ORIGINAL ARTICLE

Electrocardiography-Based Artificial Intelligence Algorithm Aids in Prediction of Long-term Mortality After Cardiac Surgery

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Abstract

Objective: To assess whether an electrocardiography-based artificial intelligence (AI) algorithm developed to detect severe ventricular dysfunction (left ventricular ejection fraction [LVEF] of 35% or below) independently predicts long-term mortality after cardiac surgery among patients without severe ventricular dysfunction (LVEF>35%).

Methods: Patients who underwent valve or coronary bypass surgery at Mayo Clinic (1993-2019) and had documented LVEF above 35% on baseline electrocardiography were included. We compared patients with an abnormal vs a normal AI-enhanced electrocardiogram (AI-ECG) screen for LVEF of 35% or below on preoperative electrocardiography. The primary end point was all-cause mortality.

Results: A total of 20,627 patients were included, of whom 17,125 (83.0%) had a normal AI-ECG screen and 3502 (17.0%) had an abnormal AI-ECG screen. Patients with an abnormal AI-ECG screen were older and had more comorbidities. Probability of survival at 5 and 10 years was 86.2% and 68.2% in patients with a normal AI-ECG screen vs 71.4% and 45.1% in those with an abnormal screen (log-rank, $P<.01$). In the multivariate Cox survival analysis, the abnormal AI-ECG screen was independently associated with a higher all-cause mortality overall (hazard ratio [HR], 1.31; 95% CI, 1.24 to 1.37) and in subgroups of isolated valve surgery (HR, 1.30; 95% CI, 1.18 to 1.42), isolated coronary artery bypass grafting (HR, 1.29; 95% CI, 1.20 to 1.39), and combined coronary artery bypass grafting and valve surgery (HR, 1.19; 95% CI, 1.08 to 1.32). In a subgroup analysis, the association between abnormal AI-ECG screen and mortality was consistent in patients with LVEF of 35% to 55% and among those with LVEF above 55%.

Conclusion: A novel electrocardiography-based AI algorithm that predicts severe ventricular dysfunction can predict long-term mortality among patients with LVEF above 35% undergoing valve and/or coronary bypass surgery.

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Artificial intelligence (AI) techniques have grown rapidly in the past decade.[1] In cardiovascular medicine, novel AI algorithms have been used to aid in processing of cardiac imaging, in predicting of adverse cardiovascular events, and in discerning subtle rhythm or myocardial and valve disorders.[1-6] Despite the promising potential of AI tools, their use in estimating risk and outcomes in the cardiac surgery population remained limited.[7] Yet, the growing intricacy and cost of surgical procedures and the increasing complexity of patients referred for surgery have emphasized the need for better selection of patients and risk prediction tools. We hypothesized that AI algorithms may be able to predict long-term outcomes using universally performed preoperative tests such as the electrocardiogram (ECG). The AI-enhanced ECG (AI-ECG) algorithm for severe left ventricular dysfunction has previously demonstrated an excellent

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ability to identify patients with reduced left ventricular ejection fraction (LVEF≤35%) using a single 12-lead surface ECG.[6] Furthermore, patients with an LVEF above 35% who had an abnormal AI-ECG screen with use of this algorithm have shown an increased likelihood for development of reduced LVEF over time.[6] We hypothesized that abnormal AI-ECG recordings among cardiac surgery patients without severe left ventricular dysfunction may reflect advanced remodeling or underlying myocardial disease that confers worse outcomes after surgery. Hence, in this study, we examined whether an abnormal AI-ECG screen for left ventricular dysfunction predicts long-term mortality in a large consecutive cohort of patients who had a baseline LVEF above 35% before coronary artery bypass and/or valve surgery.

METHODS

Data Collection and Selection of Patients

The study flow diagram is shown in Figure 1. Patients who underwent coronary artery bypass grafting (CABG), valve surgery, or both and had an LVEF above 35% between January 1, 1993, and August 30, 2019, at Mayo Clinic in Rochester were identified. To test the generalizability of our results, we excluded patients for whom ECGs were originally used in the creation of the AI-ECG algorithm for severe ventricular dysfunction, even though the model did not have the long-term outcomes during training. The algorithm was applied to the most recent ECG the patients had within the 30 days before surgery. Preoperative LVEF data were extracted from the most recent echocardiogram performed within 90 days before surgery. Baseline characteristics and in-hospital, 30-day, and long-term mortality were extracted from the Mayo Clinic cardiac surgery database. This database, by an iterative process, uses the National Death Registry to update all-cause mortality data of all patients undergoing cardiac surgery at the clinic.

Overview of the AI Model

Details of the AI-ECG reduced EF model have been previously described. Briefly, a convolutional neural network trained with Keras with a TensorFlow (Google) backend was developed and validated to screen patients with LVEF from a single 12-lead surface ECG. The outcome used to train the model was binary (LVEF≤35% or LVEF > 35%). However, the network output is a continuous number between 0 and 1 that represents the probability of the binary outcome (LVEF≤35%). A probability output above 25.6% was selected to convey a high probability of reduced LVEF (area under the curve of 0.93). The sensitivity, specificity, and accuracy of the model were 86.3%, 85.7%, and 85.7%, respectively.[6,8]

Outcomes Measures

Patients were classified into 2 groups based on the outcomes of this AI-ECG algorithm screen on preoperative electrocardiography: group 1 had a normal AI-ECG screen for LVEF of 35% or below, and group 2 had an abnormal AI-ECG screen for LVEF of 35% or below. The main end point of the study was all-cause mortality. This end point was assessed for patients with normal vs abnormal AI-ECG screens for the overall cohort and for subgroups of patients who underwent CABG only, valve surgery only, or combined CABG and valve surgery. Additional subgroup analyses were performed to confirm the results in patients with preoperative LEVF of 35% to 55% and those with LVEF above 55%.

Statistical Analyses

Baseline characteristics were reported as means and standard deviations for continuous variables and compared using the Kruskall-Wallis test. Categorical variables were reported as numbers and percentages and compared using Pearson χ^2 test. Survival curves were constructed using the Kaplan-Meier method for patients with a normal vs an abnormal AI-ECG screen. To adjust for the differences in baseline characteristics, we built univariate and multivariate Cox proportional hazards models. All variables with a *P* value of less than .20 in the univariate model were included in the multivariate model. Hazard ratios (HRs) were reported with 95% CIs. Statistical significance was inferred at a *P* value of .05 or less.

Analyses were performed using the Python lifelines package version 25.3 and SciPy 1.5.0. Mayo Clinic Institutional Review Board approved the study.

RESULTS

A total of 20,627 patients who underwent cardiac surgery at Mayo Clinic between January 1993 and August 2019 were included. Of those, 9331 (45.2%) had isolated CABG, 7764 (37.6%) had isolated valve surgery, and 3532 (17.1%) had combined CABG and valve surgery. In the overall cohort, 17,125 (83.0%) patients had a normal AI-ECG screen and 3502 (17.0%) had an abnormal AI-ECG screen. Patients who had an abnormal AI-ECG screen were older (67.1±12.3 years vs 69.5±11.5 years; P<.001) and were more likely to be female (31.1% vs 27.4%; P<.001). They also had a distinctive clinical risk profile compared with patients who had a normal AI-ECG screen (Table 1). Differences in baseline characteristics of patients with a normal vs an abnormal AI-ECG screen for the subcohorts of isolated CABG, isolated valve, and combined CABG/valve surgery patients are outlined in Supplemental Tables 1 to 3 (available online at http://www.mayoclinicproceedings.org).

The abnormal AI-ECG screen was associated with significantly lower long-term survival in the overall cohort. Probability of survival at 5 and 10 years was 86.2% and 68.2% in the normal AI-ECG screen group vs 71.4% and 45.1% in the abnormal AI-ECG screen group, respectively (Figure 2A). In the Kaplan-Meier survival analysis, the higher mortality in patients with an abnormal AI-ECG screen was consistent among patients who had isolated CABG (5-year survival, 89% vs 75.8%; 10-year survival, 72.1% vs 50.9%), isolated valve (5-year survival, 87% vs 69.9%; 10-year survival, 70.9% vs 45.6%), and combined CABG/valve surgery (5-year survival, 76.1% vs 64.8%; 10-year survival, 50.8% vs 33.2%; Figure 2B-D) and among patients with baseline LVEF of 35% to 55% (5-year survival, 82.4% vs 70.8%; 10-year survival, 61.0% vs 43.2%) and those with LVEF above 55% (5-year survival, 87% vs 72.3%; 10-year survival, 69.9% vs 48.1%; Figure 3; log-rank, P<.01).

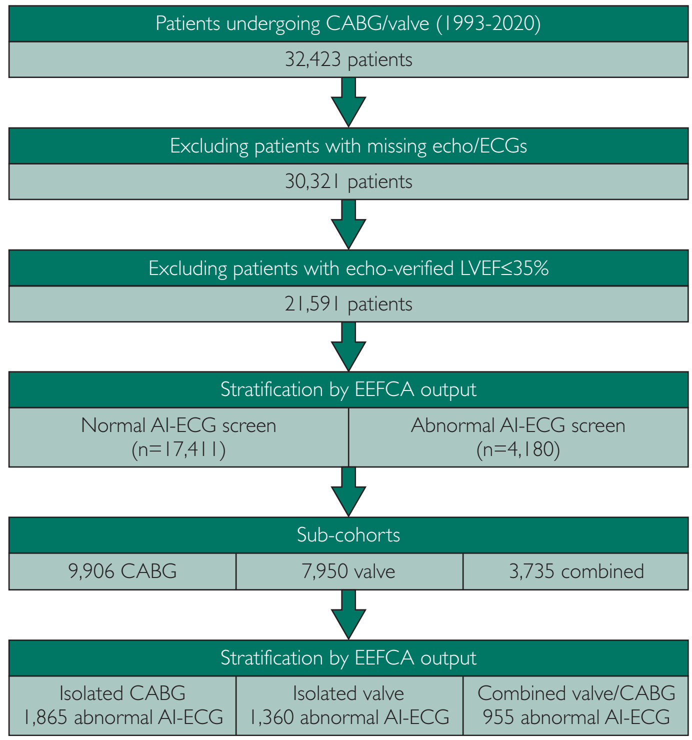


FIGURE 1. Study flow chart. AI-ECG, artificial intelligence−enhanced electrocardiogram; CABG, coronary artery bypass grafting; ECGs, electrocardiograms; AI-ECG reduced EF model, artificial intelligence-electrocardiogram reduced ejection fraction model; LVEF, left ventricular ejection fraction.

In the univariate Cox regression analysis (Table 2), the strongest predictors of long-term mortality after cardiac surgery were long-term dialysis (HR, 3.37; 95% CI, 2.89 to 3.93), baseline congestive heart failure (HR, 2.31; 95% CI, 2.20 to 2.41), and chronic lung disease (HR, 2.01; 95% CI, 1.89 to 2.14). An abnormal AI-ECG screen was also associated with increased long-term mortality (HR, 1.90; 95% CI, 1.81 to 1.98) in the overall cohort. Those predictors were consistent in the subgroups of isolated CABG, valve surgery, and combined CABG/valve surgery as well (Supplemental Tables 4 to 6, available online at http://www.mayoclinicproceedings.org). In the multivariate Cox regression model, an abnormal AI-ECG screen remained independently associated with a higher all-cause mortality in the overall group (HR, 1.31; 95% CI,

TABLE 1. Baseline Characteristics of the Study Cohort[a,b]

Baseline characteristics (N=21,591)	AI-ECG screen normal (n=17,411)	AI-ECG screen abnormal (n=4180)	*P* value
Age (y)	67.1 (12.3)	69.6 (11.5)	<.001
Female sex	5414 (31.1)	1146 (27.4)	<.001
Body mass index (kg/m^2)	28.9 (5.6)	29.1 (5.9)	.26
Smoking			<.001
Never smoker	6847 (39.3)	1472 (35.2)	
Former smoker	7192 (41.3)	1934 (46.3)	
Current smoker	1645 (9.4)	464 (11.1)	
Diabetes	3946 (22.7)	1395 (33.4)	<.001
Dyslipidemia	13,439 (77.2)	3086 (73.8)	<.001
Hypertension	11,912 (68.4)	3079 (73.7)	<.001
Family history of coronary disease	4954 (28.5)	1326 (31.7)	<.001
Peripheral vascular disease	2248 (12.9)	854 (20.4)	<.001
Coronary artery disease	11,919 (68.5)	3267 (78.2)	<.001
Cerebrovascular disease	2380 (13.7)	831 (19.9)	<.001
Carotid stenosis	266 (1.5)	63 (1.5)	.98
Arrhythmia	2301 (13.2)	1196 (28.6)	<.001
Atrial fibrillation	1935 (11.1)	1006 (24.1)	<.001
Ventricular tachycardia or fibrillation	321 (1.8)	198 (4.7)	<.001
Prior pacemaker	63 (0.4)	42 (1.0)	<.001
Congenital heart disease	550 (3.2)	146 (3.5)	.29
Previous valve procedure	905 (5.2)	507 (12.1)	<.001
Aortic aneurysm	580 (3.3)	193 (4.6)	<.001
Thoracic aortic disease	58 (0.3)	15 (0.4)	.91
Endocarditis	511 (2.9)	204 (4.9)	<.001
Chronic heart failure	2087 (12.0)	1464 (35.0)	<.001
LVEF (%)	61.6 (9.0)	50.8 (10.5)	<.001
Cardiogenic shock	88 (0.5)	55 (1.3)	<.001
History of myocardial infarction	4177 (24.0)	1913 (45.8)	<.001
Chronic lung disease	1409 (8.1)	484 (11.6)	<.001
Sleep apnea	788 (4.5)	145 (3.5)	<.01
Home oxygen therapy	24 (0.1)	10 (0.2)	.21
Dialysis dependence	132 (0.8)	122 (2.9)	<.001
Liver disease	70 (0.4)	17 (0.4)	.93
Surgery type			<.001
CABG only	8041 (46.1)	1865 (44.6)	
Valve only	6590 (37.8)	1360 (32.5)	
Combined CABG/valve	2780 (16.0)	955 (22.8)	
Alive at discharge	17,185 (98.7)	4041 (96.7)	<.001
Alive at 30 days	17,138 (98.4)	4042 (96.7)	<.001
30-day readmission	1098 (6.3)	346 (8.3)	<.001

[a]AI-ECG, artificial intelligence–enhanced electrocardiogram; CABG, coronary artery bypass grafting; LVEF, left ventricular ejection fraction.

[b]Categorical variables are presented as number (percentage). Continuous variables are presented as mean (standard deviation).

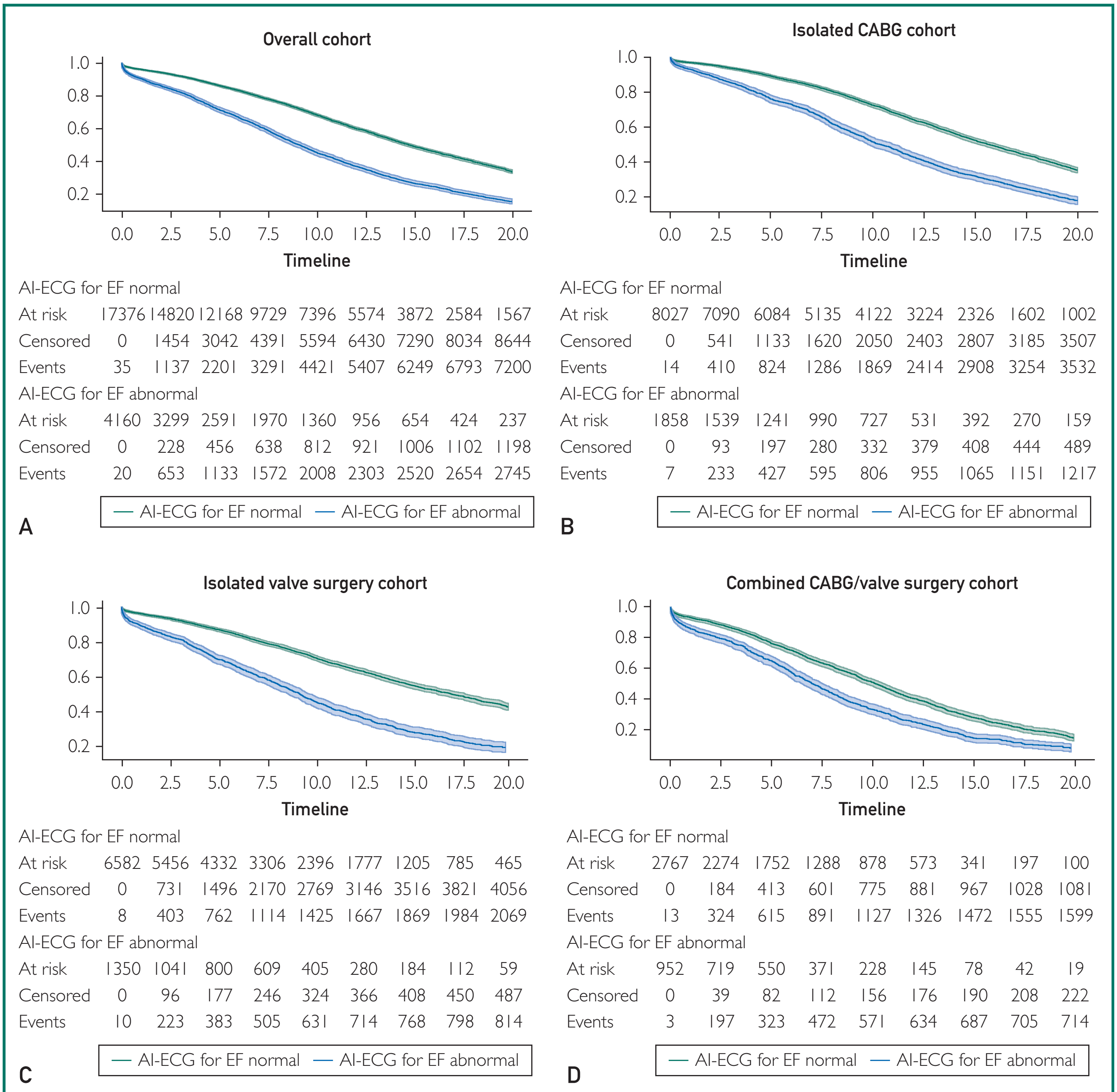
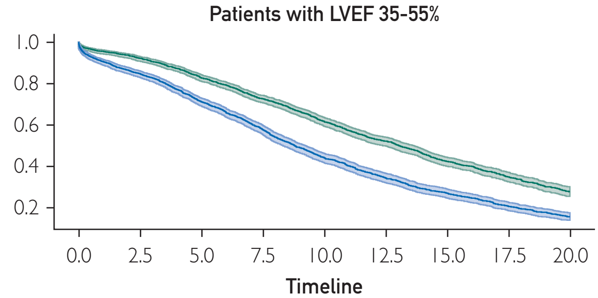


FIGURE 2. Kaplan-Meier survival analysis showing differences in long-term mortality after cardiac surgery of patients with normal vs abnormal artificial intelligence−enhanced electrocardiogram (AI-ECG) screen (A) in the overall cohort, (B) in patients who had isolated coronary artery bypass grafting (CABG), (C) in patients who had isolated valve surgery, and (D) in patients who had combined CABG/valve surgery. EF, ejection fraction.

1.24 to 1.37) and in the subgroups of isolated valve surgery (HR, 1.30; 95% CI, 1.18 to 1.42), isolated CABG (HR, 1.29; 95% CI, 1.20 to 1.39), and combined CABG/valve surgery (HR, 1.19; 95% CI, 1.08 to 1.32).

DISCUSSION

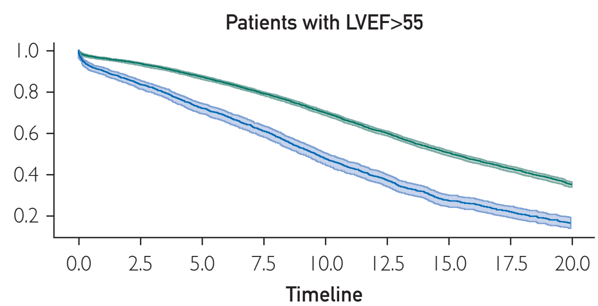
Risk prediction is an integral part of cardiac surgery practice.[9] However, validated risk scores (eg, Society of Thoracic Surgeons predicted risk of mortality calculator) have



AI-ECG for EF normal									
At risk	3072	2630	2162	1732	1315	1002	675	443	262
Censored	0	204	413	590	752	870	1016	1137	1234
Events	8	246	505	758	1013	1208	1389	1500	1584
AI-ECG for EF abnormal									
At risk	2533	2023	1565	1164	802	563	396	253	145
Censored	0	129	273	384	475	538	584	636	689
Events	10	391	705	995	1266	1442	1563	1654	1709

— AI-ECG for EF normal — AI-ECG for EF abnormal

A



AI-ECG for EF normal									
At risk	14304	12190	10006	7997	6081	4572	3197	2141	1305
Censored	0	1250	2629	3801	4842	5560	6274	6897	7410
Events	27	891	1696	2533	3408	4199	4860	5293	5616
AI-ECG for EF abnormal									
At risk	1627	1276	1026	806	558	393	258	171	92
Censored	0	99	183	254	337	383	422	466	509
Events	10	262	428	577	742	861	957	1000	1036

— AI-ECG for EF normal — AI-ECG for EF abnormal

B

FIGURE 3. Kaplan-Meier survival analysis showing differences in long-term mortality after cardiac surgery of patients with normal vs abnormal artificial intelligence−enhanced electrocardiogram (AI-ECG) screen stratified by left ventricular ejection fraction (LVEF) in patients with (A) LVEF of 35% to 55% and (B) LVEF above 55%. EF, ejection fraction.

mostly focused on predicting short-term (30-day) morbidity and mortality after common cardiac surgical procedures. Nonetheless, the increasing complexity of patients referred for surgery and of the surgical procedures themselves has fueled a growing interest in recognizing independent predictors of midterm and long-term outcomes to optimize selection of patients, clinical outcomes, and resource utilization.[9,10] Unfortunately, large-scale data on prediction of long-term mortality after cardiac surgery remain scarce.[11-14] A few studies identified traditional risk factors, such as age, vascular disease, heart failure, chronic pulmonary disease, diabetes mellitus, renal failure, and reduced LVEF, as independent predictors of poor long-term outcomes after CABG. Data encompassing other cardiac surgery procedures (eg, valve surgery) and data on novel laboratory- or imaging-based predictors are lacking. In addition, attempts to use AI algorithms in improving risk prediction after surgery were limited to predicting short-term mortality, included only traditional risk factors, and were associated with a modest incremental prognostic value.[7]

Our study documented an independent prognostic value of an AI-ECG algorithm in predicting long-term all-cause mortality after cardiac surgery. The algorithm was originally developed and validated to detect the presence of severe left ventricular dysfunction (LVEF≤35%) in large unselected cohorts of patients who had an ECG performed for a clinical indication. In this analysis, however, this novel algorithm demonstrated an incremental prognostic value beyond traditional risk factors in the prediction of long-term mortality in patients undergoing common cardiac surgical procedures. In the multivariable Cox regression survival analysis, an abnormal AI-ECG screen was associated with 30% increase in long-term mortality after valve or coronary bypass surgery. This excess mortality was consistent among patients with LVEF of 35% to 55% and among those with LVEF above 55%. To our knowledge, this is the first large-scale study that illustrates the utility of AI algorithms in improving prediction of poor outcomes after cardiac surgery using a single preoperative ECG. Because this algorithm used a routine, noninvasive, and inexpensive test (ie, ECG) that is routinely obtained preoperatively, it has the potential to be applied widely once it is externally

TABLE 2. Univariate and Multivariate Cox Survival Analysis

Cox regression survival analysis	Univariate analysis		Multivariate analysis concordance index = .74	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age (per 5-year increase)	1.42 (1.40-1.43)	<.001	1.39 (1.38-1.41)	<.001
Female sex	1.28 (1.23-1.33)	<.001	1.08 (1.04-1.13)	<.001
BMI (per 5-kg/m^2 increase)	1.02 (1.00-1.04)	.03	1.06 (1.04-1.08)	<.001
Diabetes	1.61 (1.55-1.68)	<.001	1.37 (1.31-1.44)	<.001
Dialysis	3.37 (2.89-3.93)	<.001	3.23 (2.76-3.77)	<.001
Hypertension	1.57 (1.50-1.64)	<.001	1.08 (1.03-1.13)	<.01
Chronic lung disease	2.01 (1.89-2.14)	<.001	1.53 (1.44-1.64)	<.001
Sleep apnea	0.92 (0.74-1.15)	.48	—	—
Peripheral vascular disease	1.85 (1.76-1.94)	<.001	1.33 (1.27-1.40)	<.001
History of cerebrovascular disease	1.90 (1.80-1.99)	<.001	1.28 (1.21-1.34)	<.001
Previous sternotomy	1.33 (1.23-1.43)	<.001	1.24 (1.14-1.34)	<.001
History of myocardial infarction	1.36 (1.31-1.42)	<.001	1.15 (1.10-1.20)	<.001
History of heart failure	2.31 (2.20-2.41)	<.001	1.51 (1.43-1.58)	<.001
History of arrhythmia	1.79 (1.71-1.87)	<.001	1.21 (1.15-1.27)	<.001
LVEF (per 5% decrease)	1.09 (1.08-1.10)	<.001	1.03 (1.02-1.04)	<.001
Abnormal AI-ECG screen	**1.90 (1.81-1.98)**	**<.001**	**1.31 (1.24-1.37)**	**<.001**

AI-ECG, artificial intelligence–enhanced electrocardiogram; BMI, body mass index; HR, hazard ratio; LVEF, left ventricular ejection fraction.

validated. In our practice, outputs from multiple AI algorithms are provided automatically in electronic medical records with every ECG to supplement clinical data. Other clinical investigations are underway to determine whether the information provided by these algorithms can improve diagnosis, decision-making, and clinical outcomes.

The mechanism by which this novel AI-ECG algorithm was able to gain an independent predictive power cannot be fully ascertained, considering the retrospective nature of the analysis. One hypothesis is that properly trained neural networks were able to detect subtle myocardial dysfunction beyond what is readily visible on echocardiography. This is supported by the prior observation by Attia et al,[8] who showed that an abnormal AI-ECG screen for severe ventricular dysfunction among patients with echocardiographic LVEF above 35% confers a 4-fold increase in the risk (HR, 4.1; 95% CI, 3.3 to 5.0) of developing future ventricular dysfunction. However, we are unable to confirm this hypothesis in this cohort because follow-up echocardiograms were not systematically collected at comparable intervals after surgery and access to echocardiographic data before 2001 is limited. Yet, the strong and persistent association of the abnormal AI-ECG screen with all-cause mortality in this analysis remains important clinicaly regardless of the specific underlying mechanism. In addition, we speculate that surface electrocardiography might be able to detect the presence of other risk factors that have been shown to be associated with mortality (eg, long-term pressure load on the left ventricle in hypertensive patients). However, corroborating these speculations requires further investigations.

Although we used an AI-ECG algorithm that was developed for a specific purpose (predicting severe ventricular dysfunction) in the general population, this analysis provides a proof of concept that electrocardiography-based AI algorithms might provide prognostic value among patients undergoing cardiac surgery. Considering these data and the wide availability of ECGs, additional research investigations can focus on constructing specific electrocardiography-based AI models to assess whether 12-lead surface ECGs can provide incremental predictive value for a wide range of postoperative outcomes, such as cardiac mortality, myocardial recovery, and atrial fibrillation. In addition, the utility of such models in predicting outcomes after other major cardiac and noncardiac interventions deserves further investigations.

Our study has a number of limitations. First, this is a retrospective study from a tertiary high-volume center and hence is subject to the known limitations of retrospective analyses, including selection bias and generalizability of results. Second, during the development and validation of this algorithm, only patients with both available ECGs and available echocardiograms within the prespecific window were included. It is possible that the performance of this algorithm will vary among patients without prior echocardiography because of the lower prevalence of reduced ejection fraction in patients without symptoms that would otherwise prompt echocardiography. Third, there were variations in ECGs among some patients who had several ECGs before surgery. Whether this represents a limitation of the algorithm or just a difference in myocardial disease state (compensated vs not) remains to be investigated. Fourth, a limitation of the algorithm and AI research at large is the inability to provide explanation for the pathophysiologic basis that led to outcome. One plausible explanation for the higher mortality in the group with an abnormal AI-ECG screen is the development of left ventricular dysfunction in these patients during follow-up. However, this hypothesis could not be confirmed in this study as data on the temporal trends in LVEF and cause of death are not available. However, the strong association between an abnormal AI-ECG screen for severe ventricular dysfunction and mortality remains prognostically important regardless of the underlying mechanism of this association. Finally, this model was only internally validated. External validation of this algorithm is necessary to confirm the generalizability of its prognostic value.

CONCLUSION

A novel electrocardiography-based AI algorithm that predicts left ventricular dysfunction from a single 12-lead ECG can predict long-term mortality after cardiac surgery and hence may aid in risk stratification of patients referred for surgery.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **AI,** artificial intelligence; **CABG,** coronary artery bypass grafting; **ECG,** electrocardiogram; **HR,** hazard ratio; **LVEF,** left ventricular ejection fraction

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