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Original Article

Prediction of Coronary Heart Disease Risk in Korean Patients with Diabetes Mellitus

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Conflict of Interest
The authors have no conflicts of interest to declare.

ABSTRACT

Objective: We developed a new equation for predicting coronary heart disease (CHD) risk in Korean diabetic patients using a hospital-based cohort and compared it with a UK Prospective Diabetes Study (UKPDS) risk engine.
Methods: By considering patients with type 2 diabetes aged ≥30 years visiting the diabetic center in Boramae hospital in 2006, we developed a multivariable equation for predicting CHD events using the Cox proportional hazard model. Those with CHD were excluded. The predictability of CHD events over 6 years was evaluated using area under the receiver operating characteristic (AUROC) curves, which were compared using the DeLong test.
Results: A total of 732 participants (304 males and 428 females; mean age, 60±10 years; mean duration of diabetes, 10±7 years) were followed up for 76 months (range, 1–99 month). During the study period, 48 patients (6.6%) experienced CHD events. The AUROC of the proposed equation for predicting 6-year CHD events was 0.721 (95% confidence interval [CI], 0.641–0.800), which is significantly larger than that of the UKPDS risk engine (0.578; 95% CI, 0.482–0.675; *p* from DeLong test=0.001). Among the subjects with <5% of risk based on the proposed equation, 30.6% (121 out of 396) were classified as ≥10% of risk based on the UKPDS risk engine, and their event rate was only 3.3% over 6 years.
Conclusion: The UKPDS risk engine overestimated CHD risk in type 2 diabetic patients in this cohort, and the proposed equation has superior predictability for CHD risk compared to the UKPDS risk engine.

Keywords: Coronary heart disease; Diabetes mellitus; Korea

INTRODUCTION

The main cause of death in patients with diabetes mellitus is coronary heart disease (CHD).[1,2] Therefore, it might be very valuable to predict which patients with diabetes will have CHD. Although recent studies have concluded that there is no clinical benefit of routine screening of asymptomatic patients with diabetes,[3,4] diabetic patients with silent ischemia have poor outcomes[5] and asymptomatic diabetic patients with CHD suffer more future cardiac events than symptomatic patients do.[6,7] Considering that the prognosis of severe coronary artery lesions is better with aggressive intervention such as revascularization[8] and

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that asymptomatic diabetic patients have a comparable risk of CHD events to non-diabetic subjects presenting chest pain,[9] it might be important to select the subjects with high risk of future CHD events regardless of cardiac symptom if they have diabetes.

A recent US report demonstrated that among US diabetic adults, the death rate from cardiovascular disease declined 32% every 10 years from 1988–1994, to 2010–2015.[10] It might be resulted from the improvements of managing CHD risk factors in diabetic subjects[11,12] and implicated that detection of individuals with high risk of CHD and management of the risk factors vigorously is important to reduce not only CHD events but also mortality in them. However, conventional risk factor-based approach cannot identify high-risk patients in screening tests in recent studies[4,13] and UK Prospective Diabetes Study (UKPDS) risk engine[14] which was most frequently used tool for calculating future CHD risk specifically in diabetic subjects has been reported to overestimate the risk of CHD events.[15,16] It might be also resulted from the improvements in the management of diabetic patients with multiple CHD risk factors and associated reduction of the vascular complications and mortality rates from any cause and cardiovascular causes in diabetic patients in recent years.[11,12]

Although UKPDS risk engine was developed specifically for diabetic subjects[14] and has superior predictability of CHD event in diabetic patients compared to Framingham risk scoring, it is based on UKPDS population enrolled between 1977 and 1991 and it has been reported to overestimate the risk of CHD events in the study subjects enrolled later than UKPDS.[15,16] Furthermore, as Asian population showed lower incidence of CHD[17] and different risk profiles of CHD[18] compared to Caucasians, new CHD risk calculation tool in Asian diabetic patients should be developed.

Here, we developed the new equation for predicting CHD risk in Korean diabetic patients using hospital-based cohort and compared its clinical usefulness with that of UKPDS risk engine.

MATERIALS AND METHODS

1. Subjects and study design

Retrospective cohort was based on the entire patients with type 2 diabetes aged ≥30 years visiting the diabetic center in Boramae Hospital in 2006. Exclusion criteria included past medical history of angina pectoris, myocardial infarction or coronary revascularization; abnormal electrocardiogram; and major severe illness. Subjects who were enrolled in the clinical trials were also excluded. A total of 916 subjects were enrolled and their median follow-up period was 6.3 years. After excluding subjects with insufficient clinical data to calculate the CHD risk equation, 732 (304 males and 428 females) were included in the analysis. CHD events during the follow-up period were evaluated by retrospective chart review in Boramae Hospital and causes of death statistics from Statistics Korea. We developed the multivariable equation for predicting CHD events using the Cox proportional hazard model with the stepwise selection. This study was conducted in accordance with the provisions of the Declaration of Helsinki for the participation of human subjects in research and was approved by the Institutional Review Board of Boramae Medical Center (No. 06-2012-88).

2. Definition

Diabetes mellitus was defined according to the American Diabetes Association criteria as: glycated hemoglobin (A1c) ≥6.5%, fasting plasma glucose concentration ≥7.0 mmol/L,

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2-hour plasma glucose ≥11.1 mmol/L during the 75-g oral glucose tolerance test, and/or as taking oral anti-diabetic agents or insulin.[19] Hypertension was defined as a systolic blood pressure ≥140 mmHg or a diastolic blood pressure ≥90 mmHg, or as taking antihypertensive medications.[20] Family history of CHD was defined as heart disease in first-degree relatives. CHD events consisted of the composite of unstable angina or nonfatal myocardial infarction confirmed by coronary angiography, coronary revascularization, and cardiac death. Cardiac death included fatal myocardial infarction; death due to heart failure or arrhythmia; or sudden cardiac death.

3. Statistical analysis

All data were analyzed using IBM SPSS Statistic 20.0 for Windows (IBM Inc., Chicago, IL, USA) and R version 3.1.0 (R Project, Vienna, Austria; http://www.r-project.org). Comparing demographic and clinical predictors between 2 groups was conducted with 2 sample *t*-test for continuous variables, and χ^2 test or Fisher's exact test for categorical variables. In order to investigate the new equation for prediction of CHD events, we fit a Cox proportional hazards model with predictors of interest such as age, sex, BMI, duration of diabetes, HbA1c, blood pressure, low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), total cholesterol (TC), triglyceride, albuminuria, creatinine, smoking history, and family history of CHD, and 2-way interaction terms between sex and all other predictors for considering differential sex effects. The final model was selected with the stepwise selection based on Akaike Information Criterion (AIC).[21] Discrimination, the ability to distinguish between those who experienced the event and those who did not, was evaluated using Harrell's concordance (*c*) index. Interval validation was performed using bootstrap technique with 10,000 replicates followed by generating the accelerated bias-corrected percentile confidence intervals (CIs).[22] A slope shrinkage estimate derived from the bootstrap sample whose value close to 1 represents less overfitting problem in the final model. The predictability of CHD events during 6 years was using area under the receiver operating characteristic (AUROC) curve and AUROC of each prediction model was compared by DeLong test.[23] Additionally, calibration, namely, how closely the prediction reflected observed events, was assessed for each event by the Hosmer-Lemeshow goodness of fit test. The level of significance was set at $p<0.05$.

RESULTS

1. Baseline characteristics according to future CHD events

A total of 732 participants (304 males and 428 females) were included in the analysis. The mean age of the subjects was 60±10 years and their mean duration of diabetes was 10±7 years. Baseline mean HbA1c was 7.4%±1.3%, mean LDL-C was 2.6±0.7 mmol/L and mean body mass index (BMI) was 24.8±3.4 kg/m^2. There was no difference in duration of diabetes, BMI, systolic blood pressure, LDL-C or triglyceride between males and females. However, females were significantly older (mean age, 58±10 years in males and 61±10 years in females; $p<0.001$) and had higher HbA1c (mean HbA1c, 7.3%±1.2% in males and 7.4%±1.3% in females; $p<0.001$) compared to males.

Their median follow-up period was 76 months (range 1–99 month). During the study period, 48 patients (6.6%) experienced CHD events. Compared with subjects who did not develop CHD, those who developed CHD at follow-up were older ($p=0.015$) and showed a higher prevalence of albuminuria ($p=0.020$) (**Table 1**). However, baseline HbA1c, blood pressure,

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Table 1. Baseline characteristics of subjects who did and did not develop CHD events during 6 years of follow-up

Variables	Total	No CHD at follow-up	CHD at follow-up	*p*-value*
No. (% of males)	732 (41.5)	684 (42.0)	48 (35.4)	0.374
Age (yr)	59.9±10.2	59.7±10.3	63.4±8.3	0.015
Duration of diabetes	9 (0–36)	9 (0–35)	9 (0–36)	0.746
BMI (kg/m^2)	24.8±3.4	24.8±3.4	25.4±3.2	0.231
Systolic blood pressure (mmHg)	124.6±11.7	124.5±11.8	125.5±9.9	0.561
Diastolic blood pressure (mmHg)	74.8±8.5	75.0±8.6	72.9±7.1	0.106
HbA1c (%)	7.4±1.3	7.4±1.3	7.5±1.5	0.726
TC (mmol/L)	4.3±0.8	4.3±0.8	4.3±0.8	0.991
HDL-C (mmol/L)				
Males	0.90±0.26	0.91±0.27	0.78±0.20	0.054
Females	0.94±0.25	0.95±0.26	0.91±0.20	0.436
Triglyceride (mmol/L)	1.6±0.9	1.6±0.9	1.8±0.8	0.180
Serum creatinine (mg/dL)	1.1±2.8	1.1±2.9	1.1±1.3	0.762
Retinopathy				
Normal	301 (52.7)	282 (53.2)	19 (46.3)	0.932†
NPDR	197 (34.5)	178 (33.6)	19 (46.3)	
PDR	73 (12.8)	70 (13.2)	3 (7.3)	
UAE				0.020
0–29 ug/mgCr	571 (78.0)	540 (78.9)	31 (64.6)	
≥30 ug/mgCr	161 (22.0)	144 (21.1)	17 (35.4)	
Hypertension	135 (18.4)	128 (18.7)	7 (14.6)	0.476
Triglyceride ≥1.7 mmol/L	271 (37.0)	247 (36.1)	24 (50.0)	0.054
HDL-C < (M) 1.0, (W) 1.3 mmol/L	619 (84.6)	575 (84.1)	44 (91.7)	0.159
LDL-C ≥2.5 mmol/L	397 (54.2)	374 (54.7)	23 (47.9)	0.363
LDL-C ≥3.3 mmol/L	109 (14.9)	103 (15.1)	6 (12.5)	0.630
Anti-diabetic agent				
Insulin	142 (19.4)	133 (19.4)	9 (18.8)	0.906
Metformin	491 (67.1)	460 (67.3)	31 (64.6)	0.704
Thiazolidinedione	83 (11.3)	79 (11.5)	4 (8.3)	0.497
Insulin secretagogue	435 (59.4)	408 (59.6)	27 (56.2)	0.643
Other medication				
Statin	326 (44.5)	303 (44.3)	23 (47.9)	0.626
ACEI or ARB	365 (49.9)	343 (50.1)	22 (45.8)	0.564
Beta-blocker	63 (8.6)	57 (8.3)	6 (12.5)	0.291
Anti-platelet agent	413 (56.4)	384 (56.1)	29 (60.4)	0.564
Family history of CHD	17 (2.3)	15 (2.2)	2 (4.2)	0.308
Smoking history				
Non-smoker	535 (73.1)	500 (73.1)	35 (72.9)	0.273†
Ex-smoker	94 (12.8)	85 (12.4)	9 (18.8)	
Smoker	103 (14.1)	99 (14.5)	4 (8.3)	

Values are presented as number (%) or mean±standard deviation.
CHD; coronary heart disease, BMI; body mass index, TC; total cholesterol, HDL-C; high-density lipoprotein cholesterol, NPDR; non-proliferative diabetic retinopathy, PDR; proliferative diabetic retinopathy, UAE; urinary albumin excretion, LDL-C; low density lipoprotein cholesterol, ACEI; angiotensin converting enzyme inhibitor, ARB; angiotension II receptor blocker, M; men, W; women.
*p-value between group from chi square test and independent t-test for nominal and continuous variables, respectively; †p-value from linear-by-linear analysis.

HDL-C and LDL-C levels, prevalence of family history of CHD, smoking history did not significantly differ between subjects with or without CAD events. At baseline, 19.4% of patients managed their glucose level with insulin and 67.1% with metformin; there was no difference in that medication according to CAD events (**Table 1**). The proportion of subjects taking statin at the baseline did not differ either; that was 44.3% in the subjects without CHD events and 47.9% in the subjects with CHD events (p=0.626).

2. Development of new equation for prediction of CHD events

Age, sex, BMI, duration of diabetes, HbA1c, blood pressure, LDL-C, HDL-C, TC, triglyceride, albuminuria, creatinine, smoking history, family history of CHD, and 2-way interaction terms between sex and all other predictors were considered for development of new equation using

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Table 2. HRs of risk factors incorporated in the best-fitting Cox proportional hazard model with the stepwise selection

Variables	Estimated regression coefficient (SE)	HR (95% CI)	*p*-value
Total			
Age	0.033 (0.017)	1.034 (1.000–1.068)	0.048
Sex	3.962 (1.833)	54.566 (1.446–1910.6)	0.031
FHx of CHD	2.637 (1.060)	13.967 (1.749–111.6)	0.013
BMI	0.067 (0.041)	1.069 (0.987–1.158)	0.103
HbA1c	0.242 (0.156)	1.273 (0.938–1.728)	0.121
DBP	−0.029 (0.018)	0.972 (0.939–1.006)	0.104
HDL-C	−1.319 (0.739)	0.267 (0.063–1.138)	0.074
Creatinine	0.106 (0.094)	1.111 (0.924–1.336)	0.262
Albuminuria	0.764 (0.333)	2.146 (1.118–4.117)	0.022
Sex: FHx of CHD	−2.968 (1.492)	0.051 (0.003–0.957)	0.047
Sex: HbA1c	−0.369 (0.209)	0.692 (0.459–1.043)	0.079
Sex: creatinine	−0.955 (1.024)	0.385 (0.052–2.864)	0.351
Men			
FHx of CHD	2.632 (1.082)	13.907 (1.669–115.8)	0.015
SBP	0.058 (0.025)	1.060 (1.009–1.112)	0.020
DBP	−0.075 (0.032)	0.928 (0.872–0.988)	0.020
HDL-C	−2.779 (1.382)	0.062 (0.004–0.931)	0.044
Albuminuria	0.851 (0.509)	2.342 (0.863–6.355)	0.095
Females			
Age	0.035 (0.020)	1.036 (0.996–1.077)	0.076
BMI	0.100 (0.047)	1.105 (1.009–1.210)	0.032

HR; hazard ratio, SE; standard error, CI; confidence interval, FHx; family history, CHD; coronary heart disease, BMI; body mass index, DBP; diastolic blood pressure, HDL-C; high density lipoprotein cholesterol, SBP; systolic blood pressure.

Cox proportional hazard model with the stepwise selection. The hazard ratios (HRs) and β-coefficients with 95% CI of the predictors selected for the new equation were listed in **Table 2**. Of the predictors incorporated in UKPDS risk engines, age, sex, HbA1c and HDL-C were also selected for the new equation; whereas, smoking status was not. Instead, family history of CHD, albuminuria, BMI and creatinine were added in the new equation. The Harrell's *c*-index for discrimination of our new equation was 0.698 (95% CI, 0.614–0.781) and the bias-corrected *c*-index from the internal validation was 0.664 (95% CI, 0.600–0.731), which showed that our new equation had low overfit bias. In addition, a slope shrinkage estimate was 0.977, which indicated new equation had good calibration.

As there was a significant interaction with sex on the equation, we also developed the sex-specific equation for males and females respectively (**Table 2**). Family history of CHD, systolic and diastolic blood pressure, HDL-C, and albuminuria were selected for males. Whereas, in the case of females, only age and BMI were for the new equation. Harrell's *c*-indices were 0.778 (95% CI, 0.634–0.921) for males-specific equation and 0.634 (95% CI, 0.532–0.736) for females-specific equation, respectively.

3. Comparison between new equation and UKPDS risk engine for prediction of CHD events

According to the new equation, 396 (54.1%) subjects had <5% of 6-year CHD event risk, 230 (31.4%) had 5%–10% and 106 (14.5%) had ≥10% of 6-year CHD event risk. Among the subjects with <5% of risk, 13 (3.3%) experienced CHD events during 6 years whereas 17.0% of subjects with ≥10% of risk experienced CHD events during the same period (**Table 3**). Among the subjects with <5% of risk from the new equation, 30.6% (121 out of 396) had ≥10% of risk from UKPDS risk engine. The prevalence of CHD events during 6 years in them was only 3.3%

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Table 3. Observed CHD events within 6 years according to the expected risk calculated from the new equation and UKPDS risk engine

Variables	New equation		
	<5%	5%–10%	≥10%
Total			
No.	396	230	106
No. (%) of events	13 (3.3)	12 (5.2)	18 (17.0)
UKPDS risk engine			
<5%			
No.	138	36	7
No. (%) of events	5 (3.6)	2 (5.6)	1 (14.3)
5%–10%			
No.	137	83	17
No. (%) of events	4 (2.9)	4 (4.8)	4 (23.5)
≥10%			
No.	121	111	82
No. (%) of events	4 (3.3)	6 (5.4)	13 (15.9)

CHD; coronary heart disease, UKPDS; UK Prospective Diabetes Study.

(**Table 3**). Among entire subjects with ≥10% risk according to UKPDS risk engine, 7.3% (23 out of 314) experienced CHD events within 6 years of follow-up.

Hosmer-Lemeshow goodness of fit test showed that the new equation revealed good calibration within 6 years CHD events (p=0.468). Similarly, there were no significant discrepancies in sex-specific equations for 6-year CHD events (p=0.108 for males and p=0.798 for females, respectively).

AUROC of the new equation for prediction of 6-year CHD events were 0.721 (95% CI, 0.641–0.800) which is significantly larger than that of UKPDS risk engine, 0.578 (95% CI, 0.482–0.675; p from DeLong test=0.001). We estimated and compared its predictability with UKPDS risk engine in each year from the baseline. AUROC of the new equation was superior in 3–6 years from the baseline (**Fig. 1** and **Supplementary Table 1**). We subsequently analyzed the predictability of the new equation in each sex. In males, AUROC for 6-year CHD events were 0.822 (95% CI, 0.721–0.922) and 0.743 (95% CI, 0.612–0.874) in the new equation and UKPDS risk engine, respectively (p from DeLong test=0.232). In females, AUROC of the new equation is superior to that of UKPDS risk engine (0.652 [95% CI, 0.539–0.765] in the new equation and 0.535 [95% CI, 0.421–0.650] in the UKPDS risk engine; p from DeLong test=0.012). We also investigated the sex-specific equation for the prediction of CHD events compared UKPDS risk engine and found the similar performance with the new equation for entire population (**Supplementary Table 2**).

Next, we performed the stratified analysis according to age to investigate whether age affected the predictability of the new equation (**Table 4**). In females aged <60 years, AUROC of UKPDS risk engine was only 0.383 (95% CI, 0.231–0.536), which was significantly lower compared to 0.672 (95% CI, 0.518–0.840) of sex-specific new equation (p from DeLong test=0.004). By contrast, in the case of males, the difference in AUROC between UKPDS risk engine and the new equation was prominent in males aged ≥60 years (0.817 [95% CI, 0.686–0.947] in the sex-specific new equation and 0.591 [95% CI, 0.401–0.780] in the UKPDS risk engine; p from DeLong test=0.024).

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Table 4. Predictability of the new equation for 6-year CHD events according to age

Age (yr)	Males					Female				
	New equation	New equation, sex-specific	UKPDS	*p*-value*	*p*-value†	New equation	New equation, sex-specific	UKPDS	*p*-value*	p-value†
<60	0.887 (0–1.000)	0.781 (0.585–0.978)	0.875 (0–1.000)	0.927	0.552	0.535 (0.323–0.746)	0.679 (0.508–0.849)	0.383 (0.231–0.536)	0.063	0.004
≥60	0.730 (0.571–0.890)	0.817 (0.686–0.947)	0.591 (0.401–0.780)	0.162	0.024	0.669 (0.544–0.795)	0.628 (0.502–0.754)	0.519 (0.383–0.655)	0.018	0.106

CHD; coronary heart disease, UKPDS; UK Prospective Diabetes Study.
*p-value from DeLong test between the new equation and UKPDS risk engine; †*p*-value from DeLong test between the sex-specific new equation and UKPDS risk engine.

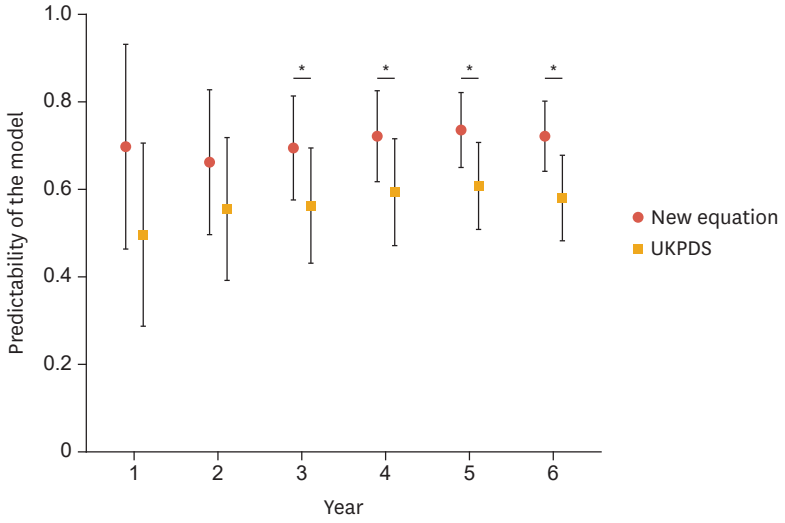

Fig. 1. Predictability of the new equation for 6-year CHD events compared to UKPDS risk engine. The predictability of the new equation and UKPDS risk engine in each year from the baseline was estimated by AUROC. AUROC was compared using DeLong test.
CHD; coronary heart disease, UKPDS; UK Prospective Diabetes Study, AUROC; area under the receiver operating characteristic.
*p<0.05.

DISCUSSION

We investigated the performance of UKPDS risk engine in the hospital-based cohort of 2006 including entire type 2 diabetic patients aged ≥30 years who had no history of CHD and found that the UKPDS risk engine showed moderate to poor discrimination for 6-year CHD (AUROC, 0.578 [95% CI, 0.482–0.675]). Furthermore, among subjects with ≥10% risk according to UKPDS risk engine, only 7.3% (23 out of 314) eventually experienced CHD events within 6 years of follow-up. It was corresponded the previous studies in European[15] and Asian[16] which showed that UKPDS risk engine made an overestimation of the CHD risk. We successfully developed the new equation for predicting CHD risk fitting for type 2 diabetic patients in this study cohort.

Discrepancy between observed CHD event rate and UKPDS risk prediction might be from improvements of managing CHD risk factors in diabetic subjects.[11,12] External validation of the UKPDS risk engine in European cohort also showed that UKPDS risk engine overestimates the risk of CHD more than 2 times (224%)[15] as in our study. Epidemiologic studies have shown that mortality were reducing prominently in diabetic patients compared to that in normal population in recent years.[12] Although UKPDS was conducted in the subjects with newly diagnosed diabetes aged 25–65 year between 1977 and 1991, the

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incidence of MI was 14%–17% and that of stroke was 4%–6%,[24,25] which was higher than that in the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) trial conducted in diabetic patients aged ≥55 years, with a history of major macrovascular or microvascular disease or at least one other risk factor for vascular disease. In ADVANCE study, major macrovascular event rate was only 4.7%–5.5%.[26]

In addition, recent studies have shown that a conventional risk factor-based approach cannot identify high-risk diabetic patients developing CHD[4,13]; also in a prospective cohort of Korea, there were no significant differences between subjects with and without CAD with respect to LDL-C or blood pressure in diabetic subjects.[9] Instead, autonomic neuropathy,[4,27] retinopathy,[28,29] and renal complications[30,31] were useful CHD risk indicators in diabetic patients, which corroborates our studies. Comparing the predictors incorporated in UKPDS risk engines and our new equation, family history of CHD, albuminuria, BMI and creatinine were only shown in the new equation. Obesity is well-known risk factor of CAD in type 2 diabetic patients.[32,33] Furthermore, the association between obesity and CHD might be different according to ethnicity[34,35] and Asian population affected their CHD risk significantly by relative lower BMI cutoff compared to Caucasians.[35]

Furthermore, UKPDS risk engine was developed in the predominantly Caucasian population, whereas ours was for Asian, known to have lower risks of CHD.[17,36-38] In addition, effect size of risk factors on CHD can be different by race.[39] Hong Kong Diabetes Registry established in 1995 also showed that the UKPDS CHD risk engine overestimated the risk of CHD with suboptimal discrimination.[16] In Hong Kong Diabetes Registry, age, creatinine, albuminuria, duration of diabetes and non-HDL-C was incorporated in the equation to predict CHD event[16]; whereas in Japanese diabetic patients, sex, age, HbA1c, blood pressure, non-HDL-C and smoking history were selected to predict CHD risk.[40]

In our cohort, we found significant interaction with sex on the risk equation. It has been already known that there is sex difference in risk factors for predicting CHD events.[41-43] Furthermore, in our study, females are significantly older and have a high glucose level compared to males. Although we did not have information of menopausal status, mean age of females in our study was over 60 years and it has been known that menopausal females have higher CHD risk compared to premenopausal females.[44] Females are at lower risk for CHD than males[14,29,45]; however, this disparity tends to disappear after menopause.[46] In addition, the association between diabetes and CHD mortality is reported to be higher in females compared to that in diabetic males.[41,42] Females in our cohort are relatively older even comparing to other previous cohorts including UKPDS[14] or Hong Kong Diabetes Registry,[16] which might result in higher HR for CHD in females compared to males in our new equation compared to that from other cohorts.[14,16] We subsequently developed the sex-specific equation for males and females respectively. Notably, in the females-specific equation, only age and BMI were selected as variables predicting CHD risk. Comparing UKPDS risk engine in and the females-specific equation in our study, new equation shows a better predictability. In males, family history of CHD, systolic and diastolic blood pressure, TC, LDL-C, triglyceride, and albuminuria were selected for the sex-specific equation. Although the predictability of males-specific equation reached at 0.812 (95% CI, 0.703–0.920) of AUROC, there was no statistical difference compared to that of UKPDS (0.743 [95% CI, 0.612–0.874]). Smoking history was not included in the new equation including sex-specific model. Relative low prevalence of current smokers, that is, about 14% which was about a half of that in UKPDS[14] might be the cause.

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Considering that previous risk engines developed even in Asian diabetic populations such as Hong Kong[16] and Japan[40] were quite different from each other, external validation of our new equation is warranted to evaluate the clinical usefulness in general population. In Hong Kong Diabetes Registry, age, creatinine, albuminuria, duration of diabetes and non-HDL-C was incorporated in the equation to predict CHD event[16]; whereas in Japanese diabetic patients, sex, age, HbA1c, blood pressure, non-HDL-C and smoking history were selected to predict CHD risk.[40]

The main limitation of our study was retrospective cohort design, which resulted in selection bias during excluding the subjects who had insufficient data to calculate the CHD risk. In addition, absence of external validation of the equation is important weak point of our study. However, we confirmed that UKPDS risk score overestimates the risk of CHD event in type 2 diabetic patients in this cohort. Among the subjects with <5% of risk from the new equation, as much as 30.6% had ≥10% of risk from UKPDS risk engine and the prevalence of CHD events in them was only 3.3%. The performance of the new equation for prediction of CHD events was superior in 3–6 years from the baseline.

In conclusion, we successfully developed the equation for predicting CHD risk fitting for type 2 diabetic patients in this study cohort. It might be useful to guide for managing CHD risk factors and screening CHD in Korean type 2 diabetic patients.

SUPPLEMENTARY MATERIALS

Supplementary Table 1

Predictability of the new equation for 6-year CHD events compared to UKPDS risk engine

Click here to view

Supplementary Table 2

Predictability of the sex-specific new equation for 6-year CHD events compared to UKPDS risk engine

Click here to view

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