Framingham risk score for predicting cardiovascular disease in older adults in Hong Kong

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KEY MESSAGES

1. The Framingham risk score, a widely used cardiovascular disease (CVD) risk prediction tool, overestimated the risk in a large cohort of older Chinese adults in Hong Kong despite recalibration. It should be used with caution for this population.
2. Our study was limited by the lack of comprehensive laboratory predictors and CVD incidence data. New risk prediction models should be developed for specific settings with CVD incidence data.

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Introduction

Cardiovascular disease (CVD), including ischaemic heart disease and stroke, is a leading cause of death. Many clinical guidelines recommend that clinicians use risk prediction tools to identify individuals at high risk of CVD. The predicted CVD risk can then guide clinical decisions on the intensity of preventive interventions, especially the use of statins or other lipid-lowering therapies.

The Framingham risk score (FRS) is the most widely used risk prediction tool.[1] It predicts the risk of incident CVD events over the subsequent 10 years. The original FRS was derived from middle-class Caucasian individuals and has been shown to systematically overestimate the risk of CVD in other ethnic groups, including Chinese.[2,3] Patterns of CVD in the Hong Kong population differ from those in Caucasian populations, with lower incidence of ischaemic heart disease and higher incidence of haemorrhagic stroke and diabetes mellitus.[4] The Hong Kong Department of Health recommends that primary care physicians use the FRS to assess individual CVD risk but also acknowledges that the FRS probably overestimates the risk in the local population. With population ageing, CVD is more prevalent. In a prospective study of 2895 Hong Kong Chinese people aged 25 to 74 years, the FRS overestimated the CVD risk by 1.5-fold in men but was fairly accurate when applied to women.[5] Nonetheless, whether the FRS can be applied specifically to older Chinese adults in Hong Kong remains unclear. This study compared the predictive performance of the FRS, specifically a simple office-based CVD risk prediction function, directly and after recalibration, in a large cohort of Chinese older adults in Hong Kong.

Methods

This study was approved by the Institutional Review Board of The University of Hong Kong/Hospital Authority Hong Kong West Cluster. We used data from the Department of Health Elderly Health Service cohort that included 66 820 older Chinese adults (aged ≥65 years) enrolled at elderly health centres in Hong Kong from July 1998 to December 2001 and followed up passively for >10 years until May 2012. Details of the cohort have been described in a previous study.[4] The 18 elderly health centres provide primary care services for older adults; all Hong Kong residents aged ≥65 years are encouraged to enrol in the service for a small annual fee. More women than men are enrolled; otherwise, participants were similar to the general elderly population in terms of age, socioeconomic status, current smoking status, and hospital use.[4]

At the elderly health centres, specifically trained nurses and doctors provided health assessments and physical check-ups using structured interviews and comprehensive clinical examinations. Height, weight, and blood pressure were measured according to standard protocols. Self-reports of chronic diseases were confirmed and supplemented by clinical diagnoses based on history. Serum samples were tested for total cholesterol.

The office-based FRS was derived from the following non-laboratory predictors: age, body mass index, systolic blood pressure, treatment for hypertension, smoking, and diabetes status.[1] To

ensure comparability, stratification of predictors or risk factors was based on the FRS.

Death from CVD events at 10 years of follow-up was as defined by the Framingham Heart Study. Vital status was ascertained from death registration by record linkage using Hong Kong identity card numbers. Causes of death were routinely coded by the Department of Health according to the International Classification of Disease. Fatal CVD was defined as death from ischaemic heart disease, cerebrovascular events, peripheral artery disease, intermittent claudication, or heart failure.[1] To estimate the incidence of all CVD events, a ratio of 8:1 for non-fatal to fatal events was assumed based on the number of inpatient discharges and CVD deaths in the Hospital Authority Statistical Report 2012-2013 because participants were not actively followed up at 10 years from enrolment.

Only participants aged 65 to 74 years at baseline were included. Participants with a history of CVD or missing predictors at baseline were excluded. Baseline CVD was defined as self-reported physician-diagnosed ischaemic heart disease, circulatory disease, or peripheral vascular disease.

The FRS has been reported to predict 10-year risk of CVD events based on a sex-specific Cox proportional hazards regression model on 8491 participants aged 30 to 74 years who were free from CVD at the time of examination between 1968 and 1987 and were followed up for a maximum of 12 years.[1] The algorithm used to derive the FRS has good calibration and discrimination.[1] In the present study, a simpler office-based version was used. This non-laboratory-based score uses body mass index (instead of total and high-density lipoprotein cholesterol) and thus is more suitable for resource-limited settings and primary care.[3] It has comparable performance with models that use cholesterol.[1]

Statistical analyses were performed using Stata (version 13.0) and R (version 3.1.1). The observed 10-year risk of CVD events and baseline survival rate were calculated using sex-specific Kaplan-Meier estimates. Participants who died from non-CVD causes were censored at the time of death. The predicted risk of CVD events for each participant was calculated using the FRS. Participants were grouped into deciles of observed and predicted risk within 10 years of follow-up. The FRS was recalibrated by substituting the baseline survival rate and mean risk factor levels with data from the cohort, and the predictive performance of the models was evaluated. Calibration refers to the degree of agreement between observed and predicted events and was measured by the Hosmer-Lemeshow test, with χ^2 <20 indicating good calibration.

Results

A total of 10 291 men and 20 445 women were included in the analysis. Table 1 shows the baseline characteristics of the cohort according to the FRS predictors. The observed 10-year risk of CVD events was 31.0% in men and 18.6% in women. Applying the original FRS function and assuming a ratio of 8:1 for non-fatal to fatal CVD events, the mean predicted 10-year risk of CVD events was 38.5% (95% confidence interval [CI]=38.2%-38.8%) in men and 21.6% (95% CI=21.5%-21.8%) in women. The original FRS function overestimated the 10-year risk of CVD events, especially at the highest risk deciles (Fig). Calibration was poor for both men (χ^2=367.6) and women (χ^2=258.6) [Table 2]. Recalibration using cohort data improved the model's performance slightly in men (χ^2=218.6) but not in women (χ^2=303.0). Applying the recalibrated FRS function, the mean predicted 10-year risk of CVD events was 36.1% (95% CI=35.8%-36.4%) in men and 22.2% (95% CI=22.0%-22.3%) in women.

Discussion

In this large cohort of Hong Kong Chinese older adults, the FRS overestimated the 10-year risk of CVD events by approximately 1.2-fold in both men and women, particularly at the highest risk deciles. This is consistent with the findings of the Chinese Multi-provincial Cohort Study of 30 121 Chinese adults aged 35 to 64 years, which reported that the FRS systematically overestimated CVD risk in men and women, with larger differences in higher risk deciles.[2] The Asia-Pacific Cohort Studies Collaboration also showed that the FRS overestimated risk of CVD by 11% and 10% for men and women, respectively, among six cohorts of 25 682 Chinese adults.[3] Recalibration substantially improved the model's performance in these two studies. In the Hong Kong Cardiovascular Risk Factors Study with a cohort of 2895 Chinese adults aged 25 to 74 years, the FRS overestimated CVD risk by about 1.5-fold in men, although it was relatively accurate when applied to women.[5] In our

TABLE 1. Baseline characteristics of the Elderly Health Service cohort by sex

Characteristics	Men (n=10 291)*	Women (n=20 445)*
Age, y	69.4±2.7	69.3±2.7
Body mass index, kg/m^2	23.9±3.3	24.6±3.7
Systolic blood pressure, mm Hg	146.5±23.1	147.2±23.9
Untreated	144.4±23.3	144.1±23.6
Treated	152.6±21.4	154.9±22.8
Hypertension	2643 (25.7)	5953 (29.1)
Smoking	2227 (21.6)	663 (3.2)
Diabetes	1389 (13.5)	2682 (13.1)

* Data are presented as mean±standard deviation or No. (%) of participants

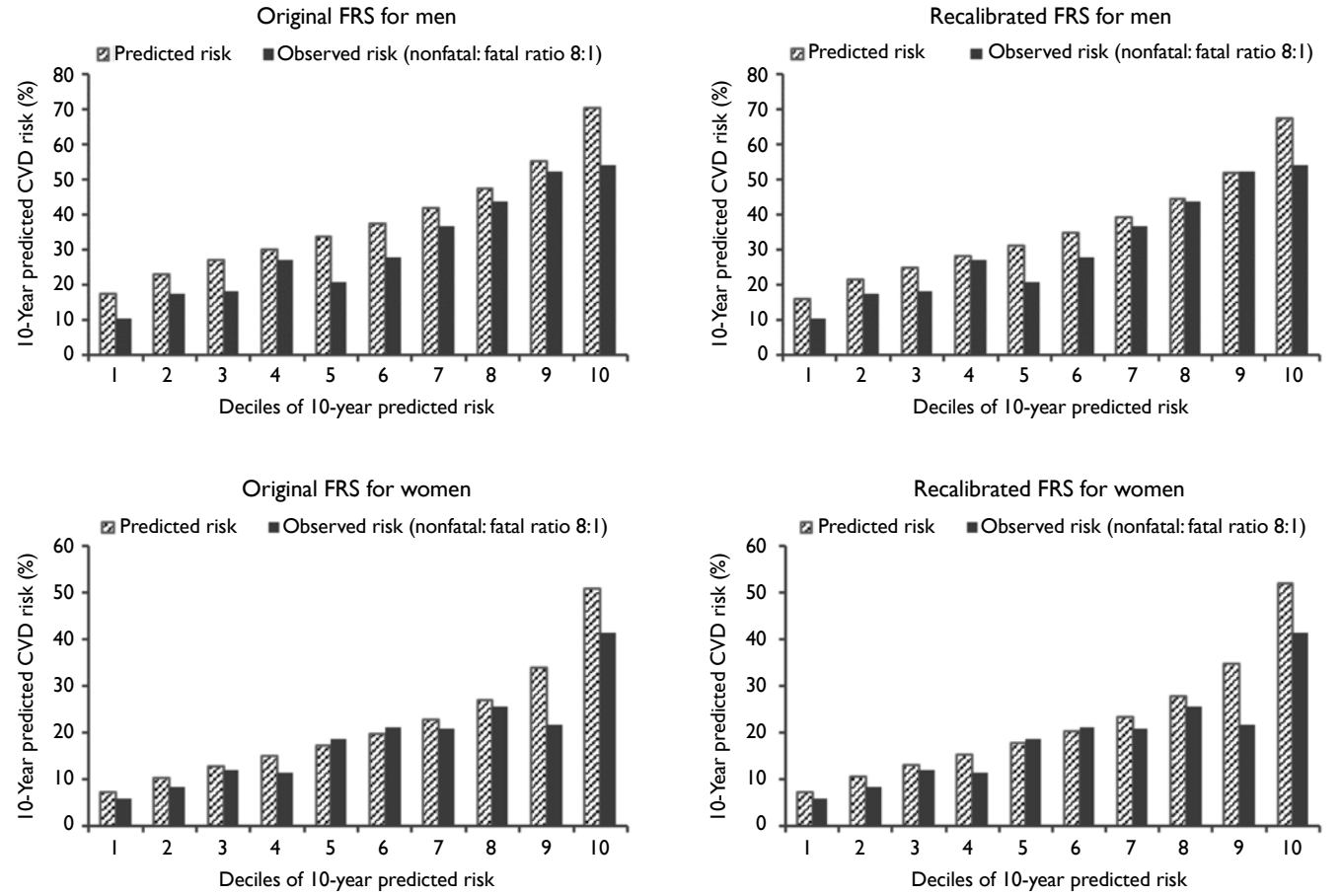

FIG. Prediction of 10-year risk of cardiovascular disease (CVD) events by sex using the original and recalibrated Framingham risk scores (FRS)

TABLE 2. Calibration of the Framingham risk score by sex*

Parameter	Men		Women	
	Original	Recalibrated	Original	Recalibrated
Mean 10-year risk of cardiovascular disease events, % (n)				
Observed†	31.0 (3186)	31.0 (3186)	18.6 (3809)	18.6 (3809)
Predicted	38.5 (3961)	36.1 (3712)	21.6 (4426)	22.2 (4531)
Calibration				
Hosmer-Lemeshow χ^2 statistic	367.6	218.3	258.6	303.0
Hosmer-Lemeshow P value	<0.001	<0.001	<0.001	<0.001

* Discrimination could not be determined, as we did not have data on individual cardiovascular disease events

† Based on a ratio of 8:1 for non-fatal to fatal cardiovascular disease events and Kaplan-Meier estimation for 10 years of follow-up

cohort, recalibration did not improve the model's calibration for women, perhaps because we did not assess laboratory predictors. As we did not measure high-density lipoprotein cholesterol, we were unable to evaluate the FRS based on laboratory predictors, as was in the Chinese Multi-provincial Cohort Study and the Hong Kong Cardiovascular Risk Factors Study cohorts,[2,5] although the office-based FRS has shown good internal validity.[1] Nonetheless, our results should be interpreted with caution owing to the lack of CVD incidence data.

To our knowledge, this was the first study to assess the predictive performance of the FRS for older adults in Hong Kong. Our cohort has the advantages of large sample size and long duration of follow-up. Nonetheless, there were several limitations. First, participants in the cohort were volunteers and may have been healthier and/or more health-conscious

than the general population, although the two groups were largely comparable in terms of socioeconomic status and health services use.[4] The FRS was derived from a cohort of volunteers. Older adults in long-term care facilities or with very poor health were unlikely to attend the elderly health centres. Survivor bias may be a problem if those who are particularly prone to certain types of exposure died before they could be recruited.[4] This is a problem inherent to all cohorts of older adults. Second, high-density lipoprotein cholesterol was not measured; hence, the laboratory-based version of the FRS could not be validated. Nonetheless, the office-based FRS has similar predictive performance to that of the laboratory-based version.[1] Third, only estimates of CVD events were provided because participants were not actively followed up, although the FRS still overestimated the risk according to a conservative assumption of the case-fatality ratio. We were unable to assess discrimination by the FRS, as we did not have individual data on CVD events. Nonetheless, even if participants had been followed up actively, the adjudication of CVD events in such a large sample would have been extremely labour-intensive and costly. Fourth, CVD risk prediction tools are used to guide clinical decisions on risk factor modification, such as lipid-lowering therapy. However, we were unable to assess whether participants were already on such therapy at baseline, which could result in overestimation of CVD risk. Finally, we relied on routine mortality data for classification of CVD deaths, which is more prone to misclassification than autopsy data. Nonetheless, most deaths in Hong Kong occur in hospitals; this enables relatively accurate ascertainment of the causes of death.

Conclusions

The FRS systematically overestimated CVD risk in older Hong Kong Chinese adults despite recalibration. The FRS should be used with caution. Overestimation of risk may result in unnecessary healthcare costs and potential harms associated with statin therapy. The risk factors for CVD may vary across populations. New risk prediction models that account for CVD incidence data should be developed.

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