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Original paper

Comparison of metabolic syndrome with glucose measurement for prediction of type 2 diabetes: The Isfahan Diabetes Prevention Study

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ABSTRACT

Aims: The aim of this study was to compare the ability of the metabolic syndrome (MetS) and fasting and 2-h glucose to predict progression to diabetes in non-diabetic first-degree relatives (FDRs) of patients with type 2 diabetes.
Methods: A total of 706 non-diabetics FDR 20–70 years old in 2003–2005 were followed through 2008 for the occurrence of type 2 diabetes mellitus. At baseline and through follow-ups, participants undergo a standard 75 g 2-h oral glucose tolerance test. MetS was defined by NCEP-ATP III.
Results: The fasting and 2-h glucose values were better predictors of progression to diabetes than MetS. Compared to participants without MetS, the age-adjusted relative risk (RRs) of diabetes was similar for participants with MetS (1.09 (95% CI 0.92, 1.29)). The age-adjusted relative risk of diabetes among those with impaired glucose tolerance (IGT) and MetS was 1.89 (95% CI 1.47, 2.42) and among those with IGT but without MetS was 1.59 (95% CI 1.32, 1.91). Areas under the receiver operating characteristic curves were 0.789 for fasting and 0.760 for 2-h glucose versus 0.595 for number of metabolic abnormalities ($P < 0.001$).
Conclusions: These data indicate that fasting or 2-h glucose during the OGTT may be more effective and efficient than MetS in predicting progression to diabetes.

1. Introduction

Diabetes prevention has become a major public health priority in both developed and developing nations and therefore, there is great interest in identification of individuals at high risk of developing diabetes. Family history, metabolic syndrome (MetS), and impaired glucose regulation increases the risk for diabetes [1–9] but their clinical value remains unsettled [10]. The MetS and impaired glucose regulations are asymptomatic disorders and their clinical significances are presumably due to their ability to identify subjects for preventing treatments that they might otherwise not receive. Many studies have been shown that the presence of the MetS is a good predictor of diabetes. The question then arises whether the MetS is a better predictor of type 2 diabetes risk than its individual components independent of the genetic basis for the clustering of its components. Recent studies [10–14] concluded that MetS is inferior to established rules for the prediction of type 2 diabetes, and the use of MetS as a focus of screening for metabolic risk modification has become questionable. These studies are limited to the cohorts in Finland [15], the United States [17–22,24], UK [16,23], and Australia [11]. No research has been undertaken in developing countries, where the MetS patterns and ethnicity are different. To our knowledge, there are no studies describing the possible association between MetS and the risk of type 2 diabetes in Iran and other middle east populations.

The objective of this study was to compare the ability of the MetS, as defined by the NCEP-ATP III criteria, and impaired glucose regulation, as defined by American Diabetes Association (ADA), to predict the incidence of type 2 diabetes in non-diabetic first-degree relatives (FDR) of patients with type 2 diabetes.

2. Patients and methods

2.1. Data collection

The Isfahan Diabetes Prevention Study (IDPS) is an ongoing cohort that was established in 2003–2005 when 2368 (614 men and 1754 women) FDR of a consecutive sample of patients with type 2 diabetes attending clinics in Isfahan Endocrine and Metabolism Research Center affiliated to Isfahan University of Medical Sciences, Iran, completed laboratory tests including standard 75 g 2-h OGTT and a questionnaire on their health status

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and on various potential risk factors for diabetes. Participants receive follow-up tests according to Standard of Medical Care in Diabetes [25] to update information on demographic, anthropometric, and lifestyle factors and on newly diagnosed diabetes. Accordingly, if OGTT was normal at baseline, repeat testing was carried out at least at 3-year interval. Otherwise, repeat testing was carried out annually. The IDPS baseline methods have been described in detail elsewhere [26]. Tenets of the Declaration of Helsinki were followed, Institutional Ethical Committee approval was granted, and an informed consent form was signed by each participant.

2.2. Ascertainment of diabetes

Cases of diabetes were identified from baseline and follow-up OGTTs according to ADA criteria [27,28]. Individuals who were not diabetic at baseline and who had at least one subsequent examination were included. Pregnant women were excluded. For the present study, analyses were limited to the 706 participants (150 men and 556 women, mean (S.D.) age 42.7 (6.4) years) in the average 2.3-year follow-up for whom complete data for assessment of the MetS were available.

2.3. Procedures

Information on age, gender, body size, HbA_{1c}, cholesterol, LDL HDL, triglyceride and blood pressure (BP), family and personal medical history was collected at the baseline and through follow-ups. The same methodology was used for both the prevalence and incidence studies. The FDR of patients with type 2 diabetes included siblings or children and reported to clinics in the morning after an overnight fast. Subjects were asked to abstain from vigorous exercise in the evening before and in the morning of the investigations. Smokers were encouraged to abstain from smoking in the morning of the investigations. On arrival in the clinic the information given by the participants in the questionnaire on family history was first verified. Then height and weight were measured with subjects in light clothes and without shoes using standard apparatus. Weight was measured to the nearest 0.1 kg on a calibrated beam scale. Height, waist, and hip circumference were measured to the nearest 0.5 cm with a measuring tape. Waist was measured midway between the lower rib margin and the iliac-crest at the end of a gentle expiration. Hip circumference was measured over the greater trochanters directly over the underwear. Resting BP was measured after subjects had been seated for 10 min by using a mercury sphygmomanometer and appropriately sized cuffs, using standard techniques. Fasting plasma glucose (FPG) was measured using the glucose oxidase method. Subjects with FPG <126 mg/dl underwent a standard OGTT (75 g glucose 2-h) at baseline and the follow-ups. Venous blood was sampled at fasting, 30, 60, and 120 min after oral glucose administration. Plasma samples obtained after centrifuge were analyzed on the same day.

Glycosylated hemoglobin (HbA_{1c}) (measured by ion-exchange chromatography), total cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol, and low-density lipoprotein (LDL) cholesterol (calculated by the Friedewald equation [29] provided total triglycerides did not exceed 400 mg/dl) were assessed. All the blood sampling procedures were performed in the central laboratory of the Isfahan Endocrine and Metabolism Research Center using enzyme-linked method.

2.4. Definitions

We calculated BMI as the ratio of weight (kg) to squared height (m^2), the latter being assessed at baseline only. Normal BMI was defined as BMI <25, overweight as BMI 25–29.99, and obesity as BMI ≥30. Abdominal obesity was defined by waist circumference (≥102 cm in men and ≥88 cm in women) or by the waist-to-hip ratio (WHR) (≥0.95 in men and ≥0.80 in women). Those participants with FPG ≥200 mg/dl or pharmacological treatment were considered as diabetic. If FPG was ≥126 and <200 mg/dl, a second FPG was measured on another day. If the second FPG was also ≥126 mg/dl, participants were considered as diabetic. FPG ≥126 mg/dl or 2-h plasma glucose of ≥200 mg/dl defined diabetes mellitus. IGT was defined as FPG <126 mg/dl, but the 2-h plasma glucose concentration ≥140 and <200 mg/dl. If the FPG was in the range of 100–126 mg/dl and the 2-h plasma glucose was <140 mg/dl, it was considered as impaired fasting glucose (IFG); whereas, if the FPG was below 100 mg/dl and the 2-h plasma glucose <140 mg/dl, it was considered a sign of normal glucose tolerance (NGT) [27,28]. The NCEP-ATP III [30] definition was used for the MetS by the presence of three or more of the following abnormalities: BP ≥130/85 mmHg or a history of hypertension and current use of antihypertensive treatment; waist girth >102 cm for men and >88 cm for women, serum triglyceride ≥150 mg/dl (≥1.7 mmol/l) and/or HDL cholesterol (<40 mg/dl (<0.9 mmol/l) for men and <50 mg/dl (<1.0 mmol/l) for women), and FPG levels ≥126 mg/dl (6.1 mmol/l).

2.5. Analysis

Incidence was expressed as the number of cases of type 2 diabetes per 1000 person-years of follow-up beginning on the date of completion of the baseline examination in 2003–2005 and continuing until the occurrence of diabetes, the date of the last completed follow-up, death, or end of follow-up on December 31, 2007, whichever came first. Statistical methods used included the Student's *t*-test, chi-squared test, and Cox's proportional hazards model. Univariate and multivariate Cox's proportional hazards models were fitted to identify predictors of new-onset diabetes using the SPSS for Windows (SPSS Inc., Chicago, IL, USA). We considered the following covariates in the multivariate-adjusted analyses: age, gender, BMI, waist circumference (WC), triglyceride, LDL, HDL, total cholesterol, IGT, IFG, MetS, and diastolic BP. Variables age, BMI, WC, triglyceride, LDL, HDL, total cholesterol, and BP were entered in models as continuous variables, while gender, IGT, IFG and MetS were categorical. Adjustment for age was examined in separate models. Age-adjusted means were calculated and compared using general linear models. The number of subjects included in the individual analyses varies slightly because of missing values. The ability of FPG, 2-h glucose value, and number of metabolic abnormalities to predict incidence diabetes was examined by receiver operating characteristic (ROC) curve and their respective areas under the curve, in which sensitivity is plotted as a function of 1-specificity. Areas under the ROC curves were compared by the algorithm developed by DeLong et al. [31]. All tests for statistical significance were two-tailed, and performed assuming a type I error probability of <0.05.

3. Results

3.1. Characteristics

Differences in distribution of several age-adjusted characteristics among 527 (74.6%) participants without MetS and 177 (25.1%) with MetS are shown in Table 1. As expected, those with MetS had higher systolic and diastolic BP, BMI, WC, hip circumference, waist-to-hip ratio, FPG, plasma glucose at 60 min, cholesterol, and triglyceride, but lower HDL and have higher proportion of obesity and women and were older at baseline. The mean (S.D.) age was 42.3 (6.5) years for those without

Table 1
Age, age-adjusted and proportion characteristics of first-degree relatives of patients with type 2 diabetes by metabolic syndrome status in the Isfahan Diabetes Prevention Study.

Characteristics	Mean (S.E.)	
	With metabolic syndrome (n = 177)	Without metabolic syndrome (n = 527)
Age (year)	44.0 (0.48)	42.3 (0.28)**
Height (cm)	159.2 (0.58)	159.0 (0.34)
Waist circumference (cm)	94.4 (0.62)	86.7 (0.36)***
Hip circumference (cm)	113.5 (0.63)	106.2 (0.37)***
Waist-to-hip ratio	0.83 (0.005)	0.82 (0.003)**
Body mass index (kg/m^2)	31.9 (0.28)	28.1 (0.16)***
Follow-up duration (year)	2.2 (0.07)	2.3 (0.04)
Fasting glucose baseline (mg/dl)	97.7 (0.95)	93.8 (0.55)***
Plasma glucose 30 min (mg/dl)	150.5 (2.41)	146.0 (1.39)
Plasma glucose 60 min (mg/dl)	163.9 (3.25)	152.7 (1.88)***
Plasma glucose 120 min (mg/dl)	132.1 (2.75)	126.6 (1.59)
HbA_{1c} (%)	5.2 (0.07)	5.1 (0.04)
Cholesterol (mg/dl)	200.6 (3.02)	191.1 (1.78)**
LDL-cholesterol (mg/dl)	117.2 (2.72)	114.7 (1.63)
HDL-cholesterol (mg/dl)	39.5 (0.84)	47.5 (0.51)***
Triglyceride (mg/dl)	230.4 (7.23)	147.2 (4.32)***
Systolic BP (mmHg)	126.1 (1.12)	111.5 (0.65)***
Diastolic BP (mmHg)	81.9 (0.88)	72.3 (0.51)***
Characteristics	%	
	With metabolic syndrome (n = 177)	Without metabolic syndrome (n = 527)
Men	16.2	23.1*
Obesity	70.1	26.3***
Normal glucose tolerance	41.8	49.2
Impaired fasting glucose	7.3	8.0
Impaired glucose tolerance	50.8	42.8

Age-adjusted means were calculated using general linear models. The difference in the mean or percentage of the variables between metabolic syndrome and no metabolic syndrome. CI = confidence interval.
* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.

MetS and 44.0 (5.8.) years for those with MetS. MetS was present in over a quarter of the participants (25.1%; 95% CI: 21.9, 28.3). Prevalence of MetS was higher in women (26.9%; 95% CI: 10.1, 15.4) than men (19.2%; 95% CI: 8.1, 10.9).

3.2. Incidence of diabetes

During the follow-up, a total of 74 (10.5%) (12 men and 62 women) incident cases of type 2 diabetes occurred during 1630 (354 men and 1276 women) person-years of follow-up. The overall incidence of subsequent diabetes was 45.4 (95% CI: 35.8, 56.7) per 1000 person-years. Incidence rates were higher in women (48.6, 95% CI: 37.4, 61.8 per 1000 person-years) than men (33.9, 95% CI: 17.6, 58.4). This difference was not statistically significant. Of the 315 participants who had IGT at initial registration, 61 subsequently developed diabetes, giving an incidence of 99.7 (95% CI: 77.1, 126.0) per 1000 person-years. This was much higher than the incidence rates seen for NGT, 4.6 per 1000 person-years (95% CI: 1.28, 11.7) ($P < 0.001$). Of the 55 participants who had IFG at initial registration, 7 subsequently developed diabetes, giving an incidence of 50.7 (95% CI: 20.7, 102.0) per 1000 person-years. Incidence of type 2 diabetes was 60.3 (95% CI 39.0, 88.4) per 1000 person-years in those with MetS. This was higher than the incidence rates seen for those without MetS, 40.4 per 1000 person-years (95% CI: 30.1, 52.9). This difference was not statistically significant.

3.3. Risk factors

Table 2 shows the group means (S.E.) and proportions for those participants who did and did not develop diabetes. Those who developed diabetes had higher systolic and diastolic BP, BMI, WC, FPG, plasma glucose at 30, 60 and 120 min, HbA_{1c}, cholesterol, and LDL-cholesterol and have lower proportion of NGT, but have higher proportion of IGT, and obesity at baseline.

Table 3 provides the incidence of diabetes and estimated RR associated with the number of metabolic abnormalities. Although the incidence of diabetes increased as the number of metabolic abnormalities rose, no significant association between events of diabetes and MetS or number of metabolic abnormalities noted.

Compared with participants without MetS, the age-adjusted relative risk (RR) of diabetes remained similar in those with MetS (RR 1.09, 95% CI 0.92, 1.29) in age-adjusted models. In a multivariate model, the additional adjustment for other time-dependent covariates did not appreciably alter the relationship between MetS and diabetes compared to the model adjusted for age alone (RR 1.07, 95% CI 0.86, 1.34). Participants with IGT tended to have a higher risk of diabetes than did participants with a NGT (RR 1.59; 95% CI 1.32, 1.91). Controlling for other time-dependent covariates slightly increased the relationship between IGT and diabetes (RR 1.65; 95% CI 1.41, 1.93) compared to the model adjusted for age alone. The multivariate-adjusted risk for diabetes among those with and without MetS was also associated with IGT (Table 4).

The ROC curves for the incidence of type 2 diabetes for FPG, 2-h glucose values and number of metabolic abnormalities are shown in Fig. 1. The areas under the ROC curves were 0.595 (95% CI: 0.528, 0.662), 0.789 (95% CI: 0.735, 0.842), and 0.760 (95% CI: 0.701, 0.819) for the number of metabolic abnormalities, fasting, and 2-h glucose respectively. The areas under the curves between fasting and 2-h glucose versus number of metabolic abnormalities were statistically significant ($P < 0.001$). Also, the area under the ROC curves for FPG and 2-h glucose are not significantly different. It is apparent that in this population of FDR of patients with type 2 diabetes, the number of metabolic abnormalities was inferior to

Table 2
Age, age-adjusted means (S.E.) and proportions of selected baseline characteristics between 74 first-degree relatives of patients with type 2 diabetes who did and 632 who did not develop diabetes.

Variables	Mean (S.E.)	
	Developed diabetes	Not developed diabetes
Age (year)	43.6 (0.75)	42.6 (0.25)
BMI (kg/m^2)	31.0 (0.48)	28.9 (0.16)***
Waist circumference (cm)	92.0 (1.05)	88.3 (0.35)***
Waist-to-hip ratio	0.82 (0.007)	0.82 (0.003)
Systolic BP (mmHg)	119.5 (1.92)	114.6 (0.64)*
Diastolic BP (mmHg)	78.6 (0.15)	74.2 (0.49)**
Baseline fasting glucose (mg/dl)	106.1 (1.35)	93.3 (0.46)***
Plasma glucose 30 min (mg/dl)	168.5 (3.72)	144.7 (1.23)***
Plasma glucose 60 min (mg/dl)	193.8 (4.96)	151.2 (1.65)***
Plasma glucose 120 min (mg/dl)	156.8 (4.11)	124.5 (1.38)***
HbA_{1c} (%)	5.4 (0.12)	5.1 (0.04)*
Triglyceride (mg/dl)	170.9 (12.34)	168.7 (4.19)
Cholesterol (mg/dl)	202.5 (4.83)	192.5 (1.62)*
HDL-cholesterol (mg/dl)	45.2 (1.40)	45.3 (0.48)
LDL-cholesterol (mg/dl)	123.0 (4.25)	114.4 (1.48)*
Variables	%	
	Developed diabetes	Not developed diabetes
Men	15.3	21.7
Obesity (BMI $\geq$ 30)	53.5	35.7**
Normal glucose tolerance	5.6	52.1***
Impaired fasting glucose	9.7	7.6
Impaired glucose tolerance	84.7	40.3***
Metabolic syndrome	32.4	24.4

Age-adjusted means were calculated using general linear models. The difference in the mean or percentage of the variables between diabetes and no diabetes. CI = confidence interval.
* $P < 0.05$.
** $P < 0.01$.
*** $P < 0.001$.

Table 3
Incidence rates and age-adjusted relative risks (95% CI) of type 2 diabetes by metabolic syndrome status, the Isfahan Diabetes Prevention Study, 2003–2008.

Variables	Cases (no.)	Incidence/1000 person-year (95% CI)	Age-adjusted relative risk (95% CI)[a]
No metabolic syndrome	8	30.3 (13.1, 58.8)	1.00
Metabolic syndrome	66	40.2 (31.2, 50.8)	1.09 (0.92, 1.29)
1 metabolic abnormality	20	36.2 (22.3, 55.4)	0.95 (0.76, 1.19)
2 metabolic abnormalities	22	51.6 (32.7, 77.1)	0.97 (0.77, 1.23)
3 metabolic abnormalities	17	54.3 (31.9, 85.5)	1.01 (0.78, 1.30)
4 or 5 metabolic abnormalities	7	82.4 (33.8, 162.0)	1.18 (0.82, 1.70)

CI = confidence interval.
[a] Relative risks (with 95% CI) calculated by Cox's proportional hazards model.

Table 4
Incidence rates and relative risks (95% CI) of type 2 diabetes by metabolic syndrome status, the Isfahan Diabetes Prevention Study, 2003–2008.

Variables	Metabolic syndrome	Cases (no.)	Incidence/1000 person-year	Age-adjusted relative risk (95% CI)	Multivariate-adjusted relative risk (95% CI)[a]
Normal glucose tolerance	No	4	5.9	1.00	1.00
Impaired fasting glucose	No	6	56.1	1.07 (0.77, 1.48)	0.98 (0.67, 1.44)
Impaired fasting glucose	Yes	1	32.3	1.19 (0.68, 2.08)	1.29 (0.66, 1.21)
Impaired glucose tolerance	No	38	85.2	1.59 (1.32, 1.91)***	1.59 (1.30, 1.94)***
Impaired glucose tolerance	Yes	23	138.6	1.89 (1.47, 2.42)***	1.72 (1.21, 2.44)**

Adjusted for age, gender, BMI, WC, triglyceride, LDL, HDL, total cholesterol, BP, IGT and IFG. **$P < 0.01$, ***$P < 0.001$. CI = confidence interval.
[a] Relative risks (with 95% CI) calculated by Cox's proportional hazards model.

measurement of glucose (fasting or 2-h post-load) in identifying those who developed diabetes.

4. Discussion

In this mean 2.3-year follow-up study, MetS as defined by the NCEP-ATP III criteria did not increase the incidence of diabetes. Those with fasting and 2-h glucose as well as those with IGT with and without MetS at baseline had higher risk of progression to diabetes, further emphasizing the utility of glucose testing alone in predicting diabetes. The MetS is a much weaker diabetes risk predictor than either fasting or 2-h glucose. IGT itself being a metabolic abnormality with a high risk of progression to diabetes, the coexistence of MetS, probably would have further enhanced

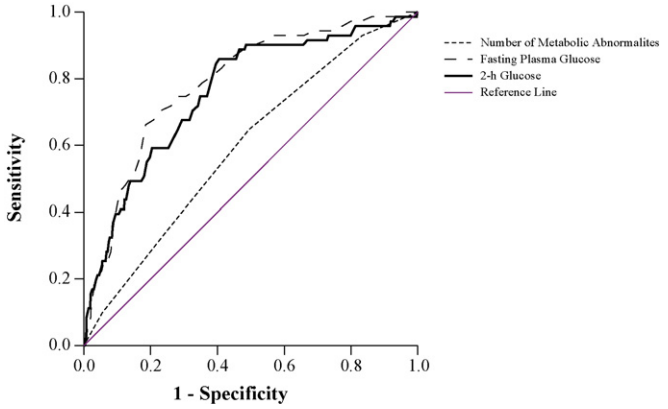

Fig. 1. Receiver operating characteristic curves for fasting, 2-h glucose and number of metabolic abnormalities for prediction of type 2 diabetes in non-diabetic first-degree relatives of patients with type 2 diabetes. The estimates of the area under the ROC curves and their 95% confidence intervals are shown.

Area under the curve (95% CI)	
Number of metabolic abnormalities	0.595 (0.528, 0.662)
Fasting plasma glucose	0.789 (0.735, 0.842)
2-h plasma glucose	0.760 (0.701, 0.819)

the risk. However, a simple FPG measurement was much better predictor of future diabetes than the expense and inconvenience necessary to diagnose the MetS. Several studies have assessed risks of diabetes in persons with MetS, and the results are inconsistent. Some of them have shown that presence of MetS was predictive of progression to diabetes [15,16,18–24,32] whereas more recent studies, which are consistent with the present study, showed no significant association of MetS in the development of type 2 diabetes [11–14,17]. Only few studies have directly compared the MetS and glucose measurements in risks of diabetes. Stern et al. [17] compared the MetS and diabetes predicting model as diabetes predictors, the NCEP-ATP III definition of the MetS was inferior using ROC curve analysis. In the Australian Diabetes, Obesity and Lifestyle (AusDiab) Study, however, the four different definitions of MetS were not superior to measurement of blood glucose alone or a diabetes risk prediction model [11]. Those with IFG or IGT but without the MetS had almost threefold higher risk of progression to diabetes than those with MetS but without IFG or IGT. Studies in China and India also found no significant association between MetS and risk of type 2 diabetes [12,13]. In an 11-year population-based follow-up of patients with type 2 diabetes in Spain, MetS did not provide better prediction of either all cause of cardiovascular mortality when compared with the single components of the MetS [14]. Moreover, the 8-year follow-up of the Framingham offspring population [33] showed that FPG is a far better predictor of diabetes mellitus than any of the combinations of factors that denote the presence of the MetS. Sattar et al. [32] compared the MetS as cardiovascular disease and diabetes predictors, the NCEP-ATP III definition of the MetS and its components was associated with type 2 diabetes as was each of its components, particularly FPG, but had weak or no association with vascular risk in elderly populations. In British Regional Heart Study, FPG alone was similar to MetS in prediction of diabetes [32]. In the San Antonio Heart Study, MetS predicted type 2 diabetes independently of other factors and beyond glucose intolerance alone [18,21]. Therefore, this analysis did not support the theory that metabolic features act synergistically in combination to result in a higher RR than would be expected from combining the RR for effects estimated individually. We found that participants with IGT and MetS had 90% higher risk of diabetes than those with NGT, even after controlling for age, gender, BMI, waist circumference (WC), triglyceride, LDL, HDL, total cholesterol, IFG, and diastolic BP. On the basis of our overall findings, fasting and 2-h glucose could be argued to be the best and most practical predictor of progression to diabetes.

The reason that the MetS, as defined by NCEP-ATP III criteria, is inferior to the FPG or 2-h glucose at predicting type 2 diabetes is because, the NCEP-ATP III criteria lack family history of diabetes as a potent risk factor for diabetes. This omission may contribute to its inferior prediction of diabetes in FDR when compared with the fasting or 2-h glucose. Another possible explanation for the superior predicting ability of the fasting or 2-h glucose is that the fasting or 2-h glucose is treated as continuous variables and not dichotomized as in NCEP-ATP III defined MetS.

Similarly, our findings confirm those of other studies [11,32,34] that the ability of MetS to predict risk of diabetes can largely be attributed to its glucose component. Diabetes risk associated with either IGT, fasting or 2-h glucose is higher than the risk associated with any of the other metabolic abnormalities. The ADA favour using FPG to avoid the costs and inconveniences of an OGTT (27). Both fasting and the 2-h glucose value have the same predictive discrimination. Similar to Lorenzo et al. study [18] the MetS slightly increases the risk associated with IGT. Thus, a simple FPG measurement is a much better predictor of progression to diabetes than the MetS.

Our study has several strengths and limitations. The strengths include the prospective cohort design, the sample consisting of both men and women of a wide age range, diagnosis of diabetes based on standard OGTT, and information on potential determinants of diabetes. Selection and information bias were unlikely because of the prospective design. Our database is one of the few that followed FDR, thereby enabling us to simultaneously control the genetic factors predicting diabetes. This study could draw criticism because of the short follow-up. A mean 2.3-year follow-up may be short to appreciate the real impact of the MetS. Other limitations include the use of a relatively small sample of FDR. Assessing the prediction in a larger sample, longer term period is therefore warranted. We also recognise that we used NCEP-ATP III criteria and not the International Diabetes Federation (IDF) to test association; however, a meta-analysis has shown that the NCEP-ATP III-based definitions modestly better than IDF in its association with vascular [35] or diabetes risk [36].

The high risk of developing type 2 diabetes in FDR with high fasting or 2-h glucose underlines the importance of prevention of type 2 diabetes in these individuals. Recent clinical trials demonstrate that lifestyle [37–40] and pharmaceutical [37,41,42] interventions in individuals with IGT can prevent the development of diabetes, providing a rationale for the identification of high-risk subjects so as to institute early lifestyle or pharmacological interventions.

In conclusion, our study indicates that the MetS as defined by the NCEP-ATP III criteria does not predict the future development of diabetes. Fasting or 2-h glucose predicts better new-onset diabetes. These findings highlight the need for lifestyle or even pharmacological intervention aiming at preventing diabetes in FDR with high fasting or 2-h glucose.

Conflict of interest

None declared.

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References

[1] Ford ES. Risks for all-causes mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. Diabetes Care 2005;28:1769–78.

[2] deVegt F, Dekker JM, Jager A, Hienkens E, Kostense PJ, Stehouwer CD, et al. Relation of impaired fasting and post-load glucose with incident type 2 diabetes in a Dutch population: the Hoorn Study. Am Med Assoc 2001;285:2109–13.

[3] Unwin N, Shaw J, Zimmet P, Alberty KGMM. Impaired glucose tolerance and impaired fasting glycemia: the current status on definition and intervention. Diabet Med 2002;19:708–23.

[4] Shaw JE, Zimmet PZ, de Courten M, Dowse GK, Chitson P, Gareeboo H, et al. Impaired fasting glucose or impaired glucose tolerance: what best predicts future diabetes in Mauritius? Diabetes Care 1999;22:399–402.

[5] Vaccaro O, Ruffa G, Imperatore G, Iovino V, Rivellese AA, Riccardi G. Risk of diabetes in the new diagnostic category of impaired fasting glucose: a prospective analysis. Diabetes Care 1999;22:1490–3.

[6] Qiao Q, Lindström J, Valle TT, Tuomilehto J. Progression to clinically diagnosed and treated diabetes from impaired glucose tolerance and impaired fasting glycaemia. Diabet Med 2003;20:1027–33.

[7] Janghorbani M, Amini M. Diabetes risk among first-degree relatives of patients with type 2 diabetes in Isfahan. Iran Rev Diabet Stud 2007;4:169–76.

[8] Li JK, Ng MC, So WY, Chiu CK, Ozaki R, Tong PC, et al. Phenotypic and genetic clustering of diabetes and metabolic syndrome in Chinese families with type 2 diabetes mellitus. Diabetes Metab Res Rev 2006;22:46–526.

[9] Meigs JB, Cupples LA, Wilson PWF. Parental transmission of type 2 diabetes mellitus: the Framingham Offspring Study. Diabetes 2000;49:2201–7.

[10] Kahn R, Buse J, Ferrannini E, Stern M. The metabolic syndrome: time for a critical appraisal: joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2005;28: 2289–304.

[11] Cameron AJ, Magliano DJ, Zimmet PZ, Welborn TA, Colagiuri S, Tonkin AM, et al. The metabolic syndrome as a tool for predicting future diabetes: the AusDiab study. J Intern Med 2008 [ahead of print].

[12] Wang JJ, Hu G, Lappalainen J, Miettinen ME, Qiao Q, Tuomilehto J. Changes in features of the metabolic syndrome and incident impaired glucose regulation or type 2 diabetes in a Chinese population. Diabetes Care 2005;28:448–50.

[13] Ramachandran A, Snehalatha C, Satyavani K, Sivasankari S, Vijay V. Metabolic syndrome does not increase the risk of conversion of impaired glucose tolerance to diabetes in Asian Indians—result of Indian diabetes prevention programme. Diabetes Res Clin Pract 2007;76:215–8.

[14] Bruno G, Merletti F, Biggeri AI, Bargero G, Ferrero S, Runzo C, et al. Metabolic syndrome as predictor of all—cause and cardiovascular mortality in type 2 diabetes. The Casale Monferrato Study. Diabetes Care 2004;27:2689–94.

[15] Laaksonen DE, Lakka HM, Niskanen LK, Kaplan GA, Salonen JT, Lakka TA. Metabolic syndrome and development of diabetes mellitus: application and validation of recently suggested definitions of the metabolic syndrome in a prospective cohort study. Am J Epidemiol 2002;156:1070–7.

[16] Sattar N, Gaw A, Scherbakova O, Ford I, O'Reilly DS, Haffner SM, et al. Metabolic syndrome with and without C-reactive protein as a predictor of coronary heart disease and diabetes in the West of Scotland Coronary Prevention Study. Circulation 2003;108:414–9.

[17] Stern MP, Williams K, González-Villalpando C, Hunt KJ, Haffner SM. Does the metabolic syndrome improve identification of individuals at risk of type 2 diabetes and/or cardiovascular disease? Diabetes Care 2004;27:2676–81.

[18] Lorenzo C, Okoloise M, Williams K, Stern MP, Haffner SM. San Antonio Heart Study. The metabolic syndrome as predictor of type 2 diabetes: the San Antonio Heart Study. Diabetes Care 2003;26:3153–9.

[19] Wilson PW, D'Agostino RB, Parise H, Sullivan L, Meigs JB. Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. Circulation 2005;112:3066–72.

[20] Schmidt MI, Duncan BB, Bang H, Pankow JS, Ballantyne CM, Golden SH, et al. The atherosclerosis risk in communities investigators. Identifying individuals at high risk for diabetes: the atherosclerosis risk in communities study. Diabetes Care 2005;28:2013–8.

[21] Lorenzo C, Williams K, Hunt KJ, Haffner SM. The National Cholesterol Education Program—Adult Treatment Panel III, International Diabetes Federation, and World Health Organization definitions of the metabolic syndrome as predictors of incident cardiovascular disease and diabetes. Diabetes Care 2007;30:8–13.

[22] Hanley AJ, Karter AJ, Williams K, Festa A, D'Agostino Jr RB, Wagenknecht LE, et al. Prediction of type 2 diabetes mellitus with alternative definitions of the metabolic syndrome: the Insulin Resistance Atherosclerosis Study. Circulation 2005;112:3713–21.

[23] Wannamethee SG, Shaper AG, Lennon L, Morris RW. Metabolic syndrome vs. Framingham risk score for prediction of coronary heart disease, stroke, and type 2 diabetes mellitus. Arch Intern Med 2005;165:2644–50.

[24] Hanson RL, Imperatore G, Bennett PH, Knowler WC. Components of the "metabolic syndrome" and incidence of type 2 diabetes. Diabetes 2002;51: 3120–7.

[25] Executive summary: Standard of Medical Care in Diabetes-2008. Diabetes Care 31 (2008) S5–S11.

[26] Amini M, Janghorbani M. Diabetes and impaired glucose regulation in first-degree relatives of patients with type 2 diabetes in Isfahan, Iran: prevalence and risk factors. Rev Diabet Stud 2007;4:169–76.

[27] Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 2003;Suppl. 1:S5–S20.

[28] Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Kahn R, et al. Expert committee on the diagnosis and classification of diabetes mellitus. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care 2003;26:3160–7.

[29] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499–502.

[30] Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults: Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). J Am Med Assoc 2001;285:2486–97.

[31] DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. Biometrics 1988;44:837–45.

[32] Sattar N, McCnnachie A, Shaper AG, Blauw GJ, Buckley BM, de Craen AJ, et al. Can metabolic syndrome usefully predict cardiovascular disease and diabetes? Outcome data from two prospective studies. Lancet 2008 [ahead of print].

[33] Wilson PW, D'Agostino RB, Parise H, Sullivan L, Meigs JB. Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. Circulation 2005;112:3066–72.

[34] Bonora E, Kiechl S, Willeit J, Oberhollenzer F, Egger G, Meigs JB, et al. Population-based incidence rates and risk factors for type 2 diabetes in white individuals: the Bruneck Study. Diabetes 2004;53:1782–9.

[35] Gami AS, Witt BJ, Howard DE, Erwin PJ, Gami LA, Somers VK, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. J Am Coll Cardiol 2007;49:403–14.

[36] Mannucci E, Monami M, Cresci B, Pala L, Bardini G, Petracca MG, et al. National Cholesterol Education Program and International Diabetes Federation definitions of metabolic syndrome in the prediction of diabetes. Results from the Firenze-Bagno: a Ripoli study. Diabetes Obes Metab 2008;10:430–5.

[37] Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. New Engl J Med 2002;346:393–403.

[38] Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. New Engl J Med 2001;344:1343–50.

[39] Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. Diabetes Care 1997;20:537–44.

[40] Li G, Zhang P, Wang J, Gregg EW, Yang W, Gong Q, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing Diabetes Prevention Study: a 20-year follow-up study. Lancet 2008;371:1783–9.

[41] Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. Lancet 2002;359:2072–7.

[42] Buchanan TA, Xiang AH, Peters RK, Kjos SL, Marroquin A, Goico J, et al. Preservation of pancreatic beta-cell function and prevention of type 2 diabetes by pharmacological treatment of insulin resistance in high-risk Hispanic women. Diabetes 2002;51:2796–803.