AntiPORT: adaptation of a transfusion prediction score to an Australian cardiac surgery population

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ABSTRACT

Introduction: Risk scoring systems exist to predict perioperative blood transfusion risk in cardiac surgery, but none have been validated in the Australian or New Zealand population. The ACTA-PORT score was developed in the United Kingdom for this purpose. In this study, we validate and recalibrate the ACTA-PORT score in a large national database.

Methods: We performed a retrospective validation study using data from the Australian and New Zealand Society of Cardiac and Thoracic Surgeons Database between 1 September 2016 and 31 December 2018. The ACTA-PORT score was calculated using an equivalent of EuroSCORE I. Discrimination and calibration was assessed using area under the receiver operating characteristic (AUROC) curves, Brier scores, and calibration plots. ACTA-PORT was then recalibrated in a development set using logistic regression and the outcome of transfusion to develop new predicted transfusion rates, termed "AntiPORT", using AusSCORE "all procedures" as the regional equivalent of EuroSCORE I. The accuracy of these new predictions was assessed as for ACTA-PORT.

Results: 30 388 patients were included in the study at 37 Australian centres. The rate of red blood cell transfusion was 33%. Discrimination of ACTA-PORT was good but calibration was poor, with overprediction of transfusion (AUROC curve, 0.76; 95% CI, 0.75–0.76; Brier score, 0.19). The recalibrated AntiPORT showed significantly improved calibration in both development and validation sets without compromising discrimination (AUROC curve, 0.76; 95% CI, 0.75–0.76; Brier score, 0.18).

Conclusions: The AntiPORT is the first red cell transfusion risk scoring system for cardiac surgery patients to be validated using Australian data. It is accurate and simple to calculate. The demonstrated accuracy of AntiPORT may help facilitate benchmarking and future research in patient blood management, as well as providing a useful tool to help clinicians target these resource-saving strategies.

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Perioperative anaemia and the requirement for allogeneic red blood cell transfusion are independently associated with increased morbidity and mortality following cardiac surgery.[1] Both nationally and internationally, surgery accounts for around a third of national blood product usage.[2] Cardiothoracic surgery patients received 5.6% of all blood products in Australia.[3] Although transfusion costs vary internationally, the burden on health service providers is universally significant.[4]

Various strategies to reduce overall blood product use by both preoperative optimisation of haemoglobin and blood conservation strategies have been developed and are grouped together under the term "patient blood management" (PBM). PBM programs incur a significant economic burden, and in order to best allocate resources, a number of scoring systems have been developed to identify patients at increased risk of perioperative transfusion.[5-8] Patients at higher risk of transfusion can be subsequently targeted for preoperative optimisation or more aggressive perioperative blood conservation strategies. A recently published example is the ACTA-PORT score developed in the United Kingdom,[9] which is a relatively simple, integer-based scoring system that proved accurate in a UK context.

To date, all relevant red blood cell transfusion risks scores (including ACTA-PORT) have been derived from UK, US, Canadian or European populations. None have yet been developed or validated using data from Australia or New Zealand. One article described a score to predict requirement for platelet transfusion in cardiac surgery using Australian and New Zealand data.[10] Despite similarities in clinical practice, risk prediction tools derived from a UK population do not necessarily retain precision when directly applied to an antipodean population.[11] As noted in a systematic review, "risk prediction tools are developed and initially validated in a specific patient population, in a specific health care setting, at a specific point in time".[12] This precludes

direct translation of risk prediction models between countries and highlights the importance of validating such models with local data before applying them.

In this study, we determine the accuracy of the original ACTA-PORT score in a cohort of Australian cardiac surgical patients. We subsequently develop and validate a recalibrated version of this score (henceforth, the AntiPORT score) in our population.

Methods

We performed a retrospective validation study using the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) database. We included data from all cardiac surgery procedures performed between 1 September 2016 and 31 December 2018. Ethics approval was obtained from the Monash Human Research Ethics Committee (project ID 16923). The ANZSCTS database currently collects perioperative data for all patients undergoing cardiac surgery across 26 public and 30 private hospitals in the region. Since mid-2016, data collection has routinely included preoperative haemoglobin. These dates were chosen due to the importance of haemoglobin data in the prediction of transfusion requirement and because of the availability of audited data at the time of analysis. The components and calculation of the ACTA-PORT score[9] are included in Table 1. With the exception of EuroSCORE I, all other data are collected routinely by the ANZSCTS database.

ACTA-PORT used EuroSCORE as a surrogate for operative mortality, which was not available in our dataset. Some of the EuroSCORE components differed slightly from components collected in the ANZSCTS database, and one (systolic pulmonary artery pressure) was not available at all. We therefore calculated EuroSCORE I (excluding pulmonary artery pressure) based on the closest available variables, as has been previously described.[13] We assessed the correlation between EuroSCORE and "all procedures" AusSCORE. To make future calculations easier using Australian data, we subsequently replaced the EuroSCORE mortality prediction ranges in ACTA-PORT with an equivalent Australian risk prediction score developed from the ANZSCTS database. This score was originally developed for coronary artery bypass grafting procedure only as AusSCORE[14] and subsequently developed to include all cardiac surgical procedures, known as the "all procedures" model.[15] This "all procedures" version was used in our analysis, which is referred to as AusSCORE-AP. In the absence of previously documented techniques of finding equivalent score ranges, we calculated the interquartile range (IQR) of the AusSCORE-AP in our population for each of the five possible categories of EuroSCORE included in the original ACTA-PORT score.

Table 1: Multivariable Risk Score showing how ACTA-PORT score is calculated, showing the number of score-points that were attributed to each group

Characteristics	Points
Age (years)	
< 70	+0
≥ 70	+1
Sex	
Men	+0
Women	+1
Haemoglobin (g/L)	
< 110	+9
110–119	+8
120–129	+6
130–139	+3
140–149	+2
≥ 150	+0
Body surface area (m^2)	
< 1.7	+6
1.7–1.89	+4
1.9–2.09	+2
2.1–2.29	+1
≥ 2.3	+0
EuroSCORE	
< 1	+0
1	+2
2	+3
3–8	+4
≥ 9	+5
Preoperative creatinine (μmol/L)	
< 88	+0
88–176	+1
≥ 177	+3
Type of operation	
CABG/valve	+2
Combination	+5
Other	+0

CABG = coronary artery bypass grafting.

Approximations of these IQRs of AusSCORE-AP replaced the EuroSCORE categories in the new model. These two techniques in turn yielded two scores: the original ACTA-PORT score using the calculated EuroSCORE (the ACTA-

PORT-ES), and the original ACTA-PORT score using the AusSCORE-AP ranges to replace EuroSCORE (the ACTA-PORT-AS). The discrimination and calibration of each of these two scores were then assessed.

Finally, given that it is likely transfusion practices will vary across the two populations, it is also likely that the calibration of the score will be affected. We determined *a priori* that we would recalibrate the ACTA-PORT score using data derived from the Australian population. In order to do this, the dataset was split randomly into two populations (by hospital) in an approximate 75:25 ratio, resulting in a training set and a validation set. Logistic regression was carried out in the training set using allogeneic red cell transfusion as the outcome and the ACTA-PORT-AS as the independent variable. Predictions based on this logistic regression were generated for the validation set using the ACTA-PORT-AS integer score. We termed this the "AntiPORT" (Antipodean Perioperative Risk of Blood Transfusion) recalibration. Discrimination and calibration were then assessed in the validation set.

Baseline characteristics were compared between patients transfused and those not transfused using χ^2 tests for categorical data, Student *t* tests for normally distributed data, and Wilcoxon rank sum tests for non-normally distributed data. Correlation was assessed using the Pearson pairwise correlation. Discrimination of AntiPORT was assessed using area under the receiver operating characteristic (AUROC) curves. Calibration was assessed using calibration plots. Both were assessed using the Brier score. All analyses were carried out using Stata version 16.1.

Results

We analysed data from 30 393 patients from 37 hospitals, whose baseline characteristics are displayed in Table 2. Five patients (0.02%) had missing red cell transfusion data and were excluded, resulting in a final analysis cohort of 30 388 patients. Of these, a total of 10 030 patients (33%) were transfused. Age, female sex, New York Heart Association class 4 status, diabetes mellitus, hypertension, and elevated creatinine were positively associated with risk of transfusion following univariate analysis. In addition, patients undergoing combined surgery or emergency surgery were more likely to require transfusion. Body mass index and preoperative haemoglobin were both negatively associated with transfusion risk.

The EuroSCORE and AusSCORE-AP were strongly correlated ($r = 0.83$; $P < 0.001$). The range of EuroSCORE used in ACTA-PORT versus the corresponding AusSCORE-AP are shown in Figure 1. Due to the significant overlap between a EuroSCORE of 1 and 2, these two categories were combined. Assigned ACTA-PORT scores for AusSCORE-AP based on these equivalents are shown in Table 3. The resultant integer AntiPORT scoring system is shown in Table 4.

Discrimination in the Australian population was similar to the UK population, with an AUROC curve for ACTA-PORT-ES and red cell transfusion of 0.76 (95% CI, 0.75–0.76; $n = 30\ 071$), and for ACTA-PORT-AS of 0.76 (95% CI, 0.75–0.76; $n = 29\ 487$). Brier scores were 0.19 for both. Calibration was poorer, with overprediction of transfusion on calibration plots (Figure 2).

Splitting the dataset yielded a training set ($n = 22\ 407$, comprising 28 hospitals) and a validation set ($n = 7981$, comprising nine hospitals). The median hospital volume per year was 353 (IQR, 169–492) in the training set compared with 324 (IQR, 222–468) in the validation set. Logistic regression in the training set showed ACTA-PORT-AS was strongly associated with red cell transfusion (odds ratio, 1.22; 95% CI, 1.21–1.23; $P < 0.001$; $n = 21\ 743$). AUROC curve in the validation set was 0.76 (95% CI, 0.75–0.77; $n = 7744$) (Figure 3, A), and Brier score was 0.18. Calibration was improved (Figure 3, B). Sensitivity, specificity and percentage correctly classified are shown in the Online Appendix. The predicted rate of transfusion based on the AntiPORT recalibration is shown in Table 5, with the corresponding predicted rate of transfusion from the original ACTA-PORT score as reference.

Discussion

We performed a retrospective validation study of the ACTA-PORT score for patients undergoing cardiac surgery in Australia. We demonstrated that discrimination between UK and Australian populations for the original ACTA-PORT score was similar when either derived EuroSCORE or AusSCORE-AP was used, but calibration was inaccurate, with overprediction of transfusion based on observed rates. Recalibrating the ACTA-PORT score to the local population resulted in a score that was both discriminative and well calibrated.

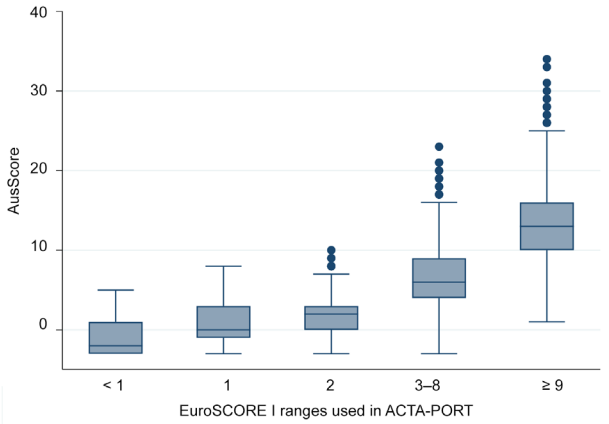
Broadly speaking, discrimination represents the ability to predict individual patient outcomes, and calibration reflects the model's ability to predict groups of patients at different levels of risk (or the agreement between estimated and actual risk). In this study, although the discrimination is acceptable (AUROC curve, 0.7–0.8), the calibration is good. This means that we can predict groups of patients at elevated or reduced risk of transfusion relatively well and potentially intervene in patients with higher risk (eg, > 50% transfusion risk). The ability to accurately predict transfusion risk allows for better directed and more cost-effective use of PBM strategies. Patients with a low score could proceed

Table 2. Baseline characteristics of the dataset used in AntiPORT derivation and validation

Columns by RBC transfusion	No RBC	RBC	Total	*P*
Total number of patients	20 358 (67.0%)	10 030 (33.0%)	30 388 (100.0%)	
Age (years), median (IQR)	66 (57–73)	69 (60–76)	67 (58–74)	< 0.001
Sex				
Male	16 247 (79.8%)	6427 (64.1%)	22 674 (74.6%)	
Female	4111 (20.2%)	3603 (35.9%)	7714 (25.4%)	< 0.001
Procedure type				
CABG	10 991 (54.0%)	4367 (43.5%)	15 358 (50.5%)	
Valve surgery	4769 (23.4%)	1948 (19.4%)	6717 (22.1%)	
Combined CABG/valve	1445 (7.1%)	1384 (13.8%)	2829 (9.3%)	
Other	3153 (15.5%)	2331 (23.2%)	5482 (18.0%)	< 0.001
Preoperative haemoglobin (g/L)	142 (19%)	126 (29%)	138 (24%)	< 0.001
Preoperative creatinine (µmol/L), median (IQR)	84 (72–99)	89 (73–115)	85 (72–103)	< 0.001
Diabetes				
No diabetes	14 605 (71.8%)	6680 (66.6%)	21 285 (70.1%)	
Diabetes	5731 (28.2%)	3343 (33.4%)	9074 (29.9%)	< 0.001
Hypertension				
No hypertension	6064 (29.8%)	2689 (26.8%)	8753 (28.8%)	
Hypertension	14 272 (70.2%)	7332 (73.2%)	21 604 (71.2%)	< 0.001
NYHA status				
1	8740 (43.0%)	3489 (34.8%)	12 229 (40.3%)	
2	7702 (37.9%)	3515 (35.1%)	11 217 (36.9%)	
3	3306 (16.3%)	2217 (22.1%)	5523 (18.2%)	
4	596 (2.9%)	803 (8.0%)	1399 (4.6%)	< 0.001
Estimated ejection fraction				
Normal	10 173 (50.8%)	4779 (48.8%)	14 952 (50.2%)	
45–60%	6862 (34.3%)	2844 (29.1%)	9706 (32.6%)	
30–45%	2368 (11.8%)	1453 (14.8%)	3821 (12.8%)	
< 30%	604 (3.0%)	710 (7.3%)	1314 (4.4%)	< 0.001
BMI (kg/m^2), median (IQR)	29 (25–32)	27 (24–31)	28 (25–32)	< 0.001
Urgency				
Non-urgent	14 969 (73.5%)	5872 (58.6%)	20 841 (68.6%)	
Urgent	4907 (24.1%)	3245 (32.4%)	8152 (26.8%)	
Emergency	468 (2.3%)	860 (8.6%)	1328 (4.4%)	
Salvage	12 (0.1%)	51 (0.5%)	63 (0.2%)	< 0.001
Previous cardiac surgery				
No	19 368 (95.2%)	8862 (88.4%)	28 230 (92.9%)	
Yes	985 (4.8%)	1163 (11.6%)	2148 (7.1%)	< 0.001
Perfusion time, median (IQR)	91 (70–119)	112 (82–157)	97 (73–130)	< 0.001
Mortality				
Survived	20 262 (99.5%)	9504 (94.8%)	29 766 (98.0%)	
Died	96 (0.5%)	526 (5.2%)	622 (2.0%)	< 0.001

BMI = body mass index; CABG = coronary artery bypass grafting; IQR = interquartile range; NYHA = New York Heart Association; RBC = red blood cell.

Figure 1. Box plot of AusSCORE plotted against EuroSCORE categories from ACTA-PORT



to surgery without further optimisation, reserving more intensive methods for those at higher risk. Many strategies to optimise anaemia require delays to be effective, and attempts to avoid such delays may necessitate expensive combination treatments such as intravenous iron, vitamin B12, folate and erythropoietin.[16] In addition to guiding the graduated use of PBM, and potentially improving resource allocation, this score could be used for benchmarking. Studies of transfusion in cardiac surgery regularly show that practices vary enormously between centres.[17,18] It is possible that practices at units with lower risk-adjusted transfusion rates could be investigated and emulated at other hospitals. Finally, there are significant implications to future PBM research. When designing an international clinical trial, the capacity to screen and assess using a common "risk prediction language" can have major impacts on feasibility, as was recently shown in a study that validated multiple risk prediction tools as part of an international cohort study.[19] Furthermore, from the perspective of the bedside clinician, applying the results of clinical trials from other countries to the individual patient is both easier and more reliable if the risk prediction models used in the trial have been validated in the local population first. Consequently, the transformation of ACTA-PORT to "AntiPORT" could allow

Table 3. Assigned EuroSCORE versus AusSCORE equivalents for the purposes of calculating the ACTA-PORT score

EuroSCORE	AusSCORE	ACTA-PORT score value
< 1	–3 to 0	0
1	1–3	3
2	1–3	3
3–8	4–9	4
≥ 9	≥ 10	5

Table 4. The AntiPORT score with AusSCORE values substituted for EuroSCORE

Characteristics	Points
Age (years)	
< 70	+0
≥ 70	+1
Sex	
Male	+0
Female	+1
Haemoglobin (g/L)	
< 110	+9
110–119	+8
120–129	+6
130–139	+3
140–149	+2
≥ 150	+0
Body surface area (m^2)	
< 1.7	+6
1.7–1.89	+4
1.9–2.09	+2
2.1–2.29	+1
≥ 2.3	+0
AusSCORE	
< 1	+0
1–3	+3
4–9	+4
≥ 10	+5
Creatinine (μmol/L)	
< 88	+0
88–176	+1
≥ 177	+3
Type of operation	
CABG/valve	+2
Combination	+5
Other	+0

CABG = coronary artery bypass grafting

Figure 2. Calibration plot showing predicted versus observed transfusions for ACTA-PORT-AS when applied to the local dataset

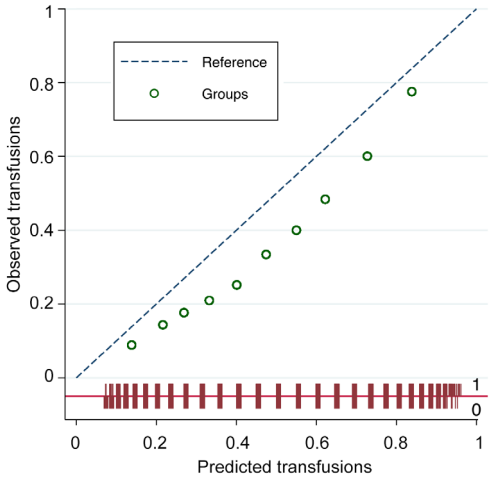
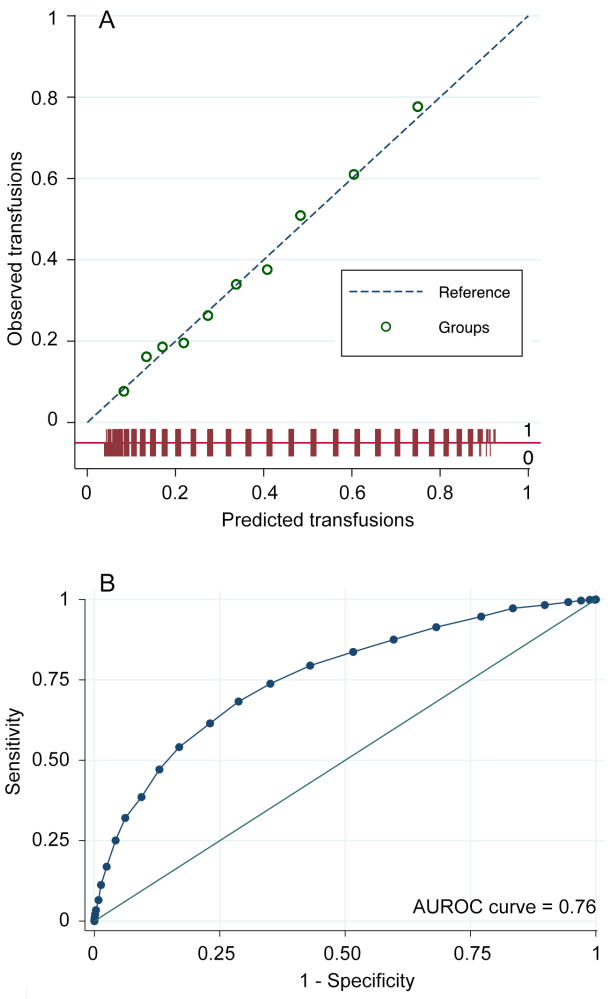


Figure 3. (A) Calibration plot showing predicted versus observed transfusions for recalibrated ACTA-PORT-AS — the "AntiPORT". (B) Receiver operating curve for recalibrated ACTA-PORT-AS — the "AntiPORT"



AUROC = area under the receiver operating characteristic.

common enrolment of patients in Australia and the UK into trials that attempted to recruit patients at a high risk of receiving allogeneic blood transfusion as part of cardiac surgery. Alternatively, this could allow a clinician in the UK to apply the results of an Australian trial to their individual practice once the appropriate recalibration factor was considered. Critically, both ACTA-PORT and AntiPORT use data collected routinely for the purposes of clinical audit (including the EuroSCORE in the UK and AusSCORE-AP in Australia), raising the possibility of using these scores as automatically calculated metrics to screen patients for embedded clinical trials.

Even though there are similarities between UK and antipodean cardiac surgical and transfusion practices, previous studies that have attempted to adapt risk prediction scores developed in the northern hemisphere to Australasian patients have shown that this process is not simple. A recent study that attempted to adapt a surgical risk prediction score from the UK to a New Zealand cohort showed that an unadjusted model underpredicted mortality by a factor of five.[11] In cardiac surgery, the commonly used EuroSCORE model was found to significantly overpredict mortality in a representative cohort of Australian patients drawn from six hospitals,[13] necessitating the development of a prediction model that was trialled and validated in a local patient cohort: the AusSCORE.[14]

Multiple scoring systems have been developed to predict red blood cell transfusion risk in cardiac surgery with varying degrees of accuracy, simplicity and generalisability. The best known of these systems are the BRiSc,[8] TRACK,[7] TRUST[5] and Goudie scores.[6] All of these scores have significant merits but also weaknesses, most driven by the inverse relationship between simplicity and accuracy. The ACTA-PORT score was chosen for our study as we feel it bests strikes the balance between simplicity, accuracy, and practicality for use by clinicians. As mentioned in the literature, these scores have little value to patients unless they have a positive impact on clinical management and patient outcomes, and to do this they must, above all, be usable.[20]

The strengths and limitations of this study should be recognised. We used a large national database incorporating multiple surgical units. The split into development and validation cohorts was carried out by the surgical unit (randomly), rather than using individual patients. This suggests the score is valid across surgical units with differing

Table 5. Predicted risk of transfusion for AntiPORT recalibration, with corresponding ACTA-PORT predicted risk as comparison

AntiPORT/ ACTA-PORT score	Predicted risk of transfusion (ACTA-PORT)	Predicted risk of transfusion (AntiPORT)
0	4.7%	2.7%
1	5.7%	3.2%
2	6.9%	3.9%
3	8.3%	4.8%
4	10.0%	5.8%
5	11.9%	7.0%
6	14.2%	8.4%
7	16.8%	10.1%
8	19.8%	12.1%
9	23.1%	14.4%
10	26.9%	17.1%
11	31.0%	20.1%
12	35.4%	23.5%
13	40.1%	27.4%
14	45.0%	31.5%
15	50.0%	36.0%
16	55.0%	40.8%
17	59.9%	45.8%
18	64.6%	50.8%
19	69.0%	55.8%
20	73.1%	60.7%
21	76.9%	65.4%
22	80.2%	69.8%
23	83.2%	73.9%
24	85.8%	77.6%
25	88.1%	80.9%
26	90.0%	83.8%
27	91.7%	86.4%
28	93.1%	88.6%
29	94.3%	90.5%
30	95.3%	92.1%

practices. It is notable that PBM and transfusion practices have evolved significantly over the past decade, affecting the applicability of the score to current practice. Recent research regarding liberal versus restrictive transfusion practices, including the TRICS III trial,[21] suggests that restrictive transfusion practices are non-inferior to liberal ones. The publication of this trial towards the end of our study period could be argued to have influenced transfusion practices during our study period, and it is possible that transfusion practices could have changed since. However, a review of the ANZSCTS database between 2017 and 2020 (unpublished data) did not show any broad change in transfusion rates during that period. This is consistent with previous research demonstrating the significant lag between research and a change in clinical practice.[22] For this reason, we believe the data remain relevant. Nonetheless, it is likely that future recalibrations will be necessary as patient risk profile and medical practice change. It is possible that a more discriminative risk prediction tool could have been generated in this population by bespoke design, rather than recalibration of an existing tool. However, for reasons described previously, it was felt that the ability to apply a common risk score internationally was more important.

Conclusions

To conclude, we have developed a local variation of a UK-based transfusion risk prediction score. The AntiPORT score is an accurate scoring system to predict perioperative blood transfusion in patients undergoing cardiac surgery in Australia. The score has a number of potential uses, including the effective allocation of PBM resources, as a quality control initiative as part of a program of comprehensive audit, and as a means of achieving consistent appreciation of risk in patients enrolled in international clinical trials of transfusion practice across different countries. Finally, the AntiPORT score is a clinically useful transfusion-prediction score that can be utilised easily at the bedside by clinicians using the QxMD software package, including an online calculator and the "Calculate by QxMD" application for mobile devices (https://qxmd.com). In addition to its academic value, we hope that this may become a practical and useful tool for perioperative physicians in Australia when caring for patients in preparation for cardiac surgery.

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Competing interests

All authors declare that they do not have any potential conflict of interest in relation to this manuscript.

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