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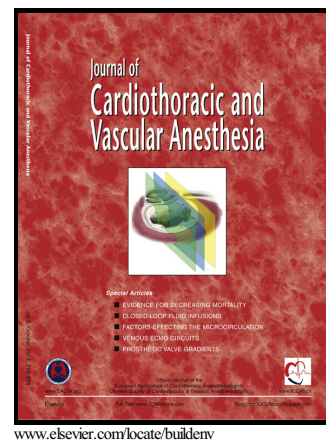
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## Author's Accepted Manuscript

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The relationship between pre-operative hemoglobin concentration, utilization of hospital resources and outcomes in cardiac surgery

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**Abstract:**

Objectives – Pre-operative anemia is an established risk factor associated with adverse peri - operative outcomes after cardiac surgery. However, limited information exists regarding the relationship between pre-operative hemoglobin and outcomes. The aim of this study was to investigate how outcomes are affected by pre-operative hemoglobin concentration in a cohort of patients undergoing cardiac surgery.

Study design – A retrospective observational cohort study.

Setting – A single center tertiary referral hospital.

Participants - 1972 adult patients undergoing elective and non – elective cardiac surgery.

Interventions / Observations - The independent relationship of pre-operative hemoglobin concentration was explored on blood transfusion rates, return to theatre for bleeding and/or cardiac tamponade, post-operative intensive care unit (ICU) and in - hospital length of stay and mortality.

Results - The overall prevalence of anemia was 32% (629 / 1972 patients). For every one unit increase in hemoglobin (g/dl), blood transfusion requirements were reduced by 11%, 8% and 3% for red blood cell units, platelet pools and fresh frozen plasma units respectively (adjusted incident rate ratio 0.89 (95% CI 0.87,0.91), 0.92

(0.88,0.97) and 0.97 (0.96,0.99). For each one unit increase in hemoglobin (g/dl) the probability (over time) of discharge from ICU and hospital increased (adjusted hazard ratio estimates 1.04 (1.00, 1.08) and 1.12 (1.12, 1.16) respectively).

Conclusion – A lower pre – operative hemoglobin concentration results in increased use of hospital resources after cardiac surgery. Each g/dl unit fall in pre – operative hemoglobin concentration results in increased blood transfusion requirements and increased post –operative ICU and hospital length of stay.

Key Words: Preoperative, hemoglobin, anemia, cardiac surgery, outcomes.

### **Introduction:**

Pre-operative anemia is recognized as an independent risk factor for increased peri - operative morbidity and mortality after both cardiac surgery (1-6) as well as non - cardiac surgery (7-11). Specifically, pre-operative anemia has been shown to be independently associated with major adverse cardiac and non – cardiac events including myocardial infarction, stroke, renal failure, prolonged ventilation, deep sternal wound infection, increased risk of red blood cell transfusions and an increase in both in - hospital and longer - term mortality. To date, most studies have examined the effect of anemia, rather than pre – operative hemoglobin concentration per se on outcomes after cardiac surgery. Studies examining the effect of pre-operative hemoglobin concentration have predominantly focused on patients undergoing elective coronary artery bypass graft (CABG) surgery (1-4, 12). In our view, the dichotomous classification of anemia poorly defines risk of adverse outcomes after cardiac surgery. We hypothesize that adverse outcomes and utilization of hospital

resources vary with pre – operative hemoglobin concentration and that the effects of both case mix and urgency of surgery on this are not known. Thus this study examines the relationship between pre - operative hemoglobin levels and utilization of hospital resources and adverse outcomes, specifically blood transfusion requirements, length of stay, return to theatre for re – exploration for bleeding and / or cardiac tamponade and mortality in a cohort of patients undergoing cardiac surgery that, to our knowledge, has not been studied before.

**Methods:**

We performed a single center retrospective observational cohort study, with the aim of examining the relationship between pre-operative hemoglobin concentration and the following peri - operative and post-operative outcomes: the likelihood and amount of red blood cell (RBC) units, fresh frozen plasma (FFP) and platelets transfused peri-operatively, the need to return to theatre for re-exploration for bleeding and/or cardiac tamponade, intensive care unit (ICU) length of stay, post-operative in-hospital length of stay and in - hospital mortality.

The study protocol was approved by the King's College London Biomedical Research Department in November 2014 (R&D Number: RJ114/N302) and was given exemption from ethical approval. All consecutive adult patients 16 years of age or older, undergoing cardiac surgery at St Thomas' Hospital, London UK, during the period from 1st October 2011 to 31st July 2013 were analyzed. Patients were excluded if they did not undergo cardiac surgery (16 patients); cardio-pulmonary bypass (22 patients) or no pre-operative hemoglobin data was available (3 patients). Therefore, 1972 patients were included in the final analysis. No formal a priori sample size calculation was undertaken as the main purpose of the project was to

model relationships rather than test specific hypotheses. The data arose from a local audit to examine compliance with anemia guidelines and contained near to 2000 individuals. In clinical practice, information on patient demographics, pre-morbid risk factors, details of operative procedures, and post - operative outcomes are routinely collected. Risk factors are defined according to those used in the European System for Cardiac Risk Evaluation (EuroSCORE) (13). Laboratory values were obtained from the Electronic Patient Records Database, which routinely stores all laboratory results. Transfusion requirements were provided by the Guy's and St Thomas' NHS Trust transfusion department database. The 24 - hour post - operative blood loss was measured from chest drain output, which is recorded in the Intellispace Critical Care and Anaesthesia (ICIP) electronic notes system. Information from these four sources was amalgamated to form the study database for analysis. Pre - operative laboratory values including hemoglobin and estimated glomerular filtration rate (eGFR) were taken to be the closest value prior to the day of surgery. Post - operative hemoglobin was taken as the first available value the day following surgery. Anemia, for presentation and tabulation purpose, was classified according to World Health Organization Criteria as being  $<13\text{g/dl}$  for males and  $<12\text{g/dl}$  for females. Length of ICU stay and post-operative hospital stay were defined as the time from the day of operation to discharge from ICU and from hospital respectively. All data including operative type, operative priority, and return to theatre were defined according to definitions used by the National Institute for Cardiovascular Outcomes Research (NICOR) for the Society for Cardiothoracic Surgery (SCTS) National Adult Cardiac Surgery Audit (14). Red cells, platelets and fresh frozen plasma were counted as whole units transfused, which may have been administered at any time from the time of operation to the time of discharge from hospital.

All patients underwent general anesthesia with either a volatile or total intravenous anesthetic or a combination of the two. Anticoagulation was achieved with unfractionated heparin to an activated clotting time (ACT) > 480 seconds. The CPB circuit was primed with 1000ml of Compound Sodium Lactate (Hartmann's solution), 500ml of Geloplasma and 250ml of 10% Mannitol. CPB was achieved using standard techniques with a flow rate of 2.4 l/min/m<sup>2</sup>. CPB was performed with either normothermia, or mild – moderate hypothermia (32 – 36 degrees centigrade), unless specific surgery warranted lower temperatures e.g. deep hypothermic circulatory arrest. Cardiac arrest was achieved with blood crystalloid cardioplegia. After separation from CPB, anticoagulation was reversed with protamine sulfate. Shed mediastinal blood was collected and measured post-operatively but not re – infused. All patients were transferred to ICU post-operatively. Details of blood conservation strategies used in the operating room, post - operative transfusion triggers and discharge protocols from ICU and hospital are contained in the appendix.

Data were summarized using mean and standard deviation for parametric data, median and interquartile ranges for non-parametric data or frequency and percentages for categorical data. Descriptive statistics; T-tests, Kruskal Wallance tests and Chi-square tests, were used to compare unadjusted outcomes. The relationship between pre-operative hemoglobin and transfusion outcomes: red cell units transfused; fresh frozen plasma units transfused and platelets pools transfused, were explored by fitting a zero-inflated Poisson (ZIP) regression which allows for over dispersion due to the large (excess) number of patients who had zero counts (15). The ZIP regression uses a mixed model approach, whereby the number of units for patients transfused is



modeled using a standard Poisson regression model, and prediction to group (transfused versus not transfused) is modeled using a logistic model. The necessity of the ZIP model over and above the standard Poisson regression model was assessed using the Vuong test. The relationship between pre-operative hemoglobin and outcomes: length of hospital stay and intensive care stay, were investigated using a Cox proportional hazards model, where discharge was the event of interest and death was treated as a censoring event. The relationship between pre-operative hemoglobin and binary outcomes: return to theatre and mortality, were explored using a logistic regression model. Two approaches to adjusting for covariates were used. In the first approach the variable logistic EuroSCORE (16) was included along with mean corpuscular volume (MCV), body mass index, body surface area, hypertension and CPB time. The advantage of using the validated single measure of the logistic EuroSCORE for our dataset was that not all the individual variables included in the score were available to us at data collection. However as it is a summary measure, we also undertook a sensitivity analysis using all the available individual variables: age; gender; body mass index, body surface area, hypertension, cardiopulmonary bypass (CPB) time, left ventricular ejection fraction, MCV, estimated glomerular filtration rate based on creatinine (eGFR), previous cardiac surgery, operative priority and operative procedure. Co-linearity of confounding variables was assessed by examining the correlation matrix and calculating the variance inflation factor (VIF). Variables with VIFs greater than two were discussed and the most informative variable based on biological plausibility was chosen for retention in the model. The assumption for proportional hazards was examined and tested using Schoenfeld residuals. Hosmer & Lemeshow goodness-of-fit test was used to assess the logistic regression models. All analyses were undertaken in Stata version 12.

**Results:**

Table 1 shows the baseline characteristics for all patients. Values are displayed as mean (standard deviation), median (inter-quartile range), or as a whole number (percentage).

The majority (69%) underwent elective surgery. Isolated CABG was the commonest procedure (43.7%) followed by isolated valve repair / replacement (27.9%) and combined CABG and valve repair / replacement (12.2%).

The overall prevalence of anemia was 31.9% (629 / 1972 patients). 36.2% of female patients were anemic (217 / 599) and 30.0% of male patients (412 / 1373). 24.9% (338 / 1360) of patients presenting for elective surgery were anemic. Patients who were anemic were older, more likely to be female with a lower body mass index, body surface area and MCV. They had greater co-morbid disease with higher logistic EuroSCOREs, and higher rates of impaired renal function and left ventricular function. In addition, they were more likely to have valve and aortic surgery, non - elective surgery, re - do surgery and had longer aortic cross clamp and CPB times.

Unadjusted estimates (Table 2) showed that a falling pre – operative hemoglobin concentration is associated with increased transfusion of RBC units, FFP and platelets. There was also a greater likelihood of returning to theatre for re-exploration for bleeding or cardiac tamponade, longer length of ICU stay, longer length of post-

operative in – hospital length of stay and increased mortality with each g/dl unit fall in pre – operative hemoglobin concentration.

The adjusted estimates between pre-op hemoglobin (Table 3), and study outcomes are expressed as incident rate ratios (IRR), odds ratios (OR) and hazard ratios (HR) with 95% confidence intervals and associated p values. Both approaches to adjusting for covariates in the models showed good agreement for all outcomes studied. Results are described for the modeling approach, which included hemoglobin as the predictor variable and logistic EuroSCORE as a covariate. Interpretations of incident rate ratios, odds ratios and hazard ratios and the sensitivity models using hemoglobin as a predictor with individual covariates (Table S1) and the results for the count and binary equations for the zero inflated Poisson regression model (Table S2) are included in this manuscript but not described (see supplementary data).

Reduced pre-operative hemoglobin levels are independently associated with the need for increased transfusion of RBC units, FFP and platelets. For every unit increase in pre-operative hemoglobin concentration (g/dl) it was estimated that there is a relative 11% decrease in RBC units transfused (IRR=0.89 (0.87 - 0.91)), 8% decrease in number of platelet units transfused IRR=0.92 (0.88 - 0.96)) and a small but statistically significant 3% decrease in FFP transfused (IRR=0.97 (0.96 - 0.99)). Using the zero inflated Poisson model for count of RBC, Figures 1a & 1b display the predicted probability of requirement for RBC units transfused peri-operatively and the predicted number of units in those at risk of transfusion by pre-operative hemoglobin adjusted for mean value of all other model covariates.

Reduced pre-operative hemoglobin levels were found to be independently associated with increased length of intensive care unit and post – operative in - hospital length of stay. It was estimated that as pre-operative hemoglobin concentration increased the probability of discharge increased for ICU (HR=1.04 (1.00 - 1.08)) and for hospital (HR=1.12 (1.09 - 1.16)). Figure 2 shows the estimated independent effect of pre-operative hemoglobin concentration (at 8, 11 and 13 g/dl) on predicted length of hospital stay adjusted for mean value of model covariates. The median length of stay increases from 9 days to 13 days as hemoglobin concentration falls from 13 to 8 g/dl. The effect is more pronounced for those remaining in hospital the longest with length of stay increasing from 14 days to 26 days for the last 25<sup>th</sup> centile of patients.

Reduced pre-operative hemoglobin levels were not found to be independently associated at the 5% significance level with either an increased rate of return to theatre for re-exploration for bleeding and / or cardiac tamponade (OR=0.91 (0.82 - 1.01) p=0.083), nor increased mortality (OR=0.88 (0.76 - 1.01) p=0.073).

### **Discussion:**

After adjusting for the confounding effects of age, gender, co-morbidity, case – mix, operative priority, re-do surgery (as defined by logistic EuroSCORE) and other risk factors including MCV, body mass index and surface area, hypertension and length of cardiopulmonary bypass, we have shown that lower pre-operative hemoglobin concentrations are independently associated with increased utilization of hospital resources. Specifically, as pre-operative hemoglobin concentration falls there are

increased transfusion requirements of blood products, prolonged ICU and post-operative in – hospital length of stay.

A few studies have examined the independent effects of pre-operative hemoglobin concentration on post-operative outcomes in patients undergoing coronary artery bypass graft surgery (CABG). Bell et al. (12) investigated the relationship between a pre – operative hemoglobin level less than 10 g/dl and 30 - day operative mortality and peri – operative morbidity in a predominantly male population of 36,358 patients undergoing CABG. They concluded that whilst pre – operative hemoglobin was significant in univariate analysis, it was not an independent predictor of adverse outcomes suggesting confounding with other variables. However, others have found pre – operative hemoglobin concentration to be independently predictive of adverse outcomes. In a retrospective multivariate analysis of 182,599 patients undergoing CABG, Williams et al. (4) found a higher odds of death, renal failure, deep sternal wound infection and post-operative length of stay for each 5% decrease in pre-operative hematocrit. Kulier et al. (2) found that lower pre-operative hemoglobin concentrations were an independent predictor of adverse non – cardiac outcomes including cerebral and renal events in 4804 patients undergoing elective CABG surgery in a prospective multicenter study.

Our findings demonstrate the independent relationship between pre – operative hemoglobin concentration, utilization of hospital resources and adverse outcomes in a cohort of patients undergoing cardiac surgery different to previous studies (2, 4, 12). We report in our study that a rise in pre-operative hemoglobin by 1g/dl is associated with a relative 11% decrease in the likelihood of red cell transfusion, an 8% decrease

in the likelihood of requiring platelets and 3% decrease in the likelihood of requiring fresh frozen plasma independent of other confounding variables. In Figures 1a and Figure 1b we have presented the estimated independent relationship between pre-operative hemoglobin concentration and the probability and amount of RBC units transfused peri-operatively. We used a ZIP model, as many patients did not receive a transfusion, thus we required a model that could account for the non-standard distribution of RBC units (due to the 'large' number of zero transfusions in the cohort). The number of predicted RBC units was found to be higher than our clinical experience would suggest. There are two possible reasons for this: the predicted count was based on mean level of covariates and this 'average' patient does not exist in clinical practice. Secondly, in the model the log count is assumed to change linearly with the predictor variable, and while this seems to hold well for the lower and middle pre-operative hemoglobin values, the linear relationship may contribute to over-estimation of RBC units for higher pre-operative hemoglobin values. As this model was developed in a single cohort and has not been externally validated, results presented in this paper should not be used for predictive purposes but rather should be viewed as describing this independent relationship.

The association with a lower pre – operative hemoglobin concentration and prolonged length of stay has been reported elsewhere. Williams et al. (4) found that a reduction of pre-operative hematocrit by 5% was associated with 10% higher odds of remaining in hospital greater than 14 days. The cohort, study design and also organizational differences in the way patients are discharged from hospital care, may in part explain differences in findings between studies with regards to post-operative length of stay. However, in this study we found that lower pre-operative hemoglobin levels were

independently associated with a reduced probability of discharge from both hospital and ICU. We have described the dramatic effect of a falling pre-operative hemoglobin concentration on post – operative length of stay and have estimated its effect in Figure 2.

This study may be underpowered to detect differences with low event rates e.g. mortality (3.7% in our cohort). Previous studies, using either larger sample sizes or different methodologies e.g. composite outcomes including mortality, have found pre – operative hemoglobin concentration to be independently associated with mortality. Williams et al. (4) who found in 182,599 patients undergoing CABG surgery that a 5% decrease in pre-operative hematocrit was independently associated with an 8% higher odds of death and van Straten et al. (3) concluded that lower pre-operative hemoglobin concentrations were independently associated with late (greater than 30 day) mortality in 10, 025 patients undergoing CABG. Karkouti et al. (5) in a retrospective analysis of 3500 cardiac surgery patients found that pre-operative anemia was not significantly associated with increased 30-day mortality after propensity matching, though this was significant when included as part of a composite outcome with acute kidney injury and stroke.

This study highlights the importance of the adverse effect of a falling pre-operative hemoglobin concentration on utilization of hospital resources including increased blood transfusion requirements and prolonged length of stay post – operatively in the intensive care unit and in hospital. We argue that clinicians should view pre – operative hemoglobin concentration, rather than anemia, as an independent risk factor as there are increasing utilization of hospital resources with each g/dl unit fall in pre –

operative hemoglobin concentration. Reasons why pre – operative hemoglobin concentration may be a more useful marker than anemia status include that anemia, as defined by WHO criteria, is a late marker of iron deficiency. It has also been argued that it may be inappropriate to define anemia by different values with respect to gender in a surgical population where blood loss has a proportionately greater effect on circulating blood volume in females(17). It is tempting to speculate whether treatment will lead to an improvement in post-operative outcomes. The potential implications of reducing transfusions requirements make targeting pre-operative hemoglobin concentration an attractive avenue for further study. Guidelines (based on a Class II a recommendation) advising the treatment of pre-operative anemia in cardiac surgery exist (18) though have a limited evidence base (level of evidence B). Nevertheless, there is evidence that pre-operative use of both iron (19) and erythropoietin (20) reduces allogeneic blood transfusion. Cladellas et al. (21) also reported improvements in mortality and hospital stay as well as reduced blood transfusions following intravenous iron and erythropoietin, although this single center study used a historical cohort for comparison, and their results have yet to be reproduced in other studies. However, adequately designed and powered efficacy and safety trials are still required to determine what role iron and erythropoietin have as transfusion avoidance strategies in cardiac surgery and other surgical settings (22).

We acknowledge the limitations of the design of the study, a single – center retrospective observational study. The inherent limitations of retrospective observational data reflects what actually happened in clinical practice, for example, the lack of a specific transfusion trigger in the operating room. The single center design means that the sample size is limited and may be underpowered to detect



outcomes with low event rates e.g. mortality. However, the benefit of this single center design is that we employ a uniform process of peri-operative care including blood conservation strategies in the operating room, transfusion triggers in the ICU and discharge protocols from intensive care (23) and hospital (Appendix). Causality cannot be established from this study and it is possible that confounding factors may still influence the outcomes studied despite multivariate analysis. We chose to examine blood transfusion as an outcome measure of hospital resources rather than include it as a covariate, thus the effects of blood transfusions themselves are a potential confounding factor. Some may view looking at blood transfusion as an outcome measure redundant in that it may seem obvious that patients with a lower pre-operative hemoglobin concentration will be transfused more often. However, we felt that it was important to examine this relationship as blood transfusions themselves have been implicated in causing adverse outcomes after cardiac surgery (24, 25) as well as having significant cost implications. Finally, the transfusion trigger that we used in our ICU at the time of the study may seem relatively high compared to a non-cardiac ICU population (26). It was chosen to reflect our patient population undergoing cardiac surgery many of whom had coronary artery disease, myocardial ischaemia and the potential for post-operative blood loss. Indeed, it remains unclear as to the optimal hemoglobin concentration peri-operatively and whether a liberal or restrictive transfusion policy is superior in patients undergoing cardiac surgery (27, 28).

In conclusion, lower pre-operative hemoglobin concentrations are independently associated with increased utilization of hospital resources after cardiac surgery. Each g/dl unit fall in pre-operative hemoglobin concentration is independently associated

with increased transfusion requirements of blood products and increased post-operative length of stay in intensive care and in hospital. To highlight this, we argue that clinicians should consider an abnormal pre – operative hemoglobin concentration and of course its underlying cause as a risk factor for increased utilization of hospital resources and potentially other adverse outcomes, rather than simply the binary phenomenon of anemia status. Further prospective evaluation is necessary to determine what hemoglobin concentration is optimal for patients undergoing cardiac surgery and whether an intervention to optimize pre - operative hemoglobin concentration is cost effective and improves patient outcomes or utilization of hospital resources.

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## FIGURE LEGENDS

Figure 1a: The predicted number of Red cell units (RCU) transfused peri-operatively in those at risk of transfusion by pre-operative hemoglobin adjusted for mean value of all other model covariates.

Figure 1b: The predicted probability of requirement for Red cell units (RCU) transfused peri-operatively by pre-operative hemoglobin adjusted for mean value of all other model covariates.

Figure 2: The estimated independent effect of pre-operative hemoglobin concentration (at 8, 11 and 13 g/dl) on predicted probability of remaining in hospital adjusted for mean value of model covariates.

Table 1: Baseline demographics and peri – operative characteristics for all patients.

	Demographics	All patients (N=1972)
Pre-op	Age (years), Median (IQR)	68.2 (59.0 - 75.4)
	Male, n (%)	1373 (69.6)
	Pre-op haemoglobin (g/dl), Median (IQR)	13.4 (12.2 - 14.4)
	MCV, Mean (SD)	91.9 (5.7)
	eGFR (ml/min/1.73m <sup>2</sup> ), Mean (SD)	73.6 (23.6)
	LVEF: poor, n (%)	500 (26.0)
	LVEF: moderate, n (%)	70 (3.6)
	Logistic Euroscore, Median (IQR)	3.8 (1.8 - 7.5)
	Hypertension, n (%)	1306 (66.5)
	Previous Cardiac Surgery, n (%)	145 (7.4)
	BMI, Mean (SD)	28.3 (5.4)
	BSA, Mean (SD)	1.92 (0.22)
	Peri-op	Operative Priority - Elective, n (%)
Operative Priority - Urgent, n (%)		512 (26.0)
Operative Priority - Emergency, n (%)		92 (4.7)
Operative Priority - Salvage, n (%)		8 (0.4)
Type of Operation - CABG only, n (%)		861 (43.7)
Type of operation - Valve only, n (%)		550 (27.9)
Type of Operation - CABG and valve, n (%)		240 (12.2)
Type of operation - Major Aortic, n (%)		153 (7.8)
Type of operation - Other, n (%)		168 (8.5)
24 Hour Drain output (mls), Median (IQR)		600 (380 - 895)
Cardiopulmonary Bypass Time (mins), Median (IQR)		87 (70 - 110)
X-Clamp Time (mins), Median (IQR)		57 (43 - 79)



Table 2: Summary of outcomes for all patients and by pre-operative haemoglobin concentration

Study outcomes	summary measure	pre-operative haemoglobin concentration (g/dl)									P-value
		All patients (N=1972)	≤9 n=47	9-10 n=68	10-11 n=108	11-12 n=215	12-13 n=357	13-14 n=504	14-15 n=398	≥15 n=275	
Red Cell Units Transfused	% with zero	51.7	2.1	5.9	14.8	19.5	38.9	58.9	75.9	79.6	<0.001
	% with one	9.7	0.0	4.4	7.4	11.9	14.9	9.3	3.5	3.3	
	% with ≥ two	38.6	9.9	7.7	8.8	3.3	2.2	2.2	6.6	1.1	
			97.8	89.7	44.8	62.3	46.2	28.2	20.6	17.1	
Fresh Frozen Plasma Units Transfused	% with zero	73.8	38.3	47.1	68.5	66.5	72.8	78.2	81.9	75.6	<0.001
	% with one	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
	% with ≥ two	26.2	61.7	52.9	31.5	33.5	27.2	21.8	18.1	24.4	
			29.8	42.7	60.2	67.4	72.0	78.7	79.2	74.9	
Platelets Pools Transfused	% with zero	72.2	29.8	42.7	60.2	67.4	72.0	78.7	79.2	74.9	<0.001
	% with one	15.6	27.7	27.9	19.4	13.5	16.8	13.7	13.3	15.6	
	% with ≥ two	12.2	42.6	29.4	20.4	19.1	11.2	8.3	7.5	9.5	
			20.5	18.5	11.9	7.8	6.4	7.9	6.7	6.8	
Return to theatre, n (%)	% return	8.1	20.5	18.5	11.9	7.8	6.4	7.9	6.7	6.8	0.001
Mortality, n (%)	% died	3.65	19.2	7.4	8.3	5.5	2.5	2.2	2.2	2.9	<0.001
Post op length of stay, days	Median	9	25	18	14	12	9	8	8	8	<0.001
	IQR	7,15	17,40	13,27	9,28	8,22	7,15	7,13	6,12	6,11	
Intensive Care Unit length of stay, days	Median	1	6	2	2	1	1	1	1	1	<0.001
	IQR	1,2	2,21	1,7	1,4	1,4	1,2	1,2	1,2	1,2	

Table 3: Multivariate regression model estimates with pre – operative haemoglobin (Hb) as a continuous predictor and covariates: logistic EuroSCORE; MCV; BMI; BSA; hypertension; CPB time.

<b>Model 1</b>	<b>Outcome</b>	<b>IRR</b>	<b>95% CIs</b>	<b>P value</b>
ZIP: count	Red Cell Units Transfused	0.89	0.87, 0.91	<0.001
ZIP: count	Fresh Frozen Plasma Units Transfused	0.97	0.96,0.99	0.010
ZIP: count	Platelets Pools Transfused	0.92	0.88,0.96	<0.001
<b>Model 1</b>	<b>Outcome</b>	<b>OR</b>	<b>95% CIs</b>	<b>P value</b>
Logistic	Return to theatre	0.91	0.82, 1.01	0.083
Logistic	Mortality	0.88	0.76, 1.01	0.073
<b>Model 1</b>	<b>Outcome</b>	<b>HR</b>	<b>95% CIs</b>	<b>P value</b>
Cox PH	Discharge from hospital	1.12	1.09, 1.16	<0.001
Cox PH	Discharge from ICU	1.04	1.00, 1.08	0.019