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Diabetes self-assessment score and the development of diabetes

A 10-year prospective study

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Abstract

To verify that the Korean Diabetes Score (KDS), a self-assessment, predicts the risk of diabetes in various comprehensive risk models, and to investigate factors that enhance its predictive ability in a large cohort. We analyzed 8735 adults without diabetes in the Korean Genome and Epidemiology Study, an ongoing large community-based 10-year cohort study. Incident diabetes was defined as fasting blood glucose ≥126 mg/dL or postload 2-hour glucose ≥200 mg/dL by 75 g oral glucose tolerance test conducted biennually, or currently taking medication for diabetes. Hazard ratios (HRs) using Cox regression were calculated for relative risk of developing diabetes as associated with the KDS, and performance of risk models was assessed by area under the receiver-operating characteristic curve (AUC). Of 8735 participants, 1497 (17.1%) developed diabetes over 10 years. The prevalence of incident diabetes was 10.3% in people with a KDS <5 and was 21.8% in those with KDS ≥5 ($P < .001$). Increasing KDS was significantly associated with developing diabetes (adjusted HR: 1.13; 95% confidence interval:1.09,1.18). The comprehensive prediction model with KDS added to fasting glucose, glycated hemoglobin, postload 2-hour glucose, and triglyceride showed a markedly higher AUC (0.782) compared to KDS alone (0.641). A low insulinogenic index (IGI) level, but not insulin resistance, was a significant determinant of developing diabetes in subjects who had baseline KDS <5. We confirmed that KDS as a 10-year risk model to predict diabetes becomes more potent when added to relevant laboratory parameters. Beta-cell function as assessed by IGI should be taken into account when predicting diabetes using the KDS.

Abbreviations: AUC = area under the receiver-operating characteristic curve, BMI = body mass index, CI = confidence interval, DM = diabetes mellitus, HbA1c = glycated hemoglobin, HDL = high-density lipoprotein, HOMA-IR = homeostasis model assessment of insulin resistance, HR = hazard ratio, IGI = insulinogenic index, KDS = Korean Diabetes Score, KoGES = Korean Genome and Epidemiology Study, OGTT = oral glucose tolerance test, ROC = receiver-operating characteristic, SBP = systolic blood pressure.

Keywords: diabetes, prediction, prospective, risk factor

1. Introduction

Type 2 diabetes mellitus (DM), a major health problem, is increasing worldwide.[1] The estimated 382 million people with diabetes in 2013 is predicted to rise to 592 million by 2035 globally.[2] In the United States, the estimated prevalence of diabetes is 12% to 14% among adults in the overall population.[3] The prevalence of diabetes in the Western Pacific region is also increasing rapidly and is expected to exceed 202 million by 2035, which is attributable to rapid urbanization and changes in

Editor: Xiaolin Zhu.

Funding/support: This study was supported by a grant from the Korea Healthcare Technology Research & Development (R&D) Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health and Welfare, Republic of Korea (HI14C2476 and HI16C1501, to Y-HL). This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (HI13C0715, to DJK).

The statistical analyses and interpretations were conducted with help from Biostatistics Collaboration Unit, Yonsei Biomedical Research Institute, Yonsei College of Medicine, and Ajou University School of Medicine (Kyoung Hwa Ha), Suwon, Republic of Korea.

The authors have no conflicts of interest to disclose.

Supplemental Digital Content is available for this article.

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Medicine (2017) 96:23(e7067)

Received: 20 December 2016 / Received in final form: 6 April 2017 / Accepted: 25 April 2017

http://dx.doi.org/10.1097/MD.0000000000007067

lifestyle and epigenetics.[4,5] Diabetes has been associated with chronic metabolic conditions such as obesity and metabolic syndrome, as well as related macrovascular and microvascular complications.[6] Consequently, these complications and mortality represent an increasing burden on socioeconomic and public healthcare systems.[7,8] Therefore, a focus on prevention and early detection of diabetes is urgently needed.

A number of diabetes risk scoring models have been developed.[9–12] Because these risk scoring models are designed primarily for Western people, and because the pathophysiology of Type 2 DM is different in Asians, these methods may not be suitable.[13] Moreover, because more than 60% of people with diabetes live in Asian countries and have a great impact on global epidemic,[14] it is critical to focus on the development of diabetes in Asians. Therefore, the KDS was developed to assess the risk of diabetes in Koreans without requiring any blood tests.[15] However, it has not been fully validated to predict diabetes in a large prospective cohort. Therefore, we aimed to investigate and validate not only the KDS but also a comprehensive risk model combining laboratory variables as useful tools for predicting diabetes in a 10-year longitudinal cohort of 10,030 people in Korea. In addition, we also sought to identify risk factors for diabetes in low-risk people with low KDS scores at baseline who ultimately develop diabetes, to predict incident diabetes.

2. Methods

2.1. Study population

The Korean Genome and Epidemiology Study (KoGES) is an ongoing prospective study that enrolled 10,030 participants aged 40 to 69 years who live in urban Ansan or rural Ansung communities in the Republic of Korea. Begun in 2001, for baseline recruitment, eligible participants were recruited as volunteers through on-site invitation, telephone calls, letters, media campaign, or community conferences.[16] The KoGES includes results of biennial self-reported questionnaires regarding medical history, family history, smoking and alcohol consumption, and exercise status and health examinations by trained staff at the survey sites, including national medical schools, hospitals, and health institutions. Exclusion criteria in this study are: current steroid users (N=15), individuals with previously diagnosed diabetes or any oral hypoglycemic agents or insulin (N=682), missing results from a 75 g oral glucose tolerance test (OGTT) (N=45), and participants with fasting glucose concentration ≥126 mg/dL or a postload 2-hour glucose concentration by a 75-g OGTT ≥200 mg/dL (N=553) (Supplementary Fig. 1, http://links.lww.com/MD/B726). Ultimately, a total of 8735 individuals were analyzed in the present study. Among 8735 participants at baseline, 5549 individuals were successfully followed up to Year 10. This study was approved by the Korean Center for Disease Control and Prevention and the Institutional Review Board of the Severance Hospital (IRB No: 4-2014-0508).

2.2. Data and measurements

Baseline measurements of height, weight, and waist circumference were obtained. Body mass index (BMI) was calculated as kg/m^2 from measured height and weight. Obesity was defined as BMI ≥25 kg/m^2 by criteria of the Asian and Pacific regions.[17–19] Blood pressure was measured 3 times in the morning, after at least 10 minutes in the sitting position. Hypertension was diagnosed in subjects who were taking hypertension medication or a measured blood pressure ≥140/90 mm Hg. Smoking and alcohol consumption were categorized into 3 categories as never, past smoker, or current smoker, and none, <1, 1–4.9, or ≥5 drinks per day, respectively. Exercise status was stratified into 3 groups according to frequency of exercise (none, 1–3 times, or ≥4 times weekly). After a 12-hour fast, plasma total cholesterol, triglyceride, and high-density lipoprotein (HDL) cholesterol were determined using a 747 chemistry analyzer (Hitachi Ltd, Tokyo, Japan). Low-density lipoprotein cholesterol level was calculated by the Friedewald equation: total cholesterol-HDL cholesterol-triglycerides/5. In a 75-g OGTT, plasma glucose and insulin levels at 0, 60, and 120 min were measured by using the hexokinase method and radioimmunoassay (LINCO kit, St Charles, MO), respectively. Glycated hemoglobin (HbA1c) level was measured by high-performance liquid chromatography (Variant II; Bio-Rad Laboratories, Hercules, CA). In this study, the diagnostic criteria for incident diabetes was current oral hypoglycemic agents or insulin, a fasting glucose level ≥126 mg/dL, or a postload 2-hour glucose level ≥200 mg/dL by biannually conducted 75-g OGTT, based on the American Diabetes Association criteria.[20] Homeostasis model assessment of insulin resistance (HOMA-IR) and 60 minutes insulinogenic index (IGI) were calculated using the following indices: fasting plasma insulin (μIU/mL) × fasting plasma glucose (mg/dL)/405 and (postload 60-minute insulin − fasting insulin [μIU/mL])/(postload 60-minute glucose − fasting glucose [mmol/L]), respectively.[21,22] Criteria for diagnosis of metabolic syndrome according to the revised National Cholesterol Education Program definition were 3 or more of the following: waist circumference >90 cm in men or >80 cm in women; serum triglycerides ≥150 mg/dL or medication use; HDL cholesterol level <40 mg/dL in men or <50 mg/dL in women; blood pressure ≥130/85 mm Hg or hypertension medication use; or serum fasting glucose ≥100 mg/dL or diabetes medication use.[23,24]

2.3. Korean diabetes score

Points for the Korean Diabetes Score (KDS) were assessed by following criteria as previously described[15,25]: age: <35 years old was determined as 0, 35–44 years old as 2, and ≥45 years old as 3; waist circumference: percentiles 1–50 were determined as 0, percentiles 51–74 as 2, and >75 as 3; alcohol consumption per day: <1 drink was determined as 0, 1–4.9 drinks as 1, and ≥5 drinks as 2; and family history of diabetes, history of hypertension, and smoking status were determined as 0 or 1. KDS score ≥5 was regarded as a cut point for being at high risk for diabetes.[15]

2.4. Statistical analyses

Data are presented as means ± standard deviations or frequencies with percentages. Differences were analyzed using Chi-square tests for categorical variables and Student *t* tests or 1-way analysis of variance followed by the Tukey honestly significant difference post hoc test for multiple comparisons, for continuous variables. Cox proportional hazard analysis was performed to estimate whether the KDS was associated with incident diabetes and to determine the independent relationship of the variables for developing diabetes. Cumulative event rates for developing diabetes were accessed by Kaplan–Meier survival curves, and equality was compared with the log-rank test. To compare the combined effect of using the KDS and various parameters for

predicting incident diabetes, we evaluated receiver-operating characteristic (ROC) curves and the areas under the receiver-operating characteristic curves (AUCs) as a discrimination index. For the comparison of ROC curves between various models, DeLong methods were used.[26] A $P < .05$ was considered statistically significant. Statistical analyses were performed using PASW Statistics version 20.0 for Windows (SPSS Inc., Chicago, IL) and MedCalc software for Windows (Version 13.1, Ostend, Belgium).

3. Results

3.1. Clinical and laboratory characteristics of participants at baseline

The mean age of participants was 51.7 ± 8.8 years; 53.3% were women, and the mean BMI was 24.5 ± 3.0 kg/m^2. Of these 8735 participants, 1513 (17.3%) progressed to diabetes during the 10-year follow-up period. There were 3388 (38.8%) participants with a KDS < 5 and 5347 (61.2%) had a KDS ≥ 5 at baseline. Participants' baseline clinical and laboratory characteristics according to presence of incident diabetes during the follow-up period and a cut point of KDS of 5 are shown in Table 1. Individuals with incident diabetes or a KDS ≥ 5 tended to be older, more likely to be men, more obese, more hypertensive, to have more family history of diabetes, more likely to smoke, and to have metabolically unhealthy parameters compared to those with nondiabetes or KDS < 5. When compared to individuals with a KDS ≥ 5 who ultimately did not develop diabetes, those with KDS < 5, but ultimately develop diabetes, showed significant younger ages, lower BMI, less hypertensive, less likely to smoke or drink, less likely to have metabolic syndrome, but with markedly higher levels of HbA1c and fasting glucose. Moreover, despite markedly lower HOMA-IR index (1.40 vs 1.64; $P < .001$), individuals with KDS < 5 and incident diabetes presented with significant lower levels of fasting insulin (6.6 vs 8.0 μIU/mL; $P < .001$) and IGI (7.0 vs 15.8; $P < .001$) relative to individuals with KDS ≥ 5 but who ultimately did not develop diabetes. In particular, levels of fasting insulin and IGI in subjects with KDS < 5 but who ultimately developed diabetes were the lowest among 4 groups in Table 1.

3.2. Relationship between KDS and incident diabetes

Figure 1 illustrates that the proportion of incident diabetes over 10 years gradually increased as KDS scores rose. The mean prevalence of incident diabetes is 10.3% in participants with a KDS < 5 and is 21.8% in those with KDS ≥ 5 ($P < .001$). Based on the KDS cutoff point of 5, participants with KDS ≥ 5 had a markedly increased cumulative incidence of diabetes compared to those with KDS < 5 (Fig. 2; $P < .001$ by log-rank test).

To test the independent association between KDS score and incident diabetes over 10 years, we performed Cox proportional hazards analysis and variables such as age, smoking and alcohol consumption, and family history of diabetes that were composed of KDS, were excluded in covariates in the analysis (Table 2). A 1-point increase in KDS score presented a significantly elevated adjusted hazard ratio (HR) for incident diabetes after adjusting for sex, exercise status, levels of HbA1c, fasting glucose, postload 2-hour glucose, total cholesterol, triglyceride, HDL cholesterol, IGI, and HOMA-IR index (HR:1.13; 95% confidence interval [CI]:1.09–1.18; $P < .001$). In addition, male sex, levels of HbA1c, fasting glucose, postload 2-hour glucose, triglyceride, and IGI were significant determinants of incident diabetes.

Table 1

Baseline characteristics of the subjects according to KDS score and the development of diabetes (N = 8735).

	Nondiabetes (N = 7222)		Incident diabetes (N = 1513)		
	KDS < 5 (N = 3039)	KDS ≥ 5 (N = 4183)	KDS < 5 (N = 349)	KDS ≥ 5 (N = 1164)	*P
Age, y	†48.7 ± 8.4	‡53.4 ± 8.6	§50.3 ± 8.6	54.4 ± 8.5	<.001
Female, *n* (%)	‖1666 (54.8)	¶2261 (54.1)	#160 (45.8)	573 (49.2)	<.001
Waist circumference, cm	†74.6 ± 5.6	‡86.5 ± 7.0	§76.2 ± 5.3	87.8 ± 7.2	<.001
BMI, kg/m^2	‖22.5 ± 2.3	‡25.6 ± 2.9	§22.9 ± 2.3	26.1 ± 3.0	<.001
Obesity, *n* (%)	a395 (13.2)	‡2307 (56.8)	§62 (16.9)	716 (62.8)	<.001
Hypertension, *n* (%)	†301 (9.9)	‡1546 (37.0)	§61 (17.5)	563 (48.4)	<.001
SBP, mm Hg	†112.7 ± 15.2	‡124.0 ± 17.9	§119.0 ± 18.7	128.7 ± 17.8	<.001
DBP, mm Hg	†75.0 ± 10.1	‡82.3 ± 11.2	§78.8 ± 10.9	84.7 ± 10.8	<.001
Family history of diabetes, *n* (%)	‖215 (7.1)	487 (11.6)	46 (13.2)	156 (13.4)	<.001
Smoking, never/past/current, *n* (%)	1963/495/581 (64.6/16.3/19.1)	2457/526/1200 (58.7/12.6/28.7)	§195/92/62 (55.9/26.4/17.8)	628/184/352 (54.0/15.8/30.2)	<.001
Alcohol, ≤1/1–4.9/≥5 drinks/d, *n* (%)	2775/257/7 (91.3/8.5/0.2)	3132/801/250 (74.9/19.1/6.0)	§304/44/1 (87.1/12.6/0.3)	835/260/69 (71.7/22.3/5.9)	<.001
Exercise, none/1–3/≥4 times/wk, *n* (%)	2175/604/260 (71.6/19.9/8.6)	3075/806/302 (73.5/19.3/7.2)	253/64/32 (72.5/18.3/9.2)	848/214/102 (72.9/18.4/8.8)	.244
Metabolic syndrome, *n* (%)	‖130 (4.3)	‡1568 (37.5)	§34 (9.7)	603 (51.8)	<.001
HbA1c, %	†5.5 ± 0.3	‡5.6 ± 0.4	§5.7 ± 0.4	5.9 ± 0.5	<.001
Fasting glucose, mg/dL	†80.9 ± 7.5	‡82.8 ± 8.4	§86.1 ± 10.2	88.0 ± 10.5	<.001
Postload 2-h glucose, mg/dL	†108.0 ± 27.9	‡112.8 ± 28.5	§134.1 ± 32.5	137.7 ± 33.7	<.001
Fasting insulin, μIU/ mL	6.7 ± 4.0	¶8.0 ± 5.1	§6.6 ± 2.9	8.5 ± 5.0	<.001
Postload 2-h insulin, μIU/ mL	‖24.1 ± 22.4; 4	‡29.9 ± 29.5	28.6 ± 24.2	35.6 ± 31.8	<.001
HOMA-IR	1.35 ± 0.83	‡1.64 ± 1.07	§1.40 ± 0.65	1.86 ± 1.15	<.001
IGI	†15.0 ± 40.4	¶15.8 ± 43.3	#7.0 ± 9.6	11.0 ± 45.4	<.001
Total cholesterol, mg/dL	†183.5 ± 32.6	‡192.5 ± 35.5	191.6 ± 35.0	198.1 ± 34.4	<.001
Triglycerides, mg/dL	†124.3 ± 67.7	‡167.8 ± 101.7	159.4 ± 90.9	196.7 ± 121.8	<.001
HDL cholesterol, mg/dL	†47.1 ± 10.4	‡44.0 ± 9.9	45.0 ± 10.2	42.5 ± 9.2	<.001
LDL cholesterol, mg/dL	111.6 ± 29.4	115.2 ± 33.5	114.2 ± 32.7	115.3 ± 33.2	<.001

BMI = body mass index, DBP = diastolic blood pressure, HbA1c = glycated hemoglobin, HDL = high density lipoprotein, HOMA-IR = homeostasis model assessment of insulin resistance, LDL = low density lipoprotein, IGI = insulinogenic index, KDS = Korean diabetes score, SBP = systolic blood pressure.

* *P* values were calculated from analysis of variance test for continuous variables and chi-squared tests for categorical variables, respectively.

[a] $P < .05$, ‖$P < .01$, †$P < .001$ between nondiabetes and incident diabetes among individuals with KDS < 5.

[#] $P < .05$, ¶$P < .01$, ‡$P < .001$ between nondiabetes and incident diabetes among individuals with KDS ≥ 5.

[§] $P < .001$ between individuals with non-diabetes and KDS ≥ 5 versus individuals with incident diabetes and KDS < 5.

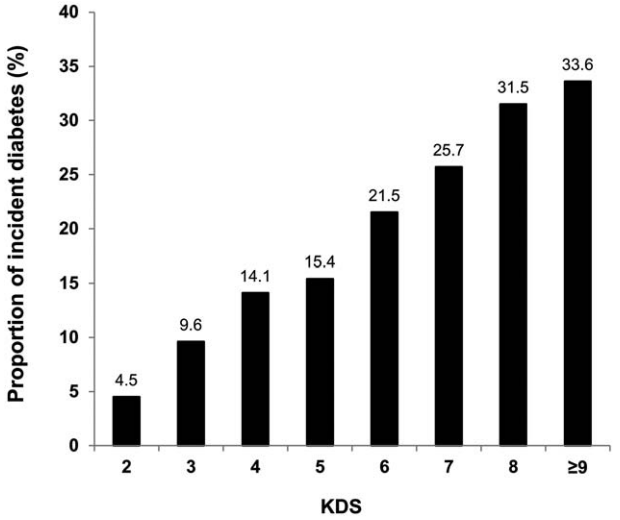

Figure 1. Relationship between Korean Diabetes Score and the development of diabetes over 10 years.

Table 2

Association of KDS with the incidence of diabetes in the Cox proportional hazards models.

	HR	95% CI	*P*
KDS, per 1 point	**1.13**	**1.09–1.18**	**<.001**
Sex (0 = male, 1 = female)	**0.85**	**0.76–0.96**	**.010**
BMI, per 1 kg/m^2	1.00	0.98–1.02	.804
Exercise, none/wk	Referent		
Exercise, 1–3 times/wk	0.94	0.82–1.09	.413
Exercise, ≥4 times/wk	1.00	0.82–1.22	.985
HbA1c, per 1%	**2.57**	**2.25–2.94**	**<.001**
Fasting glucose, per 10 mg/dL	**1.29**	**1.21–1.38**	**<.001**
Postload 2-h glucose, per 10 mg/dL	**1.20**	**1.17–1.22**	**<.001**
Total cholesterol, per 10 mg/dL	0.99	0.97–1.01	.139
Triglyceride, per 10 mg/dL	**1.01**	**1.01–1.02**	**<.001**
HDL cholesterol, per 5 mg/dL	0.97	0.94–1.01	.107
***IGI**	**0.93**	**0.89–0.97**	**.001**
*HOMA-IR index	1.01	0.91–1.11	.916

Bold font indicates the HR is significantly elevated. CI = confidence interval; HDL = high density lipoprotein; HOMA-IR = homeostasis model assessment of insulin resistance; HR = hazard ratio; IGI = insulinogenic index; KDS = Korean Diabetes Score.
* Variables are log-transformed.

Further, we investigated the performance of KDS in addition to different risk factors for the prediction of incident diabetes over 10 years by ROC analyses. As shown in Table 3, the AUC of the univariate logistic model of KDS score was 0.641 (95% CI, 0.627–0.656) and it increased to 0.780 (95% CI, 0.767–0.793) in the multivariate comprehensive model of KDS, fasting glucose, HbA1c, and postload 2-hour glucose. The multivariate combination model of KDS in addition to fasting glucose, HbA1c, postload 2-hour glucose, and triglyceride showed the highest AUC of 0.782 (95% CI 0.769–0.795). The performance of other risk scores including US screening score,[27] Thai score,[28] and Rotterdam model,[29] revealed AUCs ranged from 0.579 to 0.643 (Supplementary table 1, http://links.lww.com/MD/B726).

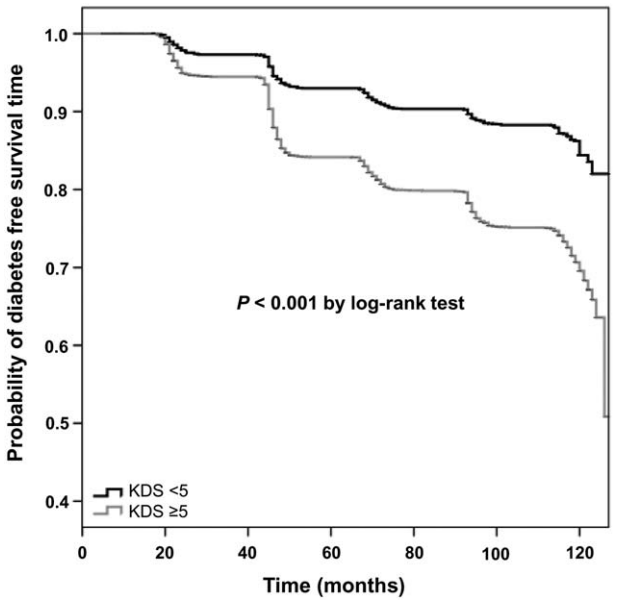

Figure 2. Ten-year diabetes-free survival according to baseline Korean Diabetes Score (<5 or ≥5). KDS = Korean Diabetes Score.

To investigate whether KDS score reflects components of insulin resistance or beta-cell function, we analyzed AUCs of risk models of HOMA-IR or IGI for predicting KDS ≥ 5 (Supplementary table 2, http://links.lww.com/MD/B726). An AUC of 0.613 (95% CI 0.601–0.625) with HOMA-IR index was higher than IGI (AUC, 0.476; 95% CI, 0.462–0.490), indicating KDS might represent an insulin resistance component more than beta-cell function. In subgroup analyses of age, individuals younger than 50 years revealed markedly higher values of AUCs than those older than 50 years for predicting incident diabetes in all of these models.

3.3. Predictive parameters for incident diabetes according to KDS

We further evaluated significant clinical and laboratory parameters to predict the likelihood of developing diabetes during 10 years of follow-up in participants having KDS < 5 at baseline (Table 4). Cox proportional hazards analysis showed that systolic blood pressure (SBP), family history of diabetes, HbA1c, fasting glucose, postload 2-hour glucose, triglyceride, and IGI were independently associated with incident diabetes in subjects with KDS < 5 at baseline. In addition, a family history of diabetes, current smoking, increased SBP, HbA1c, fasting glucose, postload 2-hour glucose, triglyceride, and decreased IGI were significant predictors of an increased likelihood of incident diabetes in subjects having baseline KDS ≥ 5. Collectively, common independent parameters for predicting diabetes were the presence of family history of diabetes, increased SBP, HbA1c, fasting glucose, postload 2-hour glucose, and decrease in IGI, which indicates decline in beta-cell function.

4. Discussion

In the present study, we investigated and validated the KDS to predict diabetes in a 10-year longitudinal data. We confirmed that subjects with a baseline KDS ≥ 5 were significantly associated with a high incidence of diabetes, and that the KDS risk model becomes more potent in combination with various laboratory parameters. In particular, there is an increased ability to predict

Table 3

Comparisons of risk models of Korean Diabetes Score and various laboratory parameters for predicting diabetes.

	AUC	95% CI	P
KDS	0.641	0.627–0.656	<.001
Fasting glucose	0.660	0.644–0.676	<.001
HbA1c	0.695	0.680–0.710	<.001
Postload 2-h glucose	0.722	0.707–0.737	<.001
TG	0.638	0.623–0.653	<.001
HOMA-IR index	0.579	0.562–0.595	<.001
IGI	0.604	0.587–0.620	<.001
KDS + fasting glucose	0.701	0.687–0.715	<.001
KDS + HbA1c	0.719	0.701–0.733	<.001
KDS + postload 2-h glucose	0.751	0.737–0.764	<.001
KDS + TG	0.665	0.651–0.680	<.001
KDS + fasting glucose + postload 2-h glucose	0.765	0.752–0.779	<.001
KDS + fasting glucose + HbA1c + postload 2-h glucose	0.780	0.767–0.793	<.001
KDS + fasting glucose + HbA1c + postload 2-h glucose + TG	0.782	0.769–0.795	<.001
Fasting glucose + HbA1c + postload 2-h glucose + TG	0.772	0.758–0.785	<.001
Subgroup analysis			
Age ≤50 years (n = 4605)			
KDS	0.656	0.635–0.677	<.001
KDS + fasting glucose + postload 2-h glucose	0.784	0.764–0.803	<.001
KDS + fasting glucose + HbA1c + postload 2-h glucose	0.798	0.779–0.817	<.001
KDS + fasting glucose + HbA1c + postload 2-h glucose + TG	0.800	0.782–0.819	<.001
Age >50 years (n = 4130)			
KDS	0.611	0.590–0.632	<.001
KDS + fasting glucose + postload 2-h glucose	0.739	0.719–0.758	<.001
KDS + fasting glucose + HbA1c + postload 2-h glucose	0.753	0.734–0.771	<.001
KDS + fasting glucose + HbA1c + postload 2-h glucose + TG	0.755	0.737–0.774	<.001

AUC = area under the receiver-operating characteristic curve, CI = confidence interval, HOMA-IR = homeostasis model assessment of insulin resistance, IGI = insulinogenic index, KDS = Korean Diabetes Score, TG = triglyceride.

diabetes using the KDS in participants younger than 50 years compared to those over 50 years. In addition, low IGI, representing impaired beta-cell function, was an independent determinant of incident diabetes in low-risk individuals with baseline KDS < 5.

Every 1-point increase in the KDS revealed a significantly increased risk of developing diabetes. Moreover, levels of HbA1c, fasting glucose, postload 2-hour glucose, and triglyceride were also shown as strong predictors for diabetes in this study, as previously suggested.[30–33] IGI and HOMA-IR index were included as covariates in the analyses, but only low IGI was shown as an independent risk factor for incident diabetes (Table 2). Consistent with this, baseline clinical and laboratory characteristics revealed that subjects with a baseline KDS < 5 who ultimately developed diabetes had the lowest fasting insulin levels and IGI, but lower HOMA-IR index, compared to those having baseline KDS ≥ 5 but who did not develop diabetes. Moreover, Cox regression analysis in participants having a baseline KDS < 5 who developed diabetes showed that a low level of IGI was a significant predictor of diabetes. These findings indicate that impaired beta-cell function at baseline but not insulin resistance is a significant determinant in the development of diabetes in the Korean population. Our study results are in line with previous studies regarding the role of beta-cell dysfunction, especially in Asian populations.[34,35] Decreased beta-cell function was shown to be the major determinant for the development of type 2 diabetes, which limits compensation in response to minor progressive insulin resistance in Asians; otherwise, a compensatory increase of beta-cell function was revealed with deeply declined insulin sensitivity in White people.[13,35,36] Consistent with this, compared to HOMA-IR index (AUC, 0.579; 95% CI, 0.562–0.595), IGI presented a higher AUC of 0.604 (95% CI, 0.587–0.620) in predicting diabetes (Table 3). Further, we evaluated independent factors to predict incident diabetes in people with baseline KDS ≥ 5 who ultimately developed diabetes using the Cox regression model, and also found that low IGI was an independent predictor. In particular, current smoking had a significant adjusted HR of 1.49 (95% CI, 1.19–1.87) for the risk of diabetes in participant having baseline KDS ≥ 5; therefore, as a modifiable risk factor, smoking cessation should be emphasized to people with baseline KDS score ≥5.

In terms of the AUC, the KDS demonstrated a modest level of accuracy in predicting diabetes (0.641; 95% CI, 0.627–0.656) with a sensitivity of 61% and a specificity of 61%. Other risk scores including Thai score, Rotterdam model, and US screening score had AUCs ranged from 0.579 to 0.643 with the sensitivities from 63% to 77% and the relatively low specificities from 36% to 57%. In the previous study regarding performance of the KDS risk model using cross-sectional data,[15] the KDS had an AUC of 0.730 with a cut point of KDS ≥ 5. Also, a recent study reported an AUC of 0.696 (95% CI, 0.655–0.737) among 3029 individuals with a mean follow-up period of 6.2 years, in which the definition of diabetes was different (e.g., fasting glucose ≥126 mg/dL or HbA1c ≥ 6.5%) from the present study.[37] In the present study, the risk prediction model for diabetes performed better up to an AUC of 0.782 (95% CI, 0.769–0.795) with a sensitivity of 69% and a specificity of 74% in the comprehensive risk model of KDS combined with laboratory parameters, including concentrations of fasting glucose, HbA1c, postload 2-hour glucose, and triglyceride. Our 10-year longitudinal results revealed lower AUCs compared to a previous study with cross-sectional data or a shorter follow-up period.[37] The tendency toward lower AUC values in longitudinal data compared to those in cross-sectional data was also seen in the previous study. This might be affected by an insufficiency of KDS for representing beta-cell function rather than insulin sensitivity, because impaired beta-cell function is more dependent than insulin resistance in the predisposition to diabetes in Asian people.[35] Furthermore, because KDS is an effective primary screening tool for predicting nonalcoholic fatty liver disease or nonalcoholic steatohepatitis, which is strongly associated with insulin resistance, this also revealed that the KDS strongly reflects insulin sensitivity.[25] In line with this, in subgroup analyses, all of the risk prediction models demonstrated higher accuracy in predicting diabetes in people younger than 50 years, whose beta-cell function is more preserved in general (IGI, 15.7 vs 13.3; $P = .014$; HOMA-IR, 1.55 vs 1.57; $P = .616$; age ≤50 years old vs age >50 years old) compared to those older than 50 years.

The present study has several distinguishable strengths. It is the first study to investigate the ability of the KDS to predict incident diabetes in a large population over 10 years of follow-up. Therefore, we could analyze the real-world longitudinal results. Further, we evaluated numerous risk prediction models with laboratory parameters based on KDS to compare the likelihood

Table 4

Cox regression analysis of the variables associated with the development of diabetes among subjects according to KDS < 5 and KDS ≥ 5.

	KDS < 5 (total, N = 3388; incident diabetes, N = 349)			KDS ≥ 5 (total, N = 5347; incident diabetes, N = 1164)		
	HR	95% CI	*P*	HR	95% CI	*P*
Age, y	1.05	0.99–1.02	.472	1.00	0.99–1.01	.976
Sex (0 = male, 1 = female)	1.05	0.73–1.52	.791	1.01	0.80–1.26	.974
BMI, per 1 kg/m^2	1.01	0.95–1.08	.676	1.01	0.99–1.04	.322
SBP, per 5 mm Hg	**1.08**	**1.04–1.12**	**<.001**	**1.06**	**1.04–1.08**	**<.001**
Family history of diabetes	**1.82**	**1.29–2.57**	**.001**	**1.24**	**1.03–1.50**	**.023**
Smoking, never	Referent			Referent		
Smoking, past	1.39	0.95–2.05	.092	1.21	0.94–1.56	.132
Smoking, current	1.41	0.92–2.15	.116	**1.49**	**1.19–1.87**	**.001**
Exercise, none/wk	Referent			Referent		
Exercise, 1–3 times/wk	0.85	0.63–1.15	.290	0.98	0.83–1.16	.813
Exercise, ≥4 times/wk	1.17	0.77–1.78	.469	1.01	0.80–1.28	.910
HbA1c, per 1%	**2.66**	**1.92–3.67**	**<.001**	**2.58**	**2.22–3.01**	**<.001**
Fasting glucose, per 10 mg/dL	**1.33**	**1.14–1.54**	**<.001**	**1.28**	**1.18–1.38**	**<.001**
Postload 2-h glucose, per 10 mg/dL	**1.23**	**1.18–1.29**	**<.001**	**1.18**	**1.16–1.21**	**<.001**
Total cholesterol, per 10 mg/dL	0.99	0.96–1.04	.774	0.98	0.96–1.00	.086
Triglyceride, per 10 mg/dL	**1.02**	**1.01–1.03**	**.020**	**1.01**	**1.01–1.02**	**<.001**
HDL cholesterol, per 10 mg/dL	0.94	0.87–1.01	.078	0.98	0.94–1.02	.270
*IGI	**0.88**	**0.81–0.96**	**.005**	**0.94**	**0.89–0.99**	**.023**
*HOMA-IR index	1.02	0.83–1.27	.843	0.99	0.89–1.11	.898

Bold font indicates the HR is significantly elevated. CI = confidence interval, HDL = high density lipoprotein, HOMA-IR = homeostasis model assessment of insulin resistance, HR = hazard ratio, IGI = insulinogenic index, KDS = Korean Diabetes Score, SBP = systolic blood pressure.

* Variables are log-transformed.

of predicting diabetes. The KDS is a simple and easy self-assessment tool for laypersons without any mathematical calculations, blood assays, or expense, in the prediction of diabetes. The KDS includes only 6 easily comprehensible components such as age, waist circumference, family history of diabetes, hypertension, smoking status, and daily alcohol consumption. Therefore, the KDS is not only a convenient tool but also a practical tool with which laypersons can self-assess their risk factors for diabetes and improve their health status with checking modifiable risk factors related to personal lifestyle. Second, participants with incident diabetes were in addition defined by a 2-hour 75-g OGTT, which was performed biannually for all participants. Moreover, insulin resistance and beta-cell function, 2 main components in the development of diabetes, could be assessed as HOMA-IR and IGI, respectively, so the relationship between the KDS and the development of diabetes regarding insulin resistance or beta-cell function could be evaluated.

Nonetheless, there are limitations in the present study. Despite a large number of 10,030 participants in KoGES, age ranged from 40 to 69 years in a community-based cohort. Therefore, subjects aged under 40 years or over 70 years were not included, which limits our results to generalization. However, we performed subgroup analyses by age under or over 50 years to verify the performance of the KDS risk prediction models for incident diabetes. As the components of KDS could be related to the bias when using subgroup analysis with participants having KDS < 5 or ≥5 at baseline, we checked the multicollinearity and found that there was no multicollinearity among these parameters including KDS score. Moreover, for log-transformed in IGI values, negative IGI values were regarded as missing, similar to the previous study,[35] which might cause potential bias in the study. In addition, as 5544 (55.3%) subjects completed the study up to Year 10 from the 10,030 participants of the cohort at baseline,[16,35] the attrition bias could be existed in the analysis of the present study.

In conclusion, we investigated and validated the KDS in a well-designed cohort over 10 years and found that additional KDS combined with various laboratory parameters may be more effective for predicting diabetes than KDS alone. Furthermore, beta-cell function is a crucial independent determinant for developing diabetes in Koreans, which also may be considered for diabetes risk prediction when estimated using KDS.

Acknowledgments

Data in this study were from the Korean Genome and Epidemiology Study (KoGES; 4851-302), National Research Institute of Health, Centers for Disease Control and Prevention, Ministry for Health and Welfare, Republic of Korea.

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