Incident Heart Failure Prediction in the Elderly

The Health ABC Heart Failure Score

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Background—Despite the rising heart failure (HF) incidence and aging United States population, there are no validated prediction models for incident HF in the elderly. We sought to develop a new prediction model for 5-year risk of incident HF among older persons.

Methods and Results—Proportional hazards models were used to assess independent predictors of incident HF, defined as hospitalization for new-onset HF, in 2935 elderly participants without baseline HF enrolled in the Health ABC study (age, 73.6±2.9 years, 47.9% males, 58.6% whites). A prediction equation was developed and internally validated by bootstrapping, allowing the development of a 5-year risk score. Incident HF developed in 258 (8.8%) participants during 6.5±1.8 years of follow-up. Independent predictors of incident HF included age, history of coronary disease and smoking, baseline systolic blood pressure and heart rate, serum glucose, creatinine, and albumin levels, and left ventricular hypertrophy. The Health ABC HF model had a c-statistic of 0.73 in the derivation dataset, 0.72 by internal validation (optimism-corrected), and good calibration (goodness-of-fit χ² 6.24, P=0.621). A simple point score was created to predict incident HF risk into 4 risk groups corresponding to 5%, 5% to 10%, 10% to 20%, and >20% 5-year risk. The actual 5-year incident HF rates in these groups were 2.9%, 5.7%, 13.3%, and 36.8%, respectively.

Conclusion—The Health ABC HF prediction model uses common clinical variables to predict incident HF risk in the elderly, an approach that may be used to target and treat high-risk individuals. (Circ Heart Fail. 2008;1:125-133.)

Key Words: heart failure ■ elderly ■ risk factors ■ statistical models ■ epidemiology

Despite significant progress in the treatment of heart failure (HF), the incidence and prevalence of this diagnosis are rising in the United States.1-3 This trend is expected to continue and is attributed primarily to the increasing proportion of elderly in the population, improved care of acute heart diseases resulting in improved patient survival, and increasing prevalence of cardiovascular risk factors such as obesity and diabetes.4,5 The majority of HF research to date has focused on treatment. To further HF prevention efforts, the American Heart Association and the American College of Cardiology proposed a new classification scheme for HF to include “Stage-A” patients: those who do not have structural heart disease but are at risk for HF.1 Unlike coronary heart disease (CHD), however, no validated risk prediction scores are available for targeting such subjects for primary prevention.

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Previous studies of HF risk factor assessment are not useful for population-based risk prediction. These studies either included a select specific patient subpopulation (eg, the Framingham Heart Failure Risk Score [FHFRS] was developed in patients with known CHD, valvular disease, or...
hypertension) or assessed individual risk factors but did not develop risk assessment scores.6-13

HF is primarily a disease of the elderly. Its incidence approaches 10/1000 annually after age 65 and 80% of patients hospitalized with HF are older than 65 years.14-16 In this study, we sought to develop and validate a risk prediction model for incident HF among elderly participants enrolled in the Health Aging and Body Composition (Health ABC) study. Moreover, we sought to assess the predictive utility of the FHFRS for incident HF in this population.

### Table 1. Baseline Participant Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Health ABC (n=2935)</th>
<th>Cohort With HTN or CHD or VHD (n=1412)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall (n=2677)</td>
<td>No HF (n=258)</td>
</tr>
<tr>
<td></td>
<td>HF</td>
<td>No HF</td>
</tr>
<tr>
<td></td>
<td>(n=175)</td>
<td>(n=1237)</td>
</tr>
<tr>
<td><strong>Age, y</strong></td>
<td>73.6 (2.9)</td>
<td>74.2 (2.9)</td>
</tr>
<tr>
<td><strong>Males, %</strong></td>
<td>47.9</td>
<td>54.3</td>
</tr>
<tr>
<td><strong>Whites, %</strong></td>
<td>58.6</td>
<td>52.3</td>
</tr>
<tr>
<td><strong>Smoking status, %</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>10.5</td>
<td>17.1</td>
</tr>
<tr>
<td>Past</td>
<td>45.0</td>
<td>44.7</td>
</tr>
<tr>
<td><strong>Marital status, %</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never married</td>
<td>5.1</td>
<td>5.8</td>
</tr>
<tr>
<td>Married</td>
<td>40.8</td>
<td>41.8</td>
</tr>
<tr>
<td>Widowed</td>
<td>54.5</td>
<td>49.2</td>
</tr>
<tr>
<td>Divorced/separated</td>
<td>31.0</td>
<td>37.1</td>
</tr>
<tr>
<td><strong>Education, %</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>10.2</td>
<td>10.7</td>
</tr>
<tr>
<td>High school</td>
<td>40.8</td>
<td>40.7</td>
</tr>
<tr>
<td>More than high school</td>
<td>48.6</td>
<td>48.6</td>
</tr>
<tr>
<td><strong>Body mass index, kg/m^2</strong></td>
<td>27.3 (4.8)</td>
<td>28.1 (4.9)</td>
</tr>
<tr>
<td><strong>Systolic blood pressure, mm Hg</strong></td>
<td>144 (24)</td>
<td>135 (20)</td>
</tr>
<tr>
<td><strong>Diastolic blood pressure, mm Hg</strong></td>
<td>73 (13)</td>
<td>71 (12)</td>
</tr>
<tr>
<td><strong>Heart rate, bpm</strong></td>
<td>65 (11)</td>
<td>68 (12)</td>
</tr>
<tr>
<td><strong>Hypertension, %</strong></td>
<td>43.4</td>
<td>58.0</td>
</tr>
<tr>
<td><strong>Diabetes, %</strong></td>
<td>14.8</td>
<td>23.4</td>
</tr>
<tr>
<td><strong>Depression, %</strong></td>
<td>2.1</td>
<td>2.0</td>
</tr>
<tr>
<td><strong>Cerebrovascular disease, %</strong></td>
<td>6.8</td>
<td>9.9</td>
</tr>
<tr>
<td><strong>Coronary heart disease, %</strong></td>
<td>16.5</td>
<td>36.0</td>
</tr>
<tr>
<td><strong>Left ventricular hypertrophy, %</strong></td>
<td>11.9</td>
<td>17.8</td>
</tr>
<tr>
<td><strong>Glucose fasting, mg/dL</strong></td>
<td>104 (34)</td>
<td>114 (46)</td>
</tr>
<tr>
<td><strong>Creatinine, mg/dL</strong></td>
<td>1.05 (0.41)</td>
<td>1.16 (0.58)</td>
</tr>
<tr>
<td><strong>Albumin, g/dL</strong></td>
<td>3.98 (0.31)</td>
<td>3.94 (0.32)</td>
</tr>
<tr>
<td><strong>Total cholesterol, mg/dL</strong></td>
<td>203 (38)</td>
<td>198 (40)</td>
</tr>
<tr>
<td><strong>High density lipoprotein, mg/dL</strong></td>
<td>122 (35)</td>
<td>119 (35)</td>
</tr>
<tr>
<td><strong>Triglycerides, mg/dL</strong></td>
<td>137 (77)</td>
<td>134 (70)</td>
</tr>
</tbody>
</table>

Numbers represent mean (standard deviation). Health ABC indicates Health, Aging, and Body Composition; HF, heart failure; HTN, hypertension; CHD, coronary heart disease; VHD, valvular heart disease.
Study Definitions

Definite CHD was defined as a history of coronary artery bypass graft surgery, percutaneous coronary intervention, myocardial infarction, or angina, or self-reported history of CHD accompanied by antianginal medication use (calcium channel blockers, β blockers, or nitrates). Possible CHD was designated if there was a self-reported history of CHD without antianginal (or missing information on) medication use and any information about history of coronary artery bypass graft, percutaneous coronary intervention, myocardial infarction, or angina was missing or negative. Cerebrovascular disease was defined as self-reported history of stroke, transient ischemic attack, or carotid endarterectomy. Hypertension was defined as definite if there was a self-reported history of physician diagnosis accompanied by use of antihypertensive medication; or possible if there was a self-reported history of hypertension but without use of antihypertensive medication (or missing information about medication use) or there was antihypertensive medication use but there was no history of hypertension. Depression was defined as definite if there was both a self-reported treatment of depression and use of antidepressants; or possible if there was a self-reported treatment of depression but without use of antidepressants (or missing information about medication) or if there was medication use but no history of depression. Diabetes mellitus was considered present if the participant reported a history of diabetes mellitus or used hypoglycemic medications at baseline. Smoking status was defined as current use, past use (smoked at least 100 cigarettes in their lifetime), or never. The Minnesota code criteria were applied to diagnose left ventricular hypertrophy from the baseline ECG:

- R>26 mm in either V5 or V6, or R>20 mm in any of leads I, II, III, aVF, or R>12 mm in lead aVL, or R in V1, or V5 plus S in V1 >35 mm. History of VHD was not collected in the Health ABC study; VHD was considered present if the participant had either history of rheumatic heart disease or valve surgery.

Study Outcome

All participants in Health ABC were asked to report any hospitalizations, and every 6 months they were asked direct questions to elicit information about interim cardiovascular events. Medical records for overnight hospitalizations were reviewed at each site. All first admissions to the hospital with an overnight stay confirmed to be related to HF were classified as incident HF. Local adjudicators classified HF, based on symptoms, signs, chest x-ray, and echocardiographic findings, using criteria similar to those used in the Cardiovascular Health Study. The HF criteria required at least HF diagnosis from a physician and treatment for HF (ie, diuretics and either digitalis or a vasodilator); these criteria have been used in previous studies. All deaths were reviewed by the Health ABC Diagnosis and Disease Ascertainment committee; cause of death was determined by central adjudication. Because HF was not allowed as a cause of death, there were no deaths considered as incident HF.

Statistical Analyses

Development and Internal Validation of the Health ABC Heart Failure Model

First, to facilitate preliminary selection of predictors, descriptive statistics were obtained and compared by the Fisher’s exact test or the Welch-corrected t test between participants who developed HF (n=258) and those who did not (n=2677). Table 1. Variables with P<0.20 were considered as candidates. The association of candidate variables with risk for incident HF was assessed in univariate Cox models using bootstrap estimation (1000 replications, resampling with replacement). The functional form of continuous predictors

### Table 2. Independent Predictors of Incident Heart Failure

<table>
<thead>
<tr>
<th>Variable</th>
<th>Wald χ²</th>
<th>P</th>
<th>BC Coefficient</th>
<th>BC HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary heart disease</td>
<td>64.9</td>
<td>&lt;0.001</td>
<td>1.104</td>
<td>3.02 (2.24–3.79)</td>
</tr>
<tr>
<td>Definite</td>
<td></td>
<td></td>
<td>0.434</td>
<td>1.55 (0.71–3.01)</td>
</tr>
<tr>
<td>Smoking</td>
<td>19.9</td>
<td>&lt;0.001</td>
<td>0.017</td>
<td>1.02 (1.01–1.02)</td>
</tr>
<tr>
<td>Systolic BP, per mm Hg</td>
<td>35.8</td>
<td>&lt;0.001</td>
<td>0.826</td>
<td>2.28 (1.56–3.26)</td>
</tr>
<tr>
<td>Heart rate, per bpm</td>
<td>13.4</td>
<td>&lt;0.001</td>
<td>0.015</td>
<td>1.12 (0.83–1.47)</td>
</tr>
<tr>
<td>Creatinine, per log, mg/dL</td>
<td>17.5</td>
<td>&lt;0.001</td>
<td>0.952</td>
<td>2.59 (1.68–4.04)</td>
</tr>
<tr>
<td>Albumin, per g/dL</td>
<td>13.1</td>
<td>&lt;0.001</td>
<td>0.022</td>
<td>1.02 (1.01–1.03)</td>
</tr>
<tr>
<td>Glucose, per mg/dL</td>
<td>10.1</td>
<td>0.001</td>
<td>-0.749</td>
<td>0.47 (0.32–0.72)</td>
</tr>
<tr>
<td>Age, per year</td>
<td>7.7</td>
<td>0.005</td>
<td>0.064</td>
<td>1.07 (1.02–1.12)</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td>6.0</td>
<td>0.014</td>
<td>0.433</td>
<td>1.54 (1.06–2.11)</td>
</tr>
</tbody>
</table>

BC indicates bias-corrected after bootstrapping (1000 samples, random seed); HR, hazard ratio; CI, confidence interval; BP, blood pressure.
(linear versus nonlinear relations with incident HF risk) was evaluated using fractional polynomial functions. All candidate variables were also evaluated for significant interactions with age, gender, and race. All terms with $P \leq 0.10$ (Wald $\chi^2$ test) were considered for inclusion in multivariable models. Observations with missing values were dropped from subsequent analyses. Second, to identify independent predictors of outcome (incident HF), we adopted a backwards elimination approach. Bootstrap estimation was adopted to obtain bias-corrected coefficients and confidence intervals in each step. The threshold to retain a term in the model was set to $P \leq 0.05$ (Wald $\chi^2$).

The goodness-of-fit of the final model was evaluated both formally by the Hosmer-Lemeshow $\chi^2$ statistic and visually by plotting the cumulative expected versus observed events across the quartiles of risk (Arjas plots). The bias-corrected coefficients of the final model presented in Table 2 formed the basis for the Health ABC HF Score.

We internally validated the performance of the model by bootstrapping. Simulation studies have shown that this approach provides the least biased and most stable estimates of optimism-corrected performance among the various proposed methods for internal validation; with "optimism" referring to the inherent bias toward an overestimated performance in the derivation dataset. Briefly, optimism in a performance measure (eg, the $c$-statistic as a measure of discrimination and the Nagelkerke $R^2$ as a measure of explained variance) can be estimated by the average of $c$-statistics of bootstrap samples: the performance of each of the bootstrap sample-derived models is evaluated on the bootstrap sample ("training" dataset) and back to the original dataset ("validation" dataset). The average of $c$-statistics of bootstrap samples: the performance of each of the bootstrap sample-derived models is evaluated on the bootstrap sample ("training" dataset) and back to the original dataset ("validation" dataset). The average of $c$-statistics of bootstrap samples: the performance of each of the bootstrap sample-derived models is evaluated on the bootstrap sample ("training" dataset) and back to the original dataset ("validation" dataset). The average of $c$-statistics of bootstrap samples: the performance of each of the bootstrap sample-derived models is evaluated on the bootstrap sample ("training" dataset) and back to the original dataset ("validation" dataset).

We validated 2 measures of performance using 1000 bootstrap samples: the $c$-statistic and the slope of the linear predictor. The $c$-statistic is a measure of discrimination of the model, ie, the ability to distinguish high- from low-risk subjects and is analogous to the area under the receiver operating characteristic curve. Values range from 0.5 (useless) to 1.0 (perfect). The slope of the linear predictor is a measure of model calibration, ie, whether predicted probabilities agree with observed probabilities. Perfect is 1.0 and calibration is worse as the value deviates from 1.0. Validating the slope of the linear predictor by bootstrapping provides also a means to moderate absolute predictions by recalibrating the linear predictor using the optimism-corrected slope as a "shrinkage factor" (see Data Supplement Appendix).

Development of the Health ABC Heart Failure Score

The entire follow-up period was used to develop the model. After recalibrating the linear predictor of the model using the optimism-corrected slope ("shrinkage factor") to provide more conservative estimates, the results were adapted to provide 5-year HF risk predictions (Data Supplement Appendix). To facilitate clinical use of the model, the coefficients in Table 2 were used to assign score points for each risk factor using an approach similar to that adopted in the development of the FRS. For each level of the total score (the Health ABC HF Score), the 5-year risk was calculated; thus the Health ABC HF Score could be divided into 4 risk categories (<5%, 5% to 10%, 10% to 20%, and >20%). The Health ABC HF Score was tested for possible loss of information against the original equation. In addition, consistency of risk prediction was evaluated across gender and race.

The Health ABC HF Score and the Framingham Heart Failure Risk Score

For the FFRS, we restricted analyses to Health ABC participants with hypertension, CHD, or VHD. To compare performance for 5-year HF prediction, we used the 5-year occurrence of HF as a binary outcome and fit the respective, sex-specific scores in univariate logistic regression models. For each score, we calculated the $c$-statistic as a measure of discrimination and the Nagelkerke $R^2$ as a measure of explained variance. The $c$-statistics were compared between models according to the method described by DeLong et al. Again, performance measures for the Health ABC HF Score were corrected for optimism by bootstrapping using the methods described above.

Survival analysis, development of the multivariable model, and calculation of 5-year estimates was performed with Stata SE 9.2 (StataCorp LP). The S-Plus 6.2R statistical language (Insightful Corp) was used for internal validation of the models using the Design library provided by F. E. Harrell (http://lib.stat.cmu.edu/S/Harrell/Design.html). The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Study Population

Table 1 describes the baseline patient characteristics stratified by incident HF status in the overall cohort and the subpopulation studied. The mean age of participants was 73.6±2.9 years with 47.9% male and 58.6% whites. The mean follow-up was 6.5 years.

Table 3. Health ABC Heart Failure Risk Score: Predicted vs Observed Heart Failure Incidence

<table>
<thead>
<tr>
<th>Health ABC HF Risk Group</th>
<th>n</th>
<th>Health ABC HF Risk Score, Points</th>
<th>Predicted 5-Year HF Risk, %</th>
<th>Observed 5-Year HF Incidence, %</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>1754</td>
<td>2</td>
<td>&lt;5</td>
<td>2.9</td>
<td>...</td>
</tr>
<tr>
<td>Average</td>
<td>618</td>
<td>3–5</td>
<td>5–10</td>
<td>5.7</td>
<td>2.06 (1.34–3.17)</td>
</tr>
<tr>
<td>High</td>
<td>375</td>
<td>6–9</td>
<td>10–20</td>
<td>13.3</td>
<td>5.11 (3.46–7.54)</td>
</tr>
<tr>
<td>Very high</td>
<td>106</td>
<td>10</td>
<td>&gt;20</td>
<td>36.8</td>
<td>17.87 (11.66–27.40)</td>
</tr>
</tbody>
</table>

Health ABC indicates Health, Aging, and Body Composition; HF, heart failure; CI, confidence interval.
Incident Heart Failure and Outcomes

Overall, 611 of 2935 participants died, representing a cumulative mortality of 20.8% and annual mortality of 3.1%. A total of 258 participants developed HF (cumulative rate 8.8%, annual 1.36%). Subsequent mortality among participants who developed HF was 18.0%/year (cumulative 46.9%) over a mean follow-up of 2.6 years after HF hospitalization, compared with the 2677 participants who did not develop HF in whom annual mortality was 2.7% (cumulative 18.3%) over a mean follow-up of 6.7 years. Men and blacks were more likely than women and whites to develop HF (men: 140/1407, 10.0% cumulative, 1.58% annual rate versus women: 118/1528, 7.7% cumulative, 1.17% annual rate, \( P = 0.01 \), and blacks: 123/1215, 10.1% cumulative, 1.63% annual rate versus white: 135/1720, 7.8% cumulative, 1.18% annual rate, \( P = 0.01 \)).

Predictors of Incident Heart Failure

As shown in Table 2, 9 variables were associated with development of incident HF including: age, history of smoking and CHD, left ventricular hypertrophy, systolic blood pressure and heart rate, and serum glucose, albumin, and creatinine levels. Sex and race were both considered for inclusion but neither was associated with HF development in the final multivariable model. Formal and graphical statistical testing revealed concordant baseline hazard functions for both these factors. A significant nonlinear relationship with HF risk was detected only for creatinine levels. After inclusion of baseline blood pressure and serum glucose levels in the prediction model, history of hypertension and diabetes were no longer independently associated with incident HF.
Health ABC Heart Failure Model

The Health ABC model for incident HF had satisfactory discrimination (c-statistic 0.73 in the derivation dataset and 0.72 by internal validation with bootstrap-derived samples and correction for optimism). The Hosmer-Lemeshow goodness-of-fit test demonstrated overall good calibration ($\chi^2=6.24$, $P=0.621$); the distribution of expected versus observed HF incidence across deciles of risk is shown in Figure 1. In concordance, the slope of the linear predictor during internal validation with bootstrap-derived samples was estimated to 0.95 suggesting good calibration; we opted to use this optimism-corrected slope to obtain 5-year estimates to provide more conservative risk predictions.

Health ABC 5-Year Heart Failure Risk Score

A score was developed from the coefficients in Table 2; we were able to define 4 risk groups (low, average, high, and very high) corresponding to <5%, 5% to 10%, 10% to 20%, and >20% 5-year risk of incident HF, respectively (Table 3; Figure 2). Actual 5-year HF risk in these groups was 2.9%, 5.7%, 13.3%, and 36.8%, respectively. Figure 3 shows the Kaplan-Meier curves for incident HF in these risk groups. The Health ABC HF score predicted risk well in both genders and in white/black race-based subgroups (Figure 4). In the Health ABC derivation cohort (n=2853), the Health ABC HF Score achieved an optimism-corrected c=0.76 for 5-year HF occurrence (95% confidence interval: 0.72 to 0.80) and $R^2=0.154$.

Health ABC HF Risk Score and the Framingham HF Risk Score

Table 4 summarizes the comparative utility of the Health ABC and FHFRS in predicting incident HF in the Health ABC cohort and the subcohort in which the original score was developed. The FHFRS was suboptimal in predicting risk (3 of 4 gender-specific analyses had a c-statistic <0.7) and inferior compared with the Health ABC model.

Discussion

In this study, we developed and internally validated a risk prediction model for incident HF in an elderly cohort using commonly available clinical variables. We demonstrated that this model provides better discrimination for incident HF than the FHFRS. Moreover, we created a simple to use scoring system to classify the population at risk into 4 risk categories for HF development over 5 years.

The Health ABC HF risk prediction model and score has several strengths. First, this is a clinically relevant and applicable model that has potentially important utility in the general elderly population for prediction of incident HF. This is of significant
be only 12.7% and 8.3%, respectively.6,34 Because most subjects with hypertension and diabetes in the elderly recently were found to have not been developed.13 The only exception is the FHFRS, which was developed in a subgroup of community-based cohort at higher risk for HF with known CHD or VHD or hypertension.10 Such patients accounted for half the population in our study. Moreover, with the obesity, metabolic syndrome, and diabetes epidemic, the population risk profile for incident HF may be changing.5 We assessed the utility of the FHFRS in predicting incident HF in a general population of elderly subjects and found it to be suboptimal in assessing the risk of incident HF, in both the overall Health ABC cohort and also in the subgroup of patients from which it was derived.

Our 9-variable model had good discrimination and calibration, with acceptable performance in both gender- and race-based groups. Importantly, internal validation in 1000 random bootstrap samples demonstrated stable performance. Although hypertension and diabetes were significantly associated with HF in univariate analyses, after inclusion of blood pressure and serum glucose levels in the analyses, history of hypertension and diabetes were not independently associated with incident HF. This finding suggests that the relation among blood pressure, glucose, and HF is continuous and graded, and that blood pressure and glucose levels may increase HF risk even in the normal range.35,36 A recent analysis also showed an independent relationship between glucose levels and HF hospitalization risk.37 Thus, optimal glucose and blood pressure levels to ameliorate risk for HF need further study. This becomes a central issue in light of recent studies that indicate both increasing prevalence and inadequate control of hypertension and diabetes.38,39

Our study has several limitations. Diagnosis of HF was based on HF hospitalization. As some participants may have developed HF without hospitalization, our rates of HF are likely underestimated. Possible misclassification of HF events might have occurred, as diagnostic criteria for HF are difficult to define. Of note, although the prognostic validity of Cardiovascular Health Study criteria for diagnosis of HF has been demonstrated, these criteria are less specific than the Framingham HF criteria and may explain some of the variability in the performance of the different models.40 Echocardiography was not performed at baseline in the Health ABC study. Thus, patients with subclinical prevalent
structural heart disease may have been included in the analysis. The outcomes of both patients with either systolic dysfunction or HF with preserved ejection fraction are uniformly poor. The discriminatory ability of the current model to predict the 2 types of HF needs to be assessed further.\textsuperscript{41,42} The Health ABC study did not collect data uniformly on VHD; however, it is unlikely that a very large proportion of participants had significant subclinical VHD that would impact these results. Finally, the model was developed in a relatively healthy cohort of a certain age. Thus, the validity of the Health ABC model in other age groups, or general population within this age group where the burden of comorbidity may be higher, needs to be studied.

In conclusion, we have developed and internally validated a HF risk prediction model based on 9 routine clinical variables, most of which are potentially modifiable. The identification of persons at high risk for HF using the Health ABC HF Score and targeting strategies for primary prevention of HF to improve outcomes needs further study.

Sources of Funding

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Disclosures

None.

References


CLINICAL PERSPECTIVE

Despite the rising heart failure incidence and aging of the United States population, there are no validated prediction models for incident heart failure in the elderly. In this work, Cox proportional hazards modeling was used to identify common clinical variables that independently predicted incident heart failure (defined as hospitalization for new-onset heart failure) among the 2935 well-functioning elderly participants enrolled in the community-based Health, Aging, and Body Composition (Health ABC) study. Of note, black participants accounted for >40% of the study population. Heart failure developed in 258 (8.8%) of participants during 6.5±1.8 years of follow-up. Independent predictors for heart failure were age, history of coronary disease and smoking, baseline systolic blood pressure and heart rate, serum glucose, creatinine, and albumin levels, and left ventricular hypertrophy. A prediction model based on these risk factors was developed and internally validated by bootstrapping; the model demonstrated good prediction properties in the total cohort and across sex- and race-based subgroups. Based on this model, we developed a 5-year risk score (the Health ABC HF score), a simple, chart-based point score that predicts incident heart failure risk into 4 risk groups corresponding to 5%, 5% to 10%, 10% to 20%, and >20% 5-year risk. We envision this model to serve both as a clinical tool to identify and treat high-risk individuals, especially when considering that most of the identified risk factors are potentially modifiable, and also as a research tool that may be used as a basis to improve and further refine risk prediction for heart failure.
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APPENDIX - The Health ABC Heart Failure risk prediction equations

**Equation 1:** Original linear predictor (LP\textsubscript{original})

\[
LP_{\text{original}} = 1.104 \text{ (if definite CHD)} + 0.435 \text{ (if probable CHD)} + 0.826 \text{ (if current smoker)} + 0.115 \text{ (if past smoker)} + 0.433 \text{ (if LVH)} + 0.0635 \times (\text{age} - 73.6) - 0.750 \times (\text{albumin} - 4.0) + 0.0046 \times (\text{glucose} - 104.1) + 0.0217 \times (\text{heart rate} - 65.3) + 0.0173 \times (\text{systolic BP} - 136.0) + 0.9579 \times (\ln(\text{creatinine}) + 0.0256)
\]

**Equation 2:** Recalibration of the linear predictor (LP\textsubscript{recalibrated})

The internal validation process (bootstrapping, 1000 replications) derived an optimism-corrected slope of 0.95 for the original linear predictor.\textsuperscript{1} Interestingly, this result was very similar to the heuristic shrinkage estimator \( \gamma \) of van Houwelingen and le Cessie:\textsuperscript{2}

\[
\hat{\gamma} = \frac{\text{model } \chi^2 - p}{\text{model } \chi^2}
\]

where \( p \) is the number of regression parameters and the model \( \chi^2 \) is the total likelihood ratio \( \chi^2 \) statistic computed using the full set of \( p \) parameters. In our model, \( \gamma \) was equal to \( \gamma = (199.27 - 11)/199.27 \approx 0.945 \), very close to 0.95.

We recalibrated the \( LP_{\text{original}} \) using the optimism-corrected slope as ‘shrinkage’ factor:

\[
LP_{\text{recalibrated}} = LP_{\text{original}} \times 0.95
\]

**Equation 3:** Exponent for the ‘survival’ equation (B)

\[
B = \exp (LP_{\text{recalibrated}})
\]

For a hypothetical 73.6 yr old never-smoker patient without history of CHD or LVH and with average values of systolic BP (136 mmHg), heart rate (65.3 bpm), glucose (104.1 mg/dl), albumin (4.0 g/dl), and creatinine (0.97 mg/dl), i.e. when the ‘survival’ function is evaluated at zero value of covariates), the \( LP_{\text{recalibrated}} \) amounts to zero and \( B \) equals 1 (=the ‘reference’ patient). For any given patient, \( B \) virtually expresses the relative risk of the patient compared to the risk of this hypothetical ‘reference’ patient.
Equation 4: Heart failure cumulative risk (P)

\[ P = 1 - S(t)^B \]

Where \( S(t) \) is the ‘survival’ (=HF-free) function evaluated at time \( t \) and \( P \) the cumulative risk for the event (incident HF) at time \( t \) for a patient with relative risk \( B \). For the above ‘reference’ patient, \( S(t)^B = S(t)^1 = S(t) \). The baseline ‘survival’ (=HF-free) table for the original model yields a probability of 0.966 to be HF-free at 5 years when the function is evaluated at zero value of adjustment variables, thus \( S(5\text{yrs}) = 0.966 \) for our ‘reference’ patient. Conversely, the cumulative 5-yr risk for HF is 0.034 or 3.4\% for this patient.

Example: A 75-yr old past-smoker patient with definite history of CHD and LVH has systolic BP 120 mmHg, heart rate 75 bpm, fasting glucose (120 mg/dl), albumin 4.5 g/dl, and creatinine 1.2 mg/dl. The \( LP_{original} \) for this patient is: 1.104 (for definite CHD) + 0.115 (for past smoker) + 0.433 (for LVH) + 0.0635*(75-73.6, for age) – 0.750*(4.5-4.0, for albumin) + 0.0046*(120-104.1, for glucose) + 0.0217*(75-65.3, for heart rate) + 0.0173*(120-136.0, for systolic BP) + 0.9579*(\ln(1.2)+0.0256, for creatinine) = 1.571.

The \( LP_{recalibrated} \) is 0.95*1.571 = 1.492 and his calculated relative risk \( B \) is \( e^{(1.492)} = 4.45 \). Consequently, his calculated 5-yr HF risk is \( P = 1 - 0.966^{(4.45)} = 1 - 0.857 = 0.143 \) or \( \approx 14\% \).

Using the score chart in Figure 4 (Health ABC HF Score) for convenience, this patient would have a total of: (age=0) + (CHD=5) + (LVH=2) + (Systolic BP=-1) + (Heart Rate=1) + (Glucose=0) + (Albumin=-2) + (Past Smoking=1) + (Creatinine=1) = 7 points, which correctly places the patient at the high (10\%-20\%) 5-yr HF risk category.

Abbreviations:

CHD=Coronary Heart Disease
BP=Blood Pressure
LVH=Left Ventricular Hypertrophy
HF=Heart Failure
References:
