

Transfusion practice varies widely in cardiac surgery: Results from a national registry


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Objectives: Evidence is accumulating of adverse outcomes associated with transfusion of blood components. If there are differences in perioperative transfusion rates in cardiac surgery, and what hospital factors may contribute, requires further investigation.

Methods: Analysis of 42,743 adult patients who underwent 43,482 procedures from 2005 to 2011 at 25 Australian hospitals, according to the Australian and New Zealand Society of Cardiac and Thoracic Surgeons Cardiac Surgery Database. Multiple logistic regression examined associations of patient and hospital characteristics with transfusion of ≥ 1 red blood cell (RBC) unit; platelet (PLT), fresh frozen plasma (FFP), and cryoprecipitate (CRYO) doses; and ≥ 5 RBC units, from surgery until hospital discharge.

Results: Procedures included 24,222 (55%) isolated coronary artery bypass grafts, 7299 (17%) isolated valve, 4714 (11%) coronary artery bypass graft and valve, and 7247 (17%) other procedures. After adjustment for various patient and procedure characteristics, transfusion rates varied across hospitals for ≥ 1 RBC unit from 22% to 67%, ≥ 5 RBC units from 5% to 25%, ≥ 1 PLT dose from 11% to 39%, ≥ 1 FFP dose from 11% to 48% and ≥ 1 CRYO dose from 1% to 20%. Hospital characteristics, including state or territory, private versus public, and teaching versus nonteaching, were not associated with variation in transfusion rates.

Conclusions: Variation in transfusion of all components and large volume RBC was identified, even after adjustment for patient and procedural factors known to influence transfusion, and this was not explained by hospital characteristics. (*J Thorac Cardiovasc Surg* 2014;147:1684-90)

 Supplemental material is available online.

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A substantial proportion of blood components worldwide are issued to patients undergoing cardiac surgery. In Australia this is the second most common surgical indication for red blood cell (RBC) use; the largest single indication for fresh frozen plasma (FFP), accounting for approximately 15% of all plasma use; and the second largest indication for platelet (PLT) transfusion after hematology and oncology.^{1,2} Despite the significant use of blood components by patients undergoing cardiac surgery, the evidence to guide transfusion therapy is limited, particularly for components other than RBCs. There have been few studies on the optimal triggers for RBC transfusion, and these have been mostly in other clinical settings.^{3,4} Studies on the use of FFP and PLT in cardiac surgery are also limited, with varying results regarding outcomes.⁵⁻⁸

There is evidence of significant variation in the transfusion rates of blood components in cardiac surgery between institutions and individual clinicians,⁹⁻¹² and this variation has been shown to continue following publication of

Abbreviations and Acronyms

ANZSCTS	= Australian and New Zealand Society of Cardiac and Thoracic Surgeons
CABG	= coronary artery bypass graft
CRYO	= cryoprecipitate
FFP	= fresh frozen plasma
PLT	= platelet
RBC	= red blood cell

transfusion practice guidelines.¹³ A previous small Australian survey conducted in 2004 reported substantial variation in RBC use between institutions following cardiac surgery.¹⁴ It is not known if these differences persist, if this also applies to the use of non-RBC components, and if hospital characteristics contribute to differences in practice. In our study, we investigated if significant variation exists in blood product use in cardiac surgery, after adjusting for patient-related variables that might reasonably influence the need for transfusion. We also investigated if hospital characteristics account for variation in transfusion rates after adjusting for patient-level characteristics.

METHODS

Patients

All cardiac surgery patients aged 18 years or older reported to the Australian and New Zealand Society for Cardiac and Thoracic Surgery (ANZSCTS) Cardiac Surgery Database, between January 1, 2005, and December 31, 2011, from 25 Australian hospitals, were included in the study. Not all 25 hospitals reported for the entire study duration; however, once reporting commenced all consecutive cases were included.

During this period there were a total of 43,482 procedures recorded in 42,743 adult patients at the 25 hospitals. These included isolated coronary artery bypass graft (CABG) in 24,222 (55%), isolated valve in 7299 (17%), CABG and valve in 4714 (11%), and other procedure in 7247 (17%). Procedures (n = 147) in patients younger than age 18 years were excluded.

ANZSCTS Cardiac Surgery Database

The ANZSCTS Cardiac Surgery Database prospectively collects information on all adult patients undergoing cardiac surgery at participating hospitals using a standardized data set and definitions, including patient demographics, preoperative risk factors, preoperative medications, intraoperative details, transfusion therapy received (including number of units of RBCs, PLTs, FFP, and cryoprecipitate [CRYO]), length of stay, complications, and patient outcomes.¹⁵

Statistical Methods

Summary statistics for continuous data are reported as mean and standard deviation or median and interquartile range as appropriate, and as number and percent for categorical variables.

Binary categorical variables for the outcomes of interest were created: ≥ 1 RBC unit, large-volume RBC transfusion (≥ 5 RBC units), low-volume RBC transfusion (1 or 2 RBC units), ≥ 1 FFP adult equivalent dose, ≥ 1 PLT adult equivalent dose, and ≥ 1 CRYO adult equivalent dose. Logistic regression analyses explored the association between covariates, including hospital site, and outcomes, using a backward stepwise approach. Variables that were associated with the outcomes of

interest with a *P* value $< .25$ were considered for the multiple logistic regression models. Pearson's correlation was used to assess variables for potential collinearity, with the more clinically relevant variable selected where present. Covariates considered for the models were those which that reasonably influence a decision to transfuse and included hospital site, patient age, sex, body mass index, peripheral or cerebrovascular disease, prior myocardial infarction, diabetes, New York Heart Association functional class, lung disease, infective endocarditis, preoperative creatinine, medications (including antiplatelet agents within 5 days, anticoagulants, and immunosuppressive therapy), previous cardiothoracic procedure, procedure type and urgency, preoperative shock, and use of intra-aortic balloon pump. Correlation of hospital-adjusted rates of RBC versus PLT and RBC versus FFP were also assessed. Analysis was performed on all procedures and repeated for first-time CABG only.

To explore the association of hospital-level characteristics and outcome, variables for the type of institution (academic affiliation and private or public) and in which area they were located, the median number of cardiac procedures performed annually, and previous covariates were added in multiple multilevel logistic regression models, where hospital site was now modeled as a random effect.¹⁶

All analyses were performed using the statistical software packages Stata 11.2 (Statacorp LP, College Station, Tex).

RESULTS

Patient demographics, comorbidities, and surgical and hospital characteristics for all procedures are shown in [Table 1](#). The total number of cardiac surgeries performed at each hospital ranged from 312 to 4193 (median, 1327; IQR, 669-2557) and the median annual number of cardiac surgeries performed at each hospital ranged from 154 to 588 (median, 238; IQR, 164-353).

The most important patient characteristics associated with RBC transfusion in multivariate analysis based on effect size included patient age (odds ratio [OR], 1.1; 95% confidence interval [CI], 1.0-1.1), New York Heart Association functional class II or greater heart failure (class IV OR, 1.7; 95% CI, 1.5-1.9) procedure other than isolated CABG or valve (OR, 2.2; 95% CI, 1.9-2.3), previous cardiac surgery (OR, 1.3; 95% CI, 1.2-1.4), urgent (OR, 2.9; 95% CI, 2.5-3.2) or emergency surgery (OR, 3.7; 95% CI, 2.1-6.5), and the use of acetylsalicylic acid (OR, 1.2; 95% CI, 1.1-1.2) or clopidogrel (OR, 1.1; 95% CI, 1.1-1.2) within 7 days before surgery.

The rate of transfusion, after adjusting for patient and surgical characteristics, of any RBC unit ranged between hospitals from 22% to 67%, ≥ 5 RBC units from 5% to 24%, 1 or 2 RBC units from 10% to 34%, ≥ 1 PLT dose from 10% to 39%, ≥ 1 FFP dose from 10% to 44%, and ≥ 1 CRYO dose from 1% to 21%. The hospital-adjusted rates of transfusion of RBC, PLTs, FFP, and CRYO for all procedures are shown in [Figure 1](#). Similar variation in adjusted rates of blood product use was also present when the analysis was limited to only isolated CABG procedures with no history of previous cardiac surgery ([Figure E1](#)). Hospital rates of RBC versus PLT transfusion and RBC versus FFP transfusion after adjustment for patient and surgical characteristics are shown in [Figure 2](#).

TABLE 1. Patient, surgical, and hospital characteristics for all procedures

Characteristic	All procedures
Total number of procedures	43,482
Patient demographics	
Age, y	66 ± 13
Male gender	31,414 (72)
Body mass index	28.2 ± 5.4
Prior myocardial infarction	16,652 (38)
Cerebrovascular disease	5027 (12)
Dialysis preoperative	752 (2)
Lung disease	5815 (13)
Congestive heart failure	10,153 (23)
Diabetes	12,344 (28)
Medications	
Anticoagulants at time of surgery	8622 (20)
Acetylsalicylic acid within 7 d	21,655 (50)
Clopidogrel within 7 d	5292 (12)
Surgical	
Previous cardiothoracic surgery	8320 (19)
Procedure type	
Isolated coronary artery bypass graft	24,222 (55)
Isolated valve	7299 (17)
Other	11,961 (28)
Urgency more than elective	14,482 (34)
Cardiopulmonary bypass duration, min	113 ± 56
Crossclamp time, min	82 ± 42
Intra-aortic balloon pump	2305 (5)
Hospital level characteristics (n = 25 hospitals)	
Academic affiliation (n = 18)	35,345 (81)
No academic affiliation (n = 7)	8137 (19)
Public (n = 19)	36,041 (83)
Private (n = 6)	7441 (17)
State 1 (n = 9)	23,082 (53)
State 2 (n = 9)	13,573 (31)
Other (n = 7)	6872 (16)

Values are presented as mean ± standard deviation or n (%).

The observed rates of transfusion of RBC, PLT, FFP, and CRYO by hospital-level characteristics are shown in [Table 2](#). After adjustment for patient characteristics (including patient and procedure characteristics) in the multilevel regression analysis, none of the 4 hospital-level characteristics was associated with the transfusion outcomes examined ([Table 3](#)).

DISCUSSION

This nationwide analysis of 43,529 cardiac surgical procedures performed at 25 hospitals within Australia demonstrated substantial variation in hospital rates of transfusion of blood components, after adjusting for patient and surgical characteristics, which was not accounted for by the hospital characteristics examined. The finding of variation in blood product use is consistent with a previous Australian study and other international studies that have

demonstrated variation in transfusion of RBCs,¹⁴ PLTs, and plasma in cardiac surgery.^{9-12,17,18}

Substantial variation in both low volume and large volume RBC transfusion across the 25 institutions was identified, and this variation persisted after adjusting for patient and surgical characteristics that might reasonably influence a decision to transfuse and limiting the analysis to isolated CABG. It is not surprising that individual clinician preference or institutional practice may influence the decision for a low volume RBC transfusion during the perioperative period. However, the requirement of large volume transfusion also appears to be in part dependent on institutional practice even after adjusting for patient and surgical characteristics, including the need for reoperation to control bleeding. Because we did not examine rates of perioperative blood loss between sites, it is not possible from our study to determine if the variation in large volume transfusion is due to differences in bleeding complications across sites or due to a difference in the preferred approach to manage large volume blood loss. However, another study¹⁷ that demonstrated variation in rates of massive transfusion following cardiac surgery found that perioperative bleeding was relatively consistent between sites, whereas methods for managing this bleeding was more subject to differences.

As observed for RBC transfusion, there was wide variation in the use of FFP, PLT, and CRYO. Hospitals that had higher use of RBCs also tended to have higher transfusion rates of other blood products, and those with a more restrictive use of RBCs had comparatively lower rates of transfusion of other components.

Although there was considerable variation between institutions in transfusion practice, this did not appear to be attributable to hospital-level characteristics, including if the hospital was private or public, had an academic affiliation, or the median number of procedures performed annually. Although differences were evident in observed rates of transfusion between private and public hospitals and also academic status, after adjusting for patient and surgical characteristics, the association of these hospital-level characteristics with transfusion did not persist. This is in contrast to a study from the United States⁹ linking perioperative RBC use to hospital academic status and geographic region. Although Australia has a relatively uniform health system, there are differences between state jurisdictions in health service structures and the funding of blood products, which may influence practice. However, after adjusting for patient and surgical characteristics, geographic location did not explain the variation in rates of transfusion between institutions.

The finding of variation in transfusion practice in our study, as in other studies, is important for a number of reasons. There is increasing evidence from observational studies of an association between RBC transfusion and

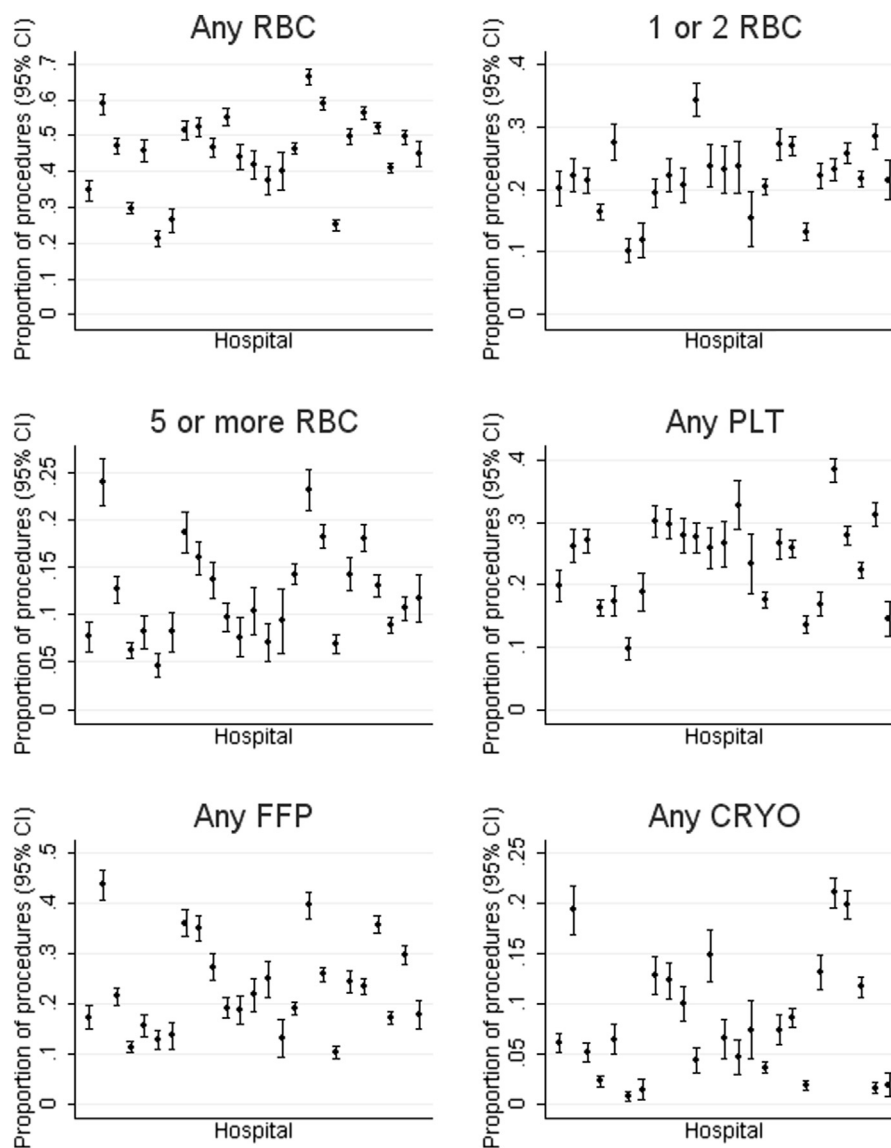


FIGURE 1. Adjusted transfusion outcome rates for all procedures at 25 hospitals. *CI*, Confidence interval; *RBC*, red blood cell; *PLT*, platelet; *FFP*, fresh frozen plasma; *CRYO*, cryoprecipitate.

adverse outcomes, including mortality (both short and long-term survival), length of stay, multiorgan failure, infection, and thrombosis.¹⁹⁻²¹ Due to ethical and practical constraints, randomized controlled trials of transfusion compared with nontransfusion in cardiac surgery have not been performed. However, studies comparing different transfusion strategies, including restrictive or reduced transfusion triggers, have shown comparable outcomes. A noninferiority randomized controlled trial of 502 patients undergoing cardiac surgery with cardiopulmonary bypass comparing a restrictive with a more liberal transfusion strategy (maintaining a hematocrit of 24% vs 30%) found comparable mortality and morbidity outcomes.³ However, this was a single-center study, used fresh nonleukoreduced RBCs, and

included less than half of all eligible patients, so the generalizability of the study findings are limited. Other observational studies have demonstrated an association between reduction in blood transfusion rates and improved outcomes.²²

There are even fewer data to guide transfusion support with other blood components in cardiac surgery. Transfusion of FFP has been associated with increased mortality in cardiac surgery⁸; however, there are conflicting findings on the association of PLT transfusions with outcomes.^{5,23} Although studies have reported on use of fibrinogen concentrate in cardiac surgery, the use of CRYO has not been examined.²⁴ The lack of evidence to support transfusion decisions for blood components other than RBCs may contribute to the observed variation in



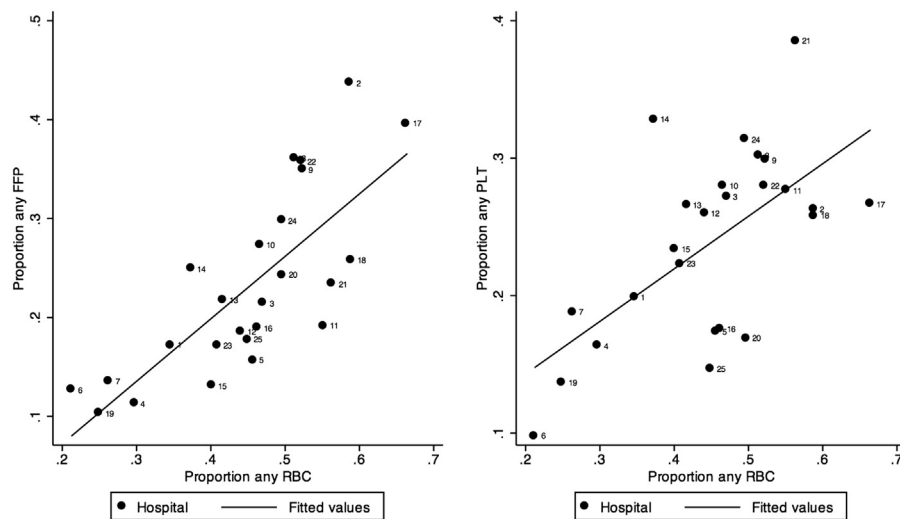


FIGURE 2. Adjusted rates of platelet (PLT), fresh frozen plasma (FFP), and red blood cell (RBC) transfusion, by hospital.

use of these components in cardiac surgery. In fact, in recently published national Perioperative Patient Blood Management Guidelines,²⁴ few recommendations or practice points could be made for the use of other blood components due to the lack of evidence. The marked variation in blood product use in cardiac surgery, coupled with limited evidence to inform practice, highlights the requirement for future studies to assess the effect of blood components on patient outcomes.

With the accumulating evidence of the association of RBC transfusion with some adverse outcomes, the increasing costs associated with transfusion and consideration of preservation of limited blood supplies, it has been proposed that RBC transfusion should be included as a quality indicator in cardiac surgery.²⁵ With an aging population and advances in medical care, the demand for blood products is expected to rise, placing further demands on a limited resource. In addition, the cost of transfusion is increasing, with reduced donor availability and measures to minimize transfusion risks as contributing factors.²⁶ Although reducing unnecessary transfusions is important, there is likely to be a point, albeit as yet undefined, where lowering the transfusion rate any further would pose risks

for patients. Therefore, when considering transfusion as a quality indicator, it should be the rate of appropriate transfusion, rather than the lowest transfusion rate, that is the desired outcome.

It has been argued that wide variation in transfusion practice is an indicator of excessive or inappropriate transfusions.²⁷ However substantial variation in practice is also a pointer to an inadequate evidence base to guide practice. In this setting, the optimal use of blood products in cardiac surgery has not been well established and therefore the ideal approach to change transfusion practice and reduce variation is not clear.

Our study has demonstrated significant institutional variation in transfusion practice within a relatively uniform health system and with ready access to blood products. However, neither patient, procedure, nor hospital-level characteristics, including academic affiliation or the hospital's location, accounted for this variation. These observed differences should be interpreted in light of the limitations of the study. First, the ANZSCTS Cardiac Surgery Database does not include preoperative or intraoperative hemoglobin, hematocrit, platelet count, or coagulation profile, nor does it collect information on the

TABLE 2. Frequency of blood product use, by hospital-level characteristics

Hospital characteristic	Any RBC	RBC (1-2 units)	RBC (≥5 units)	PLT	FFP	CRYO
Public	16,389 (46)	7812 (22)	4595 (13)	8649 (24)	8365 (23)	3180 (9)
Private	3047 (41)	1484 (20)	741 (10)	1382 (19)	1389 (19)	450 (6)
Academic affiliation						
Yes	16,118 (46)	7671 (22)	4539 (13)	8571 (24)	8266 (23)	3171 (9)
No	3318 (41)	1625 (20)	797 (10)	1460 (18)	1488 (18)	459 (6)
State 1	10,231 (44)	4874 (21)	2844 (12)	5297 (23)	4716 (20)	2188 (10)
State 2	6387 (47)	2965 (22)	1808 (13)	3234 (24)	3472 (26)	1229 (9)
Other states	2818 (42)	1457 (22)	684 (10)	1500 (22)	1566 (23)	213 (3)

Values are presented as n (%). RBC, Red blood cell; PLT, platelet; FFP, fresh frozen plasma; CRYO, cryoprecipitate.

TABLE 3. Odds ratio and 95% confidence intervals of association of hospital-level characteristics and transfusion outcomes for all procedures*

Hospital characteristic	Any RBC	RBC 1-2 units	RBC ≥5 units	PLT	FFP	CRYO
Public	1.0	1.0	1.0	1.0	1.0	1.0
Private	0.8 (0.2-2.9)	0.9 (0.4-1.8)	0.8 (0.2-2.3)	1.7 (0.7-4.3)	0.9 (0.3-3.1)	2.2 (0.3-17)
Academic affiliation						
Yes	1.0	1.0	1.0	1.0	1.0	1.0
No	1.1 (0.4-4.5)	1.0 (0.5-2.0)	1.1 (0.3-3.3)	0.5 (0.2-1.2)	0.8 (0.2-2.6)	0.5 (0.1-3.5)
State 1	1.0	1.0	1.0	1.0	1.0	1.0
State 2	1.4 (0.8-2.4)	1.2 (0.8-1.6)	1.1 (0.7-1.9)	1.1 (0.7-1.6)	1.6 (0.9-2.6)	1.3 (0.6-3.4)
Other states	1.0 (0.6-1.8)	1.0 (0.7-1.5)	0.7 (0.4-1.2)	1.1 (0.6-1.7)	1.2 (0.6-2.3)	0.5 (0.2-1.3)
Median number	0.9 (0.9-1.0)	0.9 (0.9-1.0)	0.9 (0.9-1.0)	0.9 (0.9-1.0)	0.9 (0.9-1.0)	0.9 (0.9-1.0)

RBC, Red blood cell; PLT, platelet; FFP, fresh frozen plasma; CRYO, cryoprecipitate. *Odds ratio (95% confidence interval) are from multiple multilevel logistic regression with assignment of random effects for each hospital.

use of autologous blood. Therefore, the rates of transfusion could not be adjusted for these parameters in the multivariate analysis. Second, although the quality of the ANZSCTS data, including accuracy and completeness, has been validated with an external quality audit program, this has not included transfused blood components.¹⁵ Although we have established a generally high degree of accuracy of our data sources, it is possible that a small part of the institutional variation observed might be attributed to the way in which data on transfused blood components is collected or recorded.

CONCLUSIONS

These findings from a large and prospectively collected cardiac surgery database demonstrate wide variation in transfusion practice not accounted for by patient or hospital-level characteristics. Many areas remain where the evidence base to inform the use of blood products in cardiac surgery is lacking. Further clinical studies and formal evaluation of the effect of patient blood management programs, rates of transfusion, and patient outcomes, is warranted.

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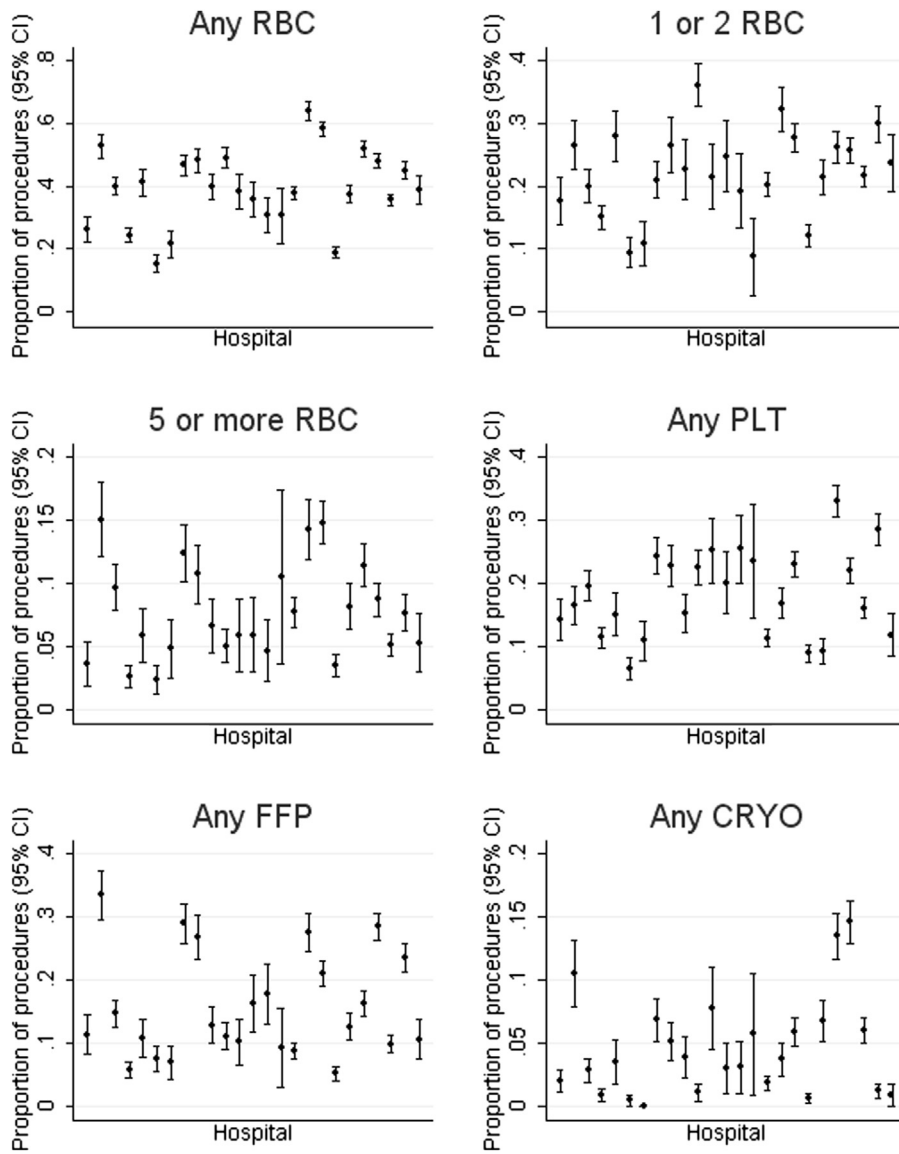


FIGURE E1. Adjusted transfusion outcome rates for primary coronary artery bypass graft only for 25 hospitals. *CI*, Confidence interval; *RBC*, red blood cell; *PLT*, platelet; *FFP*, fresh frozen plasma; *CRYO*, cryoprecipitate.