Variable selection methods for multiple regressions influence the parsimony of risk prediction models for cardiac surgery

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ABSTRACT

Objective: To compare the impact of different variable selection methods in multiple regression to develop a parsimonious model for predicting postoperative outcomes of patients undergoing cardiac surgery.

Methods: Data from 84,135 patients in the Australian and New Zealand Society of Cardiac and Thoracic Surgeons registry between 2001 and 2014 were analyzed. Primary outcome was 30-day-mortality. Mixed-effect logistic regressions were used to build the model. Missing values were imputed by the use of multiple imputations. The following 5 variable selection methods were compared: bootstrap receiver-operative characteristic (ROC), bootstrap Akaike information criteria, bootstrap Bayesian information criteria, and stepwise forward and stepwise backward methods. The final model's prediction performance was evaluated by the use of Frank Harrell's calibration curve and using a multifold cross-validation approach.

Results: Stepwise forward and backward methods selected same set of 21 variables into the model with the area under the ROC (AUC) of 0.8490. The bootstrap ROC method selected 13 variables with AUC of 0.8450. Bootstrap Bayesian information criteria and Akaike information criteria respectively selected 16 (AUC: 0.8470) and 23 (AUC: 0.8491) variables. Bootstrap ROC model was selected as the final model which showed very good discrimination and calibration power.

Conclusions: Clinical suitability in terms of parsimony and prediction performance can be achieved substantially by using the bootstrap ROC method for the development of risk prediction models. (J Thorac Cardiovasc Surg 2017;153:1128-35)

The bootstrap receiver operating characteristic method provides parsimony of risk prediction model.

Central Message

The balance between parsimony and performance can be improved using the bootstrap method with receiver operating characteristics for developing risk prediction models.

Perspective

The trade-off between parsimony and performance is a major challenge in risk prediction modeling. Different approaches to variable selection may be an avenue for improving the parsimony of a cardiac surgical risk prediction model. This work compared the clinical suitability of models generated by the use of different variable selection methods with regard to parsimony and performance to predict 30-day mortality.

See Editorial Commentary page 1136.

In the past decades, the field of cardiac surgery has made significant progress in the development of risk prediction models to enable outcome prediction and clinical quality monitoring. National cardiac surgical registries have been established in many countries, and many have developed

risk prediction models suitable for local populations.¹⁻³ The aim of these models was to provide an estimate of postoperative mortality risk based on preoperative risk factors.

In risk prediction modeling of cardiac surgery, outcomes data are adjusted for preoperative risk factors. When so many variables are included in the model, however, the accuracy along with parsimony of the model may be compromised.⁴ The principle of parsimony states that

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Abbreviations and Acronyms

AIC	= Akaike information criteria
ANZSCTS	= Australian and New Zealand Society of Cardiac and Thoracic Surgeons Registry
AUC	= Area under ROC curve
BIC	= Bayesian information criteria
CI	= confidence interval
ROC	= receiver operating characteristic

simpler explanations are preferred over more complex explanations.⁵ A parsimonious model is computationally simpler for the clinician to implement in day-to-day practice.⁵ A smaller number of variables in a risk prediction model makes the model simpler to use. Furthermore, when many variables are included in the model, the burden of clinical staff is increased considerably in regard to data collection, which can compromise data quality as well. The prevalence of cases with missing data also may increase with increasing number of variables in the model. If a simple model can explain a phenomenon with a similar level of accuracy compared with a complex model, the former model should be preferred on the ground of parsimony, unless the complex model outperforms the former.^{6,7}

Several methodologic approaches are currently in practice for identifying the predictor variables for risk prediction models. These methods excel in different tasks and have their inherent limitations. Automated variable selection methods are used widely for model development.⁸ Automated variable selection, forward selection, and backward elimination are very easy to use and available in most statistical software packages. Although popularly used, a number of concerns have been identified with the application of these methods in the field of risk prediction modeling.⁹

Bootstrap resampling is another approach used for variable selection in risk prediction modeling.¹⁰⁻¹² Usually bootstrap resampling is used in conjunction with criteria like Akaike information criteria (AIC),¹³ Bayesian information criteria (BIC),¹⁴ and receiver operating characteristics (ROCs)¹⁵ to develop models; however, the question of whether developing models using bootstrapping method in combination with these criteria improves the parsimony of a risk prediction model remains unclear. Therefore, comparison of different methodologic approaches for variable selection may be an avenue for improving the parsimony of risk prediction models.

The aim of this paper was to compare the clinical suitability of risk prediction models generated by the use of different variable selection methods with regard to their

parsimony and performance to predict postoperative outcomes of cardiac surgery patients.

METHODS**Australian and New Zealand Society of Cardiac and Thoracic Surgeons Registry (ANZSCTS) Database**

The ANZSCTS collects information on adult patients undergoing cardiac surgery in 28 hospitals across Australia. The database collects 287 preoperative, intraoperative, and postoperative variables via internationally standardized data definitions (Table E1).³ The data collection and its audit methods have been discussed elsewhere.^{3,16} Current analysis included information of 84,135 patients who underwent cardiac surgery between 2001 and 2014. Of them, 63,523 patient records between 2001 and 2012 were used for model development and 20,625 patient records between 2013 and 2014 were used for validation. The primary outcome variable for this study was 30-day mortality.¹⁷ The variable “New York Heart Association classification” (5.28%) had the highest missing data, followed by “ejection fraction” (3.07%), “procedure type” (1.24%), and “number of diseased vessels” (1.11%). The remaining predictors had <1% missing observations (Table E2).

Plausible Predictor Identification and Model Development Methods

Of 287 variables (data field) in the ANZSCTS registry, 101 were preoperative variables. These preoperative variables included administrative data and several stems of variables. On the basis of extensive literature review on cardiac surgery risk prediction models and clinical judgment, a total of 52 variables were identified primarily as preoperative risk factors. With the use of bivariate mixed-effect logistic regression, 33 variables finally were identified as plausible risk factors for 30-day mortality.

Multiple imputation of missing value was performed with the imputation by chained equations method along with multivariable mixed-effect logistic regression. Data were “filled in” with imputed values generated by the use of a specified regression model. The process was repeated 3 times to generate 3 completed datasets. Studies have shown that repeating imputation 3 times is sufficient for data with less missing data (<20%).¹⁸ The mixed-effect logistic regression was fitted separately on each of the imputed dataset. The results were then pooled into an aggregated estimate following Rubin’s rule¹⁹ through the MIM estimation command option in Stata 14.²⁰ Multivariable mixed-effect logistic regression was used for the risk prediction. The multilevel modeling accounts for potential between-hospital variations.²¹ The first order interaction effect between clinically relevant risk factors was investigated.

Nonlinearity of continuous predictors (age, body mass index, and estimated glomerular filtration rate) was addressed by fitting fractional polynomial in the mixed-effect logistic regression model.^{22,23} Sensitivity analysis was performed for nonlinear term in the model. Little improvement in discrimination and calibration was seen with inclusion of nonlinear terms in the model; hence, linear terms of the continuous variables were kept in the final model to keep the model simple and user friendly. The following 5 variable selection methods were compared: (1) bootstrap along with ROC, (2) bootstrap along with AIC, (3) bootstrap along with BIC, (4) stepwise forward selection method, and (5) stepwise backward elimination method. A model with all 33 variables also was developed.

Bootstrap Model Selection

A bootstrap sample of the same size of the original sample was drawn from each of the 3 imputed datasets. The 33 plausible risk factors were entered into the mixed-effect logistic regression and were applied to the bootstrap sample to test the significance of the variables. A variable with

P value of less than or equal to .05 was considered as significant. The process was repeated 1000 times, and the percentage of times that each variable appeared as significant in 1000 bootstraps (bootstrap coverage) in the imputed datasets was recorded. Bootstrap coverage of each predictor in 3 imputed dataset was averaged to generate an overall coverage of individual predictors. The predictors were then ranked depending on the overall bootstraps coverage.²⁴

Fourteen plausible models were developed from variables that were significant in at least 50% of the bootstrap samples.²⁵ Model 1 comprised 10 predictors that appeared as significant in 100% of bootstrap samples. Then, 13 subsequent models were generated through adding one variable at a time of decreasing rank according to the bootstrap coverage. The area under ROC curve (AUC), AIC, and BIC values were calculated for all of these 14 models. Both AIC and BIC methods select the model with their lowest values. Bootstrap ROC method selects the model with the greatest AUC value.

Automated Model Selection

Variables in the forward and backward logistic regression were selected for the imputed data as suggested by Wood and colleagues.²⁴ The selected variables were then entered into the mixed-effect logistic regression and the model was estimated with multiple imputation, MIM estimation command option, in Stata 14.²⁰ The AUC, AIC, and BIC values were calculated for final automated model.

Discrimination and Calibration of the Models

Selected models' prediction performance was evaluated by the use of discrimination and calibration powers. Model discrimination was evaluated with AUC. The calibration was evaluated with a decile-decile plot of the observed and predicted 30-day mortality. To calculate the calibration intercept and slope parameters, a linear regression model was fitted with the deciles of observed outcome as the dependent variable and the deciles of predicted outcome as the independent variable. Calibration of final model was also assessed using the method suggested by Frank Harrell with Regression Modeling Strategies (RMS) package in R statistical software.⁷

External Validation of the Final Model

External validation of the final model was done on the validation dataset comprising patients treated during 2013 to 2014.

Ethical Approval

The institutional review board of each participating hospital approved the use of these databases for research (Alfred HREC:262/09). The ANZSCTS database registry approved collection of patient data via opt-out consent approach (MUHREC:CF08/0322-2008000065). The study received Ethical approval from Monash University, Standing Committee on Ethics in Research Involving Humans (SCERH) (MUHREC:CF14/1117-2014000476).

RESULTS

A total of 33 preoperative variables were identified as potential predictors (Tables E3 and E4). There was no first-order interaction effect between these predictors. The percentage of times each of these candidate variables appeared as significant in the multiple mixed-effect logistic regression models in 1000 bootstraps were summarized in Table 1.

Figure 1 shows the AUC of 14 bootstrap models plotted against number of variables based on bootstrap coverage increment. The model with 10 predictors those appeared

TABLE 1. Summary of appearance of variables as independent predictors of mortality following cardiac surgery in bootstrap resampling

No.	Predictors	%*
1	Age	100.0
2	Sex	100.0
3	Previous cardiac surgery	100.0
4	Peripheral vascular disease	100.0
5	Stroke	100.0
6	Glomerular filtration rate	100.0
7	Infective endocarditis	100.0
8	Urgency of procedure	100.0
9	Type of procedure	100.0
10	Ejection fraction	100.0
11	Inotropic medication	99.93
12	Angina	99.83
13	NYHA class	99.57
14	Dialysis	90.17
15	Congestive heart failure	89.80
16	Shock	87.13
17	Myocardial infarction	86.27
18	Resuscitation	86.80
19	Arrhythmia	81.00
20	Left main disease <50%	70.77
21	Hypertension	68.00
22	Respiratory disease	56.00
23	Hypercholesterolemia	55.63
24	Cerebrovascular disease	30.00
25	Steroid use	31.17
26	Pacemaker in situ	27.27
27	Body mass index	21.20
28	Diabetes	19.97
29	Number of disease vessel	14.10
30	Immunosuppressant use	11.50
31	Family history of heart disease	12.87
32	Anticoagulant use	7.53
33	Intra venous nitrate use	8.13

NYHA, New York Heart Association. *Percentage of times of appearance in bootstrap resampling.

as significant in 100% of the bootstrap samples had an AUC of 0.8392. With each addition of predictors, the AUC increased steeply until the model with 13 predictors (AUC 0.8450) appeared as significant in at least 99.6% of the samples and apparently reached a plateau (Figure 1). The addition of a further variable into the model didn't result in a steep increase in AUC (0.8454), which also corresponded to the sharp decrease of bootstrap coverage (99.6% with 13 variables vs 90.2% with 14 variables). Hence, the model with 13 predictors was selected as the final bootstrap ROC model. AIC and BIC values for all of the 14 competing bootstrap models are presented in Figure 2. The model with 23 variables had the lowest AIC (12,326.5) and the model with 16 variables had the lowest BIC (12,584.8). Hence, the model with 23 variables and the model with 16 variables were selected as bootstrap

FIGURE 1. AUC gradient with increasing number of variables based on bootstrap coverage increment. *AUC*, Area under the ROC curve.

AIC and BIC model, respectively. The AUC values for bootstrap AIC and BIC models were, respectively, 0.8470 and 0.8491.

The stepwise forward selection and backward elimination methods selected same set of 21 variables into the model with AUC of 0.8490. The model with all 33 predictors had an AUC of 0.8504.

The observed 30-day mortality in development sample was 2.693%. The predicted mortality for all variable model was 2.524% (95% confidence interval [CI], 2.481-2.567) and for the automated model was 2.524 (95% CI, 2.481-2.567). The predicted risk for the bootstrap AIC, BIC, and ROC models were 2.529% (95% CI,

2.487-2.572), 2.584% (95% CI, 2.540-2.627), and 2.574% (95% CI, 2.531-2.616), respectively.

Figure 3 shows the calibration of the competing 5 models and the final model in validation sample. Bootstrap BIC, AIC, and ROC models showed calibration slopes of 1.0128, 1.0219, and 1.0191, respectively. The automated and all variable models had calibration slopes of 1.0271 and 1.0133, respectively. All of these models have intercepts close to zero.

Based on the number of variables and discrimination and calibration, the bootstrap ROC model with 13 variables was chosen as the final model (Table 2). The overfitting-corrected loess nonparametric calibration curve demonstrated excellent calibration for the bootstrap ROC

FIGURE 2. AIC and BIC gradient with increasing number of variables based on bootstrap coverage increment. *AIC*, Akaike information criteria; *BIC*, Bayesian information criteria.

FIGURE 3. Decile-decile plots of bootstrap and automated models and validation model. A, Bootstrap ROC model; B, bootstrap BIC model; C, bootstrap AIC model; D, automated model; E, all-variable model; and F, bootstrap ROC model in validation data.

model, especially for low-risk patients (Figure 4). The model also showed very good discrimination in a multifold (10) validation (AUC, 0.8384; 95% CI, 0.8356-0.8413) in creation data as well as in external validation (AUC, 0.8156; 95% CI, 0.7936-0.8375) (Table E5).

DISCUSSION

This study is the first demonstration in the surgical literature that compares different statistical approaches for developing a parsimonious risk prediction model. A risk prediction model needs to maintain a balance between the number of variables in the model and predictive accuracy.²⁶

It is important to have a model without variables that may add little or no useful information. Omitting important prognostic factors has the potential to result in a biased estimation of the regression coefficients and inaccurate prediction.²⁷ Hence, the trade-off between parsimony and prediction performance is a major challenge in risk prediction modeling. The inclusion of a predictor in the model should be judged against the amount of prediction power it adds to the model and one should refrain from including the new predictor if the gain seems negligible.⁵ When a complicated model with many predictors in practice is applied, many patients will likely need to be excluded on the basis of missing

TABLE 2. Comparison of clinical suitability (parsimony and prediction performance) of bootstrap, automated and all predictor models

Plausible variables	All variables	Backward elimination	Forward selection	Bootstrap AIC	Bootstrap BIC	Bootstrap ROC
Age	✓	✓	✓	✓	✓	✓
Sex	✓	✓	✓	✓	✓	✓
Previous cardiac surgery	✓	✓	✓	✓	✓	✓
Peripheral vascular disease	✓	✓	✓	✓	✓	✓
Stroke	✓	✓	✓	✓	✓	✓
Glomerular filtration rate	✓	✓	✓	✓	✓	✓
Infective endocarditis	✓	✓	✓	✓	✓	✓
Urgency of procedure	✓	✓	✓	✓	✓	✓
Ejection fraction	✓	✓	✓	✓	✓	✓
Type of procedure	✓	✓	✓	✓	✓	✓
Inotropic medication use	✓	✓	✓	✓	✓	✓
Angina	✓	✓	✓	✓	✓	✓
NYHA class	✓			✓	✓	✓
Dialysis	✓			✓	✓	
Congestive heart failure	✓	✓	✓	✓	✓	
Shock	✓	✓	✓	✓	✓	
Myocardial infarction	✓	✓	✓	✓		
Resuscitation	✓			✓		
Arrhythmia	✓	✓	✓	✓		
Left main disease <50%	✓	✓	✓	✓		
Hypertension	✓			✓		
Respiratory disease	✓	✓	✓	✓		
Hypercholesterolemia	✓			✓		
Steroid use	✓					
Cerebrovascular disease	✓					
Diabetes	✓					
Pacemaker in situ	✓					
Body mass index	✓	✓	✓			
Number of disease vessel	✓	✓	✓			
Family history of heart disease	✓					
Immunosuppressant use	✓					
Intravenous nitrate use	✓					
Anticoagulant within 7 d	✓					
Number of variables	33	21	21	23	16	13
AUC	0.8504	0.8490	0.8490	0.8491	0.8470	0.8450

AIC, Akaike information criteria; BIC, Bayesian information criteria; ROC, receiver operating characteristic; NYHA, New York Heart Association; AUC, area under the ROC curve.

predictors. Furthermore, if many variables are included in a model, the likelihood of co-linearity increases which may result in biased or unstable estimation and model uncertainty.²⁸

In this study, models generated by the use of automated variable selection approaches did not show better parsimony in comparison with bootstrap ROC model. The variable selection for risk prediction modeling should consider the clinical plausibility rather than solely relying on statistical variable selection methods.⁴ Automated model selection processes act as a black box, which can result in blind selection and hence using this method, a researcher possesses less control over what predictors are included and what is being eliminated.²⁹ The use of automated variable selection methods sometimes may even produce nonreproducible regression models.⁷ Furthermore, automated selection has also the potential to

create bias in the estimated regression coefficients.³⁰ Particularly when the prevalence of events is low, the variable selection may be unstable, the estimated regression coefficients are too extreme, and the performance of the selected model is overestimated.⁷ Automated model-building methods also can mask multicollinearity. In such models, the number of noise (unimportant) variables increases with an increase in the number of plausible predictors, which translates into a decrease in the probability of correctly identifying true predictor variables.²⁷ A study on simulated data demonstrated that automated model selection may result in unstable models and may select noise variables.⁹ In the present study, the automated selection method chooses the variables body mass index and number of diseased vessel which had very poor bootstrap coverage (21.2%) and (14.1%), respectively (Table 2). There are potential that variable selection method

FIGURE 4. Overfitting-corrected loess nonparametric calibration curve demonstration calibration of the model.

may eliminate variables those are historically important. For instance, bootstrap ROC model didn't include variables like "cardiogenic shock," "myocardial infarction," and "angina." The model building process actually identifies the best predictors, among the set of similar predictors, which explains most variation in the outcome. In this process, it may eliminate a variable that is historically important; however, the model keeps a surrogate that explains the variation from the excluded variable. It could be that inclusion either or all of "New York Heart Association class," "urgency of operation," and "ejection fraction" is enough to capture the variation of those eliminated variables. For example, the model with 16 and 18 variables included "cardiogenic shock" and "myocardial infarction" but didn't perform better than the models without these variables.

To minimize the limitation of automated model selection methods, backward elimination in combination with bootstrap resampling was proposed by Austin and Tu³¹; however, this approach did not improve the ability of variable selection to identify the true predictors of an outcome.³² Reasons why this combination method did not work could be that the automated model selection was repeated in all 1000 bootstrap samples, and hence the limitation of the automated variable selection persisted. To overcome this limitation, in this study, within each bootstrap sample the multivariable logistic regression was run independently of automated method. A similar approach was used to develop several models for predicting 30-day mortality in the ANZSCTS database.^{3,16,33} In this approach, the researcher has the freedom to decide on inclusion and exclusion of predictors for the final model based on theoretical and clinical plausibility and parsimony.

Small degrees of random variation in one dataset can have a substantial influence on the variables that are identified as independent predictors. Thus, it is likely that

no one regression model estimated on one dataset can conclusively identify the independent predictors.¹¹ Bootstrap resampling has been considered as a solution for the sampling variation. The bootstrap method can provide insight in the distribution of a summary measure from a sample. The bootstrap method draws samples from the original sample to introduce a random element.^{12,34}

This study showed that bootstrap ROC method generates a parsimonious risk prediction. The model performed very well in the validation dataset. With only 13 predictors, this model showed a competitive discrimination power (AUC: 0.8156) compared with other commonly used risk prediction models such as The Society of Thoracic Surgeons (AUC: 0.8120, 31 predictors)¹ and European System for Cardiac Operative Risk Evaluation II (AUC: 0.8095, 18 predictors).³⁵

The bootstrap ROC method also can be used for developing parsimonious risk prediction model for other postoperative outcomes such as new renal failure, stroke, postoperative atrial fibrillation, pneumonia, and long-term mortality in cardiac surgery. This method also could be a useful tool for risk prediction modeling in other disciplines of research.

One limitation of this research was that all the competing models were developed for all procedures and not for a specific procedure type. It is generally hypothesized that procedure specific models performs better than the global model. Furthermore, many of the popularly used models in the field are for general cardiac surgery. The objective of this study, however, was to compare the model development methods. All the models were developed with the same process; hence, the findings in this study were not affected by case-mix. Another limitation of this study was that a number of other methods are available for screening and identification of potential candidate variables including random forest classification, classification and regressing tree (CART) etc. In this study, however, we only compared the methods currently popularly being used in the field of risk prediction modeling.

In conclusion, clinical suitability in terms of parsimony and prediction performance can be achieved by the use of bootstrap resampling in conjunction with ROC for the development of risk prediction models. We recommend this method for future risk prediction model development.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: bootstrap resampling, automated model, risk prediction model, cardiac surgery

TABLE E1. ANZSCTS registry variable information

	Variables	Data field number
1	Preoperative (101)	
	Patient demography	24
	Patient risk factor	19
	Preoperative cardiac status	33
	Previous intervention	16
2	Hemodynamic state	09
	Intra- operative (114)	
	Operative status	41
	Minimally invasive	04
	CPB support	17
3	Coronary bypass	12
	Valve surgery	40
	Postoperative (72)	
	Postoperative support	15
	Complication	36
	Mortality/readmission	21
Total		287

CPB, Cardiopulmonary bypass.

TABLE E2. Number (%) of missing observations for predictors in the development dataset

Plausible variables	Missing values	
	n	%
Age	13	0
Sex	0	0
Peripheral vascular disease	215	0.34
Stroke	0	0
Glomerular filtration rate	576	0.91
Infective endocarditis	207	0.33
Urgency of procedure	37	0.06
Ejection fraction	1951	3.07
Inotropic medication use	207	0.33
Type of procedure	786	1.24
Previous cardiac surgery	182	0.29
NYHA class	3355	5.28
Angina	581	0.91
Shock	199	0.31
Congestive heart failure	195	0.31
Myocardial infarction	172	0.27
Resuscitation	201	0.32
Arrhythmia	220	0.35
Hypertension	207	0.33
Left main disease <50%	581	0.91
Hypercholesterolemia	217	0.34
Respiratory disease	195	0.31
Steroid use	211	0.33
Diabetes	327	0.52
Pacemaker in situ	429	0.68
Body mass index	339	0.53
Number of disease vessel	703	1.11
Immunosuppressant use	206	0.32
Intravenous nitrate use	211	0.33
Anticoagulant use	221	0.35
Mortality in 30 d	280	0.44

NYHA, New York Heart Association.

TABLE E3. Descriptive statistics of plausible categorical variables

Variables	Frequency	Percent
Sex		
Male	45,854	72.18
Female	17,669	27.82
Family history of heart disease		
No	38,480	60.58
Yes	19,318	30.41
Previous cardiac surgery		
No	57,918	91.18
Yes	5423	8.54
Peripheral vascular disease		
No	56,723	89.3
Yes	6585	10.37
Respiratory disease		
No	54,558	85.89
Yes	8770	13.81
Cerebrovascular disease		
No	56,116	88.34
Yes	7198	11.33
Stroke		
No	62,198	97.91
Yes	1325	2.09
Hypertension		
No	17,273	27.19
Yes	46,043	72.48
Diabetes		
No DM	45,282	71.28
DM + no insulin	13,442	21.16
DM + insulin	4534	7.14
Hypercholesterolemia		
No	20,351	32.04
Yes	42,955	67.62
IE		
No IE	61,754	97.22
IE treated	553	0.87
IE active	1009	1.59
Left main disease		
No	51,664	81.33
Yes	11,278	17.75
Number of diseased vessels		
None	15,875	24.99
One	5264	8.29
Two	11,347	17.86
Three	30,334	47.75
NYHA class		
I, II	42,367	66.7
III	13,599	21.41
IV	4202	6.61
Cardiogenic shock		
No	61,820	97.32
Yes	1504	2.37
Resuscitation		
No	62,559	98.48
Yes	763	1.2

(Continued)

TABLE E3. Continued

Variables	Frequency	Percent
Congestive heart failure		
Yes	47,953	75.49
No	15,375	24.2
Ejection fraction		
Normal, >60%	31,391	49.42
Mild, 46%-60%	18,321	28.84
Moderate, 31%-45%	8689	13.68
Severe, ≤30	3171	4.99
Arrhythmia		
No	53,078	83.56
Yes	10,225	16.1
Pacemaker in situ		
No	61,890	97.43
Yes	1204	1.9
Angina		
No angina	21,225	33.41
Stable angina	30,664	48.27
Unstable angina	11,053	17.4
Previous MI		
No	38,817	61.11
Yes	24,534	38.62
Inotrope use		
No	61,630	97.02
Yes	1686	2.65
Intravenous nitrates		
No	60,078	94.58
Yes	3234	5.09
Anticoagulant use		
No	50,973	80.24
Yes	12,329	19.41
Steroids use		
No	61,806	97.3
Yes	1506	2.37
Immunosuppressive use		
No	61,784	97.26
Yes	1533	2.41
Procedure type		
Isolated CABG	36,085	56.81
Valve(s) only	10,489	16.51
Valve(s) + CABG	6746	10.62
Other	9417	14.82
Urgency of operation		
Elective	41,829	65.85
Urgent	18,478	29.09
Emergency	2924	4.6
Salvage	255	0.4
30-d mortality		
No	61,540	97.31
Yes	1703	2.69

DM, Diabetes mellitus; IE, infective endocarditis; NYHA, New York Heart Association; MI, myocardial infarction; CABG, coronary artery bypass grafting.

TABLE E4. Descriptive statistics of plausible numerical variables

Predictors	n	Mean	SD
Age, y	63,510	65.67	12.83
Body mass index	63,351	28.48	9.74
Estimated glomerular filtration rate	62,947	82.15	37.10

SD, Standard deviation.

TABLE E5. Bootstrap ROC model

Predictors	OR (95% CI)	P value
Age	1.024 (1.018-1.029)	<.001
Sex (female)	1.414 (1.265-1.581)	<.001
eGFR	0.990 (0.987-0.992)	<.001
Infective endocarditis (ref: none)		
Treated endocarditis	1.205 (0.745-1.948)	.446
Active endocarditis	2.437 (1.874-3.169)	<.001
Urgency (ref: elective)		
Urgent	1.567 (1.371-1.791)	<.001
Emergency/salvage	4.611 (3.884-5.475)	<.001
Ejection fraction (ref: >60%)		
Mild (46%-60%)	1.242 (1.081-1.427)	.002
Moderate (31%-45%)	1.634 (1.397-1.910)	<.001
Severe ($\leq$ 30%)	2.346 (1.895-2.904)	<.001
NYHA class (ref: I and II)		
III	1.467 (1.279-1.681)	<.001
IV	1.725 (1.463-2.032)	<.001
Procedure type (ref: CABG)		
Valve	1.462 (1.209-1.767)	.001
CABG + valve	2.043 (1.738-2.402)	<.001
Others	2.968 (2.546-3.460)	<.001
Peripheral vascular disease	1.617 (1.406-1.859)	<.001
Stroke	5.865 (4.985-6.901)	<.001
Inotrope administration	2.293 (1.916-2.743)	<.001
Angina		
Stable	0.930 (0.810-1.066)	.297
Unstable	1.260 (1.066-1.489)	.007
Previous cardiac surgery	1.687 (1.459-1.951)	<.001

OR, Odds ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate; NYHA, New York Heart Association; CABG, coronary artery bypass grafting.