm for men and 90 cm for women which recommended by ATPIII criteria[1], the sensitivity to determine the differences between participants with and without MetS decreased from 81.6% to 75.9% in men and the specificity decreased from 64.7% to 53.2% among women, this is consistent with the Iranian study.[11] Moreover, our results indicate that after the WC, WHR at a cut-off point of 0.90 for men and 0.88 for women yield highest sensitivity and specificity to diversify MetS. This finding is confirmative with previous studies from Qatar[6], Korea[13-14], Iran[15] and Taiwan.[10] BMI was stated as a poor predictor of MetS in comparison to the other obesity indices. Yet, at a slightly lower cut-off value of 28 kg/m^2 than the recommended cut-off point by WHO[16] for both men and women it produced better sensitivity and specificity to predict the risk of MetS. Previous studies in Iran, Qatar and Korea also suggest that the lower cut-off points for BMI is help a better prediction of the MetS development.[6,13-15]

Overall, preventing the occurrence of cardiovascular disease and type 2 diabetes mellitus and life style intervention is important for individuals with MetS.[9,13,25] A recent large-scale observational study showed that life style intervention in individuals with MetS was related with 25 % risk reduction of type 2 diabetes and 50 % risk-reduction of cardiovascular disease.[9,25] During life style intervention period, repeated assessment of whether they satisfy MetS criteria or not is important for determining the effectiveness of the life style intervention.[9-10,25] Although many studies have shown that MetS at baseline is a useful predictor of the future occurrence of type 2 diabetes, the impact of longitudinal status change in MetS on new onset of type 2 diabetes has not been determined.[13]

There are several limitations to this study. Firstly, the design of current study is cross sectional. Secondly, the cardiovascular risk was not clarified. Finally, long-term follow-up of the subjects was not conducted.

CONCLUSION

The prevalence of MetS was high in Turkey regarding to both ATP III and IDF criteria. The waist circumference at a cut-off point of 99cm among men and 92cm among women is the best predictor of metabolic syndrome in Turkish population. ATP III criteria for Turkish population might result in underestimation of MetS among men and overestimation of MetS among women. This study confirms the need for a geographically and ethnically sensitive MetS diagnosis criteria.

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Informed Consent

Written and verbal informed consent was obtained for this study**.**

Authors' contributions

AB, and MÖ organized study, collected data, performed statistical analysis and wrote the first draft of the article, and contributed to the interpretation of the data and writing the final draft of manuscript. ME and KUR contributed to the interpretation of the data and writing the manuscript.

Conflict of Interest

No conflict of interest was declared by the authors.

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