

## Do Blood Transfusions Affect the Outcomes of Patients Who Underwent Elective Coronary Artery Bypass Grafting?

Lok Yuh Ing\*, Cheng Kok Mun

Department of Cardiothoracic Surgery, Hospital Serdang, Selangor, Malaysia

DOI: [10.36347/sjams.2020.v08i05.001](https://doi.org/10.36347/sjams.2020.v08i05.001)

| Received: 26.04.2020 | Accepted: 03.05.2020 | Published: 06.05.2020

\*Corresponding author: Lok Yuh Ing

## Abstract

## Original Research Article

**Background:** Red blood cell (RBC) transfusions are frequently essential in cardiac procedures to correct anaemia, coagulopathy, blood loss, and hemodilution from pump priming. However, RBC transfusions have deleterious effects of receptor immune system leading to infections after cardiac surgery. Nevertheless, it is difficult to show the direct association between RBC transfusions and postoperative morbidities or mortality due to the fact that most patients undergoing cardiac surgery have multiple comorbidities and are critically ill. Hence, we conducted a study to assess the outcomes of perioperative allogenic RBC transfusions that underwent elective coronary artery bypass graft surgery (CABG) requiring cardiopulmonary bypass (CPB). **Methods:** We retrospectively analysed 130 patients who underwent first-time elective isolated coronary artery bypass operations requiring cardiopulmonary bypass between July to December 2017 at our institution. Patients with transfusions were compared with those who had no transfusion. Pre-, intra-, and postoperative data were collected from medical records, operating notes and blood transfusions database. Chi-square test and student's t-test were used, and p-value < 0.05 was considered significant. **Results:** 75.3% of the patients received RBC transfusions. The median number of RBC units transfused per patient was 2. Compared to non-RBC recipients, RBC recipients were associated with a higher incidence of acute kidney injury (41% vs 60%, p=0.05), wound infection (18% vs 39%, p=0.038) and mortality (0% vs 11%, p=0.048). Nonetheless, there was no significant association between patients' underlying comorbidities and postoperative morbidities or mortality. **Conclusions:** Perioperative allogenic blood transfusions for CABG requiring CPB were significantly associated with increased post-operative morbidities and mortality.

**Keywords:** Transfusion, elective coronary artery bypass grafting, cardiopulmonary bypass, postoperative, infection, acute kidney injury, mortality.

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### INTRODUCTION

Approximately 1,000,000 patients are undergoing cardiac surgery worldwide annually. RBC transfusions are frequently essential in cardiac procedures to correct anaemia, blood loss, hemodilution from pump priming and coagulopathy, especially in CABG surgery due to perioperative use of potent antiplatelet drugs and the invasiveness of the procedure. The incidence of RBC transfusions among patients undergoing CABG surgery has been reported vary between 7.8% to 92.8% among institutions [1]. However, RBC transfusions have deleterious effects of receptor immune system leading to immunosuppression or transfusion-transmitted infections after cardiac surgery [2]. Nevertheless, it is difficult to show the direct association between transfusions and postoperative morbidities or mortality due to the fact that most patients undergoing cardiac surgery are critically ill and have multiple comorbidities e.g.

anaemia, hypertension, diabetes, and chronic kidney disease. Hence, we conducted a study to assess the outcomes of perioperative allogenic RBC transfusions that underwent elective CABG requiring CPB.

### METHODS

Retrospective analysis of electronic medical records, operating notes and blood transfusions database for all adult patients (>18 years old) who underwent first-time elective isolated coronary artery bypass operations requiring cardiopulmonary bypass at Department of Cardiothoracic Surgery Serdang Hospital between July to December 2017. Patients who were ≤ 18 years old, underwent emergency CABG (the need for intervention up to 48 hours due to imminent risk of death or hemodynamically unstable), underwent CABG without CPB, diagnosed with active systemic infection preoperatively (through laboratory tests) or, diagnosed

with Hepatitis B, Hepatitis C or HIV infection were excluded from this study.

Baseline characteristics were obtained from electronic medical records. These included age, gender, history of hypertension, diabetes mellitus, chronic kidney disease (KDIGO guideline), ejection fraction <55% (echocardiography performed within 6 months prior to surgery at Serdang Hospital), anaemia (haemoglobin level <13g/dL for male, haemoglobin level <12g/dL for female) and preoperative haemoglobin (were measured within 1 week prior to surgery). The duration of cardiopulmonary bypass and the number of cases requiring chest reopen were obtained from operative notes. Total number of perioperative allogenic RBC units transfused for each patient between 5 days before and 10 days after CABG were obtained from blood transfusions database. RBC transfusion was initiated when haemoglobin (Hb) level <8g/dL or patients in critical clinical conditions at the physician's discretion.

Three coprimary outcomes were analysed as possible complications related to RBC transfusions which were infectious outcomes, ischemic outcomes and mortality. The infectious outcomes include sepsis (diagnosed by isolated organisms in culture associated with fever), respiratory infection (diagnosed by fever with productive cough, elevated white blood cell count, and identification of lung infection in Chest X-Ray or CT thorax), wound infection (diagnosed by the presence of pain, warmth, redness and pus at the sternal wound,

presence of sternal instability with fever or through CT thorax) and transfusion-transmitted infection (diagnosed by HBsAg, Hepatitis C antibody and HIV tests repeated at 42nd week after surgery). Ischemic outcomes include stroke (diagnosed by clinical signs of neurological deficit and CT brain) and acute kidney injury (according to KDIGO guideline). Lastly, death rate that occurred during hospitalization or within 30 days after surgery was analysed.

Quantitative variables were described as mean and standard deviation and qualitative variables as absolute number and percentages. The number of unit(s) transfused per patient is expressed as the median. Independent samples t-test was performed for continuous variables whereas the chi-square test was used to compare categorical variables. The variables with  $P < 0.05$  were considered significant. The software SPSS (Statistical Package for the Social Sciences, version 20) were used for statistical analysis.

## RESULTS

From the total of 130 patients in this study, 98 patients (75.3%) received allogenic RBC transfusions during perioperative period. Baseline characteristics of the non-transfused and transfused groups were compared in Table 1. Diabetes mellitus and cardiopulmonary bypass time were associated with RBC transfusion. Other variables were not associated with exposure to RBC transfusion. The median number of RBC units transfused per patient was 2.

**Table-1: Baseline Characteristics and Perioperative Characteristics of Patients**

Variables	Non-transfused (n=32)	Transfused (n=98)	P value
<b>Age, n(%)</b>			
< 65 years	22 (69)	70 (71)	0.77
≥ 65 years	10 (31)	28 (29)	-
<b>Sex, n(%)</b>			
Male	28 (88)	74 (76)	0.15
Female	4 (12)	24 (24)	-
<b>Hypertension, n(%)</b>	24 (75)	74 (76)	0.95
<b>Diabetes mellitus, n(%)</b>	11 (34)	63 (64)	0.003
<b>Chronic kidney disease, n(%)</b>	7 (22)	31 (32)	0.29
<b>Ejection fraction &lt;55%, n(%)</b>	18 (56)	52 (53)	0.75
<b>Preoperative haemoglobin level, g/dL</b>	13.0 ± 2.12	13.2 ± 1.8	0.5
<b>Anaemia, n(%)</b>	10 (31)	22 (22)	0.316
<b>Aortic cross clamp, minutes</b>	102 ± 34	106 ± 29	0.566
<b>Cardiopulmonary bypass time, minutes</b>	133 ± 28	156 ± 41	0.009
<b>Chest reopen, n(%)</b>	0 (0)	3 (3)	0.317

Analyses of postoperative complications in relation to RBC transfusions were shown in Table 2. Patients who received blood transfusions were associated with higher incidence of acute kidney injury (41% vs 60%,  $p=0.05$ ), wound infection (18% vs 39%,  $p=0.038$ ) and mortality (0% vs 11%,  $p=0.048$ ). The

causes of death were sepsis (7 cases), mediastinitis (2 cases), refractory bleeding (1 case) and myocardial failure (1 case). Nonetheless, complications of stroke, respiratory infection, sepsis, transfusion-transmitted infection and length of hospital stay did not differ between non-RBC recipients and RBC recipients.

**Table-2: Postoperative Complications**

Variables	Non-transfused (n=32)	Transfused (n=98)	P value
Stroke, n(%)	0 (0)	2 (2)	0.42
Acute kidney injury, n(%)	13 (41)	59(60)	0.05
Wound infection, n(%)	6 (18)	38 (39)	0.038
Respiratory infection, n(%)	0 (0)	2 (2)	0.42
Sepsis, n(%)	3 (9)	13 (13)	0.561
Transfusion transmitted infection, n(%)	0 (0)	0 (0)	--
Hospital stay, days	7.9 ± 2.4	9.6 ± 6.2	0.14
Perioperative mortality, n(%)	0 (0)	11 (11)	0.048

Apart from that, analyses of comorbidities in relation to postoperative wound infection were shown in Table 3 and preoperative anaemia in relation to postoperative complications was shown in Table 4.

There was no significant association between patients' underlying comorbidities and postoperative morbidities or mortality.

**Table-3: Comorbidities in relation to postoperative wound infection**

Variables	Wound infection (n=44)	No wound infection (n=86)	P value
Preoperative anaemia, n(%)	10 (23)	22 (26)	0.72
Diabetes Mellitus, n(%)	27 (61)	47 (55)	0.47
Chronic kidney disease, n(%)	15 (34)	23 (27)	0.38

**Table-4: Preoperative anaemia in relation to postoperative complications**

Variables	Preoperative anaemia (n=32)	Normal haemoglobin level (n=86)	P value
Acute kidney injury, n(%)	17 (53)	55 (64)	0.77
Perioperative mortality, n(%)	3 (9)	8 (9)	0.83

## DISCUSSION

In our study, we found that patients who had diabetes mellitus and prolonged cardiopulmonary bypass time were more likely to receive RBC transfusions. These findings emphasize the effort to improve preoperative care and operative technique with meticulous haemostasis to avoid RBC transfusions.

Out of 130 patients underwent elective CABG surgery, none of the patients received RBC transfusion during preoperative period, all patients had RBC transfusions during either intraoperative or postoperative period. The usual RBC transfusion indications are based on transfusion triggers as well as hemodilution due to heavy fluid load in extracorporeal circulation [3]. Thus, haemoglobin alone may be an inaccurate method of replacing red cell volume loss on CPB. Slight *et al.* found that considering haemoglobin concentration alone may overestimate the requirement for red cell transfusion in elective cardiac surgery patients. Patients transfused as per the red cell volume-based guideline received significantly less red cells with no associated difference in clinical outcome [4].

In this study, the median number of RBC units transfused per patient was 2. Owing to this finding, we have reduced preoperative RBC order for elective CABG from 4 units to 2 units since year 2018. This allowed proper blood management at blood bank in which blood products were distributed to patients who

are in need and hence reduced unnecessary wastage of blood products.

Our study showed direct association of RBC transfusions with high incidence of postoperative wound infection, acute kidney injury and mortality. Meanwhile, there was no significant association between patients' underlying comorbidities and postoperative morbidities or mortality. In a study conducted by Koch *et al.* [5], the authors also concluded that each administered unit increases by 77% the postoperative mortality risk and 100% the risk of developing any renal complication, 76% the risk of developing postoperative infections, cardiac complications in 55% and 37% the risk of neurological complications. These associations remained strong even after the risk adjustment factors causing postoperative complications. In Magedanz study *et al.*[6], in which a risk score for mediastinitis was created, an association between blood transfusion and risk of postoperative mediastinitis was found (OR: 2.5; CI95%: 1.5 - 4.1, P = 0.001), that also agrees with a study that found a strong association between transfusion and risk of infections, which reflects the immunosuppressive effect of blood transfusion[7]. Apart from immunosuppressive effect, some studies report that blood loss and blood transfusion are known to cause severe systemic inflammatory response leading to ischemic complications by modifying the systemic inflammatory response of the patients and the direct introduction of bioactive substances into circulation [8-10]. On the

other hand, the study conducted by Van Straten *et al.* [8] showed the number of units transfused may be a predictor of early mortality up to 30 days in the postoperative period, but not of late mortality. The authors concluded that in patients who received three or more units of RBC, the survival rate drops significantly when compared to non-RBC recipient. These patients have also high incidence of postoperative complications, which could explain the high early mortality in this study.

In view of blood transfusions associated with multiple postoperative complications, it is important to implement strategies for reducing RBC transfusions in postoperative cardiac surgery. Some authors report the importance of a careful preoperative assessment in order to reduce the risk of bleeding and blood transfusion during intraoperative and postoperative period. Apart from that, the measurement of serum iron and preoperative administration of iron and erythropoietin may reduce the need for RBC transfusions. Besides, autologous blood donation is used to reduce homologous blood transfusion in a wide variety of elective surgical procedures including cardiac surgeries; the patient's blood is collected prior to surgery in order to be used after the procedure [11]. Other method includes using miniEC (reduction of the prime, the tubes and vacuum drainage) and centrifugal pumps (Bio Pump) to reduce the excessive use of heparin and hence reduce the risk of bleeding [12, 13]. Hypothermia (between 30<sup>o</sup> C and 32<sup>o</sup> C) during the surgical procedure may also reduce bleeding during surgery and in the postoperative period.

Limitations of our study include this study was a single centre retrospective study, the sample size was relatively small and the effects of blood component transfusions other than RBC in the postoperative period were not taken into consideration.

## CONCLUSION

Perioperative allogenic blood transfusions for CABG requiring CPB were significantly associated with increased post-operative wound infection, acute kidney injury and mortality.

### Lists of abbreviations used

RBC – Red blood cell  
 CPB – Cardiopulmonary bypass  
 CABG – Coronary artery bypass grafting  
 CT – Computed tomography  
 HIV – Human immunodeficiency virus  
 HBsAg – Hepatitis B surface antigen  
 KDIGO – Kidney Disease: Improving Global Outcomes

## ACKNOWLEDGEMENTS

This work was supported by the Department of Cardiothoracic Surgery, Serdang Hospital.

### Declaration of conflicting interests

No conflicts of interest in preparing this article

### Funding

There was no external funding source for this research.

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