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ORIGINAL ARTICLE

Prospective Study

Are body mass index and waist circumference significant predictors of diabetes and prediabetes risk: Results from a population based cohort study

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Abstract

AIM

To determine the predictive role of body mass index (BMI) and waist circumference (WC) for diabetes and prediabetes risk in future in total sample as well as in men and women separately.

METHODS

In a population based cohort study, 1765 with mean ± SD age: 42.32 ± 6.18 healthy participants were followed up from 2003 till 2013 (n = 960). Anthropometric and biochemical measures of participants were evaluated regularly during the follow up period. BMI and WC measures at baseline and diabetes and prediabetes status of participants at 2013 were determined. Multivariable logistic regression analysis was used for determining the risk of diabetes and prediabetes considering important potential confounding variables. Receiver operating characteristic curve analysis was conducted to determine the best cut of values of BMI and WC for diabetes and prediabetes.

RESULTS
At 2013, among participants who had complete data, 45 and 307 people were diabetic and prediabetic, respectively. In final fully adjusted model, BMI value was a significant predictor of diabetes (RR = 1.39, 95%CI: 1.06-1.82 and AUC = 0.68, 95%CI: 0.59-0.75; $P < 0.001$) however not a significant risk factor for prediabetes. Also, WC was a significant predictor for diabetes (RR = 1.2, 95%CI: 1.05-1.38 and AUC = 0.67, 95%CI: 0.6-0.75) but not significant risk factor for prediabetes. Similar results were observed in both genders.

CONCLUSION
General and abdominal obesity are significant risk factors for diabetes in future.

Key words: Diabetes; Prediabetes; Waist circumference; Body mass index; Anthropometric measure

Core tip: The predictive powers of body mass index (BMI) and waist circumference (WC) were similar in predicting the incidence risk of diabetes in either gender. The cut-off points for predicting diabetes in men and women were different. Defined cut-off points based on maximum sensitivity plus specificity values suggested that in men, BMI of 26.2 kg/m^2 and WC of 89.7 cm, and in women, BMI of 28.6 kg/m^2 and WC of 84.3 cm would predict Isfahanian population at high risk for developing diabetes.

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INTRODUCTION

The increased prevalence of obesity in the world[1] is a major concern as it is strongly related to multiple metabolic disorders[2]. General obesity measured by body mass index (BMI) is a known risk factor for diabetes[2]. Although BMI is often advocated as a simple measure to determine disease risk, it has several limitations. First, lean mass and fat mass could not be differentiated for a given BMI across age, sex and race[3]. Second, fat distribution could not be distinguished by BMI[4,5], whilst it has been generally accepted that visceral adiposity plays more important role in developing insulin resistance and diabetes rather than overall adiposity[6-8]. Therefore, waist circumference (WC) was developed as an abdominal adiposity measure which considers fat distribution.

Although in most populations WC is a stronger predictor for diabetes compared with BMI[7,8], no significant differences were observed between WC and BMI in Japanese[9] and Iranians[10] to predict disease risk. In addition, available risk thresholds predominantly come from European populations which might not be applicable to the Asian population due to differences in genetics and obesity pattern. Therefore, it is essential to identify the best anthropometric index and effective risk thresholds for adiposity measures to develop appropriate preventive strategies in each population.

Based on International Diabetes Federation (IDF)'s recommendation, WC cut-off values for clinical practice should be determined in different ethnicities[11]. Although IDF has suggested WC greater than 90 and 80 cm, respectively for Asian men and women, as cut-off point for abdominal obesity, there is no consensus for WC cut-off point in Iranians. Studies in this regard have suggested that 89-95 cm for men and 85-97 cm for women may be optimal cut-off points for abdominal obesity[12-15]. Nevertheless, to the best of our knowledge, there is only one longitudinal study among Iranians which has determined cut-off point of WC for detecting cardiovascular disease risk[15], and other cut-off points come from cross-sectional surveys[12-14,16]. These values might be limited because of the design of study.

The present study aimed to prospectively determine the effective anthropometric measures to predict the risk of type 2 diabetes and prediabetes also estimate the optimal cut-off point of WC and BMI by following up non-diabetic participants at baseline examination. Estimated cut-off points by this study will contribute to detect individuals at higher risk of developing type 2 diabetes as well as prediabetes in the Iranian population.

MATERIALS AND METHODS

Study subjects

Subjects in the present study were the participants in the Isfahan Diabetes Prevention Study (IDPS), an ongoing cohort study in central Iran. The aim of this study is evaluating the role of diet and physical activity in the prevention or delay the developing of diabetes in first-degree relatives (FDRs) of patients with type 2 diabetes. This study was run between 2003 and 2013. One thousand, seven hundred and sixty-five healthy participants including 446 (25.3%) males and 1371 (74.6%) females were selected from a consecutive sample who attended in the clinics of Isfahan Endocrine and Metabolism Research Center. Data from 960 people including 255 (25.5%) male and 705 (73.4%) female at 2013 were subjected to statistical analysis. Health status and potential risk factors for diabetes were assessed using a questionnaire. To update demographic, anthropometric, and lifestyle information as well as diagnosis new diabetic cases, follow-up tests were run according to a medical care standard in diabetes[17]. Accordingly, participants with impaired 2-h OGTT at baseline were annually tested, and individuals with normal 75 g 2-h oral glucose test tolerance (2-h OGTT) were tested at least at 3-year intervals. More details regarding the participants and methodology of IDPS have been described elsewhere[18]. Informed written consent was obtained from all study participants and the Ethical Committee of Isfahan University of Medical Sciences approved the protocol of study.

Anthropometric assessment

Anthropometric indices were measured by well-trained examiners at baseline while participants were minimally clothed and without footwear. Weight was measured using a balanced scale and recorded to the nearest 0.1 kg. Height was determined using a wall-fixed tape measure while participants were in a normal standing position and recorded to the nearest 0.5 cm. WC and hip circumference were determined using a metal tape measure without imposing any pressure to body surface and were recorded to the nearest 0.5 cm. The location for measuring WC was considered as the narrowest level between the lowest rib and iliac crest, whilst for hip circumference was conserved as the largest level[19]. BMI was calculated as body weight in kilogram divided by height in Square meter.

Laboratory measurement

Biochemical tests including lipid profile, fasting plasma glucose (FPG) and OGTT were carried out for all participants. To determine lipid profile and FPG, a blood sample was drawn from all participants after 10-12 h overnight fasting. Postprandial plasma glucose was measured using venous blood sample at 30, 60, and 120 min after oral glucose administration. Plasma glucose and lipid profile concentrations were determined using enzymatic colorimetric method (ParsAzmoon, Tehran, Iran) adapted to a Selectra-2 auto-analyzer (Vital Scientific, Spankeren, Netherlands). Serum concentration of low-density lipoprotein cholesterol (LDL-C) was calculated by Friedwald equation in individuals with serum TG levels < 400 mg/dL[20]. HbA1c concentrations were measured in whole blood samples *via* the pink reagent kit on a DS5 analyzer. Both intra- and inter-assay coefficients of variability (CVs) were < 2.2% for all markers.

Definition of diabetes

The criteria for the diagnosis of diabetes and impaired glucose tolerance test were based on the American diabetes association (ADA) definition. Accordingly, cut-off point for impaired fasting glucose was considered as 100 mg/dL[17]. Diabetes was defined as FPG ⩾ 126 mg/dL, or HbA1C ⩾ 6.5% or 2-h OGTT ⩾ 200 mg/dL.

Assessment of other variables

Blood pressure was measured using a Mercury sphygmomanometer while subjects were in seated position two times with at least 30 s interval between measurements. The mean of two measurements was recorded as the subject's blood pressure. Hypertriglyceridemia was defined as serum TG ⩾ 150 mg/dL, high LDL-C as LDL-C ⩾ 130 mg/dL, hypercholesterolemia asTC ⩾ 200 mg/dL and low HDL-C as HDL-C < 50 mg/dL in female and < 40 mg/dL in male. According to the JNC and WHO Guideline criteria, hypertension was defined as systolic blood pressure (SBP) ⩾ 130 mmHg, diastolic blood pressure (DBP) ⩾ 85 mmHg and/or antihypertensive medications[21].

Statistical analysis

Continuous and categorical data were presented as mean ± SD. Normality of quantitative data was evaluated using Kolmogorov-Smirnov test and Q-Q plot. Positive skewed data was subjected to logarithmic transformation. χ^2 test was used for evaluating the association between categorical data. Between groups comparisons of quantitative data were conducted using Analysis of variance (ANOVA) or nonparametric Kruskal-Wallis tests. To determine the association between BMI and WC values at baseline (2003) as an independent variable and type 2diabetes and prediabetes at 2013, we used binary logistic regression analysis in different models. In these analyses, after obtaining relative risk (RR) and 95% confidence interval (95%CI) in crude model, adjustment was made for age and sex, smoking, positive family history in the first model. Additional adjustment was made for physical activity and energy intake in the second model. In third model adjustment additionally was done for FBS and HbA1c. Finally, adjustment was made for all mentioned variables and lipid profile indices (including TG, LDL, HDL and cholesterol) and blood pressure.

The predictive values of BMI and WC values for type 2 diabetes and prediabetes were evaluated using receiver operating characteristic curve (ROC) analysis and area under the curve (AUC) and its 95%CI. The optimal sensitivity and specificity for different cut off values of BMI and WC were calculated using Youden index. Statistical analyses were performed using statistical package for social science (SPSS version 15, SPSS, Inc., IL, United States).

RESULTS

General characteristics of participants at baseline are presented in Table 1. Individuals who affected by diabetes after 10 years follow up had greater BMI, WC, hip circumference, waist to hip ratio, fasting blood sugar, glycemic response, total cholesterol, triglyceride and systolic and diastolic blood pressures at baseline. Abdominal obesity at baseline was more prevalent

Table 1 Characteristics of study population at baseline

	Normal (n = 599)[1]	Pre-diabetes (n = 307)[1]	Diabetes (n = 45)[1]	P value
Whole population				
Age (yr)	42.06 ± 6.17	42.72 ± 6.20	43.20 ± 6.19	0.197
Energy intake (kcal/d)	1844.32 ± 553.85	1793.43 ± 571.48	1908.95 ± 598.94	0.646
Weight (kg)	72.09 ± 12.10	73.51 ± 12.49	78.22 ± 11.96	0.943
Height (cm)	160.21 ± 8.31	160.09 ± 8.62	159.81 ± 8.58	0.197
Body mass index (kg/m^2)	28.09 ± 4.17	28.66 ± 4.18	30.63 ± 4.15	< 0.0001
Waist circumference (cm)	87.00 ± 9.58	88.72 ± 9.75	92.86 ± 9.08	< 0.0001
Hip circumference (cm)	106.21 ± 8.54	107.35 ± 8.77	110.35 ± 9.27	0.003
Waist to hip ratio	0.82 ± 0.07	0.83 ± 0.07	0.84 ± 0.05	0.078
Fasting blood sugar	87.04 ± 7.99	89.30 ± 7.03	91.0 ± 6.14	< 0.0001
Blood sugar after 30 min (mg/dL)	127.41 ± 25.19	136.43 ± 26.48	141.49 ± 25.48	< 0.0001
Blood sugar after 60 min (mg/dL)	123.02 ± 32.06	136.19 ± 31.17	151.81 ± 36.61	< 0.0001
Blood sugar after 120 min (mg/dL)	98.11 ± 21.15	104.81 ± 21.08	110.94 ± 18.80	< 0.0001
HbA1c (%)	4.94 ± 0.78	5.08 ± 0.75	5.17 ± 0.78	0.014
Triglyceride (mg/dL)	150.15 ± 77.29	156.50 ± 83.83	200.82 ± 130.48	< 0.0001
Total cholesterol (mg/dL)	190.30 ± 38.16	192.47 ± 35.97	205.51 ± 50.56	0.034
LDL-C (mg/dL)	116.34 ± 33.45	117.04 ± 32.26	123.52 ± 52.88	0.436
HDL-C (mg/dL)	45.04 ± 11.75	44.78 ± 10.31	45.12 ± 11.55	0.944
Systolic blood pressure (mmHg)	110.23 ± 10.49	110.73 ± 10.66	110.76 ± 10.64	< 0.0001
Diastolic blood pressure (mmHg)	70.37 ± 10.11	70.64 ± 10.20	70.65 ± 10.26	0.002
Abdominal obese (WC > 90 cm) (%)	32.9	41.8	57.4	< 0.0001
Men				
Age (yr)	43.04 ± 6.73	42.48 ± 6.20	43.85 ± 7.16	0.71
Energy intake (kcal/d)	2384.54 ± 558.37	2176.44 ± 648.34	2536.88 ± 651.42	0.343
Weight (kg)	77.98 ± 12.95	79.43 ± 13.44	81.38 ± 6.13	0.53
Height (cm)	170.78 ± 6.47	170.56 ± 6.30	169.55 ± 5.22	0.802
Body mass index (kg/m^2)	26.66 ± 3.53	27.22 ± 3.82	28.32 ± 1.82	0.201
Waist circumference (cm)	92.63 ± 9.43	93.14 ± 9.86	97.65 ± 7.64	0.19
Hip circumference (cm)	102.76 ± 6.68	103.91 ± 7.76	108.15 ± 7.19	0.025
Waist to hip ratio	0.90 ± 0.06	0.89 ± 0.05	0.90 ± 0.03	0.754
Fasting blood sugar	87.55 ± 8.25	90.34 ± 6.91	92.54 ± 4.11	0.005
Blood sugar after 30 min (mg/dL)	133.20 ± 28.96	140.95 ± 28.86	144.42 ± 31.05	0.091
Blood sugar after 60 min (mg/dL)	128.50 ± 35.76	136.26 ± 35.35	147.69 ± 44.80	0.081
Blood sugar after 120 min (mg/dL)	91.18 ± 24.14	92.40 ± 21.22	110.08 ± 20.20	0.019
HbA1c (%)	4.94 ± 0.66	5.09 ± 0.89	5.15 ± 1.01	0.293
Triglyceride (mg/dL)	178.85 ± 97.60	177.54 ± 92.37	219.23 ± 101.25	0.328
Total cholesterol (mg/dL)	189.49 ± 383.49	189.45 ± 31.95	204.31 ± 51.08	0.312
LDL-C (mg/dL)	114.74 ± 30.58	113.56 ± 31.07	118.60 ± 43.79	0.87
HDL-C (mg/dL)	40.92 ± 12.01	41.49 ± 9.21	45.92 ± 12.16	0.301
Systolic blood pressure (mmHg)	110.46 ± 10.51	110.87 ± 10.75	120.69 ± 10.48	0.011
Diastolic blood pressure (mmHg)	70.48 ± 10.13	70.83 ± 10.30	80.08 ± 10.08	0.04
Abdominal obese (WC > 90 cm) (%)	59.1	63.5	92.3	0.058
Women				
Age (yr)	41.70 ± 5.92	42.81 ± 6.21	42.94 ± 5.86	0.059
Energy intake (kcal/d)	1738.47 ± 488.91	1674.05 ± 491.68	1715.73 ± 447.60	0.643
Weight (kg)	70.05 ± 11.11	71.17 ± 11.30	77.06 ± 13.36	0.002
Height (cm)	156.52 ± 5.12	156.96 ± 5.25	156.27 ± 6.59	0.43
Body mass index (kg/m^2)	28.58 ± 4.26	29.23 ± 4.19	31.47 ± 4.45	< 0.0001
Waist circumference (cm)	85.10 ± 8.88	87.00 ± 9.16	91.03 ± 9.02	< 0.0001
Hip circumference (cm)	107.37 ± 8.79	108.68 ± 8.79	111.21 ± 9.94	0.02
Waist to hip ratio	0.79 ± 0.05	0.80 ± 0.05	0.82 ± 0.03	0.018
Fasting blood sugar	86.87 ± 7.91	88.89 ± 7.05	90.41 ± 6.71	0.001
Blood sugar after 30 min (mg/dL)	125.21 ± 23.32	134.55 ± 25.26	140.42 ± 23.59	< 0.0001
Blood sugar after 60 min (mg/dL)	120.96 ± 30.41	136.16 ± 29.46	153.38 ± 33.60	< 0.0001
Blood sugar after 120 min (mg/dL)	100.58 ± 19.45	109.63 ± 18.99	111.26 ± 18.55	< 0.0001
HbA1c (%)	4.94 ± 0.82	5.08 ± 0.68	5.18 ± 0.69	0.05
Triglyceride (mg/dL)	140.11 ± 66.06	148.32 ± 79.00	193.34 ± 141.41	< 0.0001
Total cholesterol (mg/dL)	190.74 ± 39.60	193.63 ± 37.41	206.00 ± 51.16	0.092
LDL-C (mg/dL)	117.04 ± 34.27	118.31 ± 32.67	125.64 ± 56.94	0.44
HDL-C (mg/dL)	46.48 ± 11.34	45.99 ± 10.45	44.77 ± 11.48	0.658
Systolic blood pressure (mmHg)	110.15 ± 10.48	110.67 ± 10.63	110.40 ± 10.58	< 0.0001
Diastolic blood pressure (mmHg)	70.33 ± 10.10	70.56 ± 10.15	70.48 ± 10.31	0.044
Abdominal obese (WC > 90 cm) (%)	24.1	33.3	44.1	0.004

[1]Values are mean ± SD. LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; HbA1c: Glycosylated haemoglobin.

Table 2 Crude and multivariable-adjusted relative risk and 95%CI for relative risk obtained from logistic regression

	Total		Men		Women	
	Pre-diabetes	Diabetes	Pre-diabetes	Diabetes	Pre-diabetes	Diabetes
BMI						
Crude	1.03 (1.00, 1.07)	1.14 (1.07, 1.21)	1.04 (0.97, 1.13)	1.14 (0.97, 1.34)	1.04 (1.00, 108)	1.15 (1.07, 1.23)
Model 1	1.04 (1.00, 1.07)	1.14 (1.06, 1.22)	1.14 (0.97, 1.35)	1.04 (0.97, 1.12)	1.03 (0.99, 1.07)	1.14 (1.06, 1.23)
Model 2	1.06 (0.98, 1.15)	1.24 (1.06, 1.46)	1.06 (0.80, 1.40)	1.30 (0.75, 2.26)	1.07 (0.98, 1.17)	1.25 (1.02, 1.53)
Model 3	1.05 (0.96, 1.14)	1.36 (1.05, 1.77)	1.00 (0.75, 1.35)	1.44 (0.42, 4.88)	1.07 (0.97, 1.17)	1.44 (1.05, 1.98)
Model 4	1.04 (0.96, 1.14)	1.38 (1.05, 1.82)	1.00 (0.75, 1.35)	Inestimable	1.07 (0.97, 1.18)	1.51 (1.06, 2.14)
WC						
Crude	1.02 (1.00, 1.03)	1.06 (1.03, 1.09)	1.01 (0.98, 1.03)	1.06 (1.00, 1.13)	1.02 (1.01, 1.04)	1.07 (1.03, 1.11)
Model 1	1.02 (1.00, 1.03)	1.07 (1.03, 1.10)	1.01 (0.98, 1.03)	1.06 (1.00, 1.13)	1.02 (1.00, 1.04)	1.07 (1.03, 1.11)
Model 2	1.04 (1.00, 1.08)	1.16 (1.06, 1.27)	1.00 (0.90, 1.12)	1.08 (0.87, 1.33)	1.05 (1.01, 1.09)	1.20 (1.07, 1.35)
Model 3	1.03 (0.99, 1.07)	1.20 (1.04, 1.38)	0.97 (0.85, 1.09)	1.58 (0.37, 6.76)	1.04 (1.00, 1.09)	1.21 (1.03, 1.42)
Model 4	1.03 (0.99, 1.07)	1.20 (1.04, 1.38)	0.97 (0.86, 1.09)	Inestimable	1.04 (1.00, 1.09)	1.22 (1.03, 1.45)

Model 1: Adjusted for age, and sex only in the whole population; Model 2: Further adjustment was made for physical activity and energy intake; Model 3: Further adjustment was made for blood sugar and HbA1c; Model 4: Further control was made for lipid profile and blood pressure; BMI: Body mass index; WC: Waist circumference.

Table 3 Area under the curve (95%CI for area under the curve) for body mass index and waist circumference on predicting the pre-diabetes or diabetes

	Total		Men		Women	
	Pre-diabetes	Diabetes	Pre-diabetes	Diabetes	Pre-diabetes	Diabetes
Body mass index	0.541 (0.502, 0.581)	0.673 (0.596, 0.749)	0.538 (0.460, 0.617)	0.664 (0.551, 0.778)	0.544 (0.498, 0.590)	0.691 (0.598, 0.784)
Waist circumference	0.552 (0.513, 0.592)	0.674 (0.602, 0.746)	0.508 (0.432, 0.585)	0.613 (0.505, 0.721)	0.564 (0.518, 0.611)	0.691 (0.604, 0.778)

among those who developed (affected by) diabetes.

There were 45 incident cases of physician-diagnosed diabetic patients during follow up from 2003 to 2013. Overall, there was a positive link between BMI and WC in crude and all adjusted models (Table 2). After controlling for various confounders and mediators, relative risk for diabetes increased by 38% for 1 s.d. increase in BMI (95%CI: 1.05-1.82, P = 0.019). One s.d. increase in WC was associated with 20% higher risk for developing diabetes (95%CI: 1.04-1.38, P = 0.010), after controlling for potential confounders and mediators. In men, 1 s.d. increase either in BMI or in WC could not significantly affect the risk of prediabetes and diabetes; however, in women, 1 s.d. increase in both BMI and WC were associated with higher risk of diabetes, but not prediabetes. In the full adjusted model, 1 s.d increase in BMI and WC increased risk of diabetes by 51% (95%CI: 1.06-2.14) and 22% (95%CI: 1.03-1.45) in women, respectively.

The AUCs (and 95%CIs) of BMI and WC in the prediction of pre-diabetes and diabetes are shown in Table 3. AUCs for both measures were larger for diabetes rather than pre-diabetes. As can be seen the significant predictive roles were detected for both BMI and WC on predicting diabetes while positive but not significant for prediabetes. Nevertheless, AUC of WC did not differ substantially from AUC of BMI either for pre-diabetes or for diabetes in the whole population. When analyses were run for men and women separately, similar results were obtained. Figure 1 supports the similar predictive powers of BMI and WC in predicting the incidence risk of diabetes in the whole population and either gender.

Table 4 indicates the optimal cutoff points for general obesity and abdominal adiposity to predict incidence of pre-diabetes and diabetes. Defined cut-off points based on maximum sensitivity plus specificity values suggested that in men, BMI of 26.2 kg/m^2 and WC of 89.7 cm, and in women, BMI of 28.6 kg/m^2 and WC of 84.3 cm would predict the incident risk of diabetes. In the whole population, BMI of 28.5 kg/m^2 and WC of 86.25 and 86.75 cm had the highest maximum sensitivity plus specificity. The optimal cutoff points for BMI to predict pre-diabetes in the whole population, men and women were 28.3, 29.6, 28.3 kg/m^2, respectively. Corresponding values for WC were 86.0, 89.7, 88.2 cm, respectively.

DISCUSSION

In this prospective study, BMI was strongly associated with diabetes incidence in the whole population and women. WC was moderately related to diabetes incident in the whole population and women. These associations remained significant after controlling either for confounding variables or mediators. The associations of BMI and WC with incidence of diabetes in men were not significant, and in overall both BMI and WC were weakly correlated with pre-diabetes incidence.

Adjustment for mediators increased the risk of

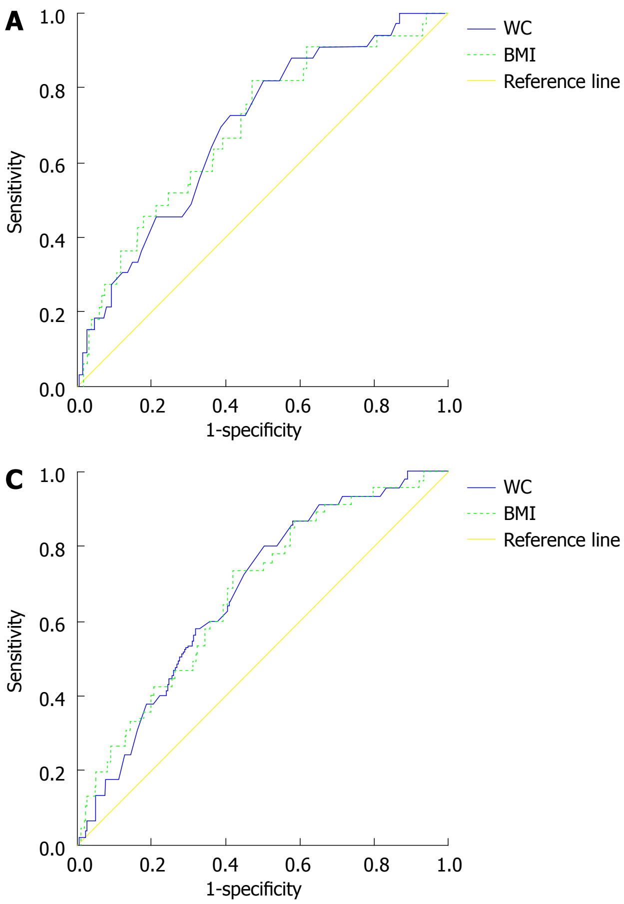

Figure 1 Comparison of receiver-operating characteristic curves for waist circumference (continuous line) and body mass index (dashed line) in women (A), men (B) and the whole population (C).

Table 4 Optimal cutoff points for general obesity and abdominal adiposity to predict incidence of pre-diabetes and diabetes

	Whole population		Men		Women	
	BMI	WC	BMI	WC	BMI	WC
Diabetes						
Cutoff point 1	28.5	86.25	26.2	89.7	28.6	84.3
Sensitivity	0.733	0.787	0.917	1	0.818	0.818
Specificity	0.579	0.495	0.477	0.356	0.53	0.5
Cutoff point 2	29	86.75	27	90	29	85
Sensitivity	0.6	0.766	0.75	0.917	0.667	0.758
Specificity	0.614	0.514	0.53	0.423	0.566	0.532
Pre-diabetes						
Cutoff point 1	28.3	86	29.6	89.7	28.3	88.2
Sensitivity	0.528	0.787	0.294	0.706	0.583	0.45
Specificity	0.559	0.495	0.819	0.356	0.516	0.686
Cutoff point 2	29	87	30	90	29	89
Sensitivity	0.427	0.723	0.235	0.635	0.468	0.376
Specificity	0.614	0.453	0.826	0.409	0.564	0.718

BMI: Body mass index; WC: Waist circumference.

diabetes incidence which might be attributed to adiposity alone or adipocytokines or other unmeasured risk factors such as dietary intake, lifestyle, inflammatory factors and family history[22,23]. Effects of these variables on anthropometric measures have been well-established[24,25]. In the DECODA (Diabetes Epidemiology: Collaborative Analysis of Diagnostic criteria in Asia) study, BMI and WC were not differently associated with the incidence risk of diabetes in men, but in women, WC was stronger anthropometric predictor of diabetes than BMI[7]. A meta-analysis of the Asian cohorts suggested that BMI and WC were similarly related to incident of diabetes[26]; however, in European, WC is stronger predictor for developing diabetes than BMI[8]. Using prospective analyses, similar associations were found for BMI and WC to predict the progression of diabetes in an Iranian population[10]. Nevertheless, in the current analyses, we observed that BMI was a stronger predictor for the incident diabetes in women and the whole population. The discrepancies regarding BMI and WC relation with diabetes in the current analyses might reveal that the length of follow-up duration might be a relevant determinant of estimating incident risk. Regardless of the contradictory results on which of anthropometric measures is better, all studies indicated that both BMI and WC are directly associated with the incidence risk of diabetes. For pre-diabetes, in the whole population, cut points were similar to cut points of diabetes. In men, in spite of similar cut points for WC to predict pre-diabetes *vs* diabetes, there was considerable difference for BMI while greater BMI value was identified as the best cut point. In contrast, in women, BMI cut point for predicting pre-diabetes was similar to the one for diabetes, but WC cut point was considerably higher. This finding confirms that WC in women and BMI in men are better index for predicting pre-diabetes as well as for diabetes.

To determine appropriate cutoff points for anthropometric measures, some variables such as age and sex need to be taken into account. In men and older age adults, higher cut-off points are more suitable. However, in the current study, we determined cut-off points only based on sex since majority of participated subjects at baseline were younger than 60 years which is defined as the age of elderly[27].

In this study, there was no difference in the overall predictive discrimination (as determined by AUC) of BMI and WC in either gender, that is in line with other studies[28,29]. Yoon *et al*[29] indicated that BMI and WC have similar predictive power for insulin resistance and diabetes among Korean adults. Another population-based cross-sectional study on Iranian men and women aged 20-80 years found no difference in the predictive power of BMI and WC for diabetes[28]. Nevertheless, Johnston Alperet *et al*[30] revealed that central obesity measures (WC and waist to height ratio) are better than BMI for the diagnosis of uninvestigated diabetes mellitus in three major Asian ethnic groups (Chinese, Malays, and Asian-Indians).

Available evidences to determine suitable cut-off points for WC and BMI have been obtained from cross-sectional studies[12,13,16]. To the best of our knowledge, there is only one prospective cohort study to predict appropriate cut-off points for diabetes among Iranians[10]. Difference in study design may lead to inconsistency regarding the determined clinically relevant cut-off points in different studies. Moreover, the follow-up duration and the sample size of study may influence these cut points in studies with similar design. Our study suggested that in the whole population, the BMI cut points of 28.5 kg/m^2 and 86 cm for WC yielded the maximum sensitivity plus specificity for predicting the presence of diabetes. Corresponding values in men were 26.2 kg/m^2 and 89.7 cm, and in women were 28.6 kg/m^2 and 84.3 cm, respectively. Generally, women had higher values of BMI but lower values of WC cut points; and this means that in women, central obesity performed better than BMI to predict diabetes risk, whilst in men BMI perform better. In this analysis, ROC analysis was run to identify cut points. It should be taken into account that ROC method is dependent on the distribution of anthropometric measures in the study population. On the other hand, increasing mean values of anthropometrics by corresponding higher distributions would automatically increase derived cut points by the ROC analysis[31]. Therefore, higher cut points of WC in men and BMI in women could be explained by the higher mean values of WC and BMI in men and women, respectively. Moreover, ROC method is equally weighted for sensitivity and specificity[32]. This might lead to low sensitivity for anthropometric measures to predict the incidence risk of diabetes in clinical practice. Furthermore, defined cut points in our study could not be optimal points in clinic, since sensitivity *vs* specificity need to be weighed against other factors such as seriousness of the complaint, the applied test for evaluation (whether it is invasive or feasible) and how often the test must be done[33]. Furthermore, due to high prevalence of diabetes in Iran[25], it is relevant to identify a sensible proportion of the population at risk. Our defined cut-off points' sensitivity are higher than 80% that means only 20% diabetic subjects would be missed by these cut points. However, for pre-diabetes sensitivity is very low.

This study has several limitations that should be taken into account. The main limitation is few numbers of cases with diabetes that decrease the statistical power of analyses. Furthermore, our study population was not a representative sample of Iranians and therefore more studies are needed to confirm whether our findings are generalizable to other Iranian populations. In addition, a recent research has shown that non-alcoholic fatty liver disease (NAFLD) might be a new criterion for metabolic syndrome[34]. Regarding the high prevalence of NAFLD among Iranians[35] and due to its close relation with insulin resistance, further studies are needed to determine the suitable cut points for BMI and WC for predicting the NAFLD incidence among Iranians. Nevertheless, this study has some strength. Using measured anthropometric variables, not self-reported values, in a large sample of men and women with very reliable data are the main strengths of this study. Furthermore, confounding effects of various confounders and mediators were taken into account in data analyses. Finally, based on our prospective study design an association between fat accumulation and diabetes mellitus could be concluded.

In conclusion, we observed that the predictive powers of BMI and WC were similar in predicting the incidence risk of diabetes in either gender. The cut-off points for predicting diabetes in men and women were different. Defined cut-off points based on maximum sensitivity plus specificity values suggested that in men, BMI of 26.2 kg/m^2 and WC of 89.7 cm, and in women, BMI of 28.6 kg/m^2 and WC of 84.3 cm would predict Isfahanian population at high risk for developing diabetes.

COMMENTS

Background

The increased prevalence of obesity in the world is a major concern as it is strongly related to multiple metabolic disorders, among them diabetes. Therefore, it is essential to identify the best anthropometric index and effective risk thresholds for adiposity measures to develop appropriate preventive strategies in each population.

Research frontiers

Current study aimed to prospectively determine the effective anthropometric measures to predict the risk of type 2 diabetes and prediabetes also estimate the optimal cut-off point of body mass index (BMI) and waist circumference (WC) by following up non-diabetic participants at baseline examination.

Innovations and breakthroughs

To the best of our knowledge, there is only one longitudinal study among Iranians which has determined cut-off point of WC for detecting cardiovascular disease risk and no study on BMI threshold, and other cut-off points come from cross-sectional surveys' on the other hand no study available on determining the best cut of values for prediabetes. These values are strengthening by the authors longitudinal study design.

Applications

Estimated cut-off points by the study will contribute to detect individuals at higher risk of developing type 2 diabetes as well as prediabetes.

Terminology

BMI and WC's best cut of values for predicting diabetes and prediabetes.

Peer-review

The article is an important epidemiological study in which the authors studied a cohort of 1765 healthy participants followed up from 2003 till 2013. The study is well conducted, with appropriate statistics methodology and the results, previously known, confirm the relationship between anthropometric data and diabetes mellitus.

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