New risk models for predicting diabetes and prediabetes in the first-degree relatives of patients with type 2 diabetes and a comparison with the FINDRIC

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Research Article

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Abstract

Background

We aimed to develop a risk model, monitoring the FDRs of patients with type 2 diabetes, who have normal glucose tolerance, to predict the onset of developing diabetes and prediabetes. In this study, 1765 FDRs of patients with type 2 diabetes mellitus, who had normal glucose tolerance, were subjected to statistical analysis. Diabetes risk factors including anthropometric indices, physical activity, fast plasma glucose, plasma glucose concentrations two-hour after oral glucose administration, glycosylated hemoglobin, blood pressure, and lipid profile at the baseline were considered as independent variables. Kaplan-Meier, log Rank test, univariate, and multivariable proportional hazard Cox regression were conducted. The optimal cut point for risk score was created according to receiver operating characteristic curve (ROC) analysis.

Results

The best diabetes predictability was achieved by a model in which waist to hip ratio (WHR), HbA1c, OGTT and the lipid profile were included. The best prediabetes risk model included HbA1c, systolic blood pressure, the lipid profile, and the oral glucose tolerance test (OGTT). These multivariable risk models were compared with FPG, HbA1c, and OGTT. The predictive efficiencies of models were higher than FPG and HbA1c; however the best predictive model of the current study showed comparable predictive efficiency to OGTT-AUC. Additionally, both diabetes models showed better performance than FINDRISC.

Conclusion

We recommend regular tests for FDRs of patients with type 2 diabetes to predict the risk of diabetes and prediabetes by using the OGTT-AUC. As a health check assessment tool, our diabetes models showed a more precise predictor compared to FINDRISC in our population.

Introduction

Type 2 diabetes mellitus (T2DM) has high morbidity and mortality worldwide. In addition, diabetes is responsible for microvascular (blindness, nephropathy and neuropathy) (1, 2) and macrovascular (cardiovascular and stroke) degenerative complications (3). The risk of diabetes in the FDRs of patients with type 2 diabetes mellitus is 2–8 times higher than general population; therefore it is important to establish appropriate predictive strategies for this "at-risk" sub-population (4–6). So that well-timed preventive measures can be implemented at the community level.

Various risk models (7–12) are suggested, using non-invasive tests and blood-based metabolic characters to identify individuals at risk of developing diabetes. Although these models (7–12) are proven

to be efficient in identifying high risk individuals, risk scores developed in one population may not be applicable to others (4, 13). The evaluation of one risk score (the Rotterdam Predictive Model) in nine populations with different ethnic origins (13) have shown significantly varied performance of the risk score among populations. Various models were also investigated in a single population of European (4), indicated that the effect of each model varies with country, age, sex, and adiposity. Because, ethnicity is strongly related to the risk of diabetes, the recalibration of predicting model is necessary for different populations; otherwise, populations with diverse ethnic origins should develop a unique scoring system of their own. Moreover, there are even more limited numbers of risk scores have been developed to identify patients at high risk of prediabetes (14).

Here, we have developed models to predict the risk of diabetes and prediabetes in the FDRs of patients with diabetes in the Isfahan Diabetes Prevention Study (IDPS). We included non-invasive parameters such as anthropometric indices, and physical activity as well as blood-based metabolic characters; followed our participants for 13 ± 2.3 years and developed risk models to predict diabetes and prediabetes in this at-risk population. We have also compared the performance of our models with the gold method, FINDRISC, for predicting diabetes.

Methods And Materials

Study design and participants

Subjects of the present study are participants of the Isfahan Diabetes Prevention Study (IDPS), an ongoing cohort study in the center of Iran. A total of 1765 FDRs of patients with type 2 diabetes who had normal glucose tolerance (NGT) at the baseline were recruited between 2003 and 2005 and followed up to 2019. In the IDPS, those people who were diagnosed as pre-diabetes at the baseline with 75-gram oral glucose test tolerance (OGTT) were tested annually. Individuals with normal OGTT (NGT) were tested at 3-year interval (15). Demographic information, anthropometric measures, biochemical, and clinical data were obtained from the registry of the IDPS at the Isfahan Endocrine and Metabolism Research Center. The Ethics Committee of the Isfahan University of Medical Sciences approved the protocol of this study (IR.MUI.MED.REC.1398.525) and the tenants of the Declaration of Helsinki were followed. All participants had provided written informed consents.

Data collection and definition of variables

Anthropometric indices at the baseline (weight, height, waist circumference, and hip circumference) were measured by trained examiners (16). Waist to hip ratio (WHR) is another anthropometric variable used in the present study. Body mass index (BMI) was considered as weight in kilogram divided by height in meter squared.

A blood sample was collected from all participants after 10 hours overnight fasting for biochemical tests, including fasting plasma glucose (FPG), obtaining blood glucose levels at 30, 60, and 120 min after oral glucose administration, glycosylated hemoglobin (HbA1c), total cholesterol, triglyceride, high density

lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol. Additionally, OGTT was performed for all participants. In this case, plasma glucose was measured using blood samples after 10 hours overnight fasting and 30, 60, and 120 minutes after oral glucose administration (16). All biochemical tests were measured using standard procedures in the central laboratory of the Isfahan Endocrine and Metabolism Research Center (17).The individual was diagnosed by impaired fasting glucose (IFG), if the FPG was between 100 mg/dL and 125 mg/dl, and 2-hour post 75 g glucose load was less than 140 mg/dl. When the 2-h post glucose load was between 140 mg/dL and 199 mg/dL with normal fasting glucose (FPG < 100 mg/dl), the patient was diagnosed by impaired glucose tolerance (IGT). Pre-diabetes were defined as either IFG or IGT or both (18, 19). Subjects were diagnosed with diabetes, if the FPG was ≥ 126 mg/dl and/ or the 2-h post glucose load was ≥ 200 mg/dl. The FPG < 100 mg/dl and the 2-h post glucose load < 140 mg/dl were considered as NGT (19).

Blood pressure was measured using a mercury sphygmomanometer twice, while subjects were in seated position, and the mean was recorded as the blood pressure. Hypertension was defined as systolic blood pressure (SBP) ≥ 130 mmHg, Diastolic blood pressure (DBP) ≥ 85 mmHg and/or taking anti-hypertensive medications, according to the Joint National Committee (JNC) criteria (20).

The overall physical activity level of a person was assessed by using the short form of International Physical Activity Questionnaire (IPAQ) and scored as a continuous variable, metabolic equivalent minutes (MET minutes) a week. We considered resting energy expenditure to be 1 MET minute, walking to be 3.3 MET minutes, moderate physical activity to be 4 MET minutes and vigorous physical activity to be 8 MET minutes (21).

Demographic information including age, gender, educational level (illiterate, under-diploma, diploma (a formal 12-year education), university graduate), and smoking status was recorded through survey questions.

Statistical analysis

Statistical analyses were performed by the Statistical Package for Social Science (SPSS version (15). Continuous and normally distributed data were presented as mean ± standard deviations (SD). Normality of quantitative data was evaluated using Kolmogorov-Smirnov test and Q-Q plot. To evaluate the association between categorical data, χ^2 test was used. Comparisons of normally distributed quantitative data between groups were conducted using the analysis of variance. A two-tailed p-value < 0.05 was considered to be statistically significant.

The oral glucose tolerance test with the area under a curve (OGTT-AUC) was derived from the OGTT curve, using the trapezoidal method between 0-120 minutes according to our previous study (22). The lipid index is a combined measure, which constructed lipid profiles including TG, cholesterol, HDL, and LDL by using exploratory analysis factor (EFA). The OGTT-AUC and lipid index have been used as independent variables in our models.

The optimal cut-points associated with each risk factor were calculated according to the receiver operating characteristics curve (ROC), and these variables were categorized according to the determined cutoff values. We used categorical variables instead of continuous variables to develop a simple model. Kaplan-Meier and log Rank test were conducted to determine the incidence rates of diabetes and prediabetes in 2019 according to the values of risk factors at the baseline as independent variables. The corresponding hazard ratio (HR) was calculated using univariate and multivariable proportional hazard Cox regression. Those risk factors were significant in univariate analyses entered in multivariable Cox regression. During this process we developed a prediction model containing only significant risk factor of developing diabetes and prediabetes in future. Then individuals who had each risk factor (their values were higher than the determined optimal cut of values for significant risk factors) were coded as 1 and others as 0. Then each risk factor's weigh was determined by its corresponding Cox regression coefficient. Finally, all significant risk factors in the final models summed up. The predictive values of our models, which reflected in the calculated risk scores, were evaluated using the ROC curve and the optimal cut points for risk score for each model were determined. The AUC and its 95% CI were reported and the optimal sensitivity, and specificity based on derived cut-off values were calculated using the Youden's index.

The performance of our risk models was compared with other glucose indices (FPG, HbA1c and OGTT-AUC) by using ROC analysis. We also compared the performance of our models for predicting diabetes with Finnish Diabetes Risk Score (FINDRISC). The risk score for variables of the concise FINDRISC model was determined for each participant and the overall risk score was calculated as the sum of the individual scores.

Results

The cumulative incidence rate of diabetes was 7.4% in the NGTs during the follow-up. In addition, 32.6% of participants developed prediabetes and 59.7% remained with the NGT. The characteristics of participants at the baseline were reported at the categories of final status of participants in Table 1. Individuals who developed diabetes after 13 ± 2.3 years, compared to those who remained healthy, had higher WHR, cholesterol, TG, lipid profile, and the OGTT-AUC at the baseline (all P-values < 0.05). Participants who became prediabetes after this period of time were older and had higher waist circumference, OGTT-AUC, HbA1c, cholesterol, TG, and the lipid index at the baseline compared to those who remained healthy (NGT) (all P-values < 0.05) (Table 1**)**. Higher values of these factors at the baseline were correlated significantly to the risk of developing diabetes (all P-values < 0.02) and prediabetes (all P-values < 0.03) (Figs. 1 and 2).

Table 1
participants' characteristics.

		Final status				
variables		Normal	Pre-diabetes	Diabetes	P-value[1] (prediabetes)	P-value[2] (diabetes)
Age		41.89 ± 6	43.29 ± 6.42	43.04 ± 6.12	0.001*	0.094
sex	Male	25.4%	28.2%	33%	0.342	0.124
	Female	74.6%	71.8%	67%		
education	Illiterate	3.2%	4.4%	3.3%	0.778	0.142
	Under-Diploma	46.8%	47.2%	53.3%		
	Diploma	32.6%	32.2%	35.6%		
	University graduate	17.4%	16.2%	7.8%		
smoker		9.10	6.10	9.10	0.363	0.995
BMI (kg/m^2)		28.10 ± 4.20	29.09 ± 4.30	28.65 ± 4.9	0.051*	0.037*
Waist (cm)		86.91 ± 9.69	90.53 ± 9.47	88.75 ± 9.57	0.005*	0.001*
Hip (cm)		106.18 ± 8.59	17.57 ± 8.94	106.88 ± 8.56	0.228	0.153
WHR		0.82 ± 0.07	0.84 ± 0.06	0.83 ± 0.07	0.011*	0.005*
FPG (mg/dl)		87.31 ± 7.67	89.70 ± 7.22	90.35 ± 9.94	< 0.001*	< 0.001*
BS30 (mg/dl)		126.20 ± 24.59	138.04 ± 26.04	142.13 ± 25.93	< 0.001*	< 0.001*
BS60 (mg/dl)		121.58 ± 31.40	137.48 ± 31.08	149.312 ± 34.97	< 0.001*	< 0.001*
BS120 (mg/dl)		98.32 ± 20.94	103.21 ± 21.83	107.62 ± 20.05	0.001*	< 0.001*

P-value 1, comparison between prediabetes and the NGT (healthy population); P-value 2, comparison between diabetes and normal, TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; BMI, body mass index; WHR, waist to hip ratio; FPG, the fasting plasma glucose; OGTT 30, 60, 120, oral glucose tolerance test after 30min, 60min, 120 min; HbA1c, glycosylated hemoglobin, OGTT-AUC, Glucose area under the curve, SBP, systolic blood pressure; DBP, diastolic blood pressure.

	Final status				
OGTT-AUC	749.70 ± 124.26	817.49 ± 122.32	863.11 ± 131.03	< 0.001*	< 0.001*
TG (mg/dl)	145.75 ± 80.76	159.83 ± 84.42	179.13 ± 98.52	< 0.001*	< 0.001*
Cholesterol (mg/dl)	189.14 ± 38.12	196.00 ± 38.63	201.09 ± 42.84	0.008*	0.007*
HDL (mg/dl)	45.20 ± 11.48	44.85 ± 11.45	44.14 ± 10.22	0.660	0.415
LDL (mg/dl)	115.63 ± 33.12	119.97 ± 34.26	121.94 ± 43.32	0.064	0.115
SBP (mmHg)	11.29 ± 1.50	11.68 ± 1.63	11.52 ± 1.60	< 0.001*	0.177
DBP (mmHg)	7.45 ± 7.50	7.58 ± 1.14	7.45 ± 1.23	0.086	0.996
HbA1c (mg/dl)	4.93 ± 0.78	5.07 ± 0.70	5.16 ± 0.70	0.006*	0.012
Physical activity (MET in/week)	86.93 ± 108.5	86.59 ± 87.78	180.149 ± 421.93	0.979	0.018*

P-value 1, comparison between prediabetes and the NGT (healthy population); P-value 2, comparison between diabetes and normal, TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein; BMI, body mass index; WHR, waist to hip ratio; FPG, the fasting plasma glucose; OGTT 30, 60, 120, oral glucose tolerance test after 30min, 60min, 120 min; HbA1c, glycosylated hemoglobin, OGTT-AUC, Glucose area under the curve, SBP, systolic blood pressure; DBP, diastolic blood pressure.

We categorized these unfavorable variables for developing diabetes and prediabetes based on the optimal cutoff values (Tables 2 and 3). The incidence of diabetes and prediabetes were significantly higher in upper categories of all studied risk factors. These variables were examined in various combinations and several Cox's proportional hazard models were developed. Finally, the best predictive models were selected (Tables 4 and 5). The final models to predict the risk of developing diabetes were created by 4 variables. Diabetes risk model 1 included WHR, HbA1c, lipid index, and OGTT-AUC with AUC of 0.71 (95%CI: 0.66–0.77). Diabetes risk model 2 was created by WHR, HbA1c, lipid index, and FPG with AUC of 0.69 (95%CI: 0.63–0.74). The performance of our risk models was evaluated by ROC analysis and the appropriate risk score cut-points were 5.57 (78%, 52%) and 4.27 (77%, 52%) for diabetes risk model 1 and 2, respectively (Table 4).

Table 2
Unfavorable clinical factors for developing diabetes after the follow-up

		Final status		
Variables	Optimal cut-point	Normal	Diabetes	P-value
WHR	≥ 0.795	58.8	77.5	0.001*
	< 0.795	41.2	22.5	
Cholesterol (mg/dl)	≥ 185	52.5%	67%	0.010*
	< 185	47.5%	33%	
TG (mg/dl)	≥ 120	53.6%	67%	0.010*
	< 120	46.4%	33%	
FPG (mg/dl)	≥ 88.5	49.9%	34.1%	0.004*
	< 88	50.1%	65.9%	
OGTT-AUC	≥ 773	59.1%	25%	< 0.001*
	< 773	40.9%	75%	
HbA1c (mg/dl)	≥ 4.8	48.1%	37.2%	0.068
	< 4.8	51.9%	62.8%	
Lipid index	≥ 0.04	55%	38.1%	0.040*
	< 0.04	45%	61.9%	

TG: triglyceride; WHR: waist to hip ratio; FPG: fasting plasma glucose; HbA1c: glycosylated hemoglobin, OGTT-AUC: Glucose area under the curve; lipid index: a combined measure of lipid profiles including TG, cholesterol, HDL, and LDL

Table 3
Unfavorable clinical factors for developing prediabetes after the follow-up

		Final status		
Variables	Optimal cut-point	Normal	Prediabetes	P-value
Age	≥ 41	52.9%	41.2%	0.001*
	< 41	47.1%	58.8%	
Waist (cm)	≥ 85.9	46.6%	39%	0.025*
	< 85.9	53.4%	61%	
Cholesterol (mg/dl)	≥ 185.5	48.5%	39.6%	0.008*
	< 185.5	51.5%	60.4%	
TG (mg/dl)	≥ 121	47.6%	38.2%	0.005*
	< 121	52.4%	61.8%	
FPG (mg/dl)	≥ 88	44.8%	33%	< 0.001*
	< 88	55.2%	67%	
OGTT-AUC	≥ 746	50.3%	29.9%	< 0.001*
	< 746	49.7%	70.1%	
HbA1c (mg/dl)	≥ 4.8	48.1%	40.9%	0.038*
	< 4.8	51.9%	59.1%	
Lipid index	≥ 0.04	48.9%	41.3%	0.030*
	< 0.04	51.1%	58.7%	
SBP (mmg)	≥ 11	55%	45.8%	0.007*
	< 11	45%	54.2%	

TG: triglyceride; FPG: fasting plasma glucose; HbA1c: glycosylated hemoglobin, OGTT-AUC: Glucose area under the curve, SBP: systolic blood pressure; lipid index: a combined measure of lipid profiles including TG, cholesterol, HDL, and LDL

Table 4
Univariate and multivariable analyses of risk factors for diabetes and the performance of the risk score: two predictive models for developing diabetes

	Univariate analysis HR (95%CI)	Multivariable analysis HR (95%CI)	AUC (95%CI) of model	Risk scores mean ± SD	Risk scores median (max,min)	risk scores Cut points (sensitivity, specificity)	P-value
Model 1							
WHR	2.47 (1.50–4.07)	1.93 (1.11–3.37)	0.71 (0.66–0.77)	5.89 ± 3.22	5.61 (0 to 11.14)	5.57 (78%, 52%)	< 0.001*
HbA1c	1.90 (1.20–3.02)	1.90 (1.17–3.09)					
OGTT-AUC	4.12 (2.54–6.68)	3.68 (2.17–6.25)					
Lipid index	2.43 (1.56–3.78)	2.25 (1.37–3.72)					
Model 2							
WHR	2.47 (1.50–4.07)	1.91 (1.10–3.32)	0.69 (0.63–0.74)	4.70 ± 2.30	7.50 (0 to 8.53)	4.27 (77%, 52%)	< 0.001*
HbA1c	1.90 (1.20–3.02)	1.97 (1.22–3.16)					
FPG	2.29 (1.48–3.54)	2.06 (1.26–3.37)					
Lipid profile	2.43 (1.56–3.78)	2.59 (1.58–4.25)					

WHR: waist to hip ratio; FPG: fasting plasma glucose; HbA1: glycosylated hemoglobin; OGTT-AUC: Glucose area under the curve; lipid index: a combined measure of lipid profiles including TG, cholesterol, HDL, and LDL; SD: standard deviation

Table 5
Univariate and multivariable analyses of risk factors for prediabetes and the performance of the risk score: two predictive models for developing prediabetes

	Univariate analysis HR (95%CI)	Multivariable analysis HR (95%CI)	AUC (95%CI) of model	Risk scores mean ± SD	Risk scores median (max,min)	Cut point for risk scores (sensitivity, specificity)	P-value
Model 1							
OGTT-AUC	1.88 (1.47–2.40)	1.80 (1.37–2.37)	0.63 (0.59–0.67)	3.20 ± 1.65	3.07 (0 to 5.92)	2.96 (71%, 52.5%)	< 0.001*
SBP	1.46 (1.17–1.81)	1.27 (0.97–1.66)					
HbA1c	1.28 (1.01–1.61)	1.25 (0.97–1.62)					
Lipid index	1.64 (1.30–2.07)	1.48 (1.14–1.93)					
Model 2							
FPG	1.79 (1.42–2.26)	1.88 (1.45–2.43)	0.60 (0.57–0.64)	4.11 ± 1.87	4.31 (0 to 7.37)	3.99 (65%, 50%)	< 0.001*
Age	1.46 (1.17–1.82)	1.18 (0.92–1.52)					
Waist	1.40 (1.11–175)	1.34 (1.05–1.72)					
HbA1c	1.28 (1.01–1.61)	1.30 (1.01–1.66)					
Lipid index	1.64 (1.30–2.07)	1.67 (1.30–2.15)					

TG: triglyceride; FPG: fasting plasma glucose; HbA1c: glycosylated hemoglobin; OGTT-AUC: Glucose area under the curve; SBP: systolic blood pressure; lipid index: a combined measure of lipid profiles including TG, cholesterol, HDL, and LDL; SD: standard deviation

Prediabetes risk model 1 was based on HbA1c, SBP, lipid index, and OGTT-AUC and the respective AUC was 0.63 (95%CI: 0.59–0.67). In the case of model 2, the best predictive ability was observed when age, waist circumferences, FPG, HbA1c, and lipid index were included, obtaining the AUC of 0.60 (95%CI:

0.57–0.64). The total prediabetes risk score was calculated as the sum of the individual's scores ranged 0 to 5.92 for prediabetes model 1 and 0 to 7.37. The corresponding risk score cut-points were 2.96 (71%, 52.5%) and 3.99 (65%, 50%) for prediabetes risk model 1 and 2, respectively (Table 5).

We compared the predictive ability of our models with other blood glucose indices: FPG, HbA1c, and OGTT-AUC (Figs. 3 and 4). Both diabetes risk models were surpassed FPG and HbA1c risk factors at predicting diabetes [FPG-AUC: 0.61 (95%CI: 0.54–0.68 and HbA1c-AUC: 0.57 (95%CI: 0.50–0.64)]. No significant difference was detected between the AUC of diabetes risk model 1 and OGTT-AUC [0.71 (95%CI: 0.66–0.77) vs 0.73 (95%CI: 0.67–0.80)] (Fig. 3).

The predictive efficiency of both prediabetes risk models was slightly better than FPG, and HbA1c risk factors individually [FPG-AUC: 0.59 (0.55–0.63) and HbA1c-AUC: 0.56 (0.52–0.60). There was no significant difference between OGTT-AUC and prediabetes risk model 1 [0.65 (95%CI: 0.61–0.69) vs 0.63 (95%CI: 0.59–0.67)] (Fig. 4).

We compared the ability of the FINDRISC to predict developing of diabetes in our population with the current study models for predicting diabetes. The predictive performance of our diabetes models was more precise than the FINDRISC and the corresponding P-values were 0.003 for the FINDRISC against model 1, and 0.005 for FINDRISC versus model 2 (Fig. 5)

Discussion

It is evidenced that people with the family history of diabetes are 2–8 fold more likely to develop diabetes (23). This association was independent of other risk factors, such as obesity, insulin resistance, and lifestyle factors which means this risk factor solely is strong enough to predict diabetes (5). Therefore, in the present study we have focused on this at-risk subgroup of population and developed a reliable risk score for future development of diabetes and prediabetes.

In this study, higher WHR, Cholesterol, TG, Lipid index, and the OGTT-AUC at the baseline in those FDRs who developed diabetes after 16 years were related to the increased risk of developing diabetes. Unfavorable clinical factors to develop prediabetes after this period of time were age, waist circumferences, OGTT-AUC, HbA1c, cholesterol, TG, and the lipid index.

According to these factors, we developed two hazard models to predict the risks of developing diabetes and prediabetes, in which OGTT-AUC or FPG were used in each one (Figs. 3 and 4). Diabetes risk models included WHR, HbA1c, lipid profile and OGTT-AUC or FPG. The best diabetes predictive ability was obtained by a model, which included OGTT-AUC. The AUC of this model was 0.71 (0.66–0.77). The other model included FPG instead with the AUC of 0.69 (0.63–0.74). According to diabetes risk model 1, individuals with score values more than 5.57 were determined as high-risk for developing diabetes. Although the predictive efficiencies of both models were higher than other plasma glucose indices, the predictive ability of the OGTT-AUC alone was comparable to the best developed predictive model in our

study. The OGTT-AUC cut point for diabetes prediction is blood glucose more than 7.8 and 7.2 mmol/L at 30 and 60 minutes, respectively.

Prediabetes risk model 1 included HbA1c, SBP, lipid, and OGTT-AUC with the AUC of 0.63 (0.59–0.67). Prediabetes risk model 2 was based on age, waist circumferences, HbA1c, lipid index, and FPG with the AUC of 0.60 (0.57–0.64). Based on prediabetes risk model 1, the score value more than 2.96 is a wakeup call for the onset of prediabetes. In comparison with other plasma glucose indices, the AUC of all prediabetes models were significantly higher than FPG and HbA1c. However, there was no considerable difference in predictability of the OGTT-AUC alone, and prediabetes model 1. Similarly, in previous studies (24, 25), no further improvement in model predictability of developing diabetes achieved by adding other clinical factors. For instance, in Framingham Offspring study (24), the initial model was based on age, gender, parental history of diabetes, BMI, waist circumference blood pressure, HDL, Triglyceride, FPG. They observed no further improvement in diabetes prediction ability by adding 2h-OGTT, fasting insulin level, log Gutt insulin sensitivity index, HOMA index, and C-reactive protein level to the models. Moreover, the ARIC's (25) model for predicting diabetes, based on non-invasive parameters including waist, height, hypertension, blood pressure, family history of diabetes, ethnicity, and age, performed similar to fasting glucose alone (AUCs were 0.71 and 0.74, respectively). On the other hand, another model composed of the non-invasive parameter plus FPG (AUC 0.78) and the model including FPG, triglycerides and HDL (AUC 0.80) had better predictability. This diversity in influential risk factors in the final models might be resulted from the diversity in population. Diabetes risk scores demonstrated good predictability in the original populations in which they were derived. However, their predictive values were usually reduced in external populations (26). Therefore, it was suggested that to develop population-specific risk prediction tools (27).

The FINDRISC (12) is one of previous models, which followed their participants up to 10 years and also included blood-based metabolic characters in the model. FINDRISC was developed based on age, BMI, waist circumference, antihypertensive drug therapy, and history of high blood glucose levels. According to this model, the diabetes risk score value ranked from 0 to 20. The predictive value of the model was the AUC of 85% with 77% sensitivity, and 66% specificity at the score 9 (12). The data was collected through a yes/no questioner and self-reporting data. In the present study, biochemical tests have been conducted on all participants at the baseline and during the follow-up, which provide more accurate data.

In a previous study (26), we evaluated the validity of the concise FINDRISC to predict type 2 diabetes in our population (i.e. the first degree relatives of patients with type 2 diabetes who have normal glucose tolerance) (28). The predictive ability of the FINDRISC in our population was lower than Finish population. In this study we compared the ability of the FINDRISC and our diabetes models to predict the onset of diabetes and results confirm that the predictive performance of our diabetes models is more precise than the FINDRISC in our population.

The results of this study need to be interpreted in light of its strengths and weaknesses. The advantages of our study are: (1) the large sample size (n = 1765), (2) long-term follow-up, (3) valid diagnose of

diabetes and prediabetes by FPG and OGTT criteria. The limitation of our study is that it was conducted in a single urban city in Iran. As risk factors, prevalence, and progression to diabetes may well differ in other cities and rural areas, so the results should be handled with caution before they can be generalized to the rest of the country.

In conclusion, developing simple assessment models for the target population is a first step to identify FDRs of patients with diabetes with an increased likelihood of developing diabetes or prediabetes. In the context of health checkups OGTT-AUC is strong enough for predicting the future risk of diabetes and prediabetes. Moreover, present study evidenced that the diabetes model 1 have the best performance in identification of future risk of developing diabetes compared to FINDRISC and diabetes model 2 in our population.

Declarations

Ethics approval and consent to participate

The Ethics Committee of the Isfahan University of Medical Sciences approved the protocol of this study (IR.MUI.MED.REC.1398.525) and the tenants of the Declaration of Helsinki were followed. All participants had provided written informed consents.

Consent for publication

Not applicable.

Availability of supporting data

The data that support the findings of this study are available on request from the corresponding author, AA. The data are not publicly available due to their containing information that could compromise the privacy of research participants.

Competing interests

The authors declare that they have no competing interests.

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Not applicable.

Contributions

AA, MA, AF had a substantial contribution to the conception and design of the study. AF, Majid A and PSh contributed to acquisition and analysis of date. AF, PSh, AA contributed to analysis and drafting of study. HGh, SA substantially revised the work. SA contributed in English editing. The author(s) read and approved the final manuscript.

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Figures

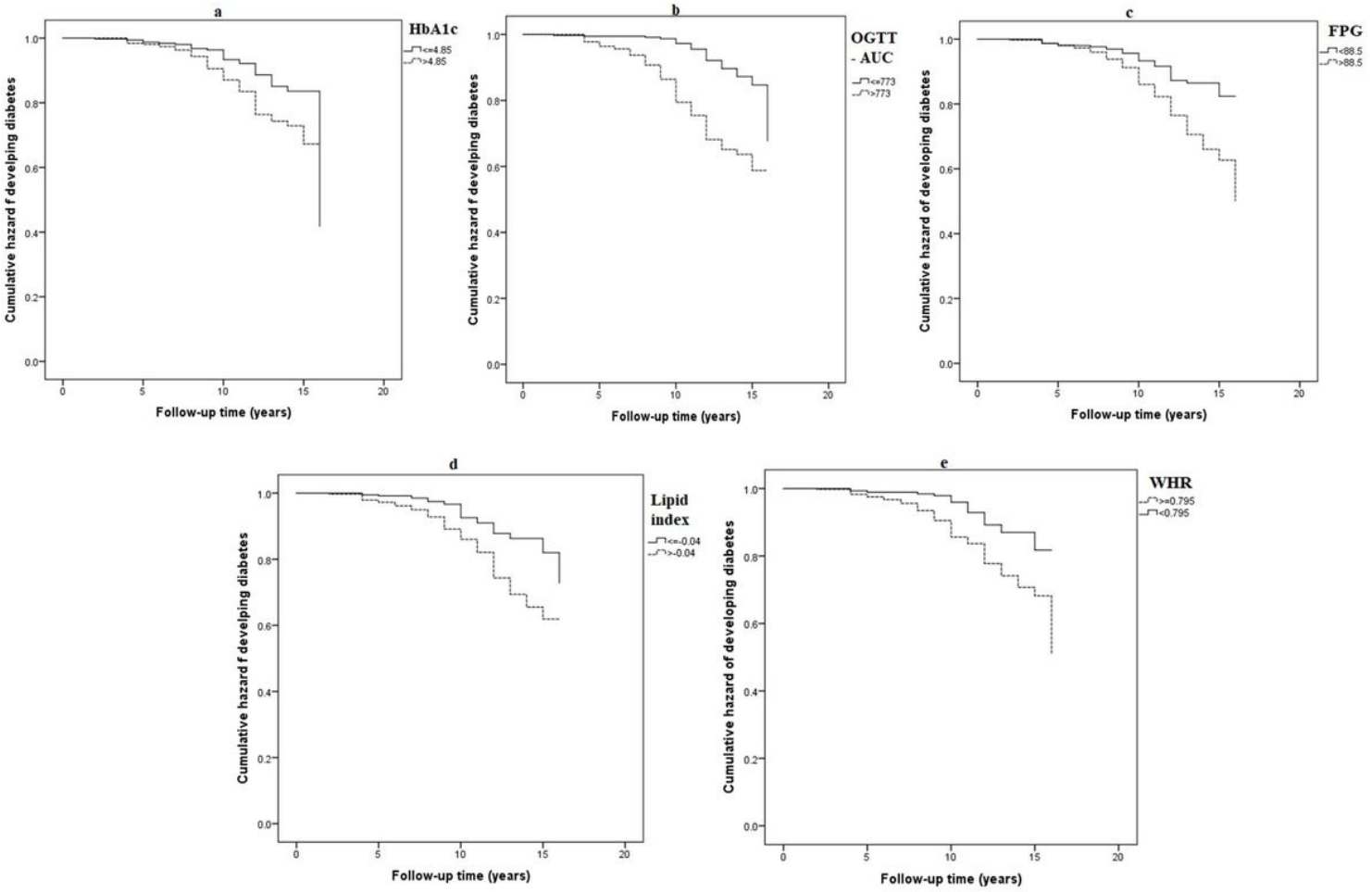

Figure 1

Higher WHR, FPG, OGTT-AUC, HbA1C and lipid index at the baseline were correlated significantly to the risk of developing diabetes after overall 16 years follow-up (all P-values <0.05).

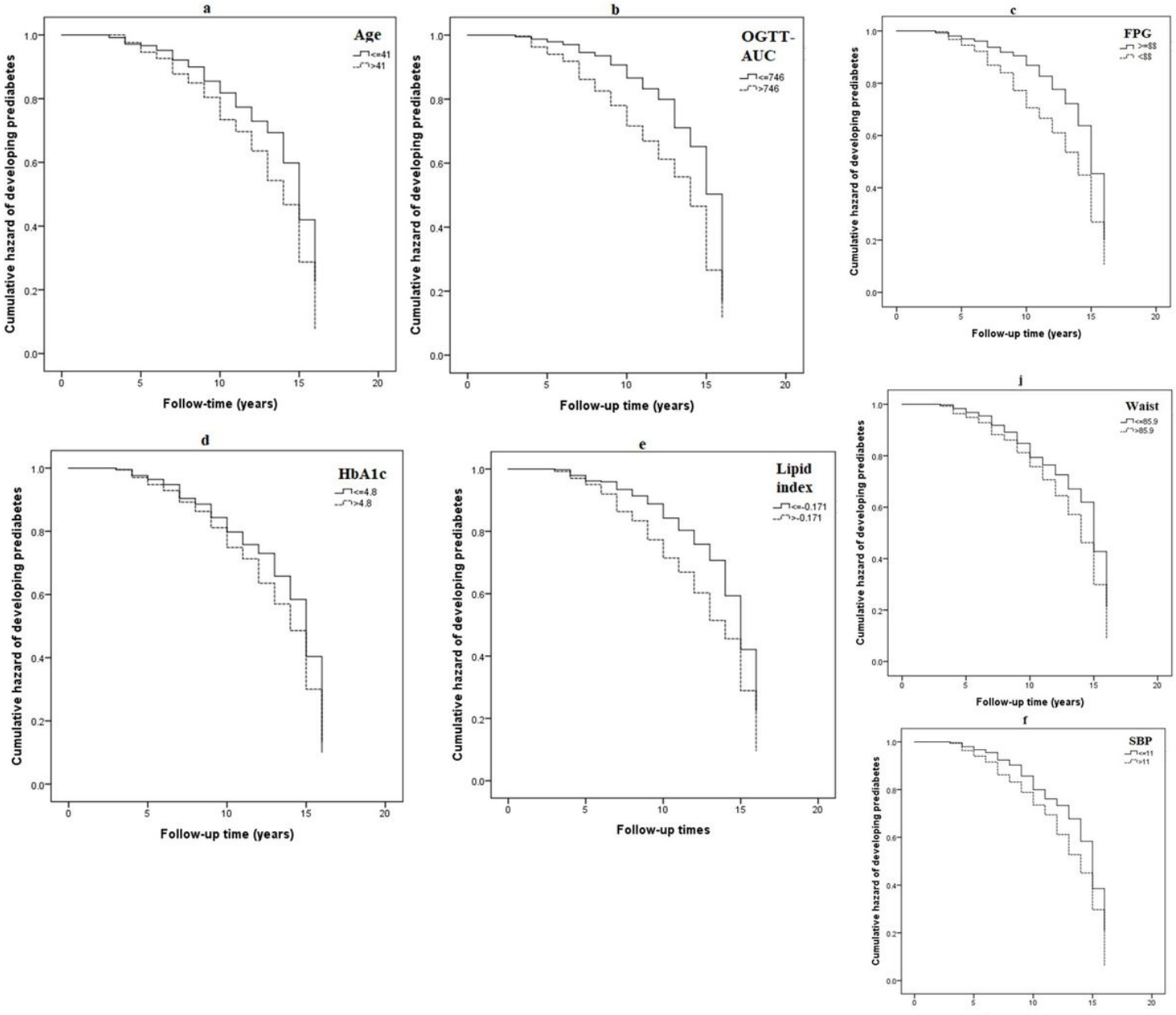

Figure 2

Higher age, waist circumferences, SBP, FPG, OGTT-AUC, HbA1C and the lipid index at the baseline were significantly correlated to the risk of developing prediabetes after overall 16 years follow-up (all P-values <0.02).

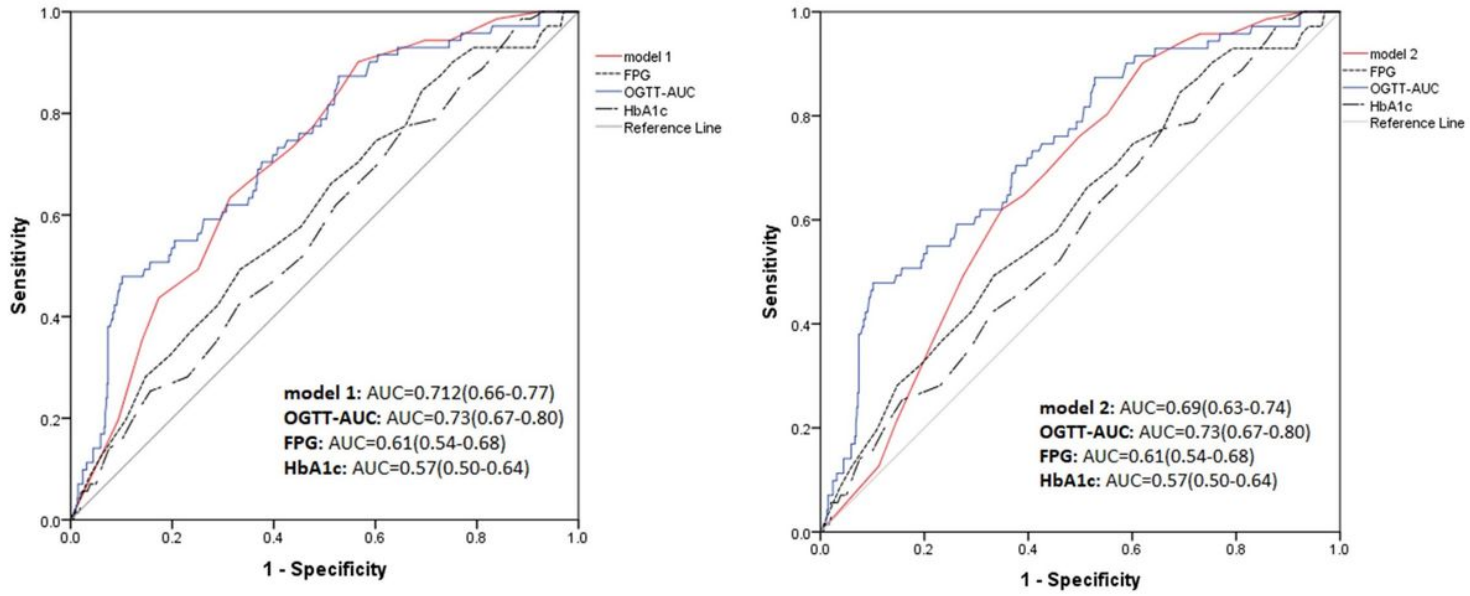

Figure 3

ROC curves and corresponding areas under the curves for model 1, model 2, FPG, 2-h PG, and HbA1c for predicting diabetes. The optimal cut-point of the model 1 is 5.57 (78%, 52%). The optimal cut-point of model 2 is 4.27 (77%, 52%).

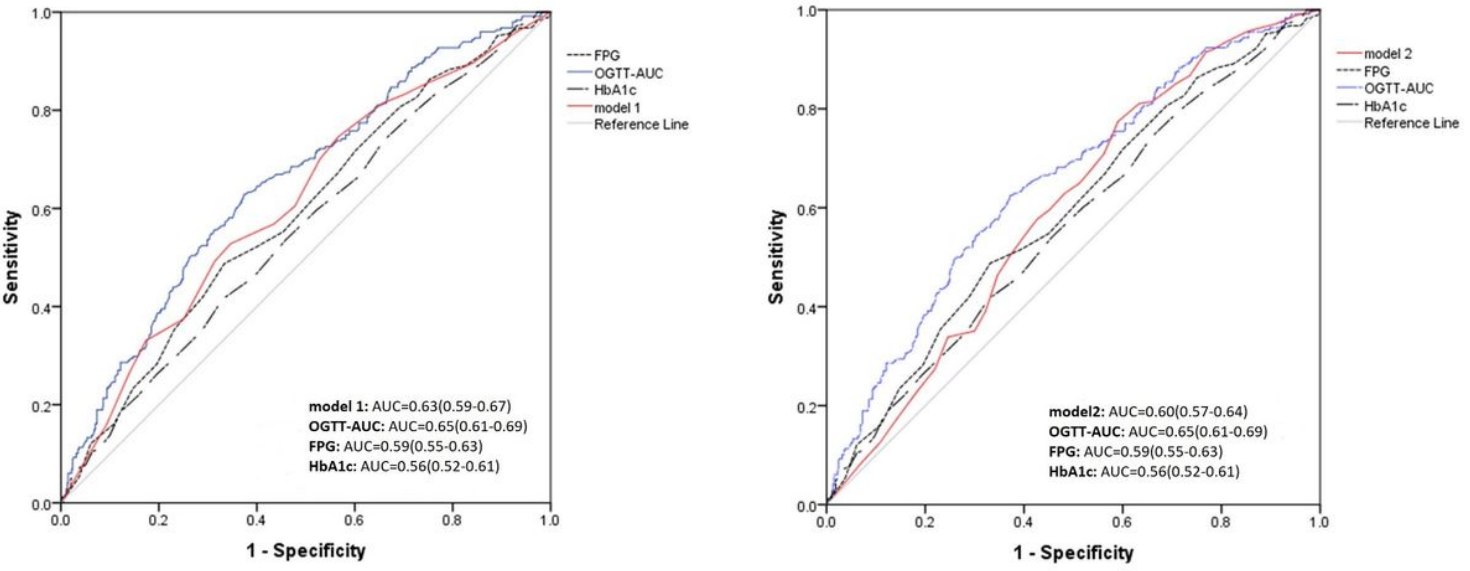

Figure 4

ROC curves and corresponding areas under the curves for model 1, model 2, FPG, 2-h PG, and HbA1c for predicting prediabetes. The optimal cut-point of the model 1 is 2.96 (71%, 52.5%). The optimal cut-point of the model 2 is 4.27 (65%, 50%).

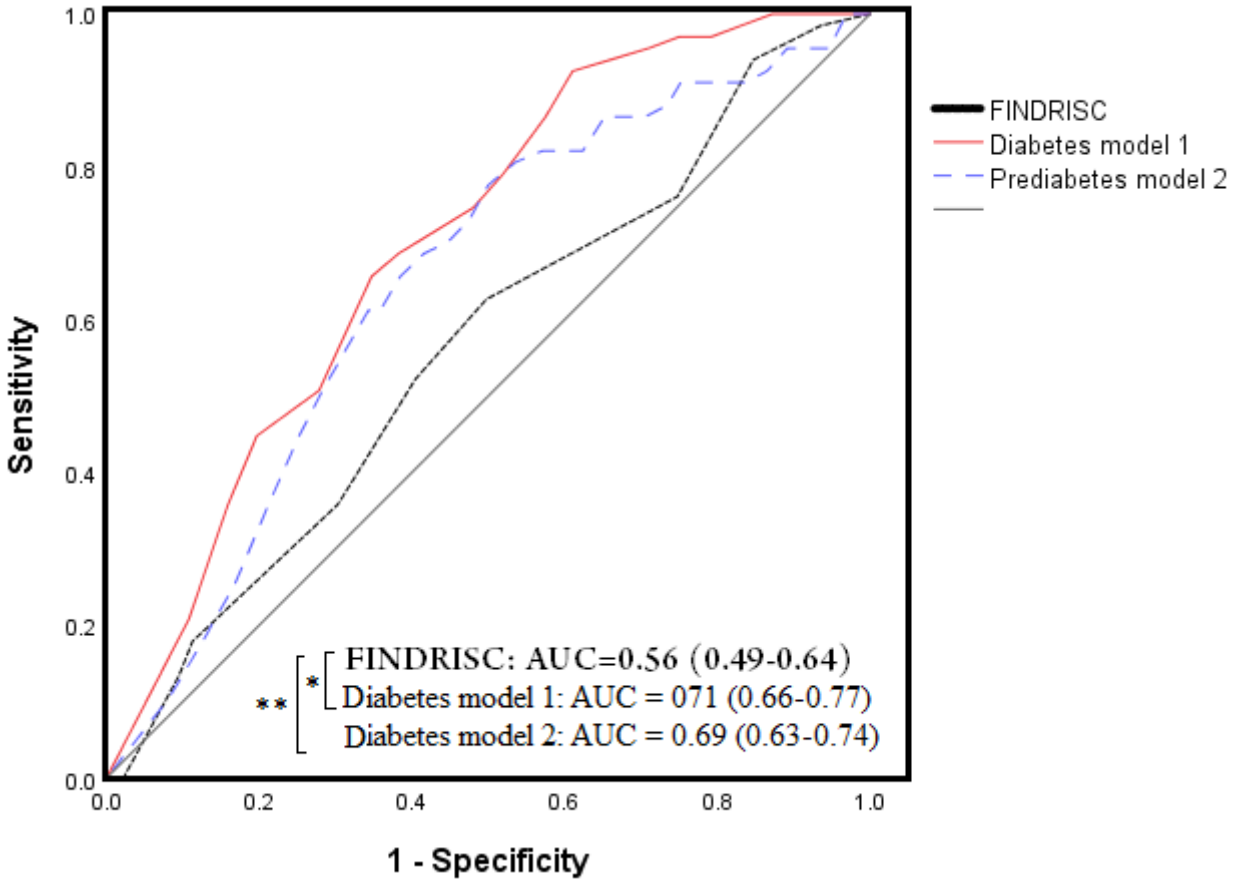

Figure 5

The performance of Diabetes models 1 and 2, compared with FINDRISC for predicting diabetes. * P-values=0.005 **P-value=0.00