BACKGROUND: Metabolic syndrome (MetS) is a challenging area in the public health field. Despite an essential role of waist circumference (WC) there is not yet an acceptable cutoff point for this index in many societies. The present study was designed to determine an optimal cutoff point for WC in MetS.

Material and methods: Among 6140 subjects, 5755 participated in all stages of the study. For the purpose of this study, only those ≥ 16 year-old (n=5525) were enrolled in the present study. ROC analysis was conducted to predict at least two other components of MetS by WC. Youden and distance indexes were used to determine the optimal cutoff point of WC in the prediction of MetS.

RESULTS: The prevalence of MetS was 28.4%, according to NCEP/ATPIII criteria, 32.1%, according to the AHA/NHLBI update of ATPIII criteria, 34.9%, according to IDF definition and 38.1% according to the Joint Interim Statement JIS definition. The maximal Youden index was related to the cutoff point value of 90cm in men (0.331) and 91cm in women (0.353). However the minimal distance index was related to cutoff point values of 92-93 cm in men (0.481) and 93 cm in women (0.463), respectively.

CONCLUSION: To identify the MetS, our study suggested a cutoff point of 90-93 cm in men and 90-93 cm in women for WC. WHR may be a more reliable index in the diagnosis of MetS.

Key words: Waist Circumference, Metabolic Syndrome, ROC Curve, Iran.
2. METHODS AND MATERIALS

Study population

This cross-sectional study was undertaken through Amol cohort study, which was initiated in 2009 and mainly focused on non-alcoholic fatty liver disease risk factors among people with age group of 10 and over in Amol city, one of the most populous city of Mazandaran province in northern Iran. The Amol population is about 400,000 with 54% urban residents. The population is served by 25 rural and 16 urban Primary Health Care (PHC) centers.

Study eligibility and sampling frame

Eligibility criteria in the present study were the age equal to or older than 16 years and no pregnancy. Multistage sampling was used to enroll participants in the baseline. In the first step, a total of rural and urban health centers were determined as data collection units where approximately all rural and urban residents are covered. In the next step, using quota sampling method 5755 study subjects were selected randomly as a baseline for each cluster. This cross-sectional study was undertaken through Amol cohort study, which was initiated in 2009 and mainly focused on non-alcoholic fatty liver disease risk factors among people with age group of 10 and over in Amol city, one of the most populous city of Mazandaran province in northern Iran. The Amol population is about 400,000 with 54% urban residents. The population is served by 25 rural and 16 urban Primary Health Care (PHC) centers.

Data collection procedure, Laboratory assessment

The anthropometric indexes, including height, weight, WC and hip circumference (HC), were measured by trained nurses who were familiar with regional language, at given health centers or through home visits. These indexes were measured with a non-stretchable accurately calibrated and ergonomic scale within 0.5 centimeters (cm) precision. We used the following formulas to compute BMI, WHR and WHtR, and respectively. The blood pressure was measured after 5 minutes rest in a quiet room, controlling the white coat effect. We used the BS200 Auto analyzer (Mindray, Pars Azmoun Pharmaceuticals, Tehran) for laboratory assessment. The coefficients of variation were 1.7% to 3.8% for all laboratory measurements. The testing kits were provided by Pars Azmoun Pharmaceuticals, Tehran.

Metabolic syndrome definitions:

In this study several criteria of metabolic syndrome were used, including: 2005 criteria of the international diabetes federation [IDF], 2001 the national cholesterol education program adult treatment panel III [NCEP /ATPIII], NCEP ATPIII modified in 2005 by the American heart association and national heart, lung, and blood institute [AHA / NHLBI] (2-4). We also used the 2009 definition of the joint interim statement [JIS] in which the cutoff points for WC were regionally defined in terms of population characteristics(5). For instance, the cutoff points 94cm and 80 cm were suggested for WC in men and women of Mediterranean and European populations respectively (5).

Statistical analysis

Mean blood pressure, demographic, anthropometric and laboratory values with related standard deviations were calculated. The prevalence of metabolic syndrome was calculated according to various definitions. To determine the agreement values between different definitions of metabolic syndrome, the χ agreement coefficients (κ statistics) were calculated. Also, using SAS LOGISTIC procedure, the predictive power of four obesity indexes (WC, BMI, WHR, W/HtR) were compared to predict at least two other components of MetS. To achieve this goal the AUC of different obesity indexes were compared by the calculation global hypothesis test (Chi-square, degree of freedom, P-value), contrasts (WC was considered as ROC contrast reference) and related P-values.

Receiver Operating Characteristic (ROC) analysis was used to determine a new cutoff point for WC to predict at least two other components of MetS. To achieve this goal the AUC of different obesity indexes were compared by the calculation global hypothesis test (Chi-square, degree of freedom, P-value), contrasts (WC was considered as ROC contrast reference) and related P-values. Finally, Receiver Operating Characteristic (ROC) analysis was used to determine a new cutoff point for WC to predict at least two other components of MetS.

Table 1. Baseline Anthropometric and some Laboratory Characteristics of study participants by sex. SD denotes standard deviation, WC waist circumference, HC hip circumference, BP blood pressure, SBP systolic blood pressure, DBP diastolic blood pressure, FBS fasting blood sugar, TG triglyceride, HDL high density lipoprotein, BMI denotes body mass index, WHR Waist to hip ratio and W/HR Waist to height ratio. † The values ≥94 cm and ≥80 cm were considered as high WC for male and female respectively. ‡ The SBP ≥130 and diastolic BP ≥85 mmHg as well as treated hypertension were considered as the high blood pressure. ‡ The values ≥50 mg/dl and ≤30 mg/dl were considered as high FBS for male and female respectively. £ The values ≤50 mg/dl and ≤40 mg/dl were considered as low HDL for male and female respectively. £ £ The significant level was considered 0.01.

Table 1. Baseline Anthropometric and some Laboratory Characteristics of study participants by sex. SD denotes standard deviation, WC waist circumference, HC hip circumference, BP blood pressure, SBP systolic blood pressure, DBP diastolic blood pressure, FBS fasting blood sugar, TG triglyceride, HDL high density lipoprotein, BMI denotes body mass index, WHR Waist to hip ratio and WHtR Waist to height ratio. * The values ≥94 cm and ≥80 cm were considered as high WC for male and female respectively. † The SBP ≥130 and diastolic BP ≥85 mmHg as well as treated hypertension were considered as the high blood pressure. ‡ The values ≥50 mg/dl and ≤30 mg/dl were considered as high FBS for male and female respectively. £ The values ≤50 mg/dl and ≤40 mg/dl were considered as low HDL for male and female respectively. £ £ The significant level was considered 0.01.

Participants characteristics Total (n=5257) Male (n=2991) Female (n=2266) £ £ P-value
Age (year) 44.35 ± 16.38 44.62 ± 16.89 43.99 ± 15.66 0.160
Weight (kg) 74.72 ± 15.01 76.48 ± 15.19 72.39 ± 14.44 <0.001
Height (cm) 164.08 ± 10.12 169.95 ± 7.91 156.34 ± 7.06 <0.001
WC (cm) Mean ±SD 91.44 ± 12.81 91.11 ± 12.36 91.88 ± 13.37 0.032
Prevalence of High WC (%)* 60.0 42.8 82.8 <0.001
HC (cm) 103.48 ± 9.92 101.01 ± 8.33 106.75 ± 10.86 <0.001
BP(mmHg) SBP (mmHg) Mean ±SD 76.36 ± 12.90 76.69 ± 12.68 75.91 ± 13.19 0.032
Prevalence of High BP (%)† 51.6 32.4 30.5 0.061
DBP (mmHg) Mean ±SD 116.90 ± 16.7 117.64 ± 15.82 115.93 ± 17.77 <0.001
FBS (mg/dl) Mean ±SD 100.73 ± 35.13 98.45 ± 29.69 103.72 ± 41.03 <0.001
Prevalence of High FBS†‡ 28.2 26.4 30.5 <0.001
TG (mg/dl) Mean ±SD 139.96 ± 86.35 141.80 ± 88.76 137.52 ± 83.00 0.075
Prevalence of High TG‡ 159
HDL (mg/dl) Mean ±SD 43.86 ± 11.41 42.58 ± 11.02 45.56 ± 11.70 <0.001
Prevalence of Low HDL (%) £ 53.9 45.7 64.8 <0.001
BMI (kg/cm²) 27.96 ± 5.34 26.59 ± 4.61 29.78 ± 5.68 <0.001
WHR 0.88 ± 0.09 0.92 ± 0.08 0.86 ± 0.09 <0.001
W/HtR 0.56 ± 0.09 0.54 ± 0.08 0.59 ± 0.09 <0.001

Table 1. Baseline Anthropometric and some Laboratory Characteristics of study participants by sex. SD denotes standard deviation, WC waist circumference, HC hip circumference, BP blood pressure, SBP systolic blood pressure, DBP diastolic blood pressure, FBS fasting blood sugar, TG triglyceride, HDL high density lipoprotein, BMI denotes body mass index, WHR Waist to hip ratio and W/HR Waist to height ratio. * The values ≥94 cm and ≥80 cm were considered as high WC for male and female respectively. † The SBP ≥130 and diastolic BP ≥85 mmHg as well as treated hypertension were considered as the high blood pressure. ‡ The values ≥50 mg/dl and ≤30 mg/dl were considered as high FBS for male and female respectively. £ The values ≤50 mg/dl and ≤40 mg/dl were considered as low HDL for male and female respectively. £ £ The significant level was considered 0.01.
nents of MetS. The optimal cutoff value of WC was determined based on two popular indexes; Youden and distance indexes, in which the indexes usually produce different cutoff points unless the sensitivity is equal to specificity (15). Hence, we reported optimal cutoff value as a range through cutoff points of indexes. Significance levels for all analysis were considered 0.05. All statistical analyses were performed using SPSS ver 18 and SAS ver 9.2.

Ethical approval

The study protocol was approved by the Ethics committee of the Iran University of Medical Sciences in conformity with the guidelines of the declaration of Helsinki. Written informed consent was obtained from all participants after describing the study.

3. RESULTS

Table 1 presents demographic, anthropometric and metabolic characteristics of study participants by sex. In comparison of these characteristics, mean weight, height, WHR and Systolic/Diastolic blood pressure were higher in men, while women had significantly higher mean HC, BMI, WHtR, HDL and FBS s. However, the mean TG difference was not statistically significant based on sex.

Table 2 shows the prevalence of MetS based on various definitions and by sex. In general, the prevalence of MetS in all categories of definitions was higher in women (39% to 46.9%) compared to men (20.4% to 35.2%). While, the lowest prevalence rates were related to NHLBI / ATP III definition for two sex groups, the highest rates for females and males were found in the JIS- definition based on proposed cutoff points for Mediterranean population and Delavari study proposed cutoff points respectively.

Table 3 contains the AUC of obesity indexes and confidence intervals to compare the predictive power of at least two other components of MetS by sex using ROC analysis. While the strongest predictor index was WC in men, the AUC difference of WC with other obesity components (BMI, WHR and WHtR) was not statistically significant. Also, the strongest predictor index was WHR in women, although the only AUC

<table>
<thead>
<tr>
<th>Definition category</th>
<th>NHLBI / ATP III</th>
<th>AHA/NHLBI update of ATP III</th>
<th>IDF</th>
<th>JIS-based on WC cutoff points for Mediterranean population</th>
<th>JIS-based on WC cutoff points that proposed by one study of Iran</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHLBI / ATP III</td>
<td>1</td>
<td>0.929</td>
<td>0.835</td>
<td>0.841</td>
<td>0.890</td>
</tr>
<tr>
<td>AHA/NHLBI update of ATP III</td>
<td>0.888</td>
<td>1</td>
<td>0.901</td>
<td>0.911</td>
<td>0.948</td>
</tr>
<tr>
<td>IDF</td>
<td>0.627</td>
<td>0.669</td>
<td>1</td>
<td>0.900</td>
<td>0.850</td>
</tr>
<tr>
<td>JIS-based on proposed cutoff points for Mediterranean population</td>
<td>0.715</td>
<td>0.821</td>
<td>0.872</td>
<td>1</td>
<td>0.860</td>
</tr>
<tr>
<td>JIS-based on Delavari study proposed cutoff points</td>
<td>0.627</td>
<td>0.728</td>
<td>0.777</td>
<td>0.902</td>
<td>1</td>
</tr>
</tbody>
</table>

* significant level was considered 0.05.

Table 3. KAPPA agreement coefficients through various definitions of metabolic syndrome by sex. *: all values were significant at 0.05, £: ATP III denotes Adult Treatment Panel III, ATP III/AHA/NHLBI Adult Treatment Panel III/ American Heart Association/ National Heart, Lung, and Blood Institute; IDF International Diabetes Federation; JIS joint interim statement. ££ 89 cm and 91 cm were proposed for men and women respectively (13).
difference between WC and BMI was significant. Moreover in the determination of an appropriate cutoff point for WC, the maximal Youden index in men (0.33) and women (0.35) were corresponded to the cutoff of 90 cm and 91 cm respectively as well as the cutoff point values of 92-93 cm in men as well as point value of 93 cm in women were related to minimal distance index (0.48 and 0.46 respectively). As could be expected from this, the range of 90-93 cm and 91-93 cm, were introduced as suitable cutoff points for males and females respectively.

### 4. DISCUSSION

We identified a separate cutoff for WC in both sex. Although the prevalence of MetS was higher in women based on all different definition of MetS, it was attenuated when study cutoff points of WC were used. While BMI as general obesity measure was not an appropriate index to predict at least two other components of MetS, the WHR was reliable, particularly in women. Considering WHR as a sex discriminating body shape measure to differentiate the android (apple shaped) and the gynoid (pear shaped) fat distribution, the high predictive power of this index was expected. A reasonable cutoff for WC was determined based on Western population’s anthropometric characteristics which are different from our populations due to differences in diet, parity, physical activity, genetic background, alcohol consumption and cigarette smoking, particularly in women. Thus, it might be the IDF and ATPIII cutoff points less applicable for Iranian population (18, 19).

The lower predictive power of BMI indicates this index cannot be a reliable obesity measure to MetS diagnosis, particularly in women (6-9, 20). These results are biologically expected, because BMI is an index of overall body fat and it is not incorporated visceral fat. In other hand, it is expected the WC and other indexes which are its adjusted form, have a good predictive power as a result of an association with the hypertrophic form of obesity and its outcomes including metabolic alterations (21, 22). In comparison to obesity indexes, the WHR indicated strongest predictive power to estimate at least two other components of MetS, particularly in women. Considering WHR as a sex discriminating body shape measure to differentiate the android (apple shaped) and the gynoid (pear shaped) fat distribution, the high predictive power of this index was expected.

Overall, high WC and low serum HDL were the most prevalent components of MetS in affected subjects as well as the total population. The inappropriate high prevalence of high WC in women of these two populations, can be partly attributed to implementation of inappropriate cutoff point particularly in women. However, Women in the present study had a higher mean WC compared to European women (23), which can be partly attributed to the sedentary lifestyle in Iranian women mainly due to the lower occupation rates (24), although the mechanism of obesity is associated with disruption of fine en-

### Table 4. The Area under curve AUC and confidence intervals of different indicators of central obesity to predict at least two other components of metabolic syndrome by sex. AUC denotes Area of under curve, WC waist circumference, BMI body mass index, WHR waist to hip ratio, WHtR waist to height ratio, SE standard error, CI confidence interval * significant level was considered 0.05

<table>
<thead>
<tr>
<th>Central obesity indicators</th>
<th>WC</th>
<th>BMI</th>
<th>WHR</th>
<th>WHtR</th>
<th>BMI-WC</th>
<th>WHR-WC</th>
<th>WHtR-WC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Area (men)</strong></td>
<td>0.719</td>
<td>0.710</td>
<td>0.708</td>
<td>0.713</td>
<td>-0.008</td>
<td>-0.010</td>
<td>-0.006</td>
</tr>
<tr>
<td>SE</td>
<td>0.009</td>
<td>0.009</td>
<td>0.009</td>
<td>0.009</td>
<td>0.009</td>
<td>0.009</td>
<td>0.006</td>
</tr>
<tr>
<td>Wald’s CI</td>
<td>0.701 to 0.737</td>
<td>0.692 to 0.729</td>
<td>0.690 to 0.727</td>
<td>0.694 to 0.731</td>
<td>-0.018 to 0.001</td>
<td>-0.022 to 0.001</td>
<td>-0.013 to 0.0006</td>
</tr>
<tr>
<td>Chi-square</td>
<td>351.76 (df=1)</td>
<td>324.11 (df=1)</td>
<td>268.49 (df=1)</td>
<td>341.10 (df=1)</td>
<td>2.91</td>
<td>2.93</td>
<td>3.14</td>
</tr>
<tr>
<td>P-value*</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.0879</td>
<td>0.0866</td>
<td>0.0763</td>
</tr>
<tr>
<td>Global hypothesis test: (chi-square = 429.12, df=4, P-Value= &lt;0.0001) Contrasts: (contrast reference: WC, chi-square = 8.38, df=3, P-Value = 0.039)</td>
<td></td>
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</table>

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<tr>
<th>Central obesity indicators</th>
<th>WC</th>
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<th>WHR</th>
<th>WHtR</th>
<th>WC-WHR</th>
<th>BMI-WHR</th>
<th>WHtR-WHR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Area (women)</strong></td>
<td>0.739</td>
<td>0.667</td>
<td>0.754</td>
<td>0.747</td>
<td>-0.015</td>
<td>-0.087</td>
<td>-0.007</td>
</tr>
<tr>
<td>SE</td>
<td>0.010</td>
<td>0.011</td>
<td>0.010</td>
<td>0.010</td>
<td>0.008</td>
<td>0.012</td>
<td>0.008</td>
</tr>
<tr>
<td>Wald’s CI</td>
<td>0.719 to 0.759</td>
<td>0.645 to 0.689</td>
<td>0.735 to 0.774</td>
<td>0.727 to 0.767</td>
<td>-0.032 to 0.013</td>
<td>-0.112 to -0.061</td>
<td>-0.023 to 0.088</td>
</tr>
<tr>
<td>Chi-square</td>
<td>317.29 (df=1)</td>
<td>178.80 (df=1)</td>
<td>318.29 (df=1)</td>
<td>338.22 (df=1)</td>
<td>3.26</td>
<td>46.07</td>
<td>0.81</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.0707</td>
<td>&lt;0.0001</td>
<td>0.3564</td>
</tr>
<tr>
<td>Global hypothesis test: (chi-square = 444.20, df=4, P-Value= &lt;0.0001) Contrasts: (contrast reference: WC, chi-square = 151.30, df=3, P-Value= &lt;0.0001)</td>
<td></td>
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</table>
ergy homeostasis and does not obey a simple process (23, 25).

The main limitation of this study can be referred to cross sectional design of the study. This implies that there is a need for more population based studies to determine WC cutoff points for the Iranian population. Until such data become available for all of the population in Iran or even Middle East, we can implement our cutoff points as the best available and useful points for WC in both men and women.

5. CONCLUSION

We proposed the optimal cutoff values of 90-93cm for diagnosis of MetS in Iran so that the prevalence of MetS was markedly related to new WC cutoff points. Although the BMI is not a good index in the prediction of MetS, WHR can be suggested as a reliable index to diagnose MetS particularly in women.

REFERENCES