

Improved prediction of sudden cardiac death in patients with heart failure through digital processing of electrocardiography

Supplementary Appendix

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Abbreviations: ECG-AI: Electrocardiography-based artificial intelligence, ROC-AUC: Receiver operating characteristic area under the curve, SCD: Sudden cardiac death, LVEF: Left ventricular ejection fraction, CI: Confidence interval.

Table S2. Subdistributional HRs of the ECG-AI index for predicting SCD events.

Subdistributional HRs are derived from the Fine-Gray models, accounting for the competing risk of non-SCD.

Abbreviations: HR: Hazard ratio, CI: Confidence interval, ECG-AI: Electrocardiogram-based artificial intelligence, SCD: Sudden cardiac death, ICD: Implantable cardioverter-defibrillator, LVEF: Left ventricular ejection fraction, NYHA: New York Heart Association.

Table S3. Patient backgrounds according to age (≤ 75 years vs. > 75 years), sex (men vs. women), and etiology (ischemic vs. non-ischemic).

Abbreviations: LVEF: Left ventricular ejection fraction, NYHA: New York Heart Association, HF: Heart failure, COPD: Chronic obstructive pulmonary disease, eGFR: Estimated glomerular filtration rate, BNP: B-type natriuretic peptide, NT-proBNP: N-terminal pro-B-type natriuretic peptide, ACEi: Angiotensin-converting enzyme inhibitor, ARB: Angiotensin receptor blocker, MRA: Mineralocorticoid receptor antagonist, ICD: Implantable cardioverter-defibrillator, CRT: Cardiac resynchronization therapy.

Figure S1. Patient allocation flow chart.

Abbreviations: WET-HF: West Tokyo Heart Failure, ECG: Electrocardiogram.

Figure S2. Architecture of the neural network model.

Abbreviations: ECG: Electrocardiogram, 1D: One-dimensional, LSTM: Long short-term memory, SCD: Sudden cardiac death.

Figure S3. Schematic illustration of the process of training and testing the neural network model.

The model was trained with data from the derivation cohort, and the performance of each model was calculated using data from the validation dataset at the end of each epoch. The final model was chosen as the model that performed best for 50 epochs in the validation cohort. The performance of the final model was calculated only once using data from the testing dataset.

Figure S4. Visualization of the region of interest that our final neural network model interpreted based on Grad-CAM results.

Figure S5. Forest plots of subdistributional HRs and 95% CI of the ECG-AI index for SCD by each subgroup.

Figure S6. Cumulative incidence of SCDs and non-SCDs according to estimated risk by the ECG-AI models.

The cutoffs of SCD risk were defined by the Youden index of the logistic regression model for predicting 3-year SCD: (a) ECG-AI index, and (b) ECG-AI combined model with LVEF and NYHA class.

Abbreviations: SCD: Sudden cardiac death, ECG-AI: Electrocardiogram-based artificial intelligence, LVEF: Left ventricular ejection fraction, NYHA: New York Heart Association.

Figure S7. Time-dependent ROC-AUC for predicting 3-year SCD events in the Cox proportional hazards models.

Abbreviations: ROC: Receiver operating characteristic area under the curve, SCD: Sudden cardiac death.

Table S1. Sensitivity analyses of the discriminative ability of the ECG-AI index and frequency of SCD and non-SCD by LVEF categories

LVEF category	Frequency			ECG-AI index performance	
	Patient, number	SCD, number (%)	Non-SCD, number (%)	ROC-AUC	95% CI
LVEF cutoff: 45%					
≤ 35%	291	25 (8.6)	49 (16.8)	0.53	0.40–0.66
35%–45%	215	13 (6.0)	51 (23.7)	0.61	0.40–0.81
≥ 45%	571	21 (3.7)	124 (21.7)	0.63	0.50–0.76
LVEF cutoff: 50%					
≤ 35%	291	25 (8.6)	49 (16.8)	0.53	0.40–0.66
35%–50%	329	21 (6.4)	73 (22.2)	0.69	0.55–0.83
≥ 50%	457	13 (2.8)	102 (22.3)	0.53	0.38–0.69
LVEF cutoff: 55%					
≤ 35%	291	25 (8.6)	49 (16.8)	0.53	0.40–0.66
35%–55%	436	26 (6.0)	100 (22.9)	0.65	0.52–0.78
≥ 55%	350	8 (2.3)	75 (21.4)	0.51	0.34–0.68
LVEF cutoff: 60%					
≤ 35%	291	25 (8.6)	49 (16.8)	0.53	0.40–0.66
35%–60%	572	31 (5.4)	129 (22.6)	0.66	0.55–0.77
≥ 60%	214	3 (1.4)	46 (21.5)	0.58	0.38–0.77

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Table S2. Subdistributional HRs of the ECG-AI index for predicting SCD events

Characteristic	Univariable			Multivariable		
	sHR	95% CI	P-value	sHR	95% CI	P-value
Indication for ICD						
LVEF \leq 35% and NYHA II–III	2.25	1.30–3.89	0.004	1.98	1.11–3.54	0.020
ECG-AI index						
Z-score (standardized)	1.31	1.12–1.53	0.001	1.23	1.04–1.49	0.015

Subdistributional HRs are derived from the Fine-Gray models, accounting for the competing risk of non-SCD.

Abbreviations: HR: Hazard ratio, CI: Confidence interval, ECG-AI: Electrocardiogram-based artificial intelligence, SCD: Sudden cardiac death, ICD: Implantable cardioverter-defibrillator, LVEF: Left ventricular ejection fraction, NYHA: New York Heart Association.

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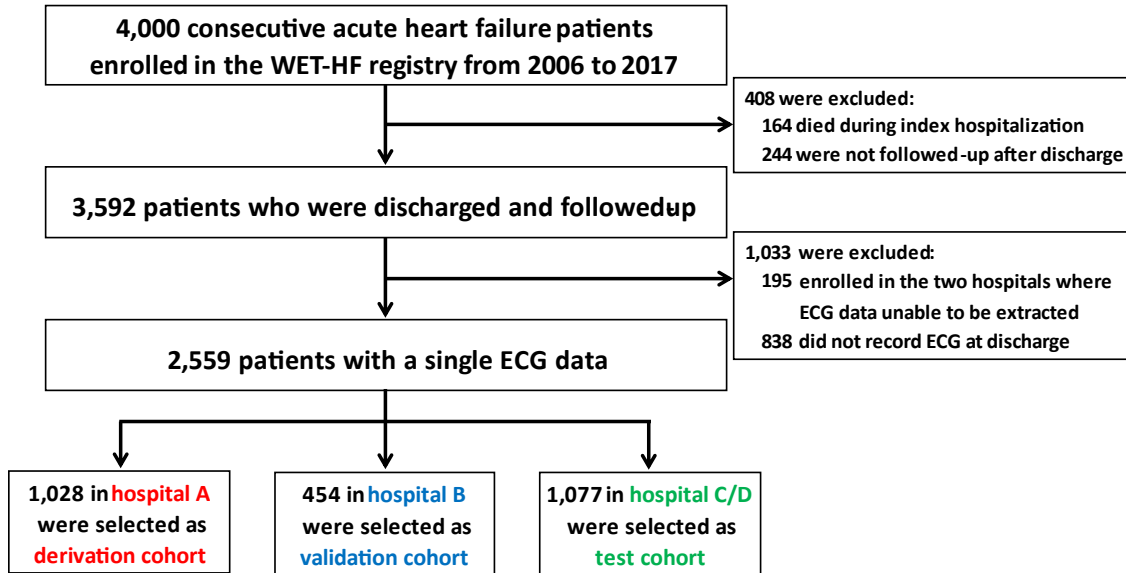
Value	≤ 75 years old n = 473	> 75 years old n = 604	Men n = 638	Women n = 439	Ischemic n = 305	Non-ischemic n = 772
Age, years	65 (56–70)	83 (79–87) *	75 (63–82)	80 (72–85) *	77 (68–83)	77 (66–84)
Men, n (%)	328 (69.3)	310 (51.3) *	638 (100)	0 (0)	212 (69.5)	426 (55.2) *
BMI, kg/m ²	22.1 (19.4–24.9)	20.4 (17.9–22.8) *	21.4 (19.3–24.1)	20.4 (17.8–23.1) *	21.3 (19.0–23.7)	21.0 (18.6–23.9)
SBP, mm Hg	110 (98–125)	116 (102–128) *	112 (100–128)	113 (101–126)	116 (100–130)	112 (100–126)
Heart rate, bpm	72 (62–80)	70 (60–78)	70 (60–80)	70 (61–80)	70 (60–79)	70 (61–80)
LVEF, %	43 (31–57)	50 (38–60) *	44 (31–57)	52 (40–61) *	41 (31–50)	50 (36–60) *
LVEF $\leq 35\%$, n (%)	166 (35.1)	125 (20.7) *	216 (33.9)	75 (17.1) *	106 (34.8)	185 (24.0) *
NYHA class II–III, n (%)	425 (89.9)	565 (93.5)	575 (90.1)	415 (94.5)	284 (93.1)	706 (91.5)
Ischemic etiology, n (%)	130 (27.5)	175 (29.0)	212 (33.2)	93 (21.2) *	305 (100)	0 (0)
HF hospitalization, n (%)	88 (18.8)	150 (25.4)	139 (22.2)	99 (22.9)	79 (26.3)	159 (21.0)
Atrial fibrillation, n (%)	155 (32.8)	273 (45.2) *	244 (38.2)	184 (41.9)	73 (23.9)	355 (46.0) *
Hypertension, n (%)	314 (66.4)	452 (74.8)	466 (73.0)	300 (68.3)	234 (76.7)	532 (68.9)
Diabetes mellitus, n (%)	204 (43.1)	224 (37.1)	283 (44.4)	145 (33.0) *	171 (56.1)	257 (33.3) *
Stroke, n (%)	51 (10.8)	90 (14.9)	89 (13.9)	52 (11.8)	55 (18.0)	86 (11.1)
COPD, n (%)	17 (3.6)	48 (8.0)	50 (7.8)	15 (3.4)	14 (4.6)	51 (6.6)
Hemoglobin, g/dL	12.7 (11.1–14.6)	11.4 (10.1–12.5) *	12.1 (10.8–14.0)	11.5 (10.1–12.8) *	11.6 (10.3–13.0)	12.0 (10.6–13.5)
BUN, mg/L	21.7 (16.4–31.3)	26.2 (18.7–37.5) *	24.8 (18.4–35.8)	23.5 (16.6–34.6)	26.2 (19.2–36.5)	23.5 (17.2–35.1)
eGFR, ml/min/1.73 m ²	56.4 (35.8–73.7)	44.7 (29.9–60.4) *	49.0 (30.6–64.9)	49.7 (31.6–68.2)	41.6 (26.3–59.3)	51.9 (34.2–70.0) *
Sodium, mEq/L	139 (136–141)	139 (136–141)	139 (136–141)	139 (137–141)	139 (136–141)	139 (137–141)
Potassium, mEq/L	4.4 (4.1–4.7)	4.3 (4.0–4.6)	4.4 (4.1–4.7)	4.3(3.9–4.6)	4.4 (4.1–4.7)	4.3 (4.0–4.6)
Uric acid, mg/L	7.3 (5.7–8.5)	7.1 (5.6–8.7)	7.4 (6.0–8.8)	6.6 (5.1–8.2) *	7.2 (5.8–8.3)	7.1 (5.7–8.7)
Albumin, mg/L	3.6 (3.2–3.9)	3.3 (2.9–3.6) *	3.4 (3.1–3.8)	3.4 (3.0–3.7)	3.3 (3.0–3.7)	3.4 (3.1–3.7)
BNP, pg/mL	226 (103–466)	256 (143–543)	254 (129–496)	236 (124–535)	285 (161–622)	230 (113–455)
Loop diuretics, n (%)	340 (71.9)	480 (79.6)	492 (77.1)	328 (74.9)	242 (79.3)	578 (75.0)
ACEi or ARB, n (%)	304 (64.3)	382 (63.3)	420 (65.8)	266 (60.7)	210 (68.9)	476 (61.7)

Beta blocker, n (%)	382 (80.8)	432 (71.6) *	490 (76.8)	324 (74.0)	258 (84.6)	556 (72.1) *
MRA, n (%)	169 (35.9)	205 (34.1)	217 (34.1)	157 (36.0)	107 (35.3)	267 (34.7)
Digitalis, n (%)	26 (5.5)	49 (8.1)	34 (5.3)	41 (9.4)	9 (3.0)	66 (8.6)
Amiodarone, n (%)	52 (11.0)	61 (10.1)	80 (12.5)	33 (7.5)	28 (9.2)	85 (11.0)
ICD, n (%)	17 (3.6)	15 (2.5)	24 (3.8)	8 (1.8)	9 (3.0)	23 (3.0)
CRT, n (%)	7 (1.5)	6 (1.0)	11 (1.7)	2 (0.5)	5 (1.6)	8 (1.0)

* $p < 0.001$.

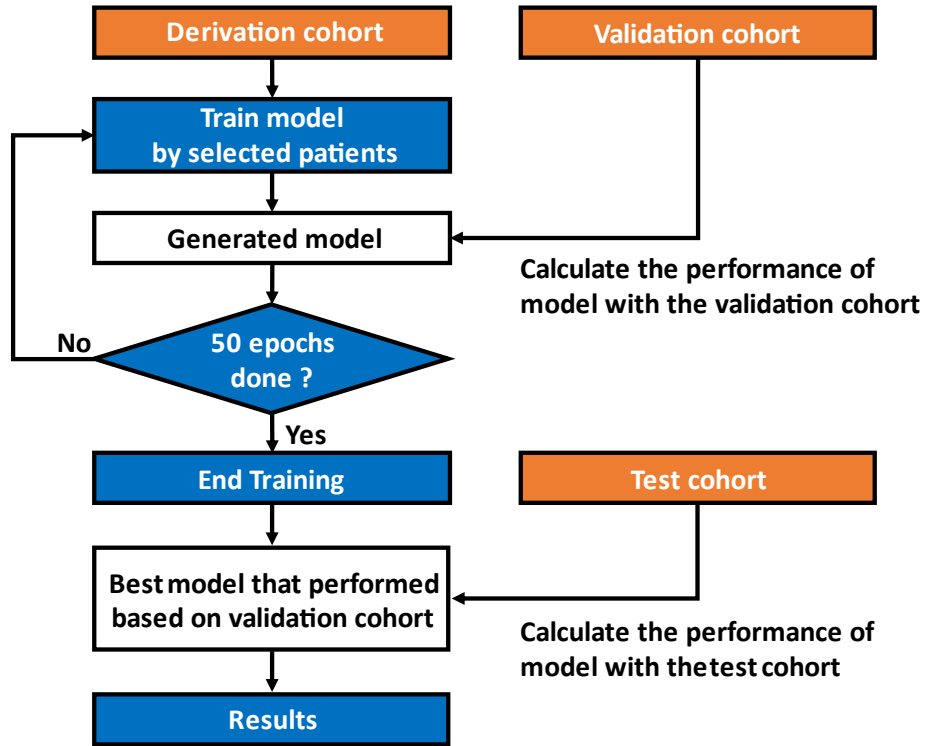
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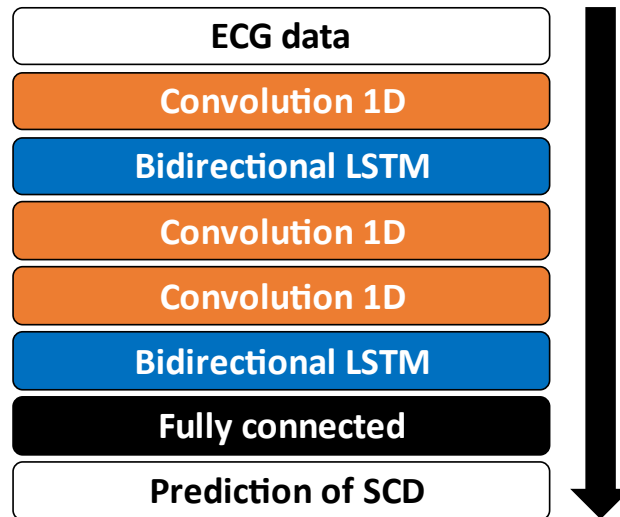
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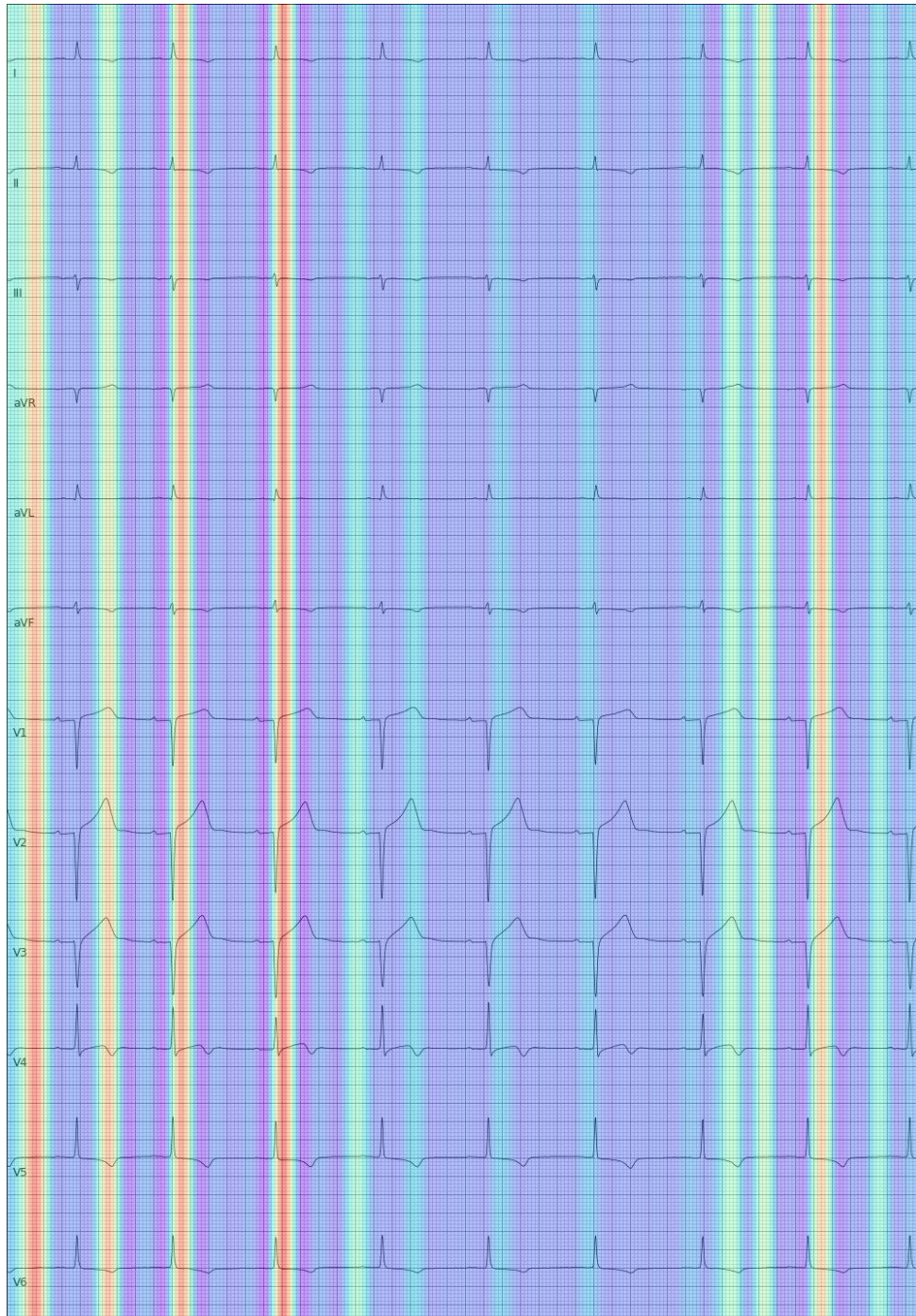
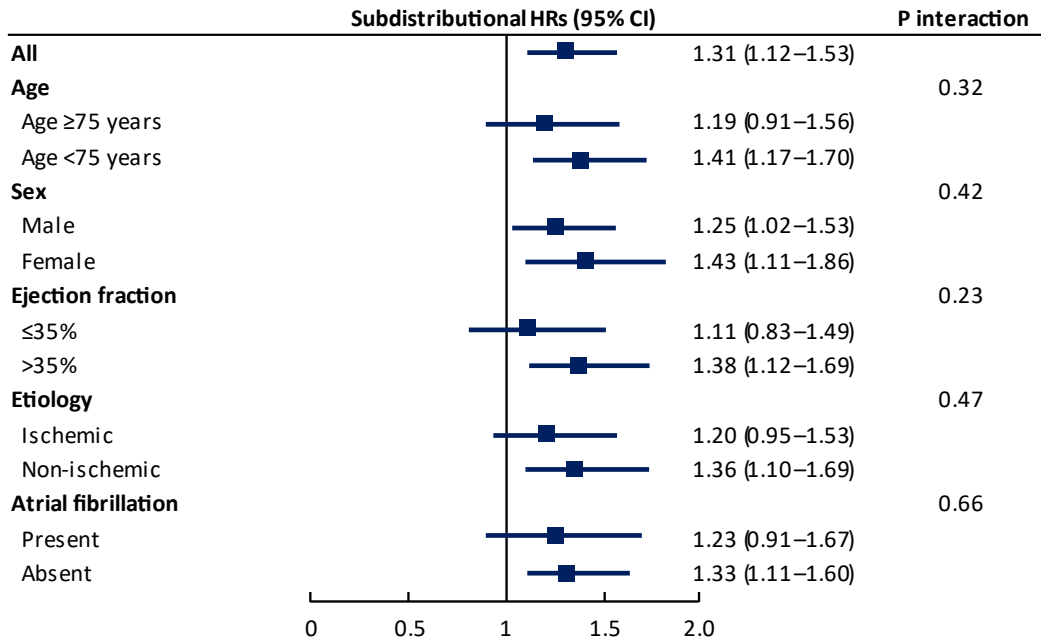
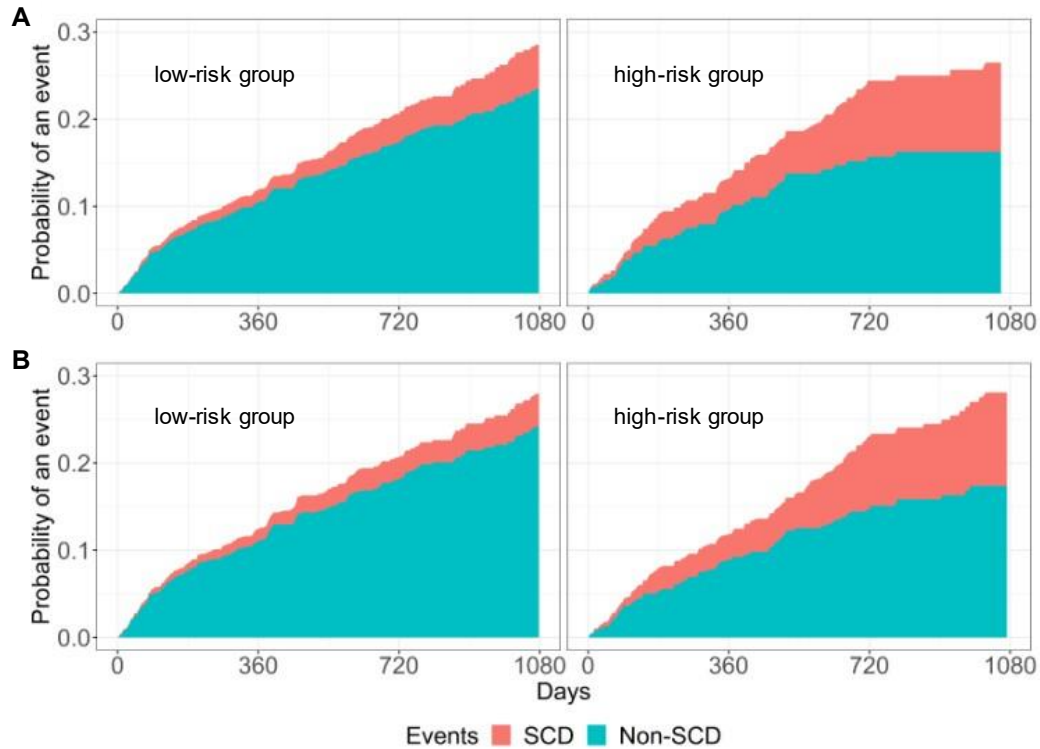


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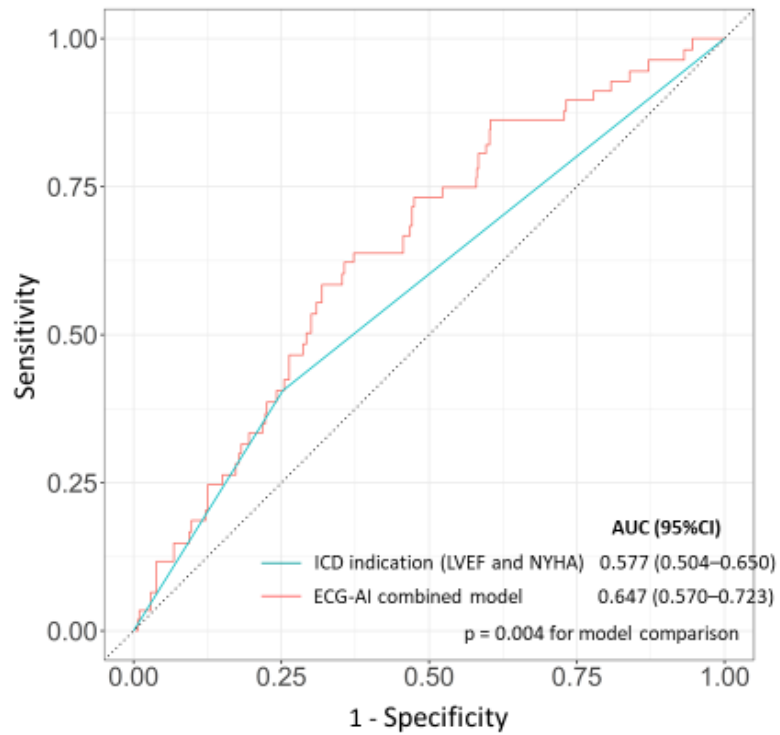
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