ONLINE SUPPLEMENTARY MATERIALS

Title: Prediction of incident atrial fibrillation in chronic kidney disease: the CRIC Study

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Supplemental Figure 1. CONSORT diagram of analytic population

Supplemental Figure 2. Calibration plot for CHARGE-AF equation with original coefficients

Supplemental Figure 3. Distribution of predicted probabilities of atrial fibrillation at 5 years from likelihood-based boosting model (all clinical and cardiac biomarker data), by category of eGFR

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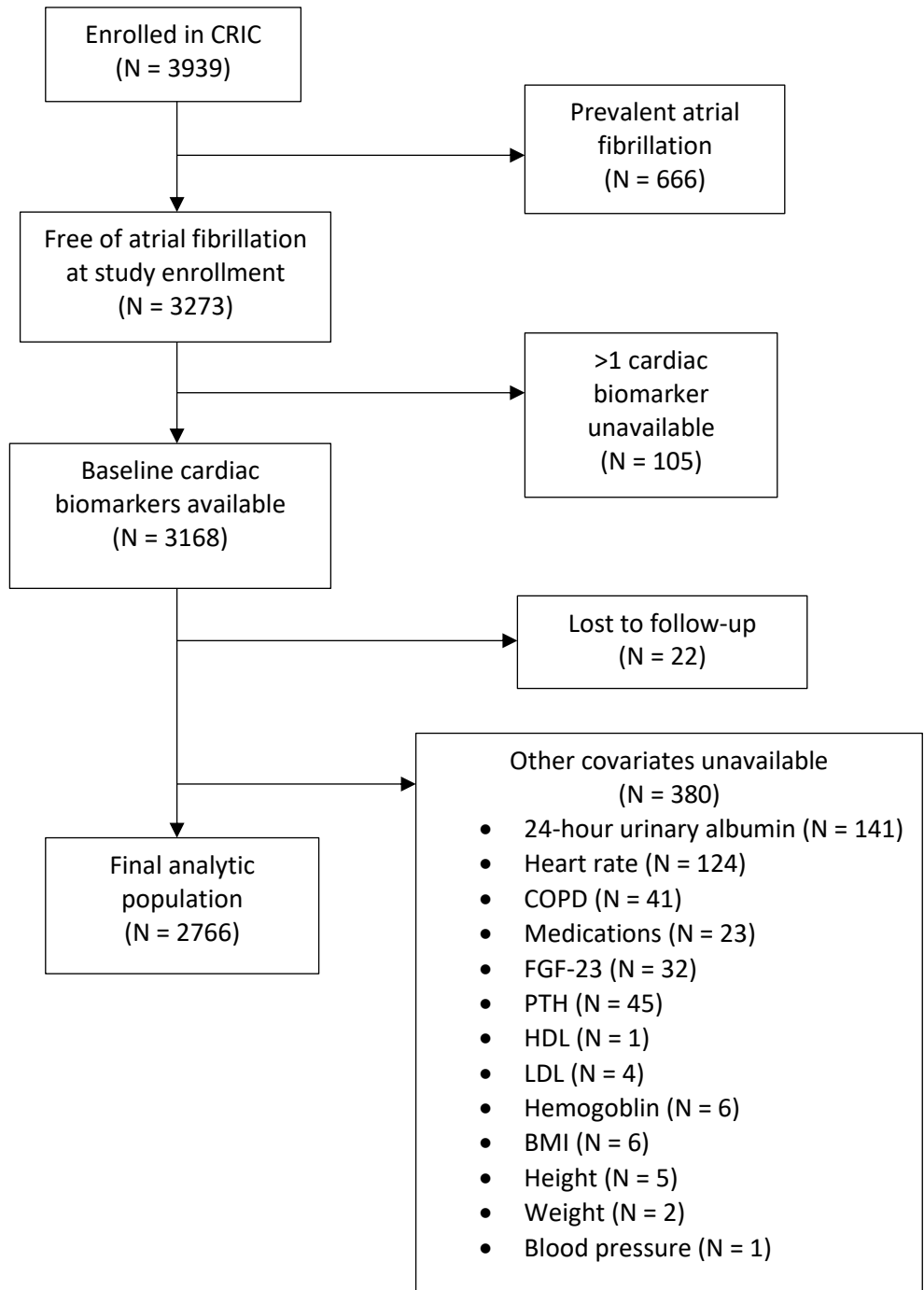
Supplemental Table 1. List of clinical and cardiac biomarker variables available for use in predictive models

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Supplemental Table 4. Final coefficient estimates of likelihood-based boosting model using clinical and cardiac biomarker data, excluding race/ethnicity

Supplemental Figure 1. CONSORT diagram of analytic population

Enrolled in CRIC
(N = 3939)

→ Prevalent atrial fibrillation (N = 666)

Free of atrial fibrillation at study enrollment
(N = 3273)

→ >1 cardiac biomarker unavailable (N = 105)

Baseline cardiac biomarkers available
(N = 3168)

→ Lost to follow-up (N = 22)

Final analytic population
(N = 2766)

→ Other covariates unavailable (N = 380)
- 24-hour urinary albumin (N = 141)
- Heart rate (N = 124)
- COPD (N = 41)
- Medications (N = 23)
- FGF-23 (N = 32)
- PTH (N = 45)
- HDL (N = 1)
- LDL (N = 4)
- Hemogoblin (N = 6)
- BMI (N = 6)
- Height (N = 5)
- Weight (N = 2)
- Blood pressure (N = 1)
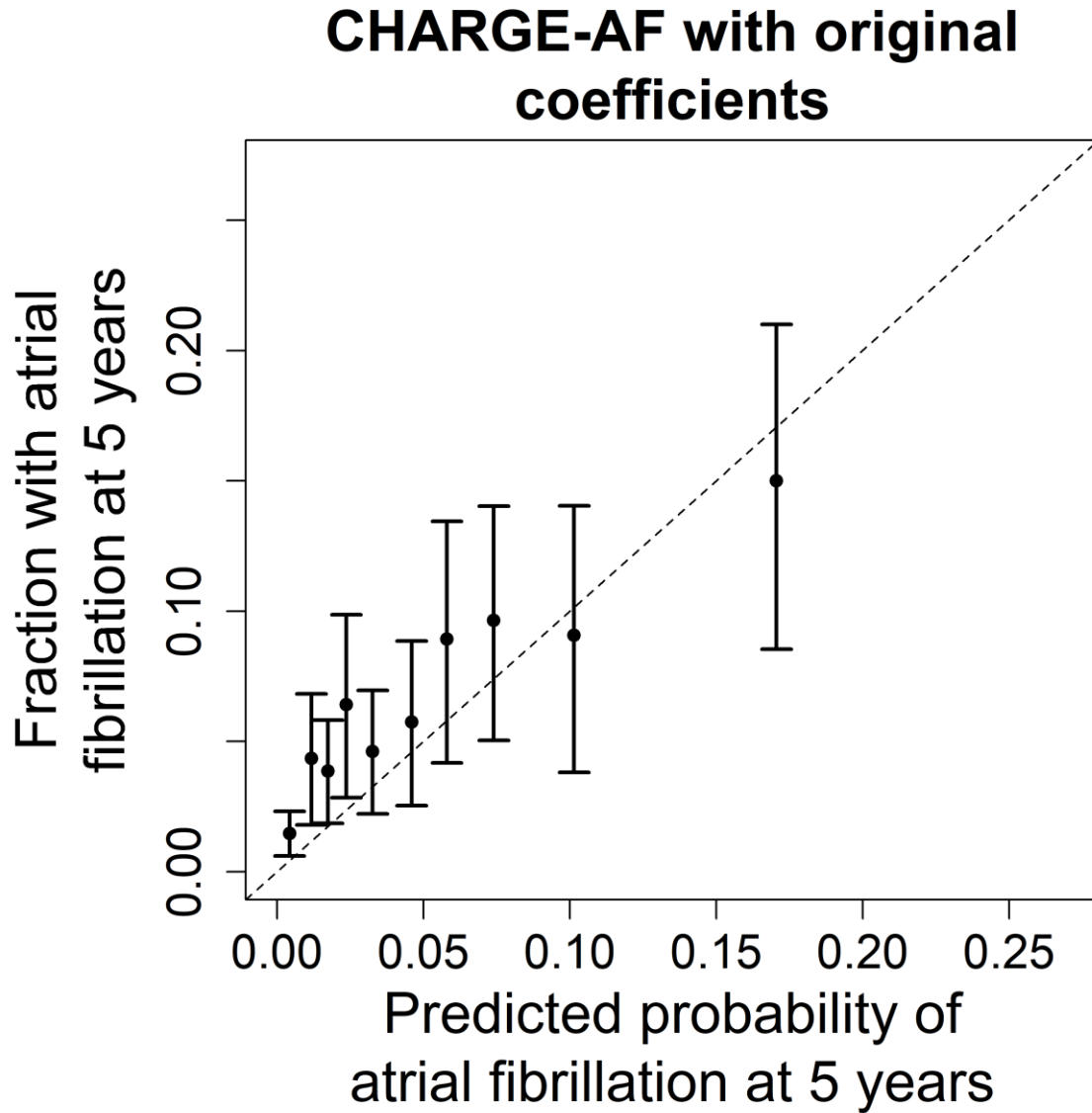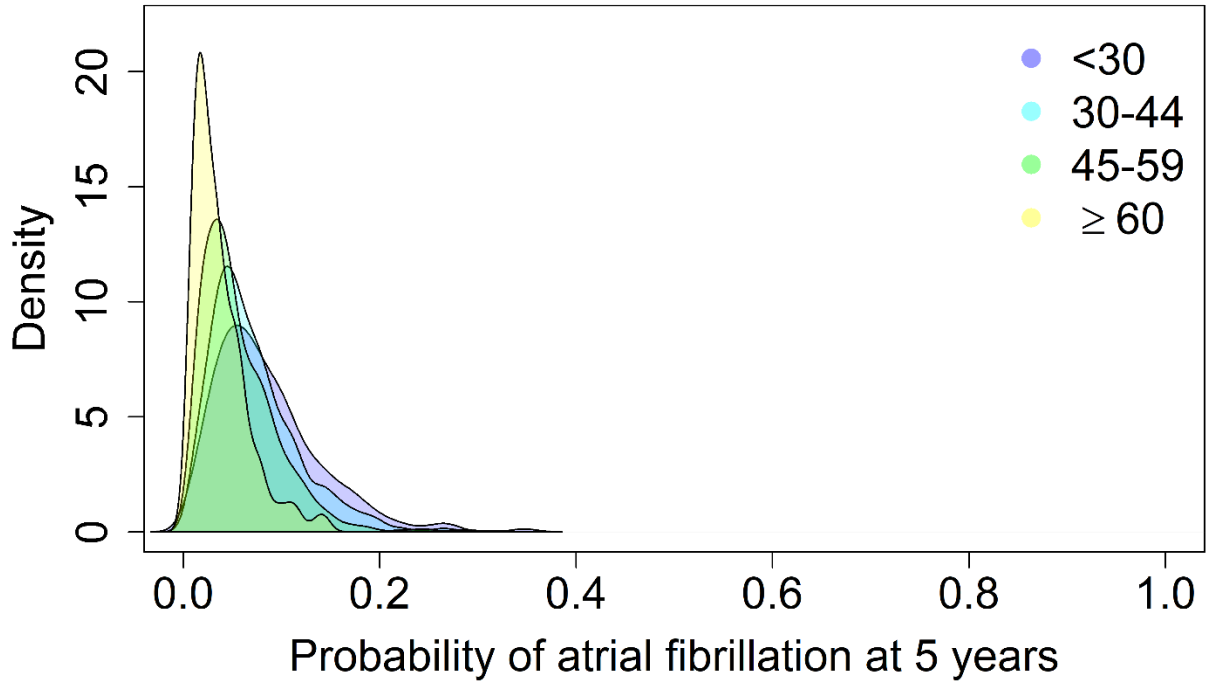
CHARGE-AF with original coefficients

Figure shows predicted and observed probabilities of atrial fibrillation at 5 years, by decile of predicted probability. The associated Grønnesby and Borgan p-value > 0.10.

Supplemental Figure 3. Distribution of predicted probabilities of atrial fibrillation at 5 years from likelihood-based boosting model (all clinical and cardiac biomarker data), by category of eGFR (mL/min/1.73m^2)

Supplemental Figure 4. Calibration plot for super learner predicted probabilities
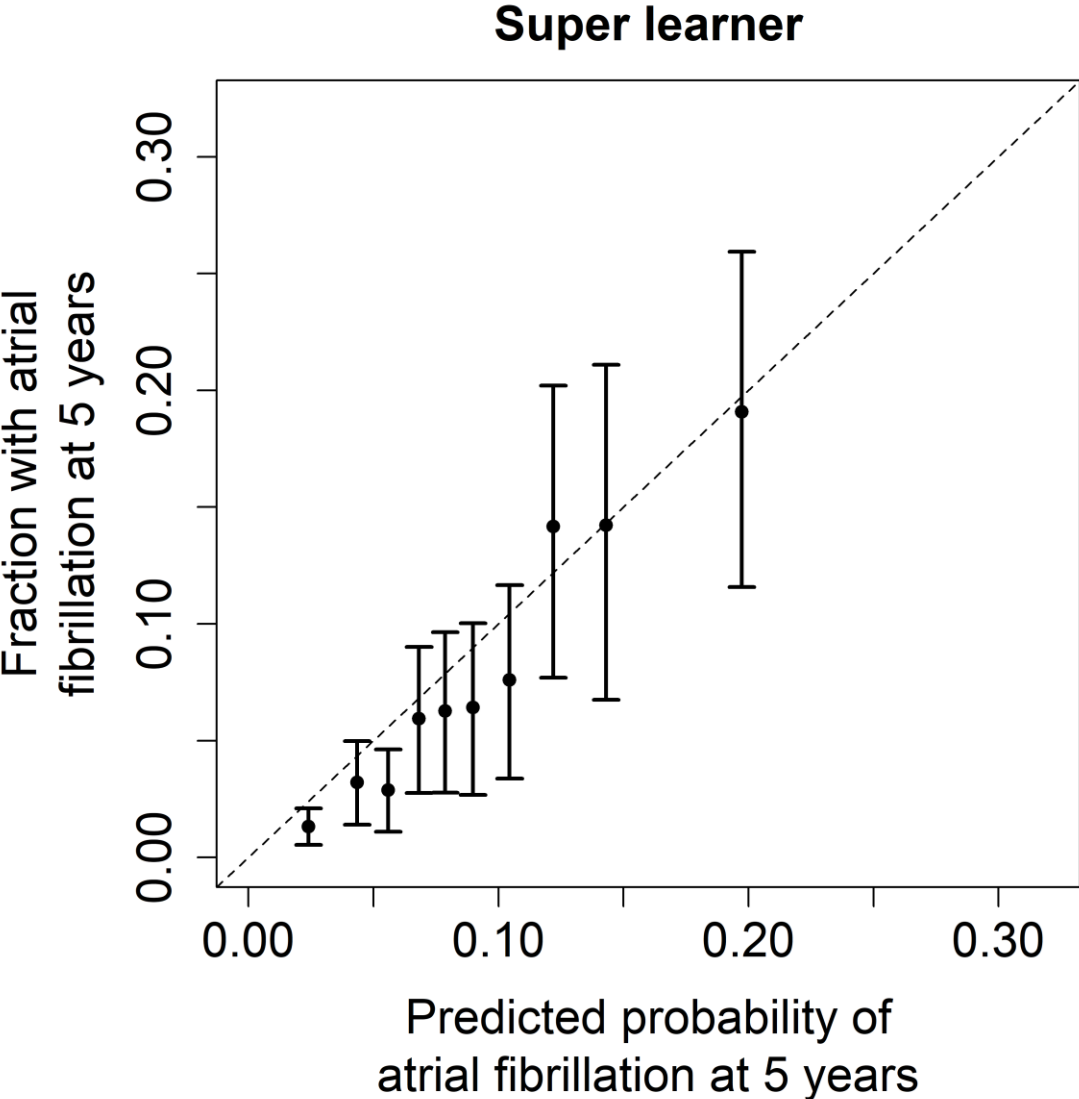
Super learner

Figure shows predicted and observed probabilities of atrial fibrillation at 5 years, by decile of predicted probability. The associated Grønnesby and Borgan p-value > 0.10.

Supplemental Table 1. List of clinical and cardiac biomarker variables available for use in predictive models

Demographics
Age
Sex
Self-reported race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, other)
Medical history
Diabetes mellitus
History of cardiovascular disease
History of congestive heart failure
History of chronic obstructive pulmonary disease
History of myocardial infarction
History of peripheral vascular disease
History of stroke
Current smoking
Markers of kidney function
eGFR (CKD-EPI) (mL/min/1.73m^2)
24-hour urine albumin (g/d)
Clinical characteristics and laboratory measurements
BMI (kg/m^2)
Systolic blood pressure (mmHg)
Diastolic blood pressure (mmHg)
ECG heart rate (bpm)
Hemoglobin (g/dL)
LDL cholesterol (mg/dL)
HDL cholesterol (mg/dL)
FGF-23 (RU/mL)
Total PTH (pg/mL)
Medications
Antihypertensive medication
ACEi/ARBs
Beta blockers
Calcium channel blockers
Diuretics
Cardiac biomarkers
NT-proBNP (pg/mL)
hsTNT (pg/mL)

Abbreviations: eGFR, estimated glomerular filtration rate; BMI, body mass index; ECG, electrocardiogram; LDL, low-density lipoprotein; HDL, high-density lipoprotein; FGF, fibroblast growth factor; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker

Supplemental Table 2. Percent weighting used for super learner predictions

Algorithm	Percent (%) weighting by super learner algorithm
CHARGE-AF	2.7
CHARGE-AF (re-estimated)	0.0
Stepwise regression	
Clinical variables only	3.3
Clinical variables + NT-proBNP	5.7
Clinical variables + hsTNT	0.5
Clinical variables + NT-proBNP + hsTNT	3.1
LASSO	
Clinical variables only	0.0
Clinical variables + NT-proBNP	0.0
Clinical variables + hsTNT	0.0
Clinical variables + NT-proBNP + hsTNT	0.0
Ridge regression	
Clinical variables only	0.0
Clinical variables + NT-proBNP	4.2
Clinical variables + hsTNT	0.0
Clinical variables + NT-proBNP + hsTNT	5.3
Likelihood-based boosting model	
Clinical variables only	0.0
Clinical variables + NT-proBNP	28.4
Clinical variables + hsTNT	0.0
Clinical variables + NT-proBNP + hsTNT	36.3
Generalized boosting regression model	
Clinical variables only	0.0
Clinical variables + NT-proBNP	2.4
Clinical variables + hsTNT	0.0
Clinical variables + NT-proBNP + hsTNT	7.8

Percent weighting of individual algorithms chosen by 10-fold cross validation; percentages sum to 100%, within rounding error.

Supplemental Table 3. Discriminatory ability of several modeling strategies not including race/ethnicity to predict incident atrial fibrillation, compared with the published CHARGE-AF model

	C-index (95% CI)	Difference from CHARGE-AF C-index (95% CI)
CHARGE-AF	0.674 (0.642, 0.706)	NA
Stepwise regression		
Clinical variables only	0.640 (0.608, 0.673)	-0.034 (-0.054, -0.014)
Clinical variables + NT-proBNP	0.702 (0.671, 0.733)	**0.028 (0.001, 0.055)**
Clinical variables + hsTNT	0.673 (0.643, 0.704)	-0.001 (-0.022, 0.020)
Clinical variables + NT-proBNP + hsTNT	0.702 (0.671, 0.733)	**0.028 (0.001, 0.055)**
LASSO		
Clinical variables only	0.645 (0.613, 0.677)	-0.029 (-0.048, -0.011)
Clinical variables + NT-proBNP	0.706 (0.676, 0.737)	**0.032 (0.007, 0.057)**
Clinical variables + hsTNT	0.670 (0.639, 0.702)	-0.004 (-0.024, 0.016)
Clinical variables + NT-proBNP + hsTNT	0.709 (0.679, 0.740)	**0.035 (0.010, 0.060)**
Ridge regression		
Clinical variables only	0.656 (0.624, 0.689)	-0.018 (-0.042, 0.007)
Clinical variables + NT-proBNP	0.699 (0.667, 0.730)	0.025 (-0.001, 0.050)
Clinical variables + hsTNT	0.667 (0.635, 0.699)	-0.007 (-0.032, 0.018)
Clinical variables + NT-proBNP + hsTNT	0.702 (0.670, 0.733)	**0.028 (0.002, 0.053)**
Likelihood-based boosting model		
Clinical variables only	0.651 (0.619, 0.683)	-0.023 (-0.042, -0.004)
Clinical variables + NT-proBNP	0.709 (0.678, 0.740)	**0.035 (0.010, 0.060)**
Clinical variables + hsTNT	0.670 (0.638, 0.702)	-0.004 (-0.025, 0.016)
Clinical variables + NT-proBNP + hsTNT	0.710 (0.679, 0.741)	**0.036 (0.011, 0.061)**
Generalized boosting regression model		
Clinical variables only	0.657 (0.625, 0.689)	-0.017 (-0.042, 0.008)
Clinical variables + NT-proBNP	0.700 (0.666, 0.733)	0.026 (-0.004, 0.055)
Clinical variables + hsTNT	0.676 (0.645, 0.706)	0.001 (-0.026, 0.029)
Clinical variables + NT-proBNP + hsTNT	0.710 (0.676, 0.743)	**0.036 (0.005, 0.066)**
Super learner algorithm	0.720 (0.689, 0.750)	**0.046 (0.025, 0.066)**

Entry for CHARGE-AF is C-index and associated 95% bootstrap confidence interval; all other entries are 10-fold cross-validated C-indices or difference in C-indices and associated 95% bootstrap confidence intervals. Bolded entries indicate statistical significance at the α=0.05 level. CHARGE-AF model predicts atrial fibrillation from age, white race/ethnicity, height, weight, systolic blood pressure, diastolic blood pressure, smoking, use of antihypertensives, diabetes, congestive heart failure, and myocardial infarction. Predictions from super learner algorithm are derived from individual algorithm predictions.

Supplemental Table 4. Final coefficient estimates of likelihood-based boosting model using clinical and cardiac biomarker data, excluding race/ethnicity

Variable	Estimated coefficient
Age (years)	0.374
History of cardiovascular disease	0.00749
History of chronic obstructive pulmonary disease	0.0298
History of myocardial infarction	0.0238
History of peripheral vascular disease	-0.0249
Use of ACEi/ARBs	0.0391
Use of diuretics	0.0258
Height (cm)	0.0641
Weight (kg)	0.188
Current smoking	-0.00792
Diastolic blood pressure (mmHg)	-0.00785
Log(NT-proBNP (pg/mL))	0.440
Log(hsTNT (pg/mL))	0.0662

Predicted 5-year risk of atrial fibrillation is $1 - 0.9496^{\ e^{(\Sigma X \beta)}}$, where β is the regression coefficient and X is the level for each risk factor listed above.

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker