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DETERMINANT OF BLOOD TRANSFUSION IN PATIENTS UNDERGOING ELECTIVE ON PUMP CORONARY ARTERY BYPASS SURGERY

Cardiology

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ABSTRACT

Background: Blood transfusion is a common and frequently used phenomenon after coronary artery bypass surgery (CABG) surgery, which significantly increases the patient's risk of morbidity and mortality. Preoperative anemia and post-operative loss of blood is main cause of need of blood transfusion in patients. In this retrospective study, determinant of the blood transfusion in CABG were studied.

Methods: Surgical and perfusion data of 164 patients were collected from the institutional HIS database. We test the association of the blood transfusion with demographic and clinical variables. Patients were classified into 2 groups namely Group 1: patients who "received" allogenic PRBC transfusion and Group II - patients who "do not received" allogenic PRBC transfusion. Binary logistic regression analysis was used to assess the predictors of the blood transfusion in study patients.

Result: Out of total 164 patients who underwent CABG, out of which 37 (22.6%) patients had received blood (Group 1), while the rest 127 (77.4%) patients had not receive any blood products (Group II). CPB time, hemoglobin level, ICU stay, ventilation time in hours and proportions of mortality between two groups were significantly different (each <0.05). Higher age, increased CPB time, increased ICU stay, lower Hb and decreased ventilators hours were independent predictors of blood transfusion. Hemoglobin was the good accurate predictor of the crossover with area under ROC curve was 78% (p <0.001) and Hb Cut-off =8.15 (Sensitivity =75%, Specificity =65%) showed good cutoff for sensitivity and specificity.

Conclusion: Higher age, increased CPB time, increased ICU stay, lower Hb and decreased ventilators hours were independent predictors of blood transfusion. Hemoglobin value of ≤7.35g/dl may be used as cutoff value to decide the blood transfusion in CABG patients.

KEYWORDS

Anemia, Hemoglobin, CABG, Blood Transfusion, Mortality

INTRODUCTION:

Blood transfusion is a common and frequently used phenomenon after coronary artery bypass surgery (CABG) surgery, which significantly increases the risk of morbidity and mortality. Preoperative anemia and post-operative loss of blood are main causes of need of blood transfusion. Anemia is a well-known risk factor for adverse outcome in cardiovascular disease in general population[1-3]. World Health Organization (WHO), defines anemia as hemoglobin (Hb) levels <13g/dl for men and <12g/dl for women[4]. Although numerous risk factors in cardiac surgery can influence the morbidity and mortality in these patients, but presence of anemia in the aftermath of surgery inordinately increases myocardial workload in a heart recovering from the effects of cardiopulmonary bypass (CPB) and reperfusion injury in a chronically ischemic heart, which results in the need of blood transfusion[5]. This also increases the cost of treatment[7]. Anemia during and after cardiac operations occur because of hemodilution and increased mediastinal blood shedding due to coagulopathy[8] caused by CPB, which requires correction by red cell and other blood product transfusions[9]. Few studies were conducted to assess the predictors of the blood transfusion in on-pump CABG patients and most of them indicated that anemia and higher CPB time are major risk factor for blood transfusion but cutoff value of hemoglobin is suggested in very small number of studies. In this study, our focus is to assess the predictors of the blood transfusion in patients undergoing on-pump CABG and to suggest appropriate cutoff value of the hemoglobin so that at appropriate time, blood transfusion can be given.

Aim of the study:

1. To assess the relationship between blood transfusion and demographic and clinical variables.
2. To assess the independent predictors of the blood transfusion in CABG patients.
3. To suggest the appropriate cutoff value of the hemoglobin to decide blood transfusion in the CABG patients.

MATERIAL AND METHOD:

This retrospective analytical study was conducted in a tertiary care postgraduate teaching institute in northern india. Observed group (exclusion criteria in data collection) comprised of isolated on-pump CABG over three-year period (November 2015 to November 2018) by a single surgeon. All institutional ethical policies of intervention and observations were followed. Data of all 164 patients admitted for isolated on-pump CABG were included in this study. All patients (n=164) were classified into two classes based on their instant hemoglobin values in the intensive care unit (ICU) after the surgery. Both groups were categorized as: Group 1: patients who "received" allogenic packed red blood cells (PRBC) transfusion. Group 2: patients who "did not receive" allogenic PRBC transfusion. In the immediate postoperative period, criteria used for PRBC transfusion trigger were based on clinical features of the patients.

Protocol for raising transfusion trigger: Our criteria for raising transfusion trigger are in the patients who show early clinical signs of any hemodynamic instability, including ongoing bleeding from the mediastinal drain, with or without any evidence of new electrocardiographic changes of myocardial ischemia.

Hb estimations were performed in all 164 patients during entire period of hospital stay (once a day) until the day of their discharge.

All surgical and perfusion related data were collected from the institutional HIS (Hospital Information System) database. These data included the gender, age at surgery, surgical procedure with CPB, hb in grams per deciliter, total CPB time in minutes, ventilation time in hours, total chest drainage in milliliter, ICU stay in hours and hospital mortality.

All patients were grafted with single skeletonized left internal mammary artery along with venous conduits (great saphenous vein).

All these patients were operated by a single surgeon through median sternotomy using intermittent cold blood cardioplegia (St. Thomas cardioplegia @150mmHg) at twenty minutes interval through aortic root and through a syringe into the distally placed venous conduit, along with topical cooling. Samples for arterial blood gas analysis estimated the immediate hemoglobin value for quick reporting which were collected into a 2 ml heparinized syringe.

Definitions:

Anemia:

Anaemia is a condition in which the number of red blood cells (and consequently their oxygen-carrying capacity) is insufficient to meet the body's physiologic needs. (WHO Definition)

PRBC: Packed Red blood cells.

Exclusion Criteria:

1) Off-pump CABG.
2) Combined surgery- CABG with any Valvular surgery.
3) Patients with any platelets / coagulation disorders.

Statistical Analysis:

Normality of the continuous variable was tested, and a variable was considered normally distributed when Standard deviation (SD) < ½ mean. Normally distributed continuous variable was presented in Mean ± SD whereas non-normal variables in Median (Inter-quartile range "IQR"). Categorical variable was presented in frequency and percentage. Independent samples 't' test / Mann Whitney U test was used to compare the means / medians between the groups. Chi-square test / Fisher exact test was used to test the association between blood transfusion and demographic and clinical variables. Univariate and multivariate binary logistic regression analysis was used to identify the predictors for blood transfusion. A $p<0.05$ considered as statistically significant. Statistical package for social sciences, version 23 (SPSS-23, IBM Chicago, USA) used for data analysis.

RESULTS:

Out of total 164 patients who underwent CABG, 37 (22.6%) patients received blood (Group 1), while the rest 127 (77.4%) patients didn't receive any blood products (Group II). Table 1 shows the distribution of the demographic and clinical variables in patient groups. Mean age of the patients was 56.18 years (Range: 2-75 years) with male proportions of 138 (84.1%).

Mean age was significantly different ($p<0.05$) but male proportions were statistically same ($p>0.05$) between the groups. Similarly, CPB time, Hemoglobin level, ICU stay, ventilation time in hours and proportions of mortality between two groups were significantly different between two patients' groups (each <0.05) whereas body mass index, serum creatinine, total chest drainage, presence of delayed wound healing in lower limb and sternum were statistically same between two groups. **(Table 1)**

Multivariate logistic regression analysis was used to identify the predictors for the crossover in the patients. All the variables found significant in univariate analysis have been included in multivariate analysis. Results showed that patients with higher age (adjusted Odds ratio=1.12, 95% CI=1.02-1.22), prolonged CPB time (adjusted Odds ratio=1.034, 95% CI=1.006-1.062) and increased ICU stay in hours (adjusted Odds ratio=1.04, 95% CI=0.1.007-1.075) had higher chances of receiving blood transfusion, whereas lower Hb in gm/% (adjusted Odds ratio=0.44, 95% CI=0.24-0.81) and decreased ventilator support in hours (adjusted Odds ratio=0.94, 95% CI=0.89-0.99) also showed higher chances of blood transfusion. To decide the actual cutoff value of the hemoglobin level in cross over CABG patients, receiver operating characteristics (ROC) curve has been used which showed that hemoglobin was the good accurate predictor of the crossover with area under ROC curve was 78% (AUC=78%, 95% CI=70% -86%, $p<0.001$). **(Figure 1).** Out of the various observed cut-off values, three cut-off values were randomly chosen with objective to get at least 50% sensitivity and 50% specificity. Hb Cut-off = 8.75 (Sensitivity =86%, Specificity =50%) was identifying to get highest sensitivity whereas highest specificity was observed at Hb Cut-off = 7.35 (Sensitivity =53%, Specificity =87%). At Hb Cut-off =8.15 (Sensitivity =75%, Specificity =65%) showed balancing in sensitivity and specificity. **(Table 2).**

Table 1: Comparison of Demographic & Clinical Characteristics of the Study Groups (N=164)

Variables	Cross over (n=37, 22.6%)	No Crossover (n=127,77.4%)	Total (n=164)	p value
Age (years)	59.81±7.64	55.13±11.18	56.18±10.64	0.018
Gender (Male)	26 (70.3)	112 (88.2)	138 (84.1)	0.008
BMI	24.37±2.83	24.47±3.11	24.45±3.05	0.864
CPP Time	122.4±28.80	109.0±30.01	112.04±30.18	0.017
Serum Creatinine	1.07±0.27	1.01±0.21	1.02±0.22	0.107
Hb (gm/dl)	7.58±1.24	8.94±1.64	8.62±1.66	<0.001
ICU stay in hours	46 (26-70)	36(27-46)	39(27-48)	0.040
Total Chest Drainage in ml	420 (270-740)	410(330-590)	410(320-600)	0.538
Ventilation time in ours	7(5.1-12.7)	6.1(4.1-9.2)	6.2(4.5-10.1)	0.046
N (%)				
Infection Leg (Yes)	4(10.8)	7(5.5)	11(6.7)	0.270
Infection Sternum (Yes)	3(8.1)	4(3.1)	7(4.3)	0.191
Outcome (Dead)	4(10.8)	1(0.8)	5(3)	0.009

Data presented in mean± standard deviation and compared using Independent samples t test. Median (inter-quartile range) and compared using Mann Whitney U test. Frequency (%) and compared by Chi square test / Fisher exact test. $P<0.05$ significant

Table 2: Cut-off values of the Haemoglobin to decide the crossover in the study patients (N=164)

Cut-off value (Haemoglobin, g/dl)	Sensitivity	Specificity
7.35	53%	87%
8.15	75%	65%
8.75	86%	51%

Smallest value indicates more chances of crossover

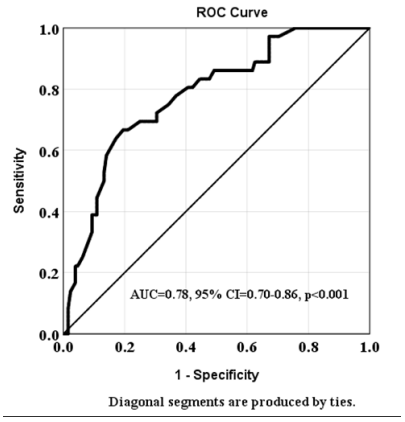

Figure 1 : ROC Curve showing cut-off value of the Haemoglobin to decide the cross over in the operating patients

DISCUSSION:

Coronary artery bypass surgery is one of the most commonly performed cardiac operation and the most common hematological condition observed in the cardiovascular surgical intensive care unit is low hemoglobin values in immediate postoperative period[10]. CPB used during CABG creates several changes that affect systemic physiology and blood formed elements that may contribute to perioperative coagulopathy by diluting the concentration of coagulation factors and platelets [3]. Anemia is common after on-pump CABG[11]. Post-operative anemia is due to certain factors such as intraoperative blood loss, CPB and hemodilutions[12].

Several authors have also made similar observation in post-surgical patients[12-15]. Postoperative anemia also results from increased post-surgical blood shedding from the mediastinum contributing to the degrees of anemia in the perioperative period.[11] It also increases the risk after surgery resulting into adverse outcomes due to other co-morbidities (such as hypertension, diabetes, obesity, poor physical fitness etc.) particularly in patients with coronary artery disease[16]. Present study has demonstrated that post-operative Hb levels of 7.35 g/dl was associated with increased mortality after on-pump CABG

(Group I, 10.8% vs. Group II, 0.8%). Blood transfusion done for anemia in post-operative had certain complications[13-15] and increase morbidity and mortality[16]. In our study, we have observed that patients with increasing age had more incidence of post-operative anemia and increased need of blood transfusion. Massive transfusions were associated with 8.1-fold increase in risk of death[17]. In Tsukinga's retrospective study of 5 years of patients undergoing CABG, low hematocrit (>30%) was associated with increased ventilatory time and increase in mortality [18]. Our study also concluded that increase blood transfusion is associated with significant increase in ventilation hours and increased ICU stay and increase mortality rates, however, there is no significant difference in drain output but minimal difference in the wound healing. In the study conducted by Murphy, increase morbidity was also associated with the transfusion, which translated more towards increase in length of ICU stay and admission costs[18]. 30 days mortality was 6 times more in PRBC transfused patients as compared to non-transfused patients in their study[18]. In addition to postoperative anemia, PRBC transfusion is also well-recognized risk factor for adverse outcome after CABG both in early and late postoperative periods[17,19]. Empirical PRBC transfusion trigger is not an uncommon practice in many post-operative cardiac ICU[20]. This empirical practice results in to PRBC transfusions in several hemodynamically stable patients who do not require blood transfusion on their clinical status[21,10]. This kind of practice not only adds to the known morbidity and mortality risk, but also increases the burden of finances, related blood donation requirements, scarcity of blood products of rare groups for other patients[22-24]. In our study, group 2 patients (n=127) did not show any early clinical signs of hemodynamic compromise, drop in oxygen saturation in arterial blood gases, ECG evidence of myocardial ischemia, so transfusion trigger was not initiated. Loor et al, in their retrospective analysis done at Cleveland Clinic, have also observed that homologous blood transfusion in patients with Hb >10.0g/dl, experienced longer ventilation time, short length of survival, when compared with untreated anemic patients Hb ≤8g/dl [25]. STS database has also recommended and stressed the importance and benefits of restricted PRBC transfusion until the patient with Hb fell below 7gm/dl or showed some hemodynamic instability [26,27]. It is a well-known that CABG patients fail to compensate adequately for the effects of anemia which can result into tissue hypoxia, cellular failure, along with organ dysfunction resulting into increased morbidity and mortality[12]. This retrospective analysis was able to demonstrate that patients who had Hb≤7.35g/dl (through ROC) were the patients who received blood had increased mortality risk when they were compared with patients who did not receive any blood products.

Two mortalities occurred in group-1; one was because of uncontrolled atrial fibrillation soon after arrival into the ICU. This atrial fibrillation did not revert itself to repeated defibrillation shocks and terminated to refractory ventricular tachycardia and ventricular fibrillation. Another patient sustained perioperative myocardial infarction within 6-hrs into the perioperative period after the revascularization. These two patients had extensive calcified atherosclerotic plaques in their dominant type III vessels supplying sparsely viable myocardium and therefore required extensive right coronary artery endarterectomies.

Although earlier studies had shown that the low Hb (≤8gm/dl) levels are predictors of poor short-term outcomes in CABG patients, level of Hb at which benefits of PRBC transfusion outweighs the risk of anemia is still unclear[28,29]. In this study, we had attempted and been successful to show that restriction of transfusion trigger along with added clinical observation can help in reducing PRBC transfusions without increasing inordinate morbidity or mortality risks.

CONCLUSION:

In this study, we have analyzed the determinants and outcome of blood transfusion in patients undergoing planned on pump coronary artery bypass surgery. Both in-hospital morbidity and mortality were higher in patients receiving blood as compared to the other group. The increased adverse effects of PRBC transfusions and favorable effects of no-transfusion were noted. We feel that an average Indian patient can tolerate much lower Hb values in the postoperative period as compared to western patients. It would be interesting to explore this further in a multi-centric study in a strictly managed environment.

Strength of study:

All patients were counseled pre-operatively about the risk and benefits of the postoperative blood transfusions (if at all required) and they willingly co-operated with the caring team about any perceptible symptoms or any discomfort during the entire course of their hospital stay.

Study Limitations:

This is a retrospective study. Although, this may appear contradictory to the observations in larger perspective, however, a much larger multi-centre study may help in future. According to WHO, anemia is defined as hemoglobin <13gm% for men and <12 gm% for women. Several cut off values has been described for postoperative hemoglobin as a risk factor for poor outcome, but in this study, we have considered Hb less than 7.35g/dl as a cut off value both for male and female patients to determine its effect on the outcome. Benefits and ill effects of PRBC transfusion and anemia were monitored during the entire period of hospital stay.

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