Mini-Review

Model for Predicting Cardiovascular Disease: Insights from a Korean Cardiovascular Risk Model

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Key Words

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Abstract

The profile and prevalence of risk factors in cardiovascular disease (CVD) are different between Western and Asian populations. In the guidelines, tailored approaches following risk stratification based on CVD risk models are recommended for the primary prevention of CVD in asymptomatic subjects. However, current risk models for predicting CVD in Asian populations are limited. A recent study of a large cohort of asymptomatic Korean individuals developed a CVD risk model to predict global cardiovascular risk that showed good performance in predicting cardiovascular events. This model may be useful for the primary prevention of CVD in East Asian individuals as well as Koreans.

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Over the past few decades, the incidence of cardiovascular disease (CVD) has rapidly increased in most Asian populations, and CVD prevention in Asia has become a major global health concern [1, 2]. The guidelines for the primary prevention of CVD generally recommend identifying high-risk individuals and improving their prognosis through aggressive interventions and personalized approaches by risk stratification using a prediction model [3, 4]. However, models for predicting CVD in Asian populations are limited at present. In addition, recently published ACC/AHA guidelines on cardiovascular risk assessment also pointed out that (a) the lack of ethnic-specific risk algorithms is an important obstacle to understanding and preventing atherosclerotic CVD in Asian populations, (b) the development of algorithms specific to these race/ethnic groups should be encouraged, and (c) when providers use the equations for non-Hispanic Whites for these individuals, their risks may be overestimated [5].

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Therefore, developing an Asian-specific risk prediction model for the primary prevention of CVD is important.

We have recently published a study performed to develop a risk model to predict global cardiovascular risk in a large cohort of asymptomatic Korean individuals [6]. In addition, we sought in that study to evaluate (a) the incidence and characteristics of CVD in a Korean population, (b) the racial or ethnic differences of risk factors attributable to the development of CVD, and (c) the validation of existing CVD risk models developed on the basis of a database of Western populations.

A total of 57,393 consecutive asymptomatic Korean individuals aged 30–80 years without known CVD who voluntarily underwent a general health examination in the Health Screening and Promotion Center at the Asan Medical Center, a 2,791-bed tertiary treatment referral hospital in Seoul, were enrolled between January 2007 and June 2011. Thirty-one possible clinical risk factors and biomarkers were assessed. A cardiovascular event was defined as a composite of cardiovascular death, myocardial infarction, and stroke. Study participants were randomly divided into train ($n = 45,914$) and validation ($n = 11,479$) cohorts. In the train cohort, a Korean CVD risk model was developed using 11 variables, including age, diabetes mellitus, hypertension, current smoking, family history of coronary heart disease (CHD), white blood cell count, creatinine level, glycohemoglobin level, atrial fibrillation, and blood pressure and cholesterol indices [C-index = 0.757; 95% confidence interval (CI) 0.726–0.788] and Akaike Information Criterion = 7,207]. In the validation cohort, this model performed well [3-year C-index = 0.760 (95% CI 0.693–0.828) and Nam and D’Agostino χ^2 statistic = 0.001; 5-year C-index = 0.782 (95% CI 0.719–0.846) and Nam and D’Agostino χ^2 statistic = 1.037; table 1] [6]. In addition, to explain our Korean cardiovascular risk model, we present a specific patient, namely a 66-year-old male who had no past medical history except hypertension. His electrocardiogram showed a normal sinus rhythm. The systolic and diastolic blood pressures were 150 and 90 mm Hg, respectively. Total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol were 200, 130, and 40 mg/dl, respectively. White blood cell count was $7.0 \times 10^3/\mu\text{l}$, glycohemoglobin was 6%, and serum creatinine was 0.6 mg/dl. For this patient, the estimated 3- and 5-year CVD risk was 5.6 and 9.5%, respectively. These prognostic scores can be calculated automatically (online suppl. table, see www.karger.com/doi/10.1159/000438683).

During the median follow-up period of 3.1 years (interquartile range 1.9–4.3), 458 individuals had 474 cardiovascular events (35 cardiovascular deaths, 79 myocardial infarctions, and 360 strokes). East Asian populations, including those from Korea, China, and Japan, are known to have a lower incidence of CHD than stroke [2, 7]. Our study also confirmed a specific characteristic – that stroke incidence was higher than myocardial infarction incidence in this Korean population. In addition, it has been reported that East Asian populations have similar types of cardiovascular risk factors, such as a higher prevalence of hypertension accompanied by high salt intake, a higher smoking rate, lower serum total cholesterol with lower fat intake, and an increasing prevalence of obesity and diabetes mellitus due to rapid and early-phase westernization [7]. Therefore, these findings suggest that our Korean CVD risk model might be applicable to other East Asian populations such as Japanese and Chinese populations.

The important predictors in our Korean CVD risk model were age, diabetes mellitus, hypertension, current smoking, a family history of CHD, white blood cell count, creatinine, glycohemoglobin, atrial fibrillation, blood pressure, and cholesterol. There were no significant differences between Korean and Western models in terms of the risk predictors of CVD [8–11]. However, we observed differences in the contributions of these predictors in our Korean CVD risk model in which age was found to be the single most important determinant

Table 1. Performance of the Korean and Framingham risk models

Models	Cardiovascular death/ myocardial infarction/ stroke ^a		
	coefficient	hazard ratio	p value
<i>Korean cardiovascular risk model</i>			
Age	0.074	1.077	<0.001
log of creatinine	0.556	1.744	0.017
Hypertension	0.343	1.409	0.008
Family history of CHD	0.140	1.150	0.417
Diabetes mellitus	0.366	1.441	0.034
log of white blood cell count	0.279	1.322	0.186
Current smoking	0.686	1.986	<0.001
Cholesterol index ^b	0.214	1.239	0.106
log of glycated hemoglobin	0.501	1.650	0.291
Blood pressure index ^c	0.255	1.290	<0.001
Atrial fibrillation	0.795	2.214	0.056
Train cohort			
C-index (95% CI)	0.757 (0.726–0.788)		
Akaike Information Criterion	7,207		
Shrinkage	0.969		
Validation cohort			
3-year C-index (95% CI)	0.760 (0.693–0.828)		
3-year Nam and D'Agostino χ^2 statistics ^d	0.001		
5-year C-index (95% CI)	0.782 (0.719–0.846)		
5-year Nam and D'Agostino χ^2 statistics ^d	1.037		
<i>Framingham risk model for CVD</i>			
log of age	3.344	28.320	<0.001
log of total cholesterol	0.560	1.750	0.061
log of high-density lipoprotein cholesterol	−0.587	0.556	0.009
log of systolic blood pressure	2.187	8.909	<0.001
Treatment of hypertension	−0.008	0.992	0.999
Diabetes mellitus	0.458	1.581	<0.001
Current smoking	0.773	2.166	<0.001
Gender	−0.016	0.985	0.902
Interaction between log of systolic blood pressure and treatment	0.106	1.111	0.906
Train cohort			
C-index (95% CI)	0.751 (0.719–0.782)		
Akaike Information Criterion	7,219		
Shrinkage	0.974		
Validation cohort			
3-year C-index (95% CI)	0.754 (0.687–0.822)		
3-year Nam and D'Agostino χ^2 statistics ^d	0.001		
5-year C-index (95% CI)	0.782 (0.718–0.846)		
5-year Nam and D'Agostino χ^2 statistics ^d	6.161		

^a The null C-index and Akaike Information Criterion were 0.5 and 7,544, respectively. When all variables were included, the maximum C-index was 0.771 (95% CI 0.739–0.802), and the Akaike Information Criterion was 7,221. Higher C-index values and lower Akaike Information Criterion values indicate better models.

^b Cholesterol index = $0.19 \times [(\text{low-density lipoprotein cholesterol} - 120)/30] - 0.25 \times [(\text{high-density lipoprotein cholesterol} - 55)/14] + 0.16 \times [(\text{total cholesterol} - 190)/34]$.

^c Blood pressure index = $0.5 \times [(\text{systolic pressure} - 115)/15] + 0.5 \times [(\text{diastolic pressure} - 75)/100]$.

^d Smaller Nam and D'Agostino χ^2 statistics indicate better models.

of a CVD event. On the other hand, the contribution of other risk factors to CVD risk prediction was much smaller. These findings indicate that there are no racial or ethnic differences in the overall risk factors for CVD, but that the contribution of each risk factor appears to be different between Korean and Western populations.

Our study also evaluated the effectiveness of conventional CVD risk models, which were developed on the basis of the database of Western countries and have rarely been validated in Asian populations living in Asian countries. We tested the validation of the Framingham risk model in our large Korean cohort. The Framingham risk model for CVD showed comparable discriminating and calibrating abilities in the train cohort, and the performance of the Framingham risk model for CVD was also reliable in the validation cohort (table 1). However, because there was a discrepancy in the study endpoints between the Korean CVD risk model and the Framingham risk model for CVD, our analysis showed a possible applicability of the Framingham risk model to Asian populations. In addition, our findings suggest that traditional CVD risk factors obtained from the Framingham risk model could also be applicable to Asian populations, and that future CVD events could be prevented by similar global approaches regardless of genetic or lifestyle differences.

Our Korean cardiovascular risk model had several limitations. First, the study was performed in a single center. Therefore, it might be weaker in methodology, and it is possible that the study participants were a homogeneous cohort. Second, because the follow-up period was limited to 5 years, the Korean risk model cannot predict the long-term cardiovascular risk. Third, the analysis of inflammation, hemostasis, thrombosis, or oxidative stress biomarkers was limited. Finally, although the database of governmental and quasi-governmental organizations was used, it is possible that these data could not fully reflect the outcomes.

In conclusion, besides developing a Korean CVD risk model, our study evaluated racial or ethnic differences in both the incidence of CVD and the differing contribution of risk factors for CVD. Our analysis confirmed that traditional CVD risk factors obtained in Western populations may in fact be applicable to Asian populations. We hope that our study encourages greater awareness of CVD risks in other Asian countries and becomes a cornerstone for future collaborative research in other Asian populations.

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Disclosure Statement

We have no conflicts of interest to disclose.

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