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Original Article

Association of Coronary Artery Calcification with Estimated Coronary Heart Disease Risk from Prediction Models in a Community-Based Sample of Japanese Men: The Shiga Epidemiological Study of Subclinical Atherosclerosis (SESSA)

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***Aim*: The clinical significance of coronary artery calcification (CAC) is not fully determined in general East Asian populations where background coronary heart disease (CHD) is less common than in USA/Western countries. We cross-sectionally assessed the association between CAC and estimated CHD risk as well as each major risk factor in general Japanese men.**

***Methods*: Participants were 996 randomly selected Japanese men aged 40−79 y, free of stroke, myocardial infarction, or revascularization. We examined an independent relationship between each risk factor used in prediction models and CAC score ≥100 by logistic regression. We then divided the participants into quintiles of estimated CHD risk per prediction model to calculate odds ratio of having CAC score ≥100. Receiver operating characteristic curve and c-index were used to examine discriminative ability of prevalent CAC for each prediction model.**

***Results*: Age, smoking status, and systolic blood pressure were significantly associated with CAC score ≥100 in the multivariable analysis. The odds of having CAC score ≥100 were higher for those in higher quintiles in all prediction models (*p*-values for trend across quintiles <0.0001 for all models). All prediction models showed fair and similar discriminative abilities to detect CAC score ≥100, with similar c-statistics (around 0.70).**

***Conclusions*: In a community-based sample of Japanese men free of CHD and stroke, CAC score ≥100 was significantly associated with higher estimated CHD risk by prediction models. This finding supports the potential utility of CAC as a biomarker for CHD in a general Japanese male population.**

Key words: Coronary artery calcification, Absolute risk prediction model, Community-based sample

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Introduction

Coronary artery calcification (CAC) quantified by the Agatston score[1)] has been known to be an excellent biomarker of atherosclerosis[2)], independently predicting clinical outcomes such as coronary heart disease (CHD)[3-5)] in Western populations. This has resulted in

the 2013 American Heart Association Guidelines to recommend CAC in people at intermediate risk as an aid for clinical decision making. In East Asia, however, only a few patient-based studies, but no community-based study, showed an association of CAC with cardiovascular morbidity and mortality[6, 7]. Since East Asians have a lower CHD risk and lower degree of subclinical atherosclerosis than those from USA/some European countries[8-10], the clinical implication of CAC remains to be fully determined in this population[11]. A global risk prediction tool such as Framingham Risk Score is designed to predict future CHD risk by taking multiple risk factors into account. In this paper, we assess the potential value of CAC as a biomarker for CHD by examining its relationship with global risk prediction tools used in Japan using a community-based sample of Japanese men.

Aim

To examine the relationship of CAC and estimated CHD risk obtained from prediction models used in Japan that take major CHD risk factors into account in a general Japanese male population.

Methods

Study Designs and Participants

This is an observational cross-sectional study of male participants of the Shiga Epidemiological Study of Subclinical Atherosclerosis (SESSA). SESSA is a study of subclinical atherosclerosis and its determinants in a sample of Japanese residents. Details of its enrollment methods have been reported previously[12-14]. In brief, from 2006 to 2008, we randomly selected and invited 2,379 Japanese men aged 40 to 79 y who were residents of Kusatsu City, Shiga, based on the Basic Residents' Register of the city. The Register contains information on name, sex, birth date, and address of residents. A total of 1094 men agreed to participate[15]. For the present study, we excluded participants with history of stroke, myocardial infarction, or revascularization ($n=80$), and those with triglycerides (TG) levels ≥ 400 mg/dL ($n=16$) because use of Friedewald's formula[16] is inappropriate in such a case. We further excluded two participants owing to missing variables pertinent to the study, leaving 996 men for the final analysis.

Measurements

Blood sample was obtained in a clinical visit after a 12-h fast. The plasma and serum were separated by centrifugation (3000 revolutions per min, for 15 min) at 4℃ within 90 min. Plasma glucose, serum creatinine, total cholesterol (TC), and TG were measured using enzymatic assays, and high-density lipoprotein cholesterol (HDL-c) was determined using a direct method. Low-density lipoprotein cholesterol (LDL-c) was estimated using Friedewald's formula: LDL-c (mg/dL) = TC (mg/dL) − HDL-c (mg/dL) − TG (mg/dL)/5[16]. Hemoglobin A1c (HbA1c) was measured by latex agglutination immunoassay according to the protocol by the Japan Diabetes Society (JDS). We converted the value of HbA1c (JDS) to HbA1c by the National Glycohemoglobin Standardization Program (NGSP) using the following formula: NGSP (%) = 1.02 × JDS (%) + 0.25%[17]. Diabetes mellitus was defined as use of medication or fasting plasma glucose ≥ 126 mg/dL or HbA1c (NGSP) ≥ 6.5%. The estimated glomerular filtration rate (eGFR) was calculated by equation for Japanese men: eGFR (mL/min/1.73 m^2) = $194 \times age^{-0.287} \times creatinine^{-1.094}$ according to the 2012 guideline by the Japanese Society of Nephrology[18]. Chronic kidney disease was defined as eGFR < 60 mL/min/1.73 m^2.

Blood pressure was measured twice consecutively in the right arm of seated participants after participants emptied their bladder for urinalysis and sat quietly for 5 min, using an automated sphygmomanometer with an appropriate-sized cuff. The average of two measurements was used for analysis. We defined hypertension as use of antihypertensive or systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg. A self-administered questionnaire was used to obtain information on demographics, medical history, medication use, smoking habits, and other factors. After completion of the questionnaire, trained staff members confirmed reported information with the participant. Smoking was first categorized as either "current," "past," or "never." We then combined the two later categories as noncurrent smoker. Body mass index (BMI) was defined as weight (kg) divided by square of height (m).

Coronary Artery Calcification

We assessed CAC by either electron beam computed tomography (EBCT, $n=691$, 69.4%) using a C-150 scanner (Imatron, South San Francisco, CA, USA) or 16-channel multidetector row computed tomography (MDCT, $n=305$, 30.6%) scans using an Aquilion scanner (Toshiba, Tokyo, Japan). Images were obtained from the level of the root of the aorta through the heart at a slice thickness of 3 mm with a scan time of 100 (EBCT) or 320 ms (MDCT). We acquired images at 70% of the cardiac cycle, using electrocardiogram triggering, during a single breath-hold. Quantification of CAC was performed using AccuImage software (AccuImage Diagnostics, South San Francisco, CA, USA). The presence of CAC was defined as a mini-

mum of three contiguous pixels (area = 1 mm^2) with density > 130 Hounsfield units. CAC score was calculated according to the Agatston method[1]. All CT images were read by one physician, who was trained in CT reading at the Cardiovascular Institute of the University of Pittsburgh and blinded to participants' characteristics. The protocol described above was adopted from a separate cohort study of ours[9], in which the reproducibility of the scans showed an intraclass correlation of 0.98[19]. CAC assessment by EBCT and MDCT has been reported to be comparable[5, 20]. We have therefore presented combined results with adjustment for CT type in the main analysis.

Coronary Heart Disease Risk Prediction Models

Three CHD risk prediction models were used: NIPPON DATA80 risk assessment chart[21], Japan Arteriosclerosis Longitudinal Study—Existing Cohorts Combine (JALS-ECC) score[22], and SUITA score[23]. The criteria for selecting those prediction models were the following: (1) a model was constructed on the basis of a community-based sample of Japanese residents, from either nationwide or regional recruitment; (2) the model should give sex-specific and CHD-specific estimates; and (3) the outcome for prediction should be either incidence or death from CHD. Key features of the selected prediction models were given in **Supplemental Table 1**.

Statistical Analysis

Characteristics of the participants were presented as mean ± standard deviation or median (interquartile range [IQR]) for continuous variables, and as percentages for categorical variables. We primarily used a threshold of CAC score ≥ 100, given relatively low CAC score documented in our sample[24] and as clinical significance of the threshold has been documented in Western and Japanese populations[25-28].

We first examined the relationship between each risk factor used in prediction models and CAC score ≥ 100 using multivariable logistic regression. All the risk factors (age, BMI, smoking status, SBP, antihypertensive use, HDL-c, TC, dyslipidemia medication use, diabetes mellitus, and eGFR) and the variable for CT type (EBCT/16-MDCT) were included in the same model to calculate adjusted odds ratio (OR).

In main analysis, we divided the participants into quintiles of risk score or probability, depending on the calculation method, according to each prediction model. Within each quintile, we presented the median (IQR) of CAC score, proportion of CAC score ≥ 100, and crude OR of having CAC score ≥ 100 using the lowest quintile as the reference. A *p*-value for trend across the quintiles was calculated by Cochran−Armitage trend test. Discriminative ability of prevalent CAC score ≥ 100 was examined by the receiver operating characteristic (ROC) curve and area under ROC curve (c-statistics) for each prediction model.

Since age is a strong risk factor for both CHD risk and CAC score, we repeated the above analysis after stratifying the participants by their age (65 y or older vs younger) to examine a potential difference in relation by age. As a sensitivity analysis, we repeated the analysis using CAC score ≥ 400 since the cutoff has been commonly used in previous studies[11, 27].

All statistical studies were conducted with the

Table 1. Characteristics of participants (996 men aged 40-79 years in 2006-2008, Shiga, Japan)

Characteristic	
Age, years	64.0 (10.0)
BMI, kg/m^2	23.5 (3.0)
Smoking, current	32.2%
SBP, mmHg	136.1 (19.0)
DBP, mmHg	79.6 (10.9)
Hypertension	53.3%
Antihypertensive use	28.3%
Total cholesterol, mg/dL	208.6 (33.4)
HDL cholesterol, mg/dL	59.1 (17.0)
LDL cholesterol, mg/dL	125.4 (31.5)
non-HDL cholesterol, mg/dL	149.5 (34.5)
Triglycerides, mg/dL	103.5 (76.0, 149.0)
Dyslipidemia medication use	12.4%
Fasting glucose, mg/dL	102.2 (20.8)
HbA1c (NGSP), %	6.0 (0.8)
Diabetes mellitus	17.9%
Diabetes medication use	9.2%
Creatinine, mg/dL	0.8 (0.8, 0.9)
eGFR, mL/min/1.73 m^2	73.4 (14.5)
Chronic kidney disease	15.6%
CAC score	
Median (IQR)	5.5 (0.0, 83.3)
Percentage of CAC score ≥ 100	22.6%
Percentage of CAC score ≥ 400	8.1%

Values are expressed as mean (standard deviation), median (25th, 75th), or percentage.
Abbreviations. BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL, low-density lipoprotein; HDL, high-density lipoprotein; HbA1c, hemoglobin A1c; NGSP, National Glycohemoglobin Standardization Program; eGFR, estimated glomerular filtration rate; IQR, interquartile range.
BMI was defined as weight (kg) divided by square of height (m). Hypertension was defined as either SBP/DBP ≥ 140/90 mmHg, or medication use. Diabetes mellitus was defined as either fasting glucose ≥ 126 mg/dL, or HbA1c (NGSP) ≥ 6.5%, or medication use. eGFR (mL/min/1.73 m^2) = $194 \times age^{-0.287} \times creatinine^{-1.094}$ (for male). Chronic kidney disease was defined as eGFR < 60 mL/min/1.73 m^2. CAC score was based on Agatston's method.

Table 2. Multivariable adjusted odds ratio of CAC score ≥ 100 according to risk factors (996 men aged 40-79 years in 2006-2008, Shiga, Japan)

Risk factors	Odds Ratio (95% CI)	*P*-value
Age, per 1-SD	2.77 (2.15-3.56)	< 0.001
BMI, per 1-SD	1.09 (0.91-1.31)	0.35
Smoking (current vs non-current)	1.86 (1.29-2.68)	< 0.001
SBP, per 1-SD	1.21 (1.03-1.43)	0.02
Antihypertensive use (yes vs no)	1.37 (0.95-1.96)	0.08
HDL cholesterol, per 1-SD	1.00 (0.84-1.20)	0.99
Total cholesterol, per 1-SD	1.00 (0.84-1.18)	0.98
Dyslipidemia medication use (yes vs no)	2.15 (1.36-3.40)	< 0.01
Diabetes mellitus (yes vs no)	1.32 (0.89-1.96)	0.17
eGFR, per 1-SD	0.99 (0.83-1.18)	0.90

An indicator variable for CT-type (EBCT/16-MDCT) was included in addition to the variable(s) listed in the table. All variables were included in the same model to calculate multivariable-adjusted odds ratios.
Abbreviations. SBP, systolic blood pressure; HDL, high-density lipoprotein; BMI, body mass index; eGFR, estimated glomerular filtration rate; SD, standard deviation.
BMI was defined as weight (kg) divided by square of height (m). Diabetes mellitus was defined as either fasting glucose ≥ 126 mg/dL, or HbA1c (NGSP) ≥ 6.5%, or medication use. eGFR (mL/min/1.73 m^2) = $194 \times age^{-0.287} \times creatinine^{-1.094}$ (for male).

SAS software version 9.4 (SAS Institute, Cary, NC, USA). A two-tailed *p*-value of ≤ 0.05 was considered significant.

Results

Demographic and cardiovascular risk factors of the 996 male participants are displayed in **Table 1**. The average age was 64 y, and the prevalence of current smokers, hypertensives, and diabetics was 32.2%, 53.3%, and 17.9%, respectively. The median (IQR) of CAC score was 5.5 (0.0, 83.3). Prevalence of CAC score ≥ 100 and ≥ 400 was 22.6% and 8.1%, respectively.

Among risk factors used in the prediction models, age, current smoking, SBP, and use of dyslipidemia medication were significantly positively associated with CAC score ≥ 100 in multivariable-adjusted model (**Table 2**). The point estimates for antihypertensive medication use, BMI, and diabetes mellitus also showed a positive nonsignificant trend of association with CAC ≥ 100.

Across the quintiles of estimated CHD risk, we observed a graded increase in both median CAC score and prevalence of CAC score ≥ 100 in all the prediction models (**Table 3**). According to the NIPPON DATA80 risk assessment chart, percentages of CAC score ≥ 100 in the lowest to highest quintiles were 3.5, 14.6, 24.0, 28.1, and 42.7. The corresponding percentages according to the JALS-ECC score and the SUITA score were 5.5, 15.2, 25.1, 31.0, and 36.2, and 5.7, 16.2, 23.8, 27.4, and 38.6, respectively. The odds of having CAC score ≥ 100 were higher for those in the higher quintiles in all the prediction models we assessed. *p*-values for trend across quintiles were < 0.0001 for all models. **Fig. 1** shows ROC curves and c-statistics for identifying prevalent CAC score ≥ 100. All prediction models showed fair discriminative ability to detect CAC score ≥ 100 with c-statistics ranging from 0.68 to 0.71.

In age-stratified analysis, we generally observed a stronger association of CAC in the younger group and an attenuated association in the older group. However, the overall significant positive association was maintained in all the prediction models (all *p*-values for trend < 0.05) (**Supplemental Tables 2** and **3**). c-statistics of the NIPPON DATA80 risk assessment chart, JALS-ECC score, and SUITA score for identifying prevalent CAC score ≥ 100 in group aged 65 y or more were lower than those in the younger group (0.61, 0.57, and 0.59 vs 0.69, 0.69 and 0.68, respectively) (**Supplemental Figs. 1** and **2**).

Sensitivity analyses using CAC score ≥ 400 did not change the overall relationship between CAC with risk factors and estimated risk (**Supplemental Tables 4** and **5**). The discriminative ability of all models for CAC ≥ 400 was relatively similar to one for CAC ≥ 100 (**Supplemental Fig. 3**).

Discussion

In this study, we showed a strong and consistent positive association between CAC and estimated CHD risk obtained by three different prediction models that have been developed in Japan and commonly used for primary prevention for the Japanese general population. Clinical utility of CAC for the general popula-

Table 3. Association between CAC score ≥ 100 and estimated CHD risk from three prediction models (996 men aged 40-79 years in 2006-2008, Shiga, Japan)

	Quintiles of estimated CHD risk					*P* for trend
	1 (lowest)	2	3	4	5 (highest)	
NIPPON DATA80 RC						
No. of participants	199	199	200	199	199	
Median (IQR) of CAC score	0.0 (0.0, 1.0)	2.3 (0.0, 42.2)	15.6 (0.0, 96.6)	23.7 (0.0, 128.2)	55.5 (4.6, 274.4)	
No. of CAC score ≥ 100, (%)	7 (3.5)	29 (14.6)	48 (24.0)	56 (28.1)	85 (42.7)	
Odds ratio of CAC score ≥ 100 (95% CI)	1.0 (ref.)	4.7 (2.0-11.0)	8.7 (3.8-19.7)	10.7 (4.8-24.3)	20.5 (9.2-45.7)	< .0001
JALS-ECC score						
No. of participants	200	198	199	200	199	
Median (IQR) of CAC score	0.0 (0.0, 1.0)	1.6 (0.0, 35.8)	16.3 (1.0, 102.1)	31.0 (0.0, 146.8)	33.7 (2.1, 191.9)	
No. of CAC score ≥ 100, (%)	11 (5.5)	30 (15.2)	50 (25.1)	62 (31.0)	72 (36.2)	
Odds ratio of CAC score ≥ 100 (95% CI)	1.0 (ref.)	3.1 (1.5-6.3)	5.8 (2.9-11.5)	7.7 (3.9-15.2)	9.7 (5.0-19.1)	< .0001
SUITA score						
No. of participants	194	204	193	190	215	
Median (IQR) of CAC score	0.0 (0.0, 1.0)	2.2 (0.0, 41.7)	14.1 (0.0, 91.5)	17.8 (1.3, 108.8)	39.2 (1.8, 214.6)	
No. of CAC score ≥ 100, (%)	11 (5.7)	33 (16.2)	46 (23.8)	52 (27.4)	83 (38.6)	
Odds ratio of CAC score ≥ 100 (95% CI)	1.0 (ref.)	3.2 (1.6-6.6)	5.2 (2.6-10.4)	6.3 (3.2-12.59)	10.5 (5.4-20.4)	< .0001

Abbreviations. CAC, coronary artery calcification; IQR, interquartile range; CI, confidence interval; RC, risk assessment chart.

tion has been studied mainly in the USA and Western countries[2-5] where CHD risk is relatively high than in East Asian countries such as Japan[8]. To our knowledge, only a few patient-based studies (i.e., those patients with proven or suspected CHD)[6] but not community-based ones have reported the prognostic value of CAC score in Japan. Clinical utility of CAC for a general Japanese population, therefore, remains to be determined[11].

A prediction model takes multiple major risk factors into account in estimating future CHD risk. In the present study, we viewed an estimated CHD risk obtained from such a model as a "surrogate" to the actually observed CHD risk, and we tested the association of CAC with those estimated risk on a community-based sample of Japanese men. Although not providing direct evidence, the strong dose−response relation between CAC and estimated CHD risk observed in our study, combined with the existing literature discussed above, supports the potential utility of CAC for risk assessment in a general Japanese population.

The independent relationship between each traditional CHD risk factor and CAC among Japanese individuals has not been well reported[12, 29]. We observed a significant and independent association of CAC with some risk factors including age, smoking, and SBP. The associations with other known risk factors such as diabetes mellitus, TC, and obesity (BMI) were not statistically significant in our multivariable-adjusted model. This may be due to the following reasons: (1) inclusion of more individuals with less-advanced stage of diabetes mellitus and dyslipidemia owing to our community-based recruitment leading to a weaker association; and (2) simultaneous inclusion of covariates in a model that partially shares a common causal pathway attenuated the estimate of association (i.e., lipid medication plus serum cholesterol; obesity plus blood pressure, lipids, and diabetes). Being consistent with our result, the lack of statistically significant associations has been reported for diabetes mellitus in the USA and in Europe[30, 31]. Overall, however, we observed positive associations, either significant or nonsignificant, between CAC and most of the major risk factors.

In age-stratified analysis, we observed a weaker relationship between CAC and estimated CHD risk in the older participants (i.e., ≥ 65 y) than in younger participants. The potential reason of the weaker association in older group may be that conventional risk factors measured at one point of time may change over one's life course both intentionally and unintentionally, and in some cases, risk factor profile changes as result of increased risk of disease (e.g., one may quit smoking because of his/her high risk; one's blood pressure may drop as a result of coexisting cardiovascular disease). In fact, it is well documented that some risk factors in middle life is more predictive than are those at older stage. Such factors include blood pressure[32-34] and cholesterol[35]. On the other hand, CAC is less likely to regress or fluctuate over one's life course and possibly reflect one's cumulative exposure to cardiovascular risk factors[11].

Care must be used in the interpretation of these

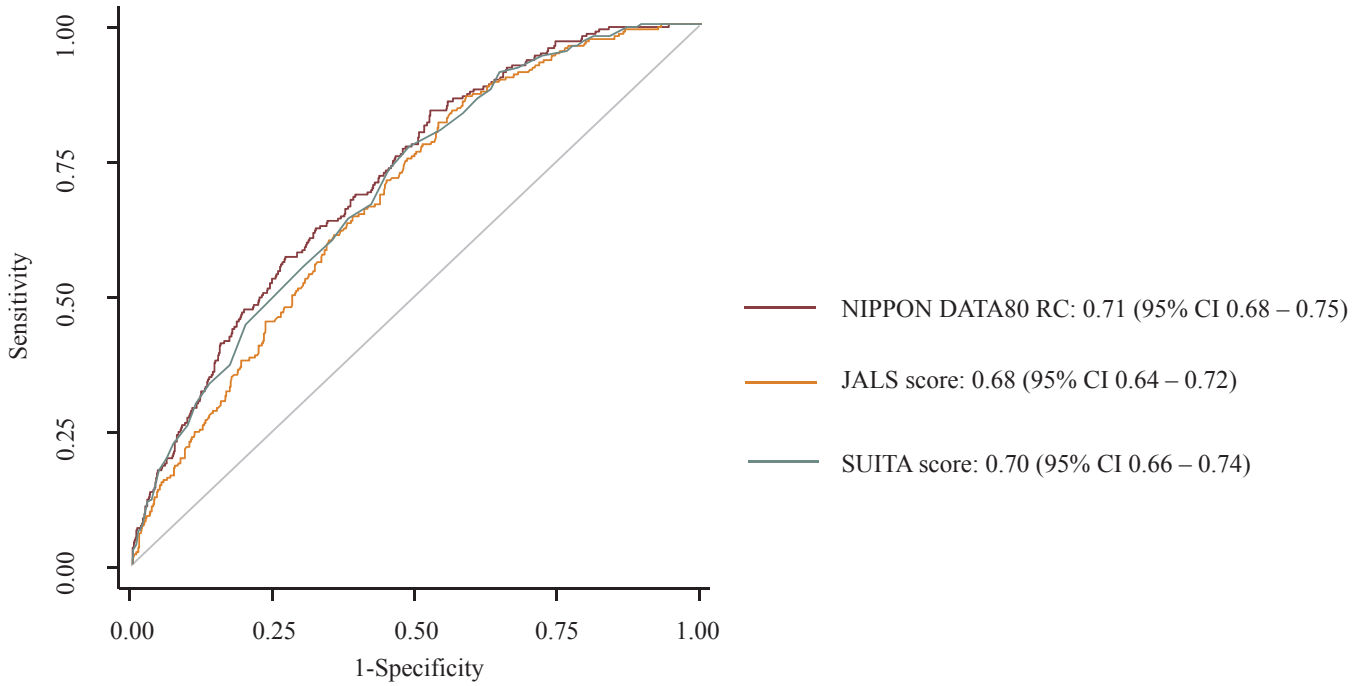

Fig. 1. Receiver operating characteristic (ROC) curves for detecting coronary artery calcification score ≥ 100 by various risk prediction models (996 men aged 40–79 y in 2006–2008, Shiga, Japan).

The area under the ROC curve and the 95% confidence intervals are shown.
Abbreviation: RC, risk assessment chart

results. First, this study was conducted only in men; hence, the results may not be applicable to women. Second, we adopted a recent definition of diabetes (using fasting-glucose, HbA1c, and medication), which is different from that of the NIPPON DATA80 risk assessment chart.

One strength of this study was the use of a randomly selected community-based sample with a broad age range, which would increase the generalizability of our findings to the general population of Japanese men. Furthermore, we have observed a consistent relation of CAC with estimated CHD risk across three prediction models. Given those prediction models were constructed on different Japanese populations targeting different CHD outcomes, the findings support robustness of CAC as a biomarker for CHD in Japanese male population. Other strengths include our standardized measurements of relevant parameters including CAC, laboratory data, and a moderate sample size.

Conclusions

In a community-based sample of Japanese men free of CHD and stroke, prevalent CAC was associated with higher estimated CHD risk obtained by various risk prediction models used in Japan. Our study suggests that CAC may be a valid marker for predicting CHD risk in the general Japanese male population.

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We do not have conflicts of interest to disclose.

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Supplemental Table 1. Characteristics of coronary heart disease risk prediction models

Risk prediction models	NIPPON DATA80 RC[21]	JALS-ECC score*[22]	SUITA score*[23]
Baseline year	1980	1985	1989
Follow-up years	19	7.6	11.8
Study design	Cohort study based on a random sample from 300 areas across Japan	Pooled data from 10 community based cohort studies across Japan	Community based cohort study in urban residents in Osaka, Japan
Population	9,353 participants (43.8% men) aged >30 years from 300 areas	22,430 participants aged 40−89 years	5,521 participants (50.6% men) aged 30−79 years
Exclusion criteria	Coronary heart diseases or stroke	Ischemic heart disease or stroke	Coronary heart diseases or stroke.
Variables used for prediction	Age, sex, smoking status, systolic blood pressure, diabetes status, total cholesterol	Age, sex, smoking status, blood pressure categories, diabetes status, HDL-C, non HDL-C	Age, sex, smoking status, blood pressure categories, diabetes status, chronic kidney disease status, HDL-C, LDL-C
Endpoints	10-year risk of coronary heart disease mortality	5-year risk of myocardial infarction	10-year risk of coronary heart disease events

* The JALS-ECC and SUITA models have two scoring systems.
We used the JALS-ECC model with non-HDL cholesterol, and the Suita score model with LDL cholesterol.

Supplemental Table 2. Association between CAC score ≥ 100 and estimated CHD risk from three prediction models in the participants aged < 65 years old (N = 516 in 2006-2008, Shiga, Japan)

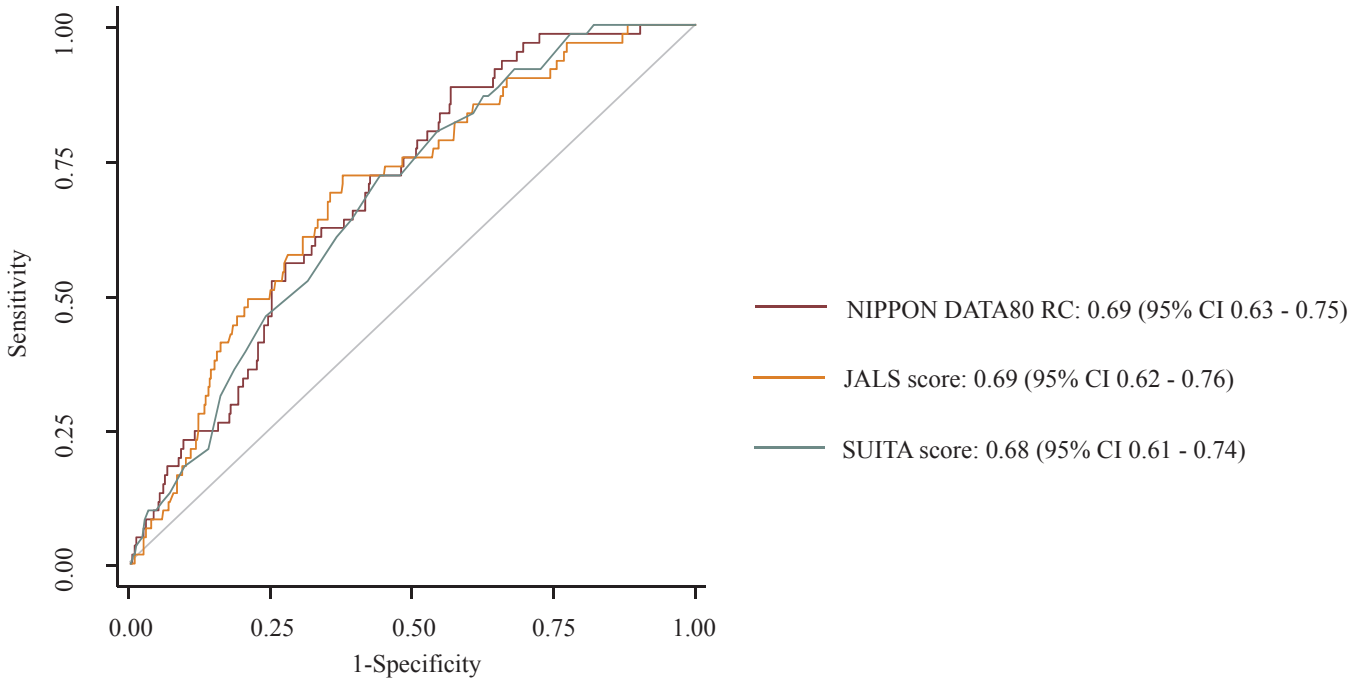
Characteristics	Quintiles of estimated CHD risk					*P* for trend
	1 (lowest)	2	3	4	5 (highest)	
NIPPON DATA80 RC						
No. of participants	103	103	104	103	103	
Median (IQR) of CAC score	0.0 (0.0, 0.0)	0.0 (0.0, 2.6)	1.9 (0.0, 20.5)	6.2 (0.0, 68.1)	14.2 (1.3, 51.8)	
No. of CAC score ≥ 100, (%)	1 (1.0)	8 (7.8)	14 (13.5)	20 (19.4)	18 (17.5)	
Odds ratio (95% CI) of CAC score ≥ 100	1.0 (ref)	8.6 (1.1-69.9)	15.9 (2.1-123.0)	24.6 (3.2-186.9)	21.6 (2.8-165.1)	< .0001
JALS-ECC score						
No. of participants	103	102	105	104	102	
Median (IQR) of CAC score	0.0 (0.0, 0.0)	0.0 (0.0, 4.6)	0.0 (0.0, 11.4)	8.0 (0.0, 59.6)	20.2 (1.6, 93.6)	
No. of CAC score ≥ 100, (%)	2 (1.9)	9 (8.8)	8 (7.6)	17 (16.4)	25 (24.5)	
Odds ratio (95% CI) of CAC score ≥ 100	1.0 (ref)	4.9 (1.0-23.2)	4.2 (0.9-20.1)	9.9 (2.2-43.9)	16.4 (3.8-71.4)	< .0001
SUITA score						
No. of participants	102	118	93	97	106	
Median (IQR) of CAC score	0.0 (0.0, 0.0)	0.0 (0.0, 7.2)	1.3 (0.0, 26.0)	5.4 (0.0, 43.3)	11.7 (1.3, 75.0)	
No. of CAC score ≥ 100, (%)	1 (1.0)	11 (9.3)	12 (12.9)	15 (15.5)	22 (20.8)	
Odds ratio (95% CI) of CAC score ≥ 100	1.0 (ref)	10.4 (1.3-81.9)	15.0 (1.9-117.5)	18.5 (2.4-142.8)	26.5 (3.5-200.3)	< .0001

Abbreviations. CAC, coronary artery calcification; IQR, interquartile range; CI, confidence interval.

Supplemental Table 3. Association between CAC score ≥ 100 and estimated CHD risk from three prediction models in the participants aged ≥ 65 years old (N = 480 in 2006-2008, Shiga, Japan)

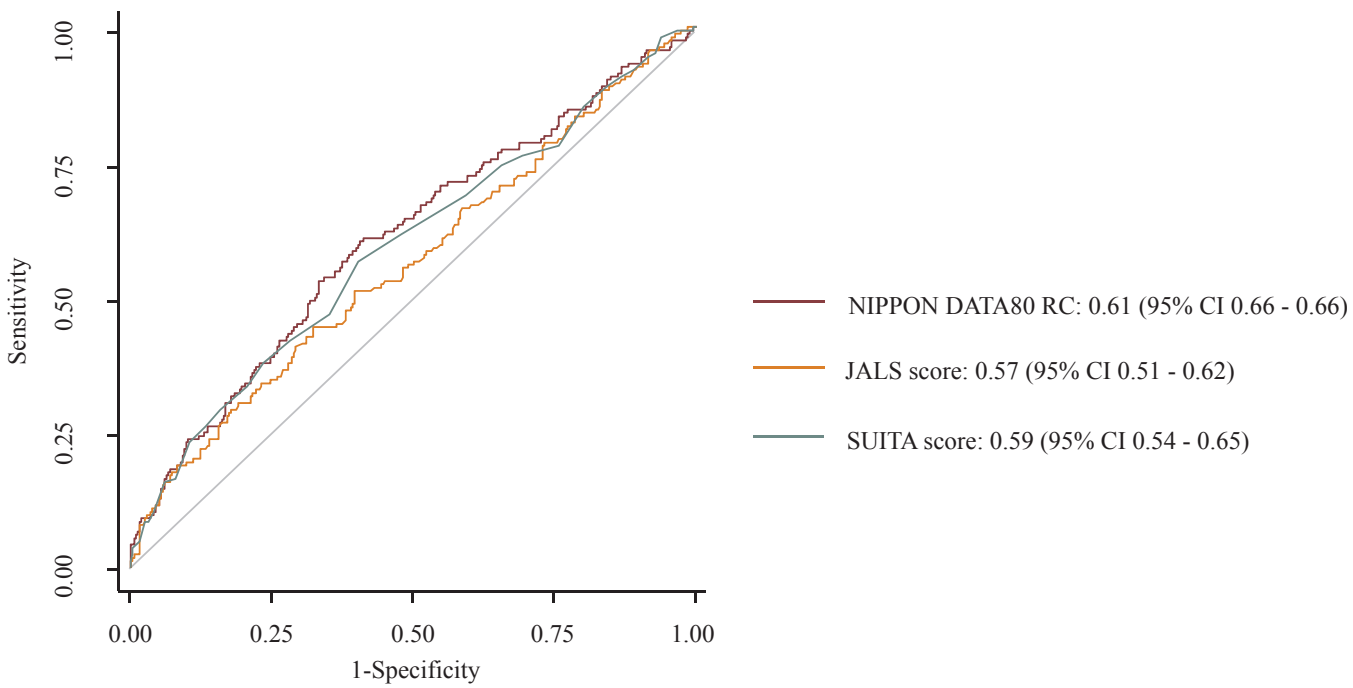
Characteristics	Quintiles of estimated CHD risk					*P* for trend
	1 (lowest)	2	3	4	5 (highest)	
NIPPON DATA80 RC						
No. of participants	96	96	96	96	96	
Median (IQR) of CAC score	11.0 (0.0, 104.8)	13.4 (0.0, 102.1)	40.7 (0.0, 146.6)	64.9 (5.9, 259.4)	77.6 (4.9, 303.2)	
No. of CAC score ≥ 100, (%)	25 (26.0)	24 (25.0)	28 (29.2)	42 (43.8)	45 (46.9)	
Odds ratio (95% CI) of CAC score ≥ 100	1.0 (ref)	1.0 (0.5-1.8)	1.2 (0.6-2.2)	2.2 (1.2-4.1)	2.5 (1.4-4.6)	< .0001
JALS-ECC score						
No. of participants	96	96	96	96	96	
Median (IQR) of CAC score	8.9 (0.0, 140.8)	34.4 (3.4, 198.4)	31.9 (0.0, 197.0)	29.7 (0.0, 145.9)	77.6 (7.7, 287.6)	
No. of CAC score ≥ 100, (%)	28 (29.2)	31 (32.3)	31 (32.3)	30 (31.3)	44 (45.8)	
Odds ratio (95% CI) of CAC score ≥ 100	1.0 (ref)	1.2 (0.6-2.1)	1.2 (0.6-2.1)	1.1 (0.6-2.1)	2.1 (1.1-3.7)	0.04
SUITA score						
No. of participants	87	93	112	90	98	
Median (IQR) of CAC score	9.8 (0.0, 137.7)	26.7 (0.0, 160.1)	36.5 (1.7, 173.0)	32.1 (0.0, 146.3)	90.0 (6.5, 297.6)	
No. of CAC score ≥ 100, (%)	24 (27.6)	27 (29.0)	36 (32.1)	29 (32.2)	48 (49.0)	
Odds ratio (95% CI) of CAC score ≥ 100	1.0 (ref)	1.1 (0.6-2.1)	1.2 (0.7-2.3)	1.3 (0.7-2.4)	2.5 (1.4-4.7)	< .001

Abbreviations. CAC, coronary artery calcification; IQR, interquartile range; CI, confidence interval.



Supplemental Fig. 1. Receiver operating characteristic (ROC) curves for detecting coronary artery calcification score ≥100 by various risk prediction models in the patients <65 y old (N=516 in 2006–2008, Shiga, Japan).

The area under the ROC curve and the 95% confidence intervals are shown.



Supplemental Fig. 2. Receiver operating characteristic (ROC) curves for detecting coronary artery calcification score ≥100 by various risk prediction models in the patients ≥65 y old (N=480 in 2006–2008, Shiga, Japan).

The area under the ROC curve and the 95% confidence intervals are shown.

Supplemental Table 4. Multivariable adjusted odds ratio of CAC score ≥400 according to risk factors (996 men aged 40-79 years in 2006-2008, Shiga, Japan)

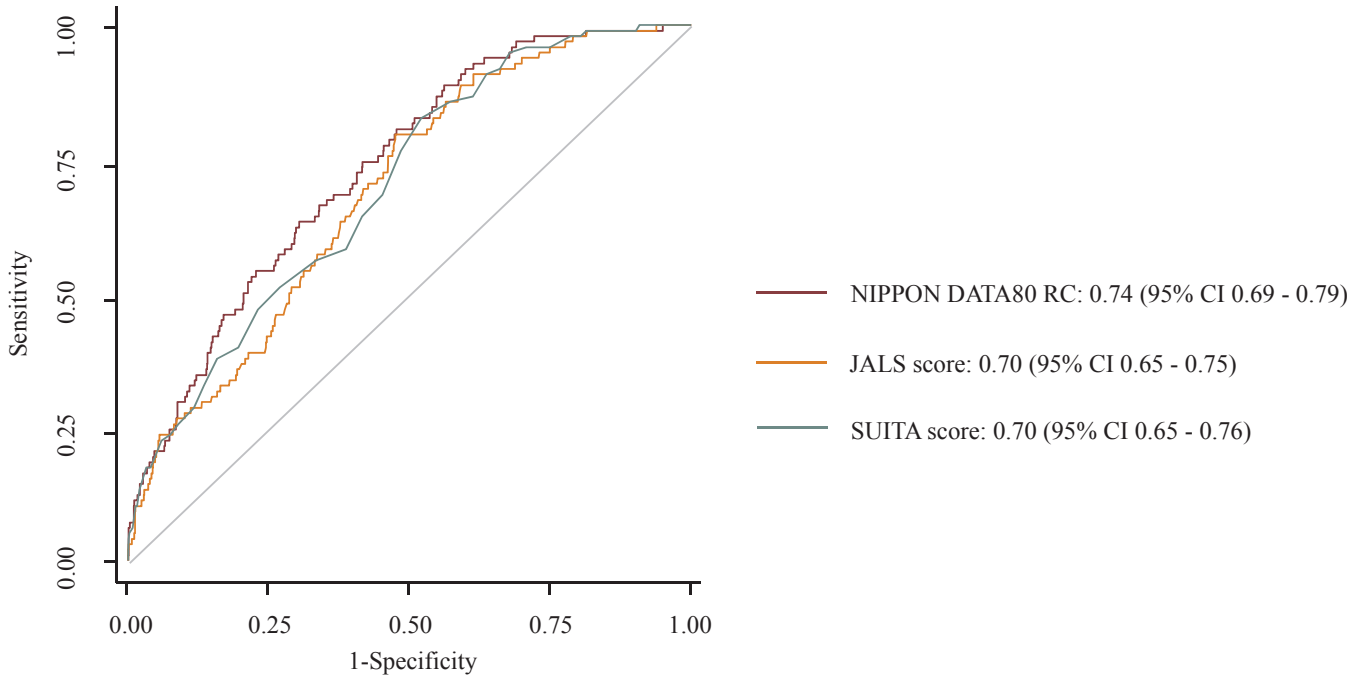
Risk factors	Odds Ratio (95% CI)	*P*-value
Age, per 1-SD	2.96 (1.98-4.43)	<0.001
BMI, per 1-SD	0.98 (0.74-1.29)	0.87
Smoking (current vs non-current)	2.20 (1.30-3.74)	<0.01
SBP, per 1-SD	1.22 (0.96-1.59)	0.10
Antihypertensive use (yes vs no)	1.78 (1.05-3.02)	0.03
HDL cholesterol, per 1-SD	0.96 (0.73-1.26)	0.75
Total cholesterol, per 1-SD	1.02 (0.79-1.32)	0.89
Dyslipidemia medication use (yes vs no)	2.32 (1.27-4.22)	<0.01
Diabetes mellitus (yes vs no)	1.72 (1.01-2.94)	0.05
eGFR, per 1-SD	1.06 (0.83-1.35)	0.63

An indicator variable for CT-type (EBCT/16MDCT) was included in addition to the variable(s) listed in the table. All variables were included in the same model to calculate multivariable-adjusted odds ratios.
Abbreviations. SBP, systolic blood pressure; HDL, high-density lipoprotein; BMI, body mass index; eGFR, estimated glomerular filtration rate; SD, standard deviation.
BMI was defined as weight (kg) divided by square of height (m). Diabetes mellitus was defined as either fasting glucose ≥126 mg/dL, or HbA1c (NGSP) ≥6.5%, or medication use. eGFR (mL/min/1.73 m^2) = $194 \times age^{-0.287} \times creatinine^{-1.094}$ (for male).

Supplemental Table 5. Association between different prediction models and presence of CAC score ≥400 (996 men aged 40-79 years in 2006-2008, Shiga, Japan)

Characteristics	Quintiles of estimated CHD risk					*P* for trend
	1 (lowest)	2	3	4	5 (highest)	
NIPPON DATA80 RC						
No. of participants	199	199	200	199	199	
No. of CAC score ≥400, (%)	1 (0.5)	6 (3.0)	18 (9.0)	17 (8.5)	39 (19.6)	
Odds ratio of CAC score ≥400 (95% CI)	1.0	6.2 (0.7-51.5)	19.6 (2.6-147.8)	18.5 (2.4-140.0)	48.2 (6.6-354.2)	<.0001
JALS-ECC score						
No. of participants	200	198	199	200	199	
No. of CAC score ≥400, (%)	1 (0.5)	8 (4.0)	20 (10.1)	24 (12.0)	28 (14.1)	
Odds ratio of CAC score ≥400 (95% CI)	1.0	8.4 (1.0-67.4)	22.2 (3.0-166.9)	27.1 (3.6-202.1)	32.5 (4.4-241.3)	<.0001
SUITA score						
No. of participants	194	204	193	190	215	
No. of CAC score ≥400, (%)	2 (1.0)	8 (3.9)	23 (11.9)	16 (8.4)	32 (15.9)	
Odds ratio of CAC score ≥400 (95% CI)	1.0	3.9 (0.8-18.7)	13.0 (3.0-55.9)	8.8 (2.0-38.9)	16.8 (4.0-71.1)	<.0001

Abbreviations. CAC, coronary artery calcification; IQR, interquartile range; CI, confidence interval.



Supplemental Fig. 3. Receiver operating characteristic (ROC) curves for detecting coronary artery calcification score ≥ 400 by various risk prediction models (996 men aged 40−79 y in 2006−2008, Shiga, Japan).

The area under the ROC curve and the 95% confidence intervals are shown.