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Development and Validation of a Simple-to-Use Nomogram for Predicting 5-, 10-, and 15-Year Survival in Asymptomatic Adults Undergoing Coronary Artery Calcium Scoring

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ABSTRACT

OBJECTIVES The purpose of this study was to develop and validate a simple-to-use nomogram for prediction of 5-, 10-, and 15-year survival among asymptomatic adults.

BACKGROUND Simple-to-use prognostication tools that incorporate robust methods such as coronary artery calcium scoring (CACS) for predicting near-, intermediate- and long-term mortality are warranted.

METHODS In a consecutive series of 9,715 persons (mean age: 53.4 ± 10.5 years; 59.3% male) undergoing CACS, we developed a nomogram using Cox proportional hazards regression modeling that included: age, sex, smoking, hypertension, dyslipidemia, diabetes, family history of coronary artery disease, and CACS. We developed a prognostic index (PI) summing the number of risk points corresponding to weighted covariates, which was used to configure the nomogram. Validation of the nomogram was assessed by discrimination and calibration applied to a separate cohort of 7,824 adults who also underwent CACS.

RESULTS A total of 936 and 294 deaths occurred in the derivation and validation sets at a median follow-up of 14.6 years (interquartile range: 13.7 to 15.5 years) and 9.4 years (interquartile range: 6.8 to 11.5 years), respectively. The developed model effectively predicted 5-, 10-, and 15-year probability of survival. The PI displayed high discrimination in the derivation and validation sets (C-index 0.74 and 0.76, respectively), indicating suitable external performance of our nomogram model. The predicted and actual estimates of survival in each dataset according to PI quartiles were similar (though not identical), demonstrating improved model calibration.

CONCLUSIONS A simple-to-use nomogram effectively predicts 5-, 10- and 15-year survival for asymptomatic adults undergoing screening for cardiac risk factors. This nomogram may be considered for use in clinical care. (J Am Coll Cardiol Img 2018;11:450–8) © 2018 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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Easy-to-use, well-validated tools for prognostication of future events are important in clinical care, in particular for treatment decisions in primary prevention (1,2). To date, however, little headway has been made in improving the utility of prognostic tools by incorporating other novel cardiac risk factors. For instance, coronary artery calcium scoring (CACS) is a robust method for prediction of near- and intermediate-term adverse clinical events, including mortality, nonfatal myocardial infarction, and other major adverse cardiovascular events, with improved prognostic and risk reclassification value above and beyond clinical risk factors alone (3-7). Moreover, McClelland et al. (8) designed the MESA (Multi-Ethnic Study of Atherosclerosis) risk score, incorporating CACS, which can be used to estimate 10-year risk for coronary heart disease (CHD) and enables clinicians to determine risk-based treatment strategies (8). However, the risk of coronary atherosclerosis, as expressed by CACS, goes beyond CHD alone. The MESA risk score does not allow for the assessment of all-cause mortality as a surrogate for high-risk individuals by increasing CACS. Although CHD risk assessment may be a practical marker within clinical practice to define preventive treatment strategies, tools for the identification of individuals with reduced survival are additionally warranted. In this study, we sought to develop and validate a nomogram incorporating CACS for prediction of near-, intermediate-, and long-term mortality from any cause.

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METHODS

STUDY POPULATION. The derivation set comprised 9,715 consecutive asymptomatic individuals referred by physicians for coronary artery disease (CAD) evaluation who underwent CACS at a single site between January 1996 and December 1999 (Tennessee Heart and Vascular Institute, Hendersonville, Tennessee). The validation set comprised 7,824 asymptomatic individuals who underwent CACS at another single site between September 1998 and July 2011 (Cedars-Sinai Medical Center, Los Angeles, California). The appropriate institutional review boards at both sites approved the current study.

CLINICAL DATA COLLECTION. Traditional CAD risk factors and verification of asymptomatic states were performed through direct interview by a physician or allied health professional or by a structured medical questionnaire. CAD risk factors queried included age, sex, smoking, hypertension, diabetes, dyslipidemia, and family history of premature CAD. Systemic arterial hypertension was defined as a documented history of high blood pressure or treatment with antihypertensive medications. Diabetes mellitus was defined by diagnosis of diabetes made previously by a physician and/or use of insulin or oral hypoglycemic agents. Dyslipidemia was defined as known but untreated dyslipidemia or current treatment with lipid-lowering medications. A positive smoking history was defined as current smoking or cessation of smoking within 3 months of testing. Family history of early CAD was determined by asking individuals whether any member of their immediate family (i.e., parents or siblings) had a history of fatal or nonfatal myocardial infarction and/or coronary revascularization in a male relative age <55 years or a female relative age <65 years. All data regarding the aforementioned variables were available for analyses in both cohorts.

ABBREVIATIONS AND ACRONYMS

CACS = coronary artery calcium scoring

CAD = coronary artery disease

CI = confidence interval

PI = prognostic index

CORONARY ARTERY CALCIUM IMAGE ACQUISITION AND INTERPRETATION. All individuals underwent Coronary artery calcium (CAC) testing using either a C-100 or C-150 Ultrafast electron beam computed tomography scanner (Imatron, South San Francisco, California). Tomographic slice thickness was 3 mm, with ~40 axial images acquired from the level of the carina to the level of the diaphragm. Coronary calcium was defined by >3 contiguous pixels with a peak attenuation of ≥130 Hounsfield units. CACS was calculated according to the method of Agatston, and was classified as 0, 1 to 100, 101 to 400, 401 to 1,000, and >1,000. Estimated radiation dose was ~1 mSv.

FOLLOW-UP PROCEDURES. Individuals belonging to the derivation and validation sets were followed for a median of 14.6 years (interquartile range [IQR]: 13.7 to 15.5 years) and 9.4 years (IQR: 6.8 to 11.5 years), respectively, for mortality from any cause. Deaths were verified through query of the National Death Index.

STATISTICAL CONSIDERATIONS. Clinical characteristics of the participants are summarized by mean ± SD for continuous measures and counts with proportions for categorical features. Multivariable time-to-event analysis was performed using Cox proportional hazards regression models to develop a nomogram using weighted estimators corresponding to each covariate derived from fitted Cox regression coefficients and estimates of variance (9,10). For Cox proportional hazards regression analysis, CACS was divided in the following 5 pre-defined categories according to the Agatston score; 0, 1 to 100, 101 to 400, 401 to 1,000, and >1,000, with CAC = 0 as a reference. A prognostic index (PI) was calculated by

summing the number of risk points corresponding to each weighted covariate used to build the nomogram. Individuals were subsequently classified for risk of mortality by PI quartiles.

Validation of the nomogram was assessed by discrimination and calibration. Harrell's C-statistic was calculated by 2,000-fold bootstrap resampling iterations to an initial fitted Cox model in the derivation set. These development estimates were then applied to yield a Harrell's C-statistic in the validation set. Model performance was further examined through survival analysis using unadjusted Kaplan-Meier curves by superimposing both datasets to facilitate visual comparison of the discrimination. In essence, a wider separation in the curves indicates better discrimination.

Calibration of the nomogram was evaluated using a refitted Cox model in the derivation set to obtain the linear prediction of the PI, then centering on its mean. Next, we applied a second-degree fractional polynomial regression to approximate the natural log baseline cumulative hazard function as a smooth function of time, and then predicted the baseline survival function (Online Figure 1). We applied a Cox regression post-estimation command to the PI and corresponding baseline survival function across time to obtain the predicted survival probabilities for each PI quartile. We then generated a calibration plot comparing the actual Kaplan Meier survival estimates (with pointwise 95% confidence intervals [CIs]) with 15-year predicted survival probabilities in both datasets. Further calibration of the PI obtained from the nomogram was evaluated using the Hosmer-Lemeshow goodness-of-fit test according to 10 risk groups. Statistical analyses for our nomogram construction were performed in R software. All other statistical calculations were computed using STATA version 13.1 (StataCorp LP, College Station, Texas).

RESULTS

CLINICAL FEATURES AND CHARACTERISTICS. Of the 9,715 individuals comprising the derivation set, the mean age was 53.4 ± 10.5 years, and 59.3% were male (Table 1). One-half of the derivation set exhibited a CACS of 0, with decreasing prevalence of CACS of 1 to 100 (28.5%), 101 to 400 (12.9%), 401 to 1,000 (5.8%), or >1,000 (2.9%). During a median follow-up period of 14.6 years (IQR: 13.7 to 15.5 years), 936 deaths occurred. The 7,824 individuals in the validation set were slightly older, with a higher frequency of men and with lower prevalence of hypertension, diabetes, smoking, and family history of premature CAD (Table 1). In the validation set, there was a higher prevalence of dyslipidemia (Table 1). During a median follow-up period of 9.4 years (IQR: 6.8 to 11.5 years), 294 deaths occurred. Each category of increasing CACS was similar between the derivation and validation sets (Table 1).

TABLE 1 Clinical Features of the Derivation and Validation Sets

	Derivation Set (n = 9,715)	Validation Set (n = 7,824)
Age, yrs	53.4 ± 10.5	54.4 ± 10.4
Male	5,765 (59.3)	5,359 (68.5)
Positive smoking history	3,817 (39.3)	638 (8.2)
Hypertension	4,220 (43.4)	3,004 (38.4)
Dyslipidemia	6,077 (62.6)	5,404 (69.1)
Diabetes	810 (8.3)	501 (6.4)
Family history of premature CAD	6,672 (68.7)	2,669 (34.1)
CAC score*	127 (119–135)	140 (131–149)
CAC score categories		
0	4,864 (50.1)	3,888 (49.7)
1–100	2,759 (28.4)	2,160 (27.6)
101–400	1,255 (12.9)	1,015 (13.0)
401–1,000	559 (5.8)	485 (6.2)
>1,000	278 (2.9)	276 (3.5)

Values are mean ± SD or n (%). *95% confidence intervals are presented for calcium scores.
CAC = coronary artery calcium; CAD = coronary artery disease.

NOMOGRAM PREDICTION OF ALL-CAUSE MORTALITY. Multivariable hazard ratios were calculated for the prognostic factors used to build the nomogram (Table 2). In the derivation set, increasing age, smoking, hypertension, diabetes, and increasing CACS were associated with a greater risk of death from all causes across 15 years of study follow-up, with an observed attenuation of mortality risk for individuals with dyslipidemia and family history of premature CAD. These relationships were similar in the validation set. The relationship between the prognostic factors and risk of all-cause death did not differ appreciably when re-examining the association at 5- and 10-year study follow-up (Table 2).

Our PI was calculated based upon the weighted risk of the individual CAD risk factors as follows: $-11.3 + (1.12 \times \text{age}) + (1 \times \text{I[male sex]}) + (17 \times \text{I[current smoker]}) + (13 \times \text{I[hypertension]}) + (11 \times \text{I[1 – dyslipidemia]}) + (22 \times \text{I[diabetes]}) + (8 \times \text{I[1 – family history of premature CAD]}) + (13 \times \text{CACS})$, where I[] denotes the indicator function equal to 1 if the condition in parenthesis is met, and 0 otherwise. Details of the individual prognostic scores relative to each risk factor are reported in Online Table 1. The distributions of the calculated PI for the derivation and validation sets are displayed in Online Figure 2. The PI had a similar spread in both datasets. No outliers or irregularities were observed.

TABLE 2 Multivariable Hazard Ratios for the Relationship Between Prognostic Risk Factors and 5-, 10-, and 15-Year All-Cause Mortality

	5-Year Follow-Up			10-Year Follow-Up			15-Year Follow-Up		
	HR	95% CI	p Value	HR	95% CI	p Value	HR	95% CI	p Value
Derivation set									
Age	1.04	1.03–1.05	<0.001	1.03	1.02–1.04	<0.001	1.04	1.03–1.04	<0.001
Male	1.15	0.90–1.45	0.26	1.03	0.88–1.20	0.72	1.02	0.90–1.17	0.72
Positive smoking history	1.92	1.54–2.41	<0.001	1.72	1.47–2.02	<0.001	1.71	1.51–1.95	<0.001
Hypertension	1.78	1.41–2.26	<0.001	1.59	1.35–1.88	<0.001	1.53	1.34–1.76	<0.001
Dyslipidemia	0.57	0.45–0.72	<0.001	0.69	0.59–0.81	<0.001	0.69	0.61–0.79	<0.001
Diabetes	1.69	1.27–2.24	<0.001	1.95	1.59–2.40	<0.001	2.01	1.69–2.38	<0.001
Family history of premature CAD	0.80	0.63–1.00	0.05	0.77	0.66–0.91	0.002	0.77	0.67–0.88	<0.001
CAC score									
0	1.00	–	–	1.00	–	–	1.00	–	–
1–100	2.29	1.65–3.16	<0.001	2.14	1.72–2.66	<0.001	1.98	1.66–2.36	<0.001
101–400	3.84	2.72–5.43	<0.001	3.38	2.68–4.25	<0.001	3.04	2.50–3.70	<0.001
401–1,000	4.07	2.70–6.11	<0.001	4.09	3.08–5.43	<0.001	4.02	3.20–5.05	<0.001
>1,000	6.36	4.15–9.73	<0.001	5.60	4.13–7.60	<0.001	5.13	3.97–6.63	<0.001
Validation set									
Age	1.09	1.06–1.11	<0.001	1.09	1.07–1.11	<0.001	1.10	1.08–1.11	<0.001
Male	1.09	0.74–1.61	0.65	0.95	0.72–1.25	0.71	0.92	0.71–1.20	0.55
Positive smoking history	1.79	1.02–3.13	0.04	1.69	1.13–2.51	0.01	1.75	1.23–2.50	0.002
Hypertension	1.71	1.18–2.50	0.005	1.58	1.22–2.04	<0.001	1.46	1.14–1.86	0.002
Dyslipidemia	0.90	0.61–1.33	0.60	0.91	0.70–1.19	0.49	0.88	0.69–1.13	0.33
Diabetes	0.97	0.52–1.82	0.94	0.84	0.54–1.30	0.44	0.80	0.52–1.22	0.29
Family history of premature CAD	0.72	0.48–1.09	0.12	0.80	0.60–1.07	0.13	0.83	0.63–1.09	0.18
CAC score									
0	1.00	–	–	1.00	–	–	1.00	–	–
1–100	1.06	0.64–1.79	0.24	1.27	0.88–1.83	0.20	1.18	0.83–1.67	0.36
101–400	1.09	0.60–1.98	0.79	1.59	1.05–2.40	0.03	1.48	1.02–2.17	0.041
401–1,000	1.75	0.91–3.37	0.10	1.64	1.00–2.68	0.05	1.76	1.13–2.75	0.012
>1,000	1.34	0.61–2.96	0.47	2.52	1.55–4.11	<0.001	2.30	1.44–3.67	0.001

Hazard ratios using 2,000 bootstrap resampling are reported. Harrell's C-index for the derivation set was 0.74. Applying the derivation set estimates to the validation set yielded a Harrell's C-index of 0.76.
CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.

Table 3 reports the risk of death from all causes by quartiles of the PI. Those comprising the very high-risk group (PI >96 total risk points) represented 57% and 58% of deaths in the derivation and validation sets, respectively. Incident deaths for the highest quartile in the derivation (17.28/1,000 person-years) and validation sets (11.71/1,000 person-years) were higher compared with lower quartiles. The highest quartiles were associated with a >10-fold (95% CI: 7.99 to 13.63; $p < 0.001$) and 15-fold (95% CI: 9.57 to 25.93; $p < 0.001$) increased risk of death in the derivation and validation sets, respectively, although the pointwise 95% CIs for the latter dataset were somewhat wider given the lower number of events observed. Based upon these findings, a nomogram was configured (Figure 1).

VALIDATION OF NOMOGRAM. Harrell's C-index for the derivation set was 0.74. Applying the derivation set estimates to the validation set yielded a similar Harrell's C-index of 0.76. A Kaplan-Meier survival curve for both datasets according to PI quartiles is reported in Figure 2. Each set of the PI quartiles appears well separated, indicating reasonable discrimination in both datasets. Figure 3 displays calibration plots comparing predicted survival probabilities with actual Kaplan-Meier estimates in both datasets according to PI quartiles. The patterns of both plots were comparable (although not identical), highlighting the similarity in the distribution of the PI in both datasets, indicating suitable model calibration. Hosmer-Lemeshow goodness-of-fit tests yielded chi-squares of 7.59 ($p = 0.47$) and 10.57 ($p = 0.23$) for the derivation and validation sets, respectively, indicating no significant deviation between observed and predicted events in both datasets.

DISCUSSION

In a cohort of 9,715 asymptomatic individuals referred for cardiac screening, we developed and validated a simple-to-use nomogram-illustrated model for

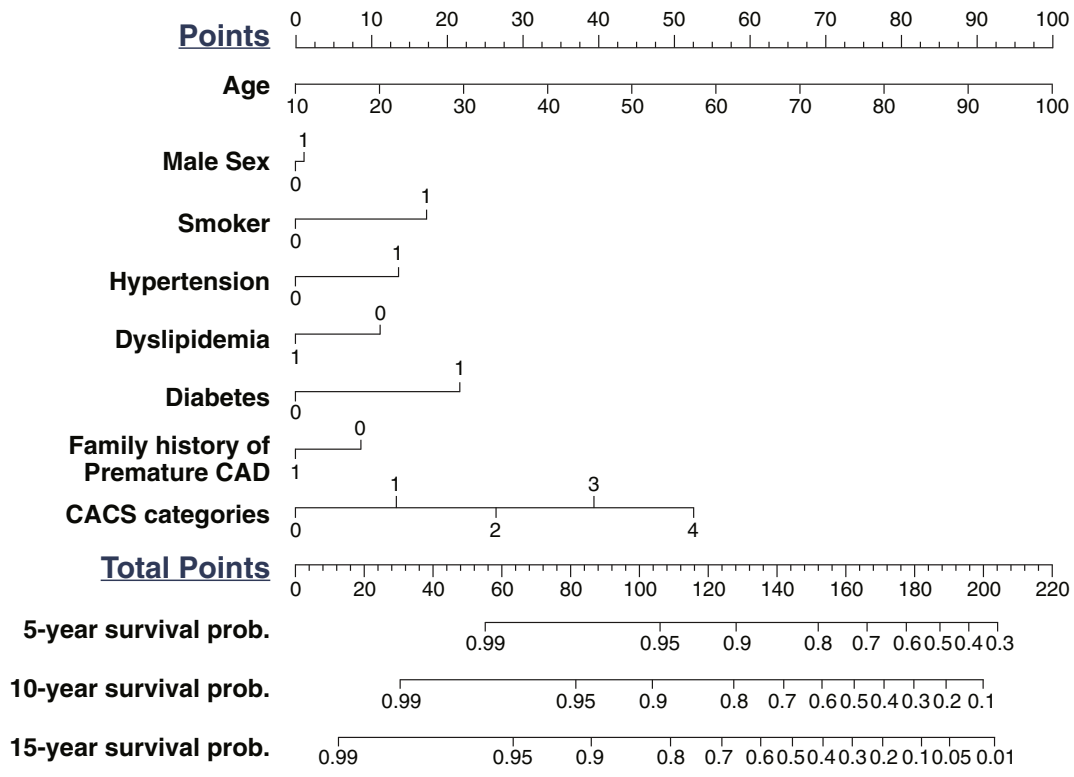
TABLE 3 Risk of Death From All Causes According to Quartiles of the Prognostic Index

Prognostic Index Groups	Median Prognostic Index Score (Range)*	No. of Persons at Risk	No. of Events	Event Rate/1,000 Person-Years (95% CI)	Unadjusted HR (95% CI)	p Value
Derivation set						
Quartile 1	52.4 (27.4–61.8)	2,424	60	1.70 (1.32–2.19)	1.00	–
Quartile 2	70.0 (62.1–77.3)	2,432	131	3.78 (3.19–4.49)	2.25 (1.66–3.05)	<0.001
Quartile 3	85.6 (77.7–95.5)	2,429	207	6.14 (5.36–7.04)	3.69 (2.77–4.93)	<0.001
Quartile 4	110.0 (96.0–167.7)	2,430	538	17.28 (15.88–18.80)	10.44 (7.99–13.63)	<0.001
Validation set						
Quartile 1	52.4 (27.6–62.0)	2,489	17	0.75 (0.47–1.21)	1.00	–
Quartile 2	69.7 (62.2–77.4)	1,947	49	2.82 (2.13–3.74)	3.76 (2.17–6.53)	<0.001
Quartile 3	85.2 (77.6–95.6)	1,615	58	4.12 (3.18–5.33)	5.50 (3.20–9.43)	<0.001
Quartile 4	112.1 (96.1–164.8)	1,773	170	11.71 (10.07–13.61)	15.75 (9.57–25.93)	<0.001

*1st and 99th centile values are reported. Median prognostic index values were extracted from the overall score summed using the equation in text.
CI = confidence interval; HR = hazard ratio; IQR = interquartile range.

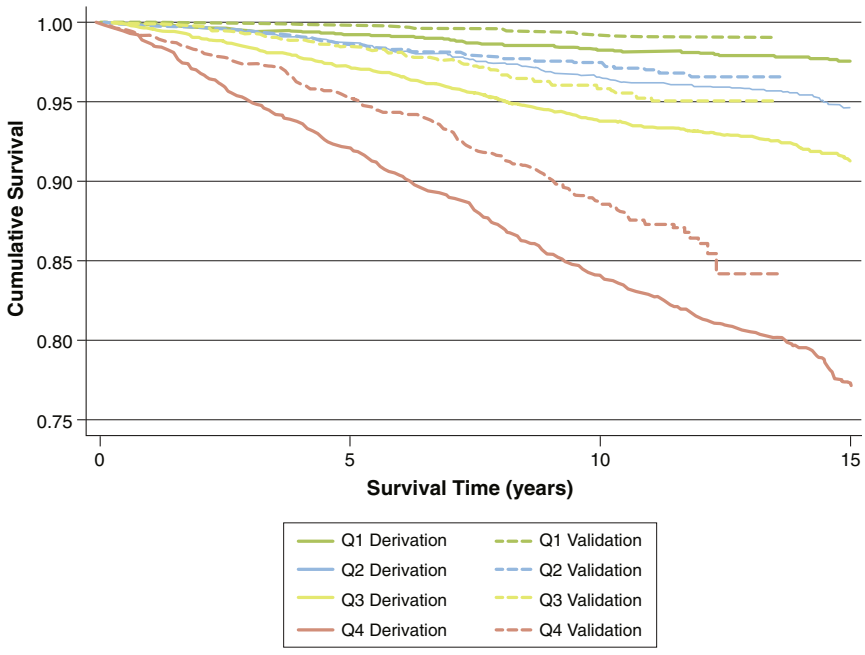
predicting 5-, 10-, and 15-year survival. Our nomogram model encompasses an extensive set of clinical risk factors that are easy to obtain and routinely collected by history, while also taking advantage of more novel cardiac screening modalities by incorporating CACS, a robust predictor of adverse health outcomes (11–13). The nomogram of the present study may be a valuable tool for clinical practice and can be

FIGURE 1 Instructions for Using the Nomogram



Draw a line perpendicular from the corresponding axis of each risk factor until it reaches the **top line** labeled "POINTS." Sum up the number of points for all risk factors then draw a line descending from the axis labeled "TOTAL POINTS" until it intercepts each of the survival axes to determine 5-, 10-, and 15-year survival probabilities. For binary variables, 0 = no and 1 = yes. For CACS categories, 0 = none, 1 = 1 to 100, 2 = 101 to 400, 3 = 401 to 1,000, and 4 = >1,000. CAD = coronary artery disease; CACS = coronary artery calcium score; prob. = probability.

FIGURE 2 Comparison of the Discrimination Between Derivation and Validation Sets According to Quartiles of the Prognostic Score



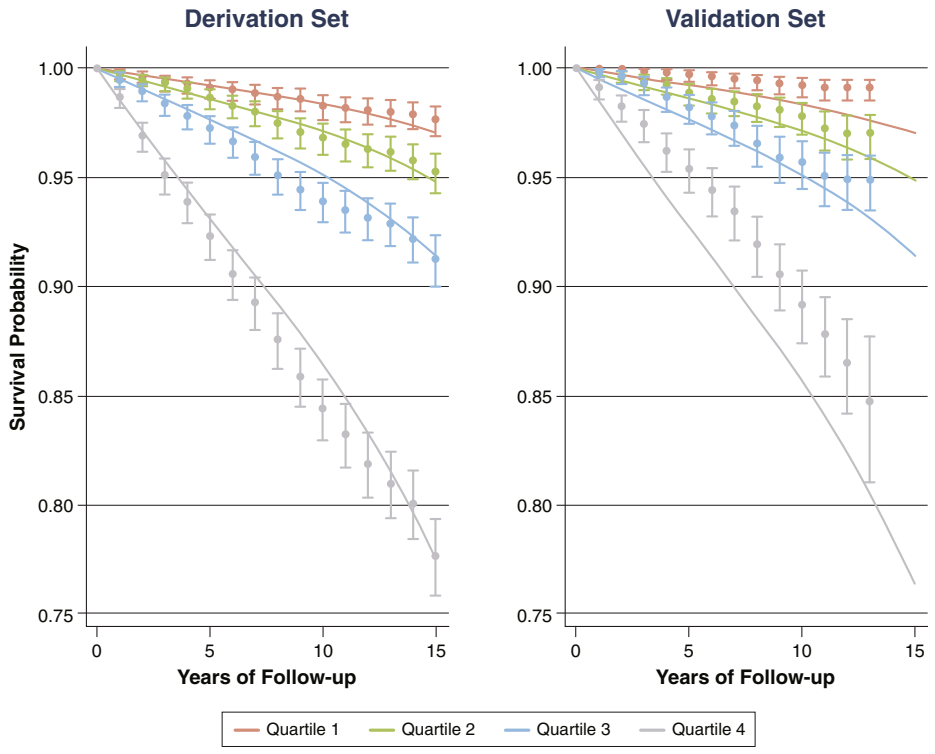
Solid lines indicate the derivation sets; **dashed lines** indicate the validation sets. Visual comparisons between the study sets were derived from a Kaplan-Meier survival curve.

consulted to inform patients about their future risk up to 15 years, incorporating the result of their CACS. In addition, the results may be used as guidance for preventive therapy, such as lipid-lowering therapy for patients with a high risk of mortality. However, comparative studies must be performed to assess the effect of preventive therapeutic strategies based on the current risk prediction mode.

Nomograms have frequently been used in cancer prognosis, primarily for estimating the likelihood of an event such as recurrence of early gastric cancer, gynecologic cancer, or renal cancers (14-16). Lauer et al. (17) developed and externally validated a parsimonious nomogram-based model for predicting all-cause mortality in adults with suspected CAD. Furthermore, McClelland et al. (8) developed the MESA risk score for the estimation of 10-year CHD risk using traditional risk factors and CACS. Still, to date, a nomogram that can predict 15-year all-cause mortality using CACS is unavailable. All-cause mortality can be considered an appropriate outcome, because a major proportion of deaths occur due to cardiac or systemic atherosclerotic diseases, and this endpoint is free from death misclassification bias (18). Also, the use of infrequently occurring cardiac-specific endpoints may introduce bias in relatively low-risk populations. Although focused treatment strategies in clinical practice may be more easily defined on the basis of cardiac-specific risk assessment, the present data unfortunately did not allow for this distinction.

Perhaps the most appealing aspect of our nomogram model is its clinical applicability and ease of use in a wide variety of health care systems. As an example, a female age 65 years who is a nonsmoker; is nonhypertensive, nondiabetic, and nondyslipidemic; has a family history of premature CAD; and has a CAC score of 90, will have a total risk score of 91 points, which corresponds to a 5-, 10-, and 15-year probability of survival of 95%, 92%, and 88% (Online Table 1, **Figure 1**). In contrast, a male age 73 years who is a current smoker; is hypertensive, nondiabetic, and nondyslipidemic; does not have a family history of premature CAD; and has a CAC score of 600, will have a total risk score of 167 points, corresponding to a 5-, 10-, and 15-year probability of survival of 70%, 45%, and 25%, respectively (**Figure 1**). The current findings support the prognostic potential of the developed and validated nomogram, which is relatively straightforward to understand and can be obtained in little time using a simple intake form (Online Table 1), or by accessing the online risk score calculator.

FIGURE 3 Calibration Plot of a Cox Model for the Derivation and Validation Sets According to Quartiles of the Prognostic Score



Smooth solid lines are predicted probabilities, and **vertical capped lines** are Kaplan-Meier (observed) estimates with 95% confidence intervals. Pink = quartile 1; green = quartile 2; blue = quartile 3; gray = quartile 4.

It is notable that dyslipidemia and a family history of premature CAD were inversely related to the risk of all-cause mortality, which may reflect the unmeasured confounding effect of lipid-lowering medications. Dyslipidemia was defined as known but untreated dyslipidemia or current treatment with lipid-lowering medications. Hypothetically, the protective value of lipid-lowering therapy in patients without established dyslipidemia could have exceeded the increased mortality risk of patients with true dyslipidemia. The same may hold true for family history of premature CAD. Indeed, others have previously reported a comparably low relative risk of mortality in patients with hypercholesterolemia and a family history of early CAD, potentially due to the same confounders (4,19).

Nowadays, there is strong consensus between researchers and physicians alike that a prognostic model should not be permitted into clinical practice unless it performs well and is "suitable for purpose" (20). External validation is frequently used to establish whether a prognostic model performs well and if it should enter clinical practice. We assessed the performance of our survival model using 2 fundamental features of model validation: discrimination and calibration (21). Using a high level of stringency, our validation set comprising 7,824 persons differed from those described in the derivation set with regard to investigators, geographic location, and time period. Furthermore, the prevalence of strongly weighted prognostic risk factors, such as hypertension, smoking, and diabetes, was lower in the validation cohort compared with the derivation cohort. This resulted in a noticeable reduction of all-cause mortality in the validation cohort. Despite this, our model performed well, showing good discrimination as reported by a C-index of 0.74 for the derivation set and 0.76 for the validation set. Further still, our model demonstrated reasonable calibration based on Kaplan-Meier survival curves for both datasets, albeit with some miscalibration. As noted elsewhere (20,22), good discrimination is more crucial to model validation than suitable calibration, considering the latter can be recalibrated, whereas the former cannot be altered (21). Still, the clinical applicability of this prognostic screening model

depends on the circumstances and the tested population. On the background of our model's favorable performance in our validation set, we advocate the use of our PI for estimating near-, intermediate-, and long-term survival in asymptomatic individuals. Undoubtedly, to ensure the robustness of our model, the need for replication and further validation of our findings in other well-defined populations, as well as for cause-specific outcomes, is warranted.

STUDY LIMITATIONS. Although individuals were considered free from CAD at baseline and representative of the general population; however, both cohorts underwent cardiac screening procedures, which raises concerns that these study individuals were referred by physicians, and consequently may have inferred a selection bias wherein the study sample may have been at higher risk than a population-based cohort. Despite this, common practice is that CAC scanning is not performed without physician prescription, and therefore, the current study sample likely reflects a generalizable group of individuals. We were unable to include other factors that could have influenced our model such as ethnic background or medication use; thus, caution should be used when extrapolating our model to different populations. Nevertheless, we developed the nomogram by evaluating individuals from Nashville, Tennessee; validated the nomogram in a distinct population from Los Angeles, California; and observed robust prediction of the study findings. These study results offer reassurance as to the generalizability of the nomogram model. We developed our nomogram using categorical variables to ensure application as a simple-to-use clinical tool. This parsimony may have led to less robust prognostic risk prediction than if continuous variables were employed (21). However, using categorical CACS groups allowed for the integration of specific thresholds associated with increased risk (23). Our nomogram is amenable only to those who strictly possess information regarding each risk factor included in the model—whether prediction of survival based on our model would improve depending on the inclusion of other cardiac risk assessment tools, such as carotid intimal medial thickness or C-reactive protein, is open to question. Arguably, from a clinical standpoint, it seems impractical to employ a different nomogram each time a new risk factor becomes available. Further still, the "revised" models themselves would require external validation, and in any case, risk prediction might not differ appreciably from the findings reported using our model (21,24). Although the availability of computed tomography scanners is ubiquitous, rendering this procedure easy to perform and highly accessible, it is important to note that there is some radiation concern associated with CAC scanning. Undoubtedly, though, the risk of future cardiovascular disease substantially outweighs the potential risk of future fatal cancer conferred by radiation doses, which mimic that of screening mammography. Despite these ambiguities, our study has developed and externally validated a robust nomogram for predicting 5-, 10-, and 15-year survival in asymptomatic adults undergoing cardiac screening.

CONCLUSIONS

This nomogram consisting of 8 clinical characteristics that are both straightforward to obtain and routinely collected in cardiovascular risk assessment offers clinicians a simple-to-use method for assessing mortality risk in asymptomatic individuals being referred for CAC scanning.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: A simple-to-use, nomogram-illustrated model encompassing broader indicators of cardiac risk, namely CACS, was developed and externally validated for predicting near-, intermediate-, and long-term death from any cause. The present nomogram model should be considered for its clinical applicability and ease of use across a wide variety of health care settings.

TRANSLATIONAL OUTLOOK: The current nomogram model was employed to predict risk of death from any cause. Forthcoming studies are needed to examine whether this model may prove useful in forecasting additional cause-specific events in persons undergoing CACS.

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KEY WORDS all-cause mortality, coronary artery calcium scoring, nomogram, prediction

APPENDIX For a supplemental table and figures, please see the online version of this paper.