Preoperative identification of cardiac surgery patients at risk of platelet transfusion: the Australian Cardiac Surgery Platelet Transfusion (ACSePT) risk prediction tool

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No reprints will be available from the authors.

The authors declare that they have no conflicts of interest relevant to the manuscript submitted to TRANSFUSION.

Abstract

Background

Platelet transfusions are limited and costly resources. Accurately predicting clinical demand while limiting product wastage remains difficult. A platelet transfusion prediction score was developed for use in cardiac surgery patients, who commonly require platelet transfusions.

Study design and methods

Using the Australian and New Zealand Society of Cardiac and Thoracic Surgeons National Cardiac Surgery Database, significant predictors for platelet transfusion were identified by multivariate logistic regression. Using a development dataset containing 2005-2016 data, the Australian Cardiac Surgery Platelet Transfusion (ACSePT) risk prediction tool was developed by assigning weights to each significant predictor that corresponded to a probability of platelet transfusion. The predicted probability for each score was compared to actual platelet transfusion occurrence in a validation (2017) dataset.

Results

The development dataset contained 38 independent variables and 91,521 observations. The validation dataset contained 12,529 observations. The optimal model contained 23 variables significant at $p<0.001$ and an area under the ROC curve of 0.69 (95% CI 0.68-0.69). ACSePT contained nine variables, had an area under the ROC curve of 0.66 (95% CI 0.65-0.66), and overall predicted probability of platelet transfusion of 19.8% for the validation dataset compared to an observed risk of 20.3%.

Conclusion

This is the first scoring system to predict a cardiac surgery patient's probability of a platelet transfusion. It can be used to identify patients at higher-risk of platelet transfusion for inclusion in clinical trials, and by platelet inventory managers to predict platelet demand.

Key words: Cardiac Surgery, Platelet, Transfusion

Abbreviations: Australian Cardiac Surgery Platelet Transfusion (ACSePT); Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS); Body Mass Index (BMI); Confidence Interval (CI); Locally Weighted Scatterplot Smoothing (LOWESS); Myocardial Infarction (MI); Negative Predictive Value (NPV); New York Heart Association (NYHA); Odds Ratio (OR); Positive Predictive Value (PPV); Red Blood Cell (RBC); Receiver Operating Characteristic (ROC); Transfusion Risk and Clinical Knowledge (TRACK); TRUST (Transfusion Risk Understanding Scoring Tool).

Introduction

The short shelf-life of liquid-stored platelets (five to seven days in most jurisdictions), combined with difficulty predicting clinical demand, results in high wastage rates due to outdating.[1-5] Cardiac surgery patients are transfused approximately 10% of all platelet units and are the second most likely patient group to receive platelet transfusions after hematology patients.[1,6,7] Although a common intervention, there are reported variations in the rate of platelet transfusion in cardiac surgery patients between institutions.[8-10] Being able to predict platelet transfusion in cardiac surgery would be useful both to blood services and hospitals to better anticipate demand for platelets. Furthermore, identifying cardiac surgery patients pre-operatively who are likely to require platelet transfusion would facilitate undertaking clinical trials of platelet transfusion interventions.

Transfusion prediction scores, such as the Transfusion Risk Understanding Scoring Tool (TRUST),[11] the Transfusion Risk and Clinical Knowledge (TRACK) score,[12] and the Red Blood Cell (RBC) transfusion models in Goudie, et al.[13], have been developed for cardiac surgery patients to predict the need for RBC transfusion.[11] Cardiac surgery patients who receive RBC transfusions are also at risk of receiving platelet transfusion, so these transfusion prediction scores might also be useful in predicting platelet requirements. However, several of the predictors used in these models (such as hemoglobin concentration or hematocrit) are less relevant to platelet transfusion, and these scores do not incorporate other clinical features (such as receipt of antiplatelet medications) that might be very relevant as to whether platelets are transfused. A platelet-specific predictive tool could be very useful—however, to date, no such score exists. Furthermore, relatively little has been published about which cardiac surgery patients are more likely to receive platelet transfusions. One single-institution retrospective study has compared patient and surgical characteristics between those who received platelet transfusion.[14] No multi-institution study has reported predictors of platelet transfusion.

Current guidelines help to inform platelet transfusion decisions but provide only weak recommendations for platelet transfusions. The AABB suggests platelet transfusion for cardiac surgery patients undergoing cardiopulmonary bypass who have perioperative bleeding and thrombocytopenia

or platelet dysfunction, but recommends against routine platelet transfusions if they have normal platelet counts.[15] British guidelines for platelet transfusion do not make specific recommendations about cardiac surgery patients, but recommend major surgery is acceptable at platelet counts above 50×10^9/L, and that platelet levels should be maintained above 50×10^9/L in the context of severe bleeding and 30×10^9/L in non-severe bleeding.[16] Australian Patient Blood Management guidelines only recommend against prophylactic platelet transfusion for cardiac surgery patients after surgery.[17] Some institutions in Australia and New Zealand use their own transfusion guidelines based on platelet counts, thromboelastography or rotational thromboelastometry, but there is no unified approach. Additionally, platelet units are at times transfused as part of a massive transfusion protocol for patients with massive hemorrhage. With such non-specific recommendations, guidelines cannot be used to predict which patients will be transfused.

The aim of this study was to develop a scoring system to predict a cardiac surgery patient's probability of receiving a platelet transfusion which could be applied across multiple institutions and over an extended time period. This risk prediction tool was developed to be used for patient recruitment in the upcoming cryopreserved platelets versus conventional liquid-stored platelets (CLIP II) trial (clinicaltrials.gov reference NCT03991481). Another potential application is to enable transfusion services to better anticipate clinical requirements to improve inventory management and reduce outdating.

Materials and methods

Study design

This was a retrospective cohort study of prospectively collected data for all cardiac surgery patients reported to the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) National Cardiac Surgery Database from 2005 to 2017. For patients with multiple cardiac surgical procedures, only the first procedure was included in the analysis.

The study was approved by Monash University's Human Research Ethics Committee (Reference number 11687).

Data sources

Data were obtained from the ANZSCTS National Cardiac Surgery Database. This is a prospectively collected database of all cardiac surgical procedures performed at participating institutions in Australia—in 2005 this included seven institutions and by 2017 the number had increased to 37. Only variables that would be relevant for the analysis and known prior to surgery were considered. Variables included patient demographics, past medical history, pre-operative cardiac status, previous cardiac surgery interventions, cardiac hemodynamics, and operation details. The primary outcome was platelet transfusion, which was defined as one or more platelet transfusion either intraoperatively or postoperatively up to 30 days. Any variables with >10% missing data were excluded initially and then observations with incomplete data were excluded.

The dataset was divided into development and validation datasets. All complete data prior to 2017 was used for the development dataset. The final year of data (2017) was used for the validation dataset.

Data analysis and statistics

STATA 15[18] was used for all data and statistical analyses. Continuous variables were converted to practical categories after assessment of Locally Weighted Scatterplot Smoothing (LOWESS) curves.

Descriptive statistics were reported as frequencies (percentages [%]). Univariate analysis was performed by chi-square tests.

Multivariate logistic regression was used to find significant predictors for platelet transfusion during the intra-operative or post-operative period using the methodology shown in Figure 1. Following the purposeful selection method in Hosmer Jr, et al.[19], all variables found to be significant at $p<0.001$ on univariate analysis were included in the initial model. The least significant variables were then removed one-by-one from the multivariate logistic regression, and the reduced model was compared to the previous by likelihood-ratios and the change in the estimated coefficients; if the likelihood ratio test was significant at $p<0.001$ or the change in estimated coefficients was greater than 20%, the variable was not removed from the model, and the model was reduced by the next least significant variable. Once the model was fully reduced, the variables that were found to be non-significant on univariate analysis were re-introduced into the model one-by-one, and if significant, they were included in the model. The final model contained all variables that were significant at $p<0.001$ within the model. This method was compared to variables selected using forwards and backwards stepwise selection for a $p<0.001$ level of significance.

The performance of the final model was determined by the area under the receiver operating characteristic (ROC) curve to measure discrimination. Clinical and biological plausibility of predictors was considered to assess for collinearity by comparing estimates from the multivariate model to the univariate results—if the parameter estimates changed direction or magnitude too greatly, or did not make clinical sense, then we considered there to be an issue with collinearity.

The final model was simplified to produce a ‘likelihood of platelet transfusion’ score. Eight simplified models were produced by rounding the constant and the estimated coefficients to different multiples. These eight models were used to estimate the probability of a platelet transfusion for both the development and validation datasets, and their performance was compared by the area under the ROC curve. The sum of the coefficients gave a score for each simplified model that correlated to a probability

of a platelet transfusion. The Australian Cardiac Surgery Platelet Transfusion (ACSePT) risk prediction tool was selected based on its performance and relative simplicity.

To account for potential variability over time, the holdout sample was chosen from the final year of the dataset. Furthermore, to increase model generalizability, site was not included in the modelling process. Finally, we did a further analysis comparing the ACSePT risk prediction tool to the TRUST score.

Results

The original dataset contained 113,409 observations and 373 variables from 2005 to 2017. After excluding observations for additional operations after a patient's first surgery (1,688 observations) there were 111,721 observations remaining. We only considered relevant variables known prior to surgery and with <10% of missing data, and excluded observations with incomplete data for these variables (7,671 observations including both missing data and not applicable data). The development dataset then contained 91,521 observations from 2005 to 2016 and 38 independent variables known pre-operatively, and the validation dataset contained 12,529 observations from 2017 (Figure 2). In both datasets, each observation represented a single patient's first cardiac surgery. In the development dataset 19,635 (21.5%) patients received a platelet transfusion, compared to 2,547 (20.3%) in the validation dataset.

Comparison of pre-operative characteristics by platelet transfusion

A comparison of the 38 pre-operative variables according to group defined by the eventual requirement for platelet transfusion is shown in Table 1. Patients who received platelet transfusions differed ($p<0.001$) from those who did not for nearly all 38 variables, with the exception of gender, Aboriginal or Torres Strait Islander heritage, and diagnosis of left main coronary artery stenosis >50%.

Prediction model

Following the purposeful selection method, 23 relevant variables were selected, all of which were significant at a $p<0.001$. This same 23 variable model was also arrived at using both forwards and backwards stepwise selection techniques. The selected variables and their odds ratios (OR) and confidence intervals (CI) are shown in Table 2.

In the development data, 21.5% of patients received a platelet transfusion and the model had an area under the ROC curve of 0.69 (95% CI 0.68-0.69). In the validation data the predicted probability of a platelet transfusion was 22.2% (observed rate 20.3%) and the area under the ROC curve was 0.70 (95% CI 0.69-0.71). There was natural variability across the 37 sites with the actual probability of platelet transfusion varying from 4% to 36% and the predicted probability varying from 17% to 27% (Table B

of the Appendix). Issues of collinearity were not detected from assessment of clinical and biological plausibility of predictors.

The Australian Cardiac Surgery Platelet Transfusion (ACSePT) risk prediction tool

To produce a simple, additive scoring system suitable for clinical use, five simplified models of the complete model were produced. These are shown in the appendix (labelled Models I to V) and were produced by rounding the complete model's constant and coefficients to the nearest 1.5, the nearest whole number, and the nearest 0.5, 0.25 and 0.1 decimal places, respectively. Three further models (Models VI to VIII) were produced by including the variables with OR≥1.5 or OR≤0.5, OR≥1.75 or OR≤0.5 and OR≥2 or OR≤0.5, respectively, and rounding the constant and their coefficients to the nearest 0.5.

Table A of the appendix shows a comparison of the eight models and the complete model based on the area under the ROC curve, the predicted probabilities and the actual probabilities for the development dataset.

Model VI was selected for the ACSePT risk prediction tool as it was relatively simple with only nine variables, but maintained performance with an area under the ROC curve of 0.66 (95% CI 0.65-0.66). Table 3 shows the additive algorithm to calculate an ACSePT score. When applied to the validation dataset, the ACSePT risk prediction tool had an area under the ROC curve of 0.67 (95% CI 0.66-0.68), compared to using the complete model of 0.70 (95% CI 0.69-0.71). The ACSePT risk prediction tool predicted the probability of a platelet transfusion to be 19.8% for the validation dataset, whereas the actual percentage of platelet transfusions was 20.3%. Figure 3 shows the actual and predicted probability of a platelet transfusion for each score-and-above using the validation dataset for the ACSePT risk prediction tool, and the corresponding percentage of patients with at least those scores. Table 4 shows the actual number (and percentage) and the predicted number (and percentage) of patients receiving platelet transfusions for each score-and-above, and the sensitivity, specificity,

positive-predictive value (PPV) and negative-predictive value (NPV) for each score using the validation dataset. There is a near-linear increase in platelet transfusion risk with increasing score. An ACSePT score of 1 or more applied to 31% of the validation dataset cohort, of whom 34% of patients were predicted to have a platelet transfusion, compared to 34% who actually did receive a platelet transfusion.

When the ACSePT risk prediction tool was compared to the TRUST score, ACSePT had a significantly greater area under the ROC curve of 0.67 (95% CI 0.66-0.68) compared to 0.60 (95% CI 0.59-0.62) using the validation dataset ($p<0.001$)—Figure 4 shows a comparison of the area under the ROC curves for ACSePT and TRUST. The maximum correctly classified patients was 81% for an ACSePT score of 2 and it was 80% for a TRUST score of 7.

A sensitivity analysis was conducted to assess the performance of the ACSePT risk prediction tool. Comparing the ACSePT risk prediction tool across the 37 hospital sites in 2017, the minimum and maximum probability of a platelet transfusion was 16.5% and 27.2%, respectively, for a mean of 19.8% with a standard deviation of 2.3%. The minimum and maximum areas under the ROC curves were 0.52 and 0.87, respectively; and the mean was equal to the median value of 0.67, with a standard deviation of 0.07. The performance of ACSePT at each hospital site can be seen in Table B of the appendix. Comparing hospital sites who transfused more than the average 600 platelet units in 2017 against sites that transfused less than 600 units: the predicted probabilities were 19.5% and 20.0% for the above and below average platelet transfusion subgroups, compared to their actual rates of 23.6% and 16.9%, respectively; and their area under the ROC curves were 0.69 for above average hospitals and 0.66 for below average hospitals. Comparing elective and non-elective surgery subgroups: for elective surgery, the predicted probability of a platelet transfusion was 18.9%, compared to the actual rate of 18.8%, and the area under the ROC curve was 0.64; for the non-elective surgery subgroup, the predicted probability was 21.8%, compared to the actual rate of 27.3%, and the area under the ROC curve was 0.71. Finally, comparing the subgroup of those who received RBC transfusions against those who did not: for the group who received RBC transfusions, the predicted probability was 24.0% compared to the actual rate of 42.8%, and the area under the ROC curve was 0.64; for the group who

did not receive a RBC transfusion, the predicted probability was 17.7% compared to the actual rate of 8.1%, and the area under the ROC curve was 0.61.

Discussion

We have developed a risk prediction tool to predict a cardiac surgery patient's probability of receiving a platelet transfusion. This is the first study to describe the predictors of platelet transfusion in cardiac surgery patients across multiple sites and to produce a scoring system to identify a patient's probability of receiving a platelet transfusion. From 38 patient and surgical factors known prior to surgery, we identified 23 relevant variables that remained independently significant after adjustment for confounding variables. From these variables, we developed a simple risk prediction tool that can be used to predict a cardiac surgery patient's probability of receiving a peri-operative platelet transfusion, using only nine pre-operative variables. The risk prediction tool was applied to a validation dataset and demonstrated that a cardiac surgery patient's probability of a platelet transfusion can be estimated pre-operatively.

Similarly to Ninkovic, et al.[14], we found patients who received platelet transfusion were more likely to have a diagnosis of infective endocarditis, recent myocardial infarction (MI) and recent exposure to aspirin or clopidogrel; and less likely to have diabetes. We also found that patients receiving platelet transfusion were more likely to be older than 70 years, where Ninkovic, et al.[14] found that patients older than 80 years were more likely to receive platelet transfusions. Ninkovic, et al.[14] found that patients with higher BMIs were more likely to receive platelet transfusions—we, however, found that patients with a BMI greater than 30 were less likely to receive platelet transfusions because they were more likely to be elective patients and less likely to have valve surgery in our patient population. Compared to the findings used to develop the TRUST and TRACK scores,[11,12] and the transfusion models produced in Goudie, et al.[13], for predictors of exposure to RBC transfusion in cardiac surgery patients, we found cardiac surgery patients who received platelet transfusions also had high pre-operative creatinine levels, were older, and had lower left ventricular ejection fractions; however, we found there was no difference for gender, and patients with diabetes were less likely to receive platelet transfusions, whereas they found patients receiving RBC transfusions were more likely to be female and have diabetes. When we compared the area under the ROC curves for the ACSePT risk prediction tool to the TRUST score, our platelet-specific model performed better. We were unable to compare the ACSePT risk prediction tool

to the TRACK score because we did not have all of the required pre-operative variables, we also were unable to compare ACSePT to the prediction models in Goudie, et al.[13] because it is not possible to construct their prediction model from their reported results. Our study investigated aggregate data from up to 37 cardiac surgery departments across Australia, whereas Ninkovic, et al.[14] and Ranucci, et al.[12] reported the results from a single center, Alghamdi, et al.[11] reported results from two centers, and Goudie, et al.[13] from 27 centers. Further studies are required to enhance prediction of platelet transfusion in both cardiac surgery and non-cardiac surgery patients and for external validation of the ACSePT risk prediction tool.

The practical application of the ACSePT risk prediction tool is determined not so much by the area under of ROC curve as by the proportion of patients with each score, the predicted versus observed platelet transfusion associated with each score, and the threshold determined by an institution as sufficiently 'high risk' to trigger an action such as enrolment in a trial, or ordering extra platelets for their blood bank. These relationships are shown in Figure 3. For example, if interested in an intervention related to intraoperative platelet transfusion, instead of seeking prospective consent from all patients prior to surgery, most of whom have a low probability of being transfused platelets, the ACSePT risk prediction tool would facilitate concentrating on only those patients most likely to be transfused. Setting the entry criterion using an ACSePT score of ≥1 would identify the 30% of patients who have a predicted risk of platelet transfusion of approximately 30%.

This study has several important implications. First of all, a platelet transfusion prediction score will be useful for clinical trials, as described. Second, some surgical and transfusion institutions may find it useful to now have a clinical tool to identify pre-operatively which patients are more likely to receive platelet transfusions. Finally, through being able to better anticipate which patients are more likely to receive platelet transfusions, there may be associated reductions in platelet wastage due to outdating at some hospitals. However, the utility of the risk prediction tool is limited by its performance and by only a small proportion of patients having a high probability of receiving a platelet transfusion—this reflects

the difficulty in predicting which patients are more likely to receive platelet transfusions, and its use for identifying patients pre-operatively might not be possible in some institutions.

This study has a number of strengths including the large sample size and the inclusion of multiple participating cardiac surgery departments, which improved the generalizability of results. We have identified relevant risk factors for platelet transfusion in cardiac surgery, which is an area for which little is known. Using the final year of data for validation, rather than a random sample of the entire dataset, had the advantage that we were able to show that historical data could predict future platelet transfusion practices despite there being significant variability in platelet transfusion rates between sites and over time.

The study has a number of limitations. Firstly, despite using a large dataset with a substantial number of relevant variables to build the model, the prediction models were not able to differentiate to a high degree of accuracy between those who received platelet transfusion and those who did not—even for the complete model with 23 relevant variables all significant at a $p<0.001$ level of significance, the area under the ROC curve was only 0.70 in the validation cohort, whereas an area under the ROC curve greater than 0.80 would generally be regarded as a well performing model. When the model was simplified to create the ACSePT risk prediction tool, this accuracy was somewhat further reduced. The accuracy of the ACSePT risk prediction tool might be limited by not including other important predictors of platelet transfusion such as pre-operative hemoglobin, platelet counts or known platelet dysfunction—these data were not collected and therefore not available, and including these variables is a possible direction for future studies. However, previous studies have shown that moderate thrombocytopenia (platelet count $<100 \times 10^9$/L) is rare (<1%) in pre-operative cardiac surgery patients, and therefore would be unlikely to improve the model.[14] Furthermore, recommendations for platelet transfusion in cardiac surgery patients are only weak and there was significant variability between institutions and over the time period—this variability may help to explain why our prediction models were not highly accurate as determined by the area under the ROC curve. In the absence of knowledge pertaining to the appropriateness of platelet transfusions, our models are further limited by the fact that

we can only assume all of the reported transfusions were appropriate. While accuracy is limited by these factors, the ACSePT risk prediction tool does provide the first quantifiable way of predicting a cardiac surgery patient's probability of a platelet transfusion. Another limitation is the relatively small number of patients with high scores—while an ACSePT score of three or above predicted 75% of patients to have a platelet transfusion and 66% of patients with this score or above in the validation dataset did have a platelet transfusion, less than 1% of patients had at least this score. We anticipated that lower scores that capture patients with a greater than average probability of a platelet transfusion will be more useful for identifying platelet transfusion recipients. Finally, while the modelling process accounts for surgery type, in practical terms, the prediction process may not be applicable for emergency surgery.

In conclusion, we have developed a platelet transfusion prediction score for patients undergoing cardiac surgery. The ACSePT risk prediction tool contained only nine variables and was validated against an internal dataset across multiple sites. Despite identifying a large number of relevant predictors, we cannot accurately predict which patients need platelet transfusions.

Acknowledgements

The ANZSCTS National Cardiac Surgery Database Program is funded by the Department of Health (Victoria), the Clinical Excellence Commission (NSW), Queensland Health (QLD), and funding from individual Units. ANZSCTS Database Research activities are supported through a National Health and Medical Research Council Senior Research Fellowship and Program Grant awarded to C.M. Reid. The Database thanks all of the investigators, data managers, and institutions that participate in the Program.

ZM is a recipient of an Australian National Health and Medical Council Early Career Fellowship.

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Figure legends

Figure 1: Model derivation methodology and selection of the ACSePT risk prediction tool.

Figure 2: Derivation of the final development and validation datasets after exclusions.

Figure 3: Observed and predicted probabilities of platelet transfusion for each score and above, and the corresponding percentage of patients with at least each score. No patients with scores of four were observed or predicted to have platelet transfusions.

Figure 4: Comparison of area under the ROC curve for the ACSePT risk prediction tool (0.66) and TRUST score (0.60) using the validation dataset (p<0.001).

Tables and legends

Table 1: Comparison of requirement for peri-operative platelet transfusion for demographics, risk factors for cardiac surgery, pre-operative cardiac status and hemodynamics, previous interventions and operation details.

Variables	All patients (N = 91,521)	Patients with platelet transfusion (N = 19,635)	Patients without platelet transfusion (N = 71,886)	p-value
Age group, years, n (%)				
Less than 50	9,103 (10.0)	1,921 (9.8)	7,182 (10.0)	<0.001
50 to <60	15,287 (16.7)	2,839 (14.5)	12,448 (17.3)	
60 to <70	27,030 (29.5)	5,347 (27.2)	21,683 (30.2)	
70 and above	40,101 (43.8)	9,528 (48.5)	30,573 (42.5)	
BMI, kg/m^2, n (%) *				
<18.5	1,231 (1.4)	423 (2.2)	808 (1.1)	<0.001
18.5 to <30	59,517 (65.0)	13,944 (71.0)	45,573 (63.4)	
30 and above	30,773 (33.6)	5,268 (26.8)	25,505 (35.5)	
Creatinine, µmol/L, n (%)				

<70	16,275 (17.8)	3,167 (16.1)	13,108 (18.2)	<0.001
70 to <110	56,276 (61.5)	11,373 (57.9)	44,903 (62.5)	
110 and above	18,970 (20.7)	5,095 (26.0)	13,875 (19.3)	
Gender, female, n (%)	24,618 (26.9)	5,298 (27.0)	19,320 (26.9)	0.77
Aboriginal or Torres Strait Islander, n (%)	2,426 (2.7)	575 (2.9)	1,851 (2.6)	0.01
History of smoking, n (%)	53,588 (58.6)	11,002 (56.0)	42,586 (59.2)	<0.001
Diabetes, n (%)	26,972 (29.5)	5,146 (26.2)	21,826 (30.4)	<0.001
Hypercholesterolemia, n (%)	61,647 (67.4)	12,649 (64.4)	48,998 (68.2)	<0.001
Dialysis, n (%)	1,450 (1.6)	562 (2.9)	888 (1.2)	<0.001
Hypertension, n (%)	67,170 (73.4)	14,216 (72.4)	52,954 (74)	<0.001
Cerebrovascular disease, n (%)	9,868 (10.8)	2,431 (12.4)	7,437 (10.4f)	<0.001
Peripheral vascular disease, n (%)	8,395 (9.2)	1,959 (10.0)	6,436 (9.0)	<0.001
Respiratory disease, n (%)	12,315 (13.5)	2,875 (14.6)	9,440 (13.1)	<0.001
Infective endocarditis, n (%)	2,214 (2.4)	938 (4.8)	1,276 (1.8)	<0.001
Previous MI, n (%)	33,211 (36.3)	7,382 (37.6)	25,829 (35.9)	<0.001

Cardiogenic shock at time of procedure, n (%)	1,633 (1.8)	882 (4.5)	751 (1.0)	<0.001
Required resuscitation within one hour prior to operation, n (%)	799 (0.9)	401 (2.0)	398 (0.6)	<0.001
Pre-operative arrhythmia, n (%)	15,217 (16.6)	4,134 (21.1)	11,083 (15.4)	<0.001
Immunosuppressive therapy in last 30 days, n (%)	2,266 (2.5)	630 (3.2)	1,6436 (2.3)	<0.001
Inotropes on day of surgery, n (%)	2,423 (2.7)	953 (4.9)	1,470 (2.0)	<0.001
Intravenous nitrates on day of surgery, n (%)	3,594 (3.9)	1,058 (5.4)	2,536 (3.5)	<0.001
Anticoagulation therapy within 24 hours prior to surgery, n (%) †	16,168 (17.8)	4,143 (21.1)	12,025 (16.7)	<0.001
Systemic steroids within 24 hours prior to surgery, n (%)	1,895 (2.1)	568 (2.9)	1,327 (1.9)	<0.001
Aspirin within 7 days prior to surgery, n (%)	50,309 (55.0)	11,019 (56.1)	39,290 (54.7)	<0.001

Clopidogrel with 7 days prior to surgery, n (%)	10,568 (11.6)	2,891 (14.7)	7,677 (10.7)	<0.001
Other antiplatelet within 7 days of surgery, n (%) ‡	5,192 (5.7)	1,333 (6.8)	3,859 (5.4)	<0.001
Previous cardiothoracic intervention, n (%)	16,873 (18.4)	4,448 (22.7)	12,425 (17.3)	<0.001
Previous cardiac valve surgery, n (%)	2,206 (2.4)	930 (4.7)	1,276 (1.8)	<0.001
Previous cardiac catheterization, n (%)	83,869 (91.6)	17,509 (89.2)	66,360 (92.3)	<0.001
Left main coronary artery stenosis >50%, n (%)	15,854 (17.3)	3,508 (17.9)	12,346 (17.2)	0.02
Transfer from cardiac catheter lab, n (%)	953 (1.0)	445 (2.3)	508 (0.7)	<0.001
Congestive heart failure, n (%)	19,642 (21.5)	5,553 (28.3)	14,089 (19.6)	<0.001
Canadian Cardiovascular Society classification of angina, n (%)				
No angina	34,878 (38.1)	8,021 (40.9)	26,857 (37.4)	<0.001
Class I	9,375 (10.2)	1,842 (9.4)	7,533 (10)	

Class II	23,117 (25.3)	4,402 (22.4)	18,715 (26.0)	
Class III	14,955 (16.3)	3,045 (15.5)	11,910 (16.6)	
Class IV	9,196 (10.1)	2,325 (11.8)	6,871 (9.6)	
New York Heart Association dyspnea classification, n (%)				
Class I	33,707 (36.8)	6,515 (33.2)	27,192 (37.8)	<0.001
Class II	31,797 (34.7)	6,522 (33.2)	25,275 (35.2)	
Class III	19,355 (21.2)	4,660 (23.7)	14,695 (20.4)	
Class IV	4,607 (5.0)	1,643 (8.4)	2,964 (4.1)	
No documented evidence of heart failure	2,055 (2.3)	295 (1.5)	1,760 (2.5)	
Left ventricular ejection fraction estimate, n (%)				
>60%	49,171 (53.7)	9,808 (50.0)	39,363 (54.8)	<0.001
46-60%	26,750 (29.2)	5,542 (28.2)	21,208 (29.5)	
30-45%	11,817 (12.9)	2,995 (15.1)	8,862 (12.3)	
<30%	3,787 (4.1)	1,333 (6.8)	2,453 (3.4)	

Number of diseased coronary systems, n (%)§				
None	26,090 (28.5)	6,385 (32.5)	19,705 (27.4)	<0.001
One	7,596 (8.3)	1,715 (8.7)	5,881 (8.2)	
Two	16,222 (17.8)	3,082 (15.7)	13,140 (18.3)	
Three	41,613 (45.5)	8,453 (43.1)	33,160 (46.1)	
Clinical urgency of operation, n (%)				
Elective	64,595 (70.6)	12,318 (62.7)	52,277 (72.7)	<0.001
Urgent	23,550 (25.7)	5,521 (28.1)	18,029 (25.1)	
Emergency or salvage ‖	3,376 (3.7)	1,796 (9.2)	1,580 (2.2)	
Operation type, n (%)				
Coronary artery bypass	49,736 (54.3)	8,149 (41.5)	41,587 (57.9)	<0.001
Valve surgery	17,273 (18.9)	3,309 (16.9)	13,964 (19.4)	
Coronary artery bypass and valve surgery	9,716 (10.6)	3,110 (15.8)	6,606 (9.2)	
Other cardiac surgery, aortic or non-cardiac surgery	14,796 (16)	5,067 (25.8)	9,729 (13.5)	

* BMI = Body Mass Index

† Anticoagulation therapy included warfarin, heparin, low molecular weight heparin, thrombin inhibitors, and/or factor Xa inhibitors

‡ Other antiplatelet medications included ticagrelor, tirofiban, eptifibatide, abciximab or any other not otherwise represented

§ Coronary systems included any of the left anterior descending system, the circumflex system or the right coronary system with >50% narrowing

|| Emergency surgery included unscheduled surgery required in the next available operating theatre on the same day, and salvage surgery included patients undergoing cardiopulmonary resuscitation on the way to or in the operating theatre prior to incision

Table 2: Selected variables in the complete model and their Odds Ratios (99.9% Confidence Intervals).

Variable	Complete Model, OR (99.9% CI)
Age Group, years, reference group <50	
50 to <60	1.15 (1.08-1.24)
60 to <70	1.28 (1.20-1.37)
70 and above	1.47 (1.38-1.57)
BMI*, kg/m^2, reference group <18.5	
18.5 to <30	0.66 (0.58-0.74)
30 and above	0.48 (0.42-0.55)
Creatinine, µmol/L, reference group <70	
70 to <110	1.07 (1.02-1.12)
110 and above	1.21 (1.15-1.29)
Gender, female	0.92 (0.88-0.96)
Aboriginal or Torres Strait Islander	1.42 (1.28-1.58)
History of smoking	0.92 (0.88-0.95)
Diabetes	0.87 (0.83-0.90)
Dialysis	1.95 (1.73-2.19)

Infective endocarditis	2.04 (1.85-2.25)
Cardiogenic shock at time of procedure	1.57 (1.40-1.76)
Systemic steroids within 24 hours prior to surgery	1.25 (1.12-1.39)
Aspirin within 7 days prior to surgery	1.22 (1.17-1.27)
Clopidogrel with 7 days prior to surgery	1.45 (1.38-1.53)
Previous cardiothoracic intervention	1.21 (1.15-1.26)
Previous cardiac valve surgery	1.91 (1.72-2.11)
Congestive heart failure	1.14 (1.09-1.19)
Canadian Cardiovascular Society classification of angina, reference group no angina	
Class I	1.06 (0.99-1.12)
Class II	1.11 (1.05-1.16)
Class III	1.15 (1.08-1.22)
Class IV	1.20 (1.12-1.28)
New York Heart Association dyspnea classification, reference group Class I	
Class II	1.04 (0.99-1.08)
Class III	1.07 (1.01-1.12)
Class IV	1.13 (1.04-1.22)

No documented evidence of heart failure	0.59 (0.52-0.67)
Left ventricular ejection fraction estimate, reference group >60%	
46-60%	1.00 (0.96-1.03)
30-45%	1.07 (1.01-1.12)
<30%	1.25 (1.16-1.36)
Number of diseased coronary systems†, reference group none	
One	0.79 (0.73-0.85)
Two	0.88 (0.81-0.95)
Three	1.08 (1.01-1.17)
Clinical urgency of operation, reference group elective	
Urgent	1.25 (1.20-1.30)
Emergency or salvage	3.17 (2.91-3.45)
Operation type, reference group coronary artery bypass	
Valve surgery	1.38 (1.28-1.50)
Coronary artery bypass and valve surgery	2.70 (2.55-2.86)
Other cardiac surgery, aortic or non-cardiac surgery	3.03 (2.84-3.23)

* BMI = Body Mass Index

† Coronary systems included any of the left anterior descending system, the circumflex system or the right coronary system with >50% narrowing

‡ Emergency surgery included unscheduled surgery required in the next available operating theatre on the same day, and salvage surgery included patients undergoing cardiopulmonary resuscitation on the way to or in the operating theatre prior to incision

Table 3: Algorithm to calculate a patient's ACSePT score.

Category	Points
A: Age 70 years or above	0.5
B: Pre-operative dialysis	0.5
C: Diagnosis of infective endocarditis	0.5
D: Cardiogenic shock at time of procedure	0.5
E: Clopidogrel within 7 days prior to surgery	0.5
F: Previous cardiac valve surgery	0.5
G: Emergency or salvage surgery	1
H: 'Coronary artery bypass AND valve surgery' OR 'Other cardiac surgery, aortic or non-cardiac surgery'	1
I: BMI $\geq$ 30 kg/m^2	-0.5

$$ACSePT\ score = A+B+C+D+E+F+G+H+I$$

Table 4: The number of patients receiving platelet transfusions and the predicted probability for each score and above in both the development and validation datasets, and the corresponding sensitivity, specificity, PPV and NPV for each score.

	Development dataset		Validation dataset						
Score	**Number (%) of patients who received a platelet transfusion with each score and above**	**Number (%) of patients predicted to receive a platelet transfusion with each score and above**	**Number (%) of patients who received a platelet transfusion with each score and above**	**Number (%) of patients predicted to receive a platelet transfusion with each score and above**	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Patients correctly classified**
-0.5	19,635 (21%)	17,901 (20%)	2,547 (20%)	2,486 (20%)	100%	0%	20%	-	20%
0	18,429 (23%)	16,939 (21%)	2,387 (22%)	2,353 (22%)	94%	15%	22%	90%	31%
0.5	14,443 (28%)	13,587 (26%)	1,913 (27%)	1,897 (27%)	75%	48%	27%	88%	54%
1	9,230 (35%)	9,087 (34%)	1,308 (34%)	1,316 (34%)	51%	75%	34%	86%	70%
1.5	5,375 (42%)	5,389 (42%)	745 (41%)	769 (42%)	29%	89%	41%	83%	77%
2	1,713 (58%)	1,618 (55%)	297 (63%)	258 (55%)	12%	98%	63%	81%	81%
2.5	606 (67%)	596 (66%)	96 (70%)	91 66%)	4%	100%	70%	80%	80%

3	204 (73%)	210 (75%)	25 (66%)	29 (75%)	1%	100%	66%	80%	80%
3.5	56 (77%)	46 (82%)	8 (80%)	8 (82%)	0%	100%	80%	80%	80%
4.0	2 (50%)	2 (88%)	0 (-)	0 (-)	0%	100%	-	80%	80%

Appendix:

Table A: Comparison of the complete model and the simplified Models I-VIII.

Table B: the performance of the ACSePT risk prediction tool at each hospital site in 2017.