Cut-off values for waist circumference in Turkish population: Is there a threshold to predict insulin resistance?

Türk toplumunda bel çevresi sınır değerleri: İnsülin direncini öngördüren bir eşik değer var mıdır?

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Objectives: To identify the cut-off values for waist circumference (WC) that may best predict cardiometabolic risk associated with insulin resistance in adult Turkish men and women.

Study design: A total of 1,039 non-diabetic subjects (592 females, 447 males; mean age 40.2±12.8 years) aged ≥18 years were enrolled. Insulin resistance was assessed with homeostasis model assessment of insulin resistance (HOMA-IR). The subjects were classified into quantiles based on the WC values and quantiles were compared with respect to the HOMA-IR levels. Receiver operating characteristic (ROC) analysis was used to identify the WC cut-off value that would best predict insulin resistance.

Results: HOMA-IR values increased in parallel with increasing WC quantiles for both genders (p=0.001). The cut-off values for WC that showed the highest sensitivity and specificity to predict insulin resistance were 93 cm for men (91.6% and 51%, respectively) and 83 cm for women (91.1% and 34.8%, respectively).

Conclusion: Our results demonstrate that the cut-off values for WC that would best predict cardiometabolic risk associated with insulin resistance are 93 cm for men and 83 cm for women in Turkish adults. However, our findings also raise the question as to whether it is indeed necessary to define a WC cut-off value for the prediction of insulin resistance, because, regardless of the cut-off WC value taken into account, insulin resistance will be overlooked in a significant number of individuals with a WC below this cut-off value.

Key words: Cut-off; HOMA-IR; insulin resistance; Turkish adults; waist circumference.

Amaç: Türk erişkin erkek ve kadınlarda insülin direnci ile ilişkili kardiyometabolik riski en iyi şekilde öngörebilecek bel çevresi sınır değerlerini belirlemek.

Çalışma planı: Çalışmaya 20 yaş ve üzeri toplam 1039 non-diyabetik olgu (592 kadın, 447 erkek, ort. yaş 40.2±12.8) alındı. İnsülin direnci HOMA-IR (Homeostasis Model Assessment of Insulin Resistance) ile belirlendi. Olgular bel çevresi değerlerine göre kuantillere ayrıldı ve kuantiller HOMA-IR düzeylerine göre karşılaştırıldı. İnsülin direncini en iyi şekilde öngörebilecek bel çevresi sınır değerini saptamada ROC (Receiver Operating Characteristic) analizi kullanıldı.

Bulgular: HOMA-IR her iki cinsiyette de artan bel çevresi kuantillerine paralel artış gösterdi (p=0.001). İnsülin direncini öngörmede en yüksek özgüllük ve duyarlık gösteren bel çevresi sınır değerleri erkeklerde 93 cm (duyarlık %91.6, özgüllük %51), kadınlarda 83 cm (duyarlık %91.1, özgüllük %34.8) idi.

Sonuç: Bu sonuçlar Türk erişkinlerinde insülin direnci ile ilişkili kardiyometabolik riski öngörmede en uygun bel çevresi sınır değerlerinin erkeklerde 93 cm, kadınlarda 83 cm olduğunu göstermektedir. Bununla birlikte, bu çalışmanın sonuçları, insülin direncini öngörmede bel çevresi için risk sınır değeri belirlemenin esasında çok gerekli olup olmadığı sorusunu akla getirmektedir. Çünkü, hangi bel çevresi sınır değerleri kabul edilirse edilsin, sınırın altında kalan önemli sayıda kişide insülin direncinin atlanabileceği aşikardır.

Anahtar sözcükler: Cut-off; HOMA-IR; insülin direnci; Türk erişkinler; bel çevresi.

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Abdominal obesity is regarded as one of the most important predictors of cardiometabolic risk associated with insulin resistance.[1,2] In clinical practice, waist circumference (WC), which has been shown to have an association with the presence and severity of insulin resistance,[3,4] is the most widely used parameter for the identification of abdominal obesity. Since WC is an anthropometric variable, each population should determine its own cut-off values for the prediction of cardiometabolic risk.[5] In Turkey, The Turkish Adult Risk Factor Study defined cut-off points for the prediction of increased cardiometabolic risk as 95 cm for males and 88 cm for females.[6] Nevertheless, the association between insulin resistance and abdominal obesity has not yet been studied in Turkish adults. The gold standard for the evaluation of insulin resistance is the hyperinsulinemic euglycemic clamp test; however, it is an invasive, time-consuming, and costly test and is used primarily for research purposes. Most epidemiological studies use the homeostasis model assessment of insulin resistance (HOMA-IR), which is a practical and inexpensive method.[7-9] The present study aimed to identify the WC cut-off values that would best predict insulin resistance assessed by HOMA-IR in adult Turkish males and females.

PATIENTS AND METHODS

Study population. Individuals aged ≥18 years admitted to the outpatient clinics of Goztepe Training and Research Hospital for check-ups were included in the present study. The relatives of patients were also included in the study. All study participants provided signed informed consent. The study was approved by the local ethics committee and conducted in accordance with Declaration of Helsinki. Exclusion criteria were diabetes mellitus, severe renal disease, liver disease, or heart failure; usage of medications known to effect insulin resistance (lipid lowering agents, antidiabetics, antihypertensives, etc.); and presence of abdominal mass or ascites. Pregnant women were also excluded from the study.

Study design. Demographic data, smoking and alcohol consumption habits, anthropometric data, and biochemical test results of subjects were recorded. Subjects were separated quantiles according to the WC values and quantiles were compared according to the HOMA-IR, triglyceride/HDL cholesterol and insulin levels. Sensitivity, specificity, and receiver operating characteristic (ROC) curves were used to identify the WC cut-off value that would best predict insulin resistance.

HOMA-IR, the evaluation of the insulin resistance by using fasting glucose and fasting insulin concentrations, was used to assess insulin resistance and simply calculated by the following formula: fasting plasma glucose × fasting insulin/ 22.5.[10] No universal HOMA-IR cut-off value has been established for insulin resistance. In the present study, a HOMA-IR value greater than 2.34, which was the median value of the study population, was accepted as the cut-off point for insulin resistance.

Criteria proposed by International Diabetes Federation (IDF) were used for the diagnosis of

Table 1. Demographic, anthropometric, and biochemical characteristics of study subjects

	Overall (n=592)	Female (n=447)	Male	*p*
Age (years)	40.22±12.77	39.59±12.77	41.05±12.74	0.068
Smoker (n, %)	263 (25.3)	130 (22.0)	133 (29.8)	0.004
Regular alchocol intake (n, %)	41 (3.9)	7 (1.2)	34 (7.6)	0.001
Waist circumference (cm)	95.91±14.27	94.65±14.79	97.58±13.39	0.001
Body mass index (kg/m2)	30.39±7.09	32.21±7.53	28.00±5.61	0.001
Systolic blood pressure (mm Hg)	128.18±21.63	127.89±22.79	128.55±20.00	0.621
Diastolic blood pressure (mm Hg)	82.02±11.41	81.79±12.10	82.33±10.43	0.444
Total cholesterol (mg/dl)	194.33±41.70	197.53±41.07	190.09±42.18	0.004
Triglyceride (mg/dl)	138.82±70.03	128.82±63.79	152.05±75.58	0.001
HDL cholesterol (mg/dl)	48.58±11.90	51.92±12.62	44.17±9.20	0.001
Triglyceride/HDL cholesterol	3.29±2.05	2.69±1.66	3.68±2.19	0.001
LDL cholesterol (mg/dl)	128.39±33.65	128.26±33.02	128.55±34.50	0.889
Fasting plasma glucose (mg/dl)	97.13±11.18	98.03±11.31	95.95±10.92	0.003
Insulin (μU/ml)	11.06±6.13	11.57±5.89	10.39±6.37	0.002
HOMA-IR	2.69±1.59	2.83±1.55	2.50±1.62	0.001
MetS frequency (n,%)	412 (39.7)	256 (43.2)	156 (34.9)	0.006

HOMA-IR: Homeostasis model assessment of insulin resistance, MetS: Metabolic syndrome. Data are expressed as mean±SD unless otherwise is indicated.

Table 2. HOMA-IR, triglyceride/HDL cholesterol, and insulin levels by waist circumference quantiles among female subjects

Waist circumference	n	HOMA-IR	Triglyceride/ HDL cholesterol	Insulin
≤76 cm	75	1.53±0.76	1.42±0.59	6.70±3.05
77–80 cm	35	1.81±0.88	2.40±1.79	7.89±3.91
81–84 cm	34	1.98±0.74	2.52±1.75	8.82±3.13
85–88 cm	46	2.30±1.02	2.43±1.32	10.09±4.51
89–92 cm	74	2.43±1.08	2.41±1.42	9.99±4.17
93–96 cm	61	2.88±1.24	2.85±1.86	11.77±4.89
97–100 cm	56	2.96±1.48	3.14±1.59	11.85±6.01
101–110 cm	127	3.72±1.69	3.15±1.71	14.62±6.18
>110 cm	84	3.96±1.58	3.29±1.72	15.82±6.12
p		0.001	0.001	0.001

HOMA-IR: Homeostasis model assessment of insulin resistance.

metabolic syndrome: WC >94 cm (male) or >80 cm (female) and presence of at least two of the following: blood pressure ≥130/85 mm Hg (or use of antihypertensive medication); fasting plasma glucose ≥100 mg/dl (or use of antidiabetic medication); fasting triglyceride ≥150 mg/dl or medical treatment for high levels of triglyceride; HDL cholesterol <40 mg/dl (male) or <50 mg/dl (female), or medical treatment for low HDL cholesterol levels.[5]

Anthropometric and biochemical measurements. Blood pressure was measured with the patient in a sitting position in both arms, after at least 10 minutes of rest, with a mercury sphygmomanometer, using the phase 1 and phase 5 Korotkoff sounds. A second measurement was performed after at least three minutes in the arm with the highest measurement. The mean value of the two measurements was taken as the systolic and diastolic blood pressure of the individual. WC was measured at the plane between anterior superior iliac spines and lower costal margins at the narrowest part of the waistline, during slight expiration, with the patient in standing position. BMI was calculated by Quetelet index (kg/m^2). Venous blood samples were obtained following 12 hours of fasting; glucose, total cholesterol, HDL cholesterol, LDL cholesterol and triglyceride levels were measured by enzymatic methods, and insulin levels were assessed by electrochemiluminescence immunoassay method.

Statistical analyses. SPSS (Statistical Package for Social Sciences) for Windows 10.0 was used for the analysis of data. The descriptive statistics of the variables was given in mean ± standard deviation. Student t-test was used for comparison of the groups. One-way analysis of variance (ANOVA) and post hoc Tukey HSD tests were used for comparison of WC quantiles. Results were evaluated at 95% confidence intervals and at a significance level of $p<0.05$.

RESULTS

A total of 1039 subjects (592 females, 447 males) with a mean age of 40.22±12.77 years, were included in the present study. Demographic, anthropometric, and biochemical characteristics of the patients are presented in Table 1.

Table 3. HOMA-IR, triglyceride/HDL cholesterol, and insulin levels by waist circumference quantiles among male subjects

Waist circumference	n	HOMA-IR	Triglyceride/ HDL cholesterol	Insulin
≤86 cm	83	1.34 ± 0.68	2.43 ± 1.41	5.95 ± 2.87
87–90 cm	50	1.55 ± 0.74	2.79 ± 1.39	6.86 ± 2.95
91–94 cm	45	2.03 ± 0.79	3.15 ± 2.07	8.52 ± 3.05
95–98 cm	64	2.33 ± 1.42	4.13 ± 2.02	9.82 ± 5.63
99–102 cm	47	2.64 ± 1.36	4.68 ± 2.54	10.88 ± 5.64
103–106 cm	65	2.90 ± 1.49	3.86 ± 2.12	11.46 ± 5.25
107–110 cm	38	3.48 ± 1.56	4.66 ± 2.91	14.10 ± 6.38
111–120 cm	31	3.98 ± 1.71	4.63 ± 1.94	16.25 ± 7.13
>120 cm	24	5.04 ± 2.19	4.49 ± 2.17	20.72 ± 8.52
p		0.001	0.001	0.001

HOMA-IR: Homeostasis model assessment of insulin resistance.

Table 4. The waist circumference cut-off value that would predict the insulin resistance determined by HOMA-IR in male subjects

Waist circumference	Sensitivity	Specificity	Positive predictive value	Negative predictive value
90 cm	95.26	41.63	54.68	92.24
91 cm	93.16	46.69	56.37	90.23
92 cm	92.11	48.64	57.00	89.29
93 cm	91.58	50.97	58.00	89.12
94 cm	86.84	54.86	58.72	84.94
95 cm	85.79	58.75	60.59	84.83
96 cm	82.63	62.26	61.81	82.90
97 cm	77.37	66.15	62.82	79.81
98 cm	76.32	72.76	67.44	80.60
99 cm	73.68	74.71	68.29	79.34
100 cm	73.68	74.71	68.29	79.34
101 cm	71.58	78.60	71.20	78.91
102 cm	67.37	81.71	73.14	77.21
103 cm	65.79	82.49	73.53	76.53
104 cm	62.11	84.44	74.68	75.09
105 cm	57.89	89.11	79.71	74.11
106 cm	52.63	91.83	82.64	72.39
107 cm	47.37	93.77	84.91	70.67
108 cm	42.11	94.94	86.02	68.93

Male subjects had greater waist circumferences, triglyceride, and triglyceride/HDL cholesterol values than female subjects ($p<0.01$ for each). Conversely, females had higher BMI values, higher total cholesterol, HDL cholesterol, fasting plasma glucose, insulin, HOMA-IR levels, and a frequency of metabolic syndrome ($p<0.01$ for each).

HOMA-IR, insulin, and triglyceride/HDL cholesterol levels by WC quantiles, for male and female subjects are shown in Tables 2 and 3. HOMA-IR, insulin, and triglyceride/HDL cholesterol levels increased as WC increased in both genders ($p<0.01$ for all).

According to ROC analysis, WC cut-off values with maximum sensitivity and specificity in predicting insulin resistance were 93 cm for males (sensitivity: 91.6%; specificity 51%; positive predictive value: 58%; negative predictive value: 89.1%) and 83 cm for females (sensitivity: 91.1%; specificity 34.8%; positive predictive value: 63%; negative predictive value: 76.2%) (Tables 4 and 5; Fig. 1).

Table 5. The waist circumference cut-off value that would predict the insulin resistance determined by HOMA-IR in female subjects

Waist circumference	Sensitivity	Specificity	Positive predictive value	Negative predictive value
80 cm	92.62	28.46	61.18	76.00
81 cm	92.00	31.46	62.03	76.36
82 cm	91.69	32.96	62.47	76.52
83 cm	91.08	34.83	62.98	76.23
84 cm	89.54	37.08	63.40	74.44
85 cm	88.62	40.07	64.29	74.31
86 cm	87.08	41.20	64.32	72.37
87 cm	85.85	44.94	65.49	72.29
88 cm	84.31	47.19	66.02	71.19
89 cm	82.15	49.44	66.42	69.47
90 cm	79.38	54.31	67.89	68.40
91 cm	77.23	55.60	67.11	67.54
92 cm	76.62	60.67	70.34	68.07
93 cm	72.31	65.17	71.65	65.91
94 cm	94.21	67.42	72.38	92.78

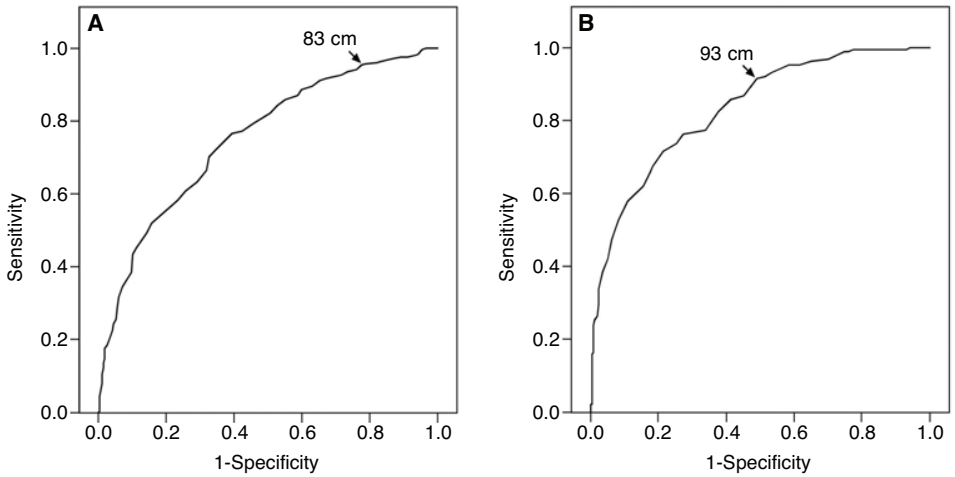

Figure 1. Receiver operating characteristics (ROC) curves **(A)**, for female subjects, **(B)** for male subjects.

DISCUSSION

The results of the present study demonstrates that most appropriate lower waist circumference limits for the prediction of cardiometabolic risk associated with insulin resistance are 93 cm and 83 cm for Turkish male and female individuals, respectively.

Abdominal obesity is regarded as one of the most important predictors of cardiometabolic risk with a key role of insulin resistance.[11] WC cut-off values predicting cardiometabolic risk have been defined by guidelines. The Adult Treatment Panel III defined the lower limit of WC predicting cardiometabolic risk, as 102 cm for males and 88 cm for females.[12] However, the IDF defined different levels for various ethnic origins, demonstrating the need for population-specific cut-off values.[5]

In Tunisian adults, the cut-off point to predict cardiovascular disease and diabetes risk associated with central obesity for both genders was found to be 85 cm.[13] In a large cross-sectional study, Lee et al.[14] reported that appropriate WC cut-off values for central obesity in Korean adults were 85 cm for women and 90 cm for men. In a recent study conducted on Iranian adults, the WC cut-off values for the diagnosis of metabolic syndrome was 91.5 cm in men and 85.5 cm in women.[15] In Turkey, Onat et al. reported the WC cut-off limits for the prediction of cardiometabolic risk as 88 cm and 95 cm for Turkish adult females and males, respectively.[6]

When adopting a definition for abdominal obesity, its association with insulin resistance, as well as its predictive power for coronary heart disease and diabetes, should also be considered. Insulin resistance may be associated with different WC cut-off values in different populations. There are no clear data on the association of abdominal obesity and insulin resistance among Turkish adults. Thus, the present study investigated the association of insulin resistance, assessed by HOMA-IR, with WC in Turkish population. According to ROC analysis, WC cut-off levels that would best predict insulin resistance were 83 cm for women and 93 cm for men.

The WC cut-off values determined in the present study are similar to IDF-defined values for males and 3 cm higher than IDF-defined values for females.[5] In a study conducted on Greek females to identify Mediterranean women with the atherogenic metabolic triad, a WC cut-off value of 84.5 cm was suggested.[16] Turkey is also a Mediterranean country, and WC results determined for Turkish females (83 cm) to predict insulin resistance are similar to the results of the Greek study. Compared to the results of Onat et al.,[6] our WC limits for increased risk were 2 cm lower for men and 5 cm lower for women. The present findings demonstrate that insulin resistance starts at a smaller WC for Turkish adults; thus, it can be suggested that Turkish adults may be at higher risk for metabolic syndrome,[17] diabetes,[18] and hypertension,[19] all of which are known to be associated with insulin resistance.

Although HOMA-IR is an inexpensive and simple tool used extensively for the determination of insulin resistance in large-scale studies, a threshold value for insulin resistance has not yet been standardized.[20] Thus, different HOMA-IR levels used to define insu-

lin resistance may result in variability of WC cut-off values to predict insulin resistance. For instance, in a retrospective study on 2746 healthy subjects, Wahrenberg et al.[21] defined a HOMA-IR value >3.99 as insulin resistance and reported the WC limit that best predicted insulin resistance as 100 cm for both men and women. Other studies have led to different estimates: Bonora et al.[22] reported a HOMA-IR value of 2.77 for insulin resistance among non-obese individuals without metabolic disorder, and Ascaso et al.[4] used a cut-off value of 2.6 for subjects with normal glucose tolerance. These different HOMA-IR cut-off values for insulin resistance in different studies may reflect varying characteristics of study populations, suggesting the need for defining population-specific HOMA-IR cut-off values for the prediction of insulin resistance. In the present study, the median value of the subjects (>2.34) was considered to predict insulin resistance, and the lower WC cut-off values for increased risk found in our study may be a reflection of the lower HOMA-IR limit.

Fasting insulin[23] and triglyceride/HDL cholesterol[24] levels are considered indirect measurements of insulin resistance. In the present study, it was demonstrated that HOMA-IR levels and fasting insulin and triglyceride/HDL cholesterol levels increased with increasing WC quantiles in both genders. This result raises the concern of whether it is necessary to define a WC cut-off value for the prediction of insulin resistance; when the lowest quantiles are taken into account regardless of the cut-off WC value, insulin resistance will be overlooked in a number of individuals with a WC below this cut-off value. It resembles to the fact that cardiovascular risk starts from 115 mmHg systolic and 75 mmHg diastolic pressure, although >140 mmHg and >90 mmHg are the diagnostic criteria for hypertension.[25] Similarly, a WC that would predict insulin resistance may be well below the lower thresholds.

Since the present study was conducted on the subjects admitted to the hospital, it may not represent the general Turkish population, which may be regarded as a potential limitation. On the other hand, by excluding diabetic individuals and those receiving treatments that may effect insulin resistance, our results may represent a comparable database on the relation of insulin resistance and WC cut-off values for Turkish adults.

In conclusion, the waist circumference values of 93 cm (for men) and 83 cm (for women) calculated in the present study may be regarded as cut-off values for the prediction of insulin resistance in the adult Turkish population. But the present study also suggests that the lower values of WC may increase cardiometabolic risk because of the gradual increase in insulin resistance far before reaching cut off values. So to take preventive measures before reaching cut off values of abdominal obesity is necessary.

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Conflict of interest statement

The author has provided professional consulting for Boehringer Ingelheim Inc. in some projects.