Original Article

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Factors influencing transfusion requirement in patients undergoing first-time, elective coronary artery bypass graft surgery

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Abstract:

CONTEXT: Coronary artery bypass graft (CABG) operation is associated with high frequency of allogeneic blood transfusion due to the acquired hemostatic challenges in patients undergoing CABG. However, allogeneic blood transfusion carries risks of infection, adverse reaction, and mortality as well as prolonged hospital stay and increased hospital cost. It is important to identify patients who require blood transfusion to mitigate their risk factors and reduce the chance of exposure to allogeneic blood.

AIMS: This study was conducted to evaluate factors that influence the decision to transfuse red cell in first-time elective CABG patients.

SETTINGS AND DESIGN: This was a cross-sectional study based on a retrospective record review. The study was done in the National Heart Institute.

MATERIALS AND METHODS: All patients who underwent first-time elective CABG were included in this study. Variables analyzed include age, gender, body weight, preoperative hemoglobin (Hb) level, patients' comorbidities, and other clinical parameters.

STATISTICAL ANALYSIS USED: Data were analyzed using SPSS software version 20.

RESULTS: A total of 463 patients underwent first-time elective CABG during the period of the study. Three hundred and eighty-six (83.4%) patients received red cell transfusion. From multiple logistic regression analysis, only age (odds ratio [OR] = 1.040, 95% confidence interval [CI]: 1.003, 1.077, P = 0.032), body weight (OR = 0.951, 95\% CI: 0.928, 0.974, P < 0.001), Hb level (OR = 0.500, 95% CI: 0.387, 0.644, P < 0.001), and cardiopulmonary bypass time (OR = 1.013, 95% CI: 1.004, 1.023, P < 0.001) were the significant independent predictors of red cell transfusion.

CONCLUSIONS: By stratifying patients according to their risk factor for red cell transfusion, the high-risk patients could be recognized and should be enrolled into effective patient blood management program to minimize their risk of exposure to allogeneic blood transfusion.

Keywords:

Coronary artery bypass graft, predictors, red cell transfusion

Introduction

Heart disease is one of the biggest killers in Malaysia^[1] and in the world.^[2] Coronary artery bypass graft (CABG) is a surgical intervention where a blockage in coronary artery is bypassed using a graft.^[3]

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Patients who undergo CABG commonly receive red cell transfusions^[4] due to the hemostatic challenges experienced by the patients.^[5,6]

However, transfusions in CABG patients are associated with higher postoperative complication, morbidity and mortality rates,^[7] including infection^[8] and increase

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Submission: 28-03-2016 Accepted: 29-05-2017 in cost.^[9,10] Therefore, the benefits and the risk of blood transfusion must be balanced carefully.

The patients who are at higher risk of red cell transfusion need to be recognized so that they can be managed optimally during perioperative period to minimize their chance to be transfused.

This study was conducted to look at the factors associated with red cell transfusion in first-time elective CABG in Malaysian patients, specifically determining the influence of preoperative hemoglobin (Hb), patients' body weight, age, and gender on transfusion. In the institution where this study was conducted, red cell transfusion was made up of packed red cell only. Packed red cell is prepared by separation of plasma from whole blood collected from blood donors.

Materials and Methods

This study was conducted in National Heart Institute (NHI), Kuala Lumpur, a 432-bedded specialist center for cardiovascular and thoracic diseases. It is one of the leading cardiovascular and thoracic center in the region and serves as the national referral center.^[11]

Patients were on antiplatelets such as aspirin and thienopyridine P2Y12 receptor antagonists and the therapy was discontinued accordingly prior to CABG. Patients on cardiopulmonary bypass (CPB) machine are transfused with red cells when the Hb level is <7. Patients with higher Hb level may be transfused when clinical condition takes precedence, for example, in massive bleeding. Platelet transfusion is indicated in platelet dysfunction due to high-dose heparin or prolonged contact with bypass circuit. Plasma transfusion is given to minimize bleeding complication in coagulopathy due to massive transfusion and disseminated intravascular coagulation. The outcome of red cell transfusion was recorded by posttransfusion patients' clinical condition and Hb level.

This was a cross-sectional study based on a retrospective review of patients' medical record. Medical record of all 463 consecutive patients who underwent first-time elective CABG operation from January 2011 to September 2011 were analyzed. Patients included in this study must be a Malaysian citizen, aged from 18 years and above. Patients' medical records must contain complete results of all the factors included in this study.

Patients who underwent emergency CABG, had other concurrent heart procedure such as valve replacement, had a history of previous heart surgery, or underwent re-exploration for surgical bleeding were excluded from this study as they were more likely to receive transfusion. Transfusions given 24 h after surgery were also excluded because these transfusions may not be related to the surgery.

Preoperative variables included in the study were preoperative Hb level, patients' body weight, age, and gender. Hb level was a numerical variable, recorded in grams per deciliter. Patients' body weight and age were also numerical variables recorded in kilograms and years, respectively. While patients' gender was a categorical variable recorded as male or female.

Patients' comorbidities which were left ventricular function (LVF), hypertension, diabetes, thromboembolic disease, renal dysfunction, chronic obstructive pulmonary condition, and smoking status were also recorded. LVF was recorded as numerical variable, in percentage while the others were categorical variables of either yes or no for each.

The use of CPB machine during CABG was recorded as a categorical variable of yes or no. CPB time was recorded as the time patient was put on CPB machine during the procedure. It was a numerical variable and recorded in minutes. The outcome of this study was recorded as a categorical variable in which patient received red cell transfusion or not within 24 h after CABG.

Patients' confidentiality was protected with all desired data were recorded in such a way that the respective patients could not be identified either directly or indirectly through linkage codes assigned to the data. Ethical approval was obtained from the institute where the study was conducted.

Data entry and statistical analysis were performed using Statistical Package for Social Sciences software version 20 (IBM Corp., Armonk, New York, USA) for Windows.^[12]

Descriptive analyses were done for all variables. The distributions of numerical variables were explored and the mean and standard deviation (SD) were checked. The difference of mean between the numerical variables with transfusion and no transfusion groups was tested by independent *t*-test. For categorical variables, the frequencies were explored and percentages were calculated. Chi-square test was used to determine the association between the categorical variables with the outcome. If the expected cell frequency <5 was more than 20%, Fisher's exact test was used. Statistical significance was taken at P < 0.05.

Univariable analysis was conducted to analyze factors associated with red cell transfusion in first-time elective CABG patients for each independent variable. Individual significant predictors were determined. Odds ratio was obtained to interpret the association between independent variables and transfusion in first-time elective CABG patients.

From the univariable analysis, all independent variables with P < 0.25 and potential biologically significant variable which has been proven in other previous studies but not statistically significant in this study were included for variable selection in multiple logistic regression to determine association with transfusion in first-time elective CABG patients. Variable selection methods (forward selection and backward elimination) were done to get the best predictors for transfusion in first-time elective CABG patients. Multicollinearity and interaction between the variables were checked. Goodness of fit of the preliminary final model was checked by doing Hosmer-Lemeshow test, checking the classification table, and assessing area under the receiver operating characteristic curve. When the assumptions were met, the final model was achieved.

Results

After analyzing inclusion and exclusion criteria, 463 patients who underwent first-time elective CABG were included in the study. There were 395 (85.3%) male patients and 68 (14.7%) female patients. The mean age was 58.3 \pm 8.5 SD years (range, 38–84) while the mean body weight for these patients was 70.5 \pm 11.99 SD kg (range, 42.50–109.00). The mean preoperative Hb level was 13.7 \pm 1.5 SD g/dL (range, 8.9–18.1).

Table 1 shows that the most common comorbidity in first-time elective CABG patients was hypertension followed by hyperlipidemia, diabetes mellitus, smoking, chronic renal failure (CRF), and thromboembolic disease. None of the patients had chronic obstructive pulmonary disease. Almost all or 444 (95.9%) patients underwent on-pump CABG.



	n (%)	Mean±SD	Range (minimum– maximum)
DM	254 (54.9)	-	-
HPT	383 (82.7)	-	-
Smoking	218 (47.1)	-	-
CRF	32 (6.9)	-	-
TED	19 (4.1)	-	-
HLP	366 (79.0)	-	-
COPD	0	-	-
LVF (mean %)	-	55.3±10.3	56 (23-79)
CPB	444 (95.9)	-	-
CPB time (min)		89.22±25.53	163 (24-187)

DM = Diabetes mellitus, HPT = Hypertension, COPD = Chronic obstructive airway disease, CRF = Chronic renal failure, TED = Thromboembolic disease, HLP = Hyperlipidemia, LVF = Left ventricular function, CPB = Cardiopulmonary bypass, SD = Standard deviation Figure 1 shows that 386 (83.4%) patients in this study received red cell transfusion within 24 h postoperation.

Associations between red cell transfusion and independent variables

Table 2 shows that the mean age and CPB time for transfused patients in this study were higher compared to the nontransfused patients. However, the mean body weight, Hb level, and LVF in the transfused patients were lower compared to the nontransfused patients.

From independent *t*-test, there were significant differences in age (P < 0.001), weight (P < 0.001), Hb level (P < 0.001), and CPB time (P = 0.041) between the transfused and nontransfused patients. However, there was no significant difference in LVF between the transfused and nontransfused patients (P = 0.067).

Table 3 shows that there was a significant association between gender and red cell transfusion among first-time elective CABG patients (P = 0.010) with a higher proportion of transfusion in females. There were also significant associations between CRF and smoking habit with transfusion among first-time elective CABG patients (P = 0.033 and 0.015, respectively). The proportion of transfused patient was higher in patients who had CRF as their comorbid illness compared to those who did not have the illness (96.9% vs. 82.4%, respectively), while the proportion of transfused patient was slightly higher in nonsmokers compared to smokers (87.3% vs. 78.9%, respectively). There was no association between diabetes mellitus, hypertension, thromboembolic disease, and use of CPB machine with transfusion among first-time elective CABG patients in this study [Table 3].

Multiple logistic regression

From the univariable analysis done, variables with P < 0.25 were selected. The variables selected were age,



Figure 1: Proportion of patients receiving red cell transfusion

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Variables	Ме	an±SD	Mean difference (95% CI)	t-test (df)	P *					
	Transfused	Not transfused								
Age (years)	59.1±8.56	54.6±7.13	-4.48 (-6.532.44)	-4.31 (461)	<0.001					
Weight (kg)	69.1±11.64	77.7±11.18	8.58 (5.75-11.42)	5.95 (461)	<0.001					
Hb level (g/dl)	13.3±1.48	14.7±0.93	1.20 (0.94-1.45)	9.19 (163.90)	<0.001					
CPB time (min)	90.3±25.95	83.6±22.59	-6.69 (-13.090.29)	-2.054 (442)	0.041					
LVF (%)	55.0±10.6	57.1±8.6	2.07 (-0.15-4.29)	1.846 (126.84)	0.067					

Table 2: Differences between transfused and nontransfused first-time elective coronary artery bypass graft patients

*Independent t-test, Hb = Hemoglobin, LVF = Left ventricular function, CPB = Cardiopulmonary bypass, CI = Confidence interval, SD = Standard deviation

Table 3: Association between independent categoricalvariables and red cell transfusion among first-timeelective coronary artery bypass graft patients

	Transfus	ed, <i>n</i> (%)	χ² (df)	Pª	
	Yes No				
Gender					
Male	322 (81.5)	73 (18.5)	6.641 (1)	0.010	
Female	64 (94.1)	4 (5.9)			
DM					
Yes	216 (85.0)	38 (15.0)	1.132 (1)	0.287	
No	170 (81.3)	39 (18.7)			
HPT					
Yes	321 (83.8)	62 (16.2)	0.313 (1)	0.576	
No	65 (81.2)	15 (18.8)			
Smoking					
Yes	172 (78.9)	46 (21.1)	5.938 (1)	0.015	
No	214 (87.3)	31 (12.7)			
CRF					
Yes	31 (96.9)	1 (3.1)	4.522 (1)	0.033	
No	355 (82.4)	76 (17.6)			
TED					
Yes	17 (89.5)	2 (10.5)	0.532 (1)	0.752 ^b	
No	369 (83.1)	75 (16.9)			
CPB					
Yes	371 (83.6)	73 (16.4)	0.279 (1)	0.537 ^b	
No	15 (78.9)	4 (21.1)			

^aPearson's Chi-squared test, ^bFisher's exact test. DM = Diabetes mellitus, HPT = Hypertension, CRF = Chronic renal failure, TED = Thromboembolic disease, CPB = Cardiopulmonary bypass

body weight, Hb level, CPB time, LVF, gender, smoking status, and CRF.

Using backward elimination, variables such as age, body weight, Hb level, CPB time, LVF, and CRF were retained at the final step. However, the *P* value of LVF and CRF was >0.05 (0.074 and 0.149, respectively). The *P* value of LVF and CRF from Wald statistic was also >0.05 (0.109 and 0.149, respectively). Therefore, the variables LVF and CRF were removed. Using forward selection, variables such as age, body weight, Hb level, and CPB time were included.

The standard error and correlation were relatively small for all the independent variables in the model. There was also no significant interaction effect in the model. Preliminary final model was obtained. From multiple logistic regression analysis, age, body weight, Hb level, and CPB time had significant association with blood transfusion in first-time elective CABG patients.

Interpretation of the final model [Table 4] is as follows:

- Increase in 1 year of age increases the chance for red cell transfusion by 4% in patients undergoing first-time elective CABG (95% confidence interval [CI]: 1.003, 1.077, *P* = 0.032) when adjusted for body weight, Hb level, and CPB time
- For each additional kilogram of body weight, a patient has 5% less the odds to have red cell transfusion in first-time elective CABG (95% CI: 0.928, 0.974, *P* < 0.001) when adjusted for age, Hb level, and CPB time
- A person with an increase in 1 g/dL of Hb level has 50% lesser odds to have red cell transfusion in first-time elective CABG (95% CI: 0.387, 0.644, *P* < 0.001) when adjusted for age, body weight, and CPB time
- A person with a 10-min increase in CPB time increases the odds of red cell transfusion by 14% in first-time elective CABG (95% CI: 1.004, 1.023, *P* < 0.001) when adjusted for age, body weight, and Hb level.

Discussion and Conclusion

Numerous studies have been conducted examining factors influencing transfusion requirement in CABG patients. Most of them are done in developed countries. This is the first of such study conducted in Malaysia.

From univariable analysis, the factors significantly associated with red cell transfusion in first-time elective CABG patients were patients' age, gender, body weight, preoperative Hb level, CPB time, CRF, and smoking status.

The probability of transfusion was higher with increasing age and CPB time while body weight and preoperative Hb level were inversely related. Nonsmoker, female, and CRF patients were more likely to receive transfusion.

From multivariate analysis, it was observed that patients' age, body weight, preoperative Hb level, and CPB time

Variable	Simple logistic regre	ession	Multiple logistic regression					
	Regression coefficient (β)	Crude OR	Adjusted <i>r</i> (β)	Adjusted OR ^a , (95% CI)	Wald statistic	Р		
Age (years)	0.67	1.069	0.039	1.040 (1.003-1.077)	4.606	0.032		
Body weight (kg)	-0.60	0.942	-0.051	0.951 (0.928-0.974)	17.283	<0.001		
Hb level (g/dl)	-0.719	0.487	-0.694	0.500 (0.387-0.644)	28.618	<0.001		
CPB time (min)	0.011	1.011	0.013	1.013 (1.004-1.023)	8.063	0.005		
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Table 4:	Associated	factors of	red c	ell trans	fusion i	n fir	st-time	elective	coronary	artery	bypass	graft	patients

^aForward LR Multiple Logistic Regression model was applied. Multicollinearity and interaction term were checked and not found. Hosmer–Lemeshow test (*P*=0.742), classification table (overall correctly classified percentage = 83.8%), and area under the ROC curve (82%) were applied to check the model fitness. OR = Odds ratio, CI = Confidence interval, Hb = Hemoglobin, CPB = Cardiopulmonary bypass, ROC = Receiver operating characteristic, LR = Logistic regression

were significant independent predictors of red cell transfusion in first-time elective CABG.

The increased life expectancy in Malaysia, from 66.90 years in 1980 to 77.4 years in 2015,^[13] has resulted in an increase in the number of elderly patients fit for CABG. In this study, older patients were likely to require blood transfusion more than the younger counterparts. This finding echoed the findings of other authors.^[14-17] This is due to the fact that older patients tend to have more comorbidities including anemia which results in transfusion.

As with other previous studies, our patients who had smaller body weight received more red cell transfusion.^[18,19] The standard large amount of priming volume used for adults on CPB machine caused a greater hemodilution in a patient with smaller body weight due to his smaller circulating blood volume. As a result, these patients had lower hematocrit post-CABG which rendered them to be more prone to receive transfusion.^[20]

Ferraris *et al.* reported that patients undergoing CABG with low Hb level preoperatively were more likely to get perioperative transfusion.^[5] Anemic patients had prolonged bleeding time and was made worse by antiplatelet drugs. The same authors later recommended 7 g/dl as the threshold for transfusion in the updated guideline on blood conservation by the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists.^[21]

Nearly all our patients (95.9%) underwent CPB procedure. This could be the reason why 83.4% of patients whose mean preoperative Hb level was within normal range (13.7 g/dl)^[22] received transfusion. CPB machine gave rise to excessive bleeding during and after the operation due to coagulopathy which increases blood loss and subsequently causes a drop in Hb level which resulted in transfusion. Bleeding in patients undergoing CABG is also caused by other factors which could be patient related, for example, preexisting thrombocytopenia and platelet dysfunction; physician related such as preferred surgical practice; procedural related, for instance, urgency of the operation and previous heart surgery; or drug related.^[5]

Female gender was only the significant predictor when associated with other variables as shown in other studies.^[16] Female patients undergoing CABG usually have lower preoperative hematocrit, smaller body size, are older, and have more comorbid illness compared to male patients.^[23-26] These factors have been shown to be associated with red cell transfusion.

From univariable analysis, smoking was shown to have a protective effect toward blood transfusion in first-time elective CABG patients in this study. This finding was supported by previous studies.^[4,27] Smoking could give rise to polycythemia^[28] and hypercoagulable state^[29] which reduces the risk of bleeding in these patients. However, there are authors who concluded differently.^[30] These conflicting findings could be due to nonstandard definition of smoking status between authors of these studies. Smoking status in this study was taken from patients' medical records documented by different physicians with no standard definition for smoking status.

This study had identified the independent predictor for red cell transfusion in first-time elective CABG. A more accurate predicting tool for transfusion in CABG can be obtained by doing a prospective study involving bigger cohort. The study should include prediction and validation phases. The predicting tool then requires to be tested at different centers to ensure its suitability for implementation.

The implementation of predicting tools for transfusion such as Transfusion Risk Understanding Scoring Tool^[31] and Transfusion Risk and Clinical Knowledge Score^[32] had been proven to be cost-effective in reducing the total cost of transfusion specifically and patient management generally in CABG. Therefore, a predicting tool which suits Malaysian population is warranted and should be developed.

Patient blood management needs to be applied to all patients going for CABG. By identifying the predictors for blood transfusion in first-time elective CABG patients, patients' risk for transfusion can be stratified. Factors that can be changed before operation such as Hb level need to be optimized and customized to suit every patient. However, age cannot be altered while body weight is usually static between the time of presentation and operation. For these patients, blood conservation technique must be considered. Patients who are expected to take a longer CPB time also need to be managed vigilantly. Blood conservation techniques in CPB procedure have been recommended by various authors^[21,33] which include minimally invasive extracorporeal circulation^[34,35] and use of retrograde autologous priming.^[33,36]

The transfusion rate from this study has been addressed in the Hospital Transfusion Committee who acts as transfusion coordinator for this institute. The committee is chaired by a cardiothoracic surgeon, while the members include consultant pathologist, anesthetists, cardiologists, pediatric cardiologists, and nurses. As a result of that, the rate of transfusion in CABG has been reduced to 78.2% in 2013 and 60.55% in 2014.^[37]

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Conflicts of interest

There are no conflicts of interest.

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