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Original Research Article

Factors determining blood transfusion in patients undergoing off pump coronary artery bypass graft (OPCABG) surgery: A prospective cross-sectional study

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ABSTRACT

Introduction: Cardiovascular disease, especially coronary heart disease is increasing to a great extent globally and in India. Off pump Coronary artery bypass graft is one of the surgical modalities in the treatment of Coronary artery heart disease. Blood/ blood component transfusion is one of the essential roles during/immediate postoperative period of off pump coronary artery bypass graft surgery. Though there are few benefits due to blood transfusion, the demerits outweigh the merits of blood transfusion. Hence identification of predisposing factors for need of blood /blood component transfusions will enhance us to understand the indications and the ways to minimize it.

Objectives: To determine the predisposing factors that influence the need for blood transfusion during off pump coronary artery bypass graft and to measure their strength of association.

Materials and Methods: This cross-sectional study was done in a tertiary care cardiac center in India between March and September 2016 on 196 patients. The participants were from both sexes, aged between 40-70 years, undergoing elective or emergency OPCABG under general anaesthesia. Information on Demographic data and comorbid illnesses were elicited. Vitals and other hemodynamic parameters were recorded during preoperative, intra operative and post operative periods. Total amount of anticoagulant (heparin) used, activated clotting time (ACT) after 3 minutes of anticoagulation, total duration of graft harvest (time from start of first graft harvesting to end of last graft harvest), total number of grafts taken, total duration for anastamoses (time from start of anastamosis to end of last graft anastamosis), total blood loss and total amount of blood transfused were noted.

Result: The intra-operative factors included total intra-operative heparin used, total protamine used, total number of grafts used for anastamoses, total duration of graft anastamoses, total duration of surgery, total duration of anaesthesia, total intra-operative blood loss and insertion of IABP intra-operatively. The post operative factors included total amount of postoperative blood loss and post operative insertion of IABP. Multivariate analysis of significant factors showed male gender, preoperative anaemia and total duration of surgery were independent predictors of need of blood and blood product transfusion.

Conclusion: Prior identification of risk factors and correction of them if applicable would help to assess and manage preoperatively and also thereby reduce the need for blood transfusions and help in managing optimal utilization of resources.

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1. Introduction

Cardio vascular disease, especially coronary heart disease is increasing world wide.[1] Cardiovascular mortality in India has shown a spike from 2.26 million (1990) to 4.77 million (2020).[2]

In 1960, the prevalence of coronary heart disease in urban India was 2% and it shown to increase 7% to 14% by 2013. In rural areas, it has increased more than 4 times from 1.7% to 7.4%.[3]

"Open-heart surgery in which a healthy blood vessel from aorta is used to create an a bypass route, around blocked or narrowed segment of the coronary arteries in order to increase the coronary blood supply is known as Coronary artery bypass graft (CABG). By late 1930 s, the invention of heart-lung machine by Dr. John Gibbon made the coronary surgeries more feasible for cardiopulmonary bypass (CPB).[4] Great achievements in coronary artery surgery were made in 1960s and in 1961, the first successful human coronary artery bypass operation was done in 1961.[5]

Recently, the Off-pump coronary artery bypass surgery (OPCAB) has gained more importance than on pump procedures due to the potential benefits like avoiding the trauma of cardiopulmonary bypass (CPB) and also by reducing the manipulation of aorta. It has been found that these off pump procedures minimize the perioperative neurological events, requirements for blood product transfusions, renal failure, duration of hospital stay and mortality rate.[6]

One of the essential step in CABG surgery is dealing with blood component transfusion issues. It is found that that blood transfusion requirements are more during cardiac surgeries inspite of major advances in perioperative blood conservation and the institutions have various transfusion procedures for CABG operations.[4] World wide, the utilization of allogeneic blood products plays an crucial part in cardiac surgeries. Increased intravascular volume to support cardiac output, Improved oxygen-carrying capacity and a better hemostasis are the major benefits of blood transfusion. But postoperatively this carries a risk of transmission of viral and bacterial infections, immunologic reactions including anaphylaxis, immune modulation and haemolysis.[5] The requirements for blood transfusion during off pump coronary artery bypass graft (OPCABG) surgery is determined by preoperative, intraoperative and postoperative factors, which will help us to assess the indications of blood transfusion and thereby the other corrective efforts to reduce the blood transfusion.[7,8]

Hence this present research was undertaken in a tertiary care setup to assess the determinants of blood transfusion during off pump coronary artery bypass graft (OPCABG) and measure strength of association of the cause.

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2. Materials and Methods

This cross-sectional study was done in a tertiary care cardiac center between March and September 2016 on 196 cases (who were willing to participate in the study) who falls under physical status III or IV according to American Society of Anaesthesiologists (ASA). The participants were from both sex, aged between 40-70 years, undergoing elective or emergency OPCABG under general anaesthesia (GA). The sample size was calculated considering, the rate of blood transfusion in OPCABG as 50%[based on study done by Chung S et al[9] and by a pilot study done in our own institute], at an absolute precision as 7% and confidence interval of 95% using the following formula.

$$n = \frac{Z^2{}_{1-\alpha/2}\, p(1-p)}{d^2}$$

The calculated sample size was 196.

Patients who had hematological abnormalities and those for whom the off pump was converted to on pump were excluded from the study.

Participants were explained about the procedure during the pre-anesthetic checkup and those who were willing to participate in the study were requested to sign the informed consent document after going through it. Patient's demographic data such as name, age, sex, weight, height, BMI, ASA classification, European System for Cardiac Operative Risk Evaluation (EURO SCORE II) were collected. A detailed history of coronary artery disease (CAD), comorbid illnesses like diabetes mellitus (DM), hypertension (HTN), prior surgical and anaesthetic experience, if any, were elicited. During general examination, patient's general condition was assessed; pulse rate (PR) and blood pressure (BP) were measured and documented. A detailed assessment of airway, respiratory system (RS), central nervous system (CNS), cardiovascular system (CVS), gastrointestinal system(GIT), were carried out as a part of pre anesthetic checkup.

Basic laboratory data including coagulation profile, ECG, Chest- X ray, 2D-ECHO and angiography were reviewed and noted. As per the institutional protocol, angiotensin receptor blockers (ARB) and angiotensin converting enzyme inhibitors (ACEi) were withheld during the day of surgery. All other cardiac medications which patient might have been receiving were continued. Anaemia was defined as per WHO standards: Hb<13 for males and <12 for females.[10]

All patients were instructed to be kept nil per oral (NPO) for atleast 6 hours before the surgery except for emergency cases. All patients are premedicated with tablet pantoprazole 40mg and tablet diazepam 0.1mg/kg. As per the institutional protocol, tablet metaprolol was administered for heart rate control according to following guidelines: 12.5mg if heart rate >50 and ejection fraction 40-50%; 25mg if heart rate >50 and ejection fraction >50%. No metaprolol was administered for patients with heart rate <50 or ejection fraction <40%. No beta blockers were

initiated or stopped on the day of surgery.

After the patient has been shifted to the operation theater, monitors such as electrocardiogram (ECG), pulse oximetery (SpO_2), non-invasive blood pressure (NIBP) and temperature probe were connected. IBP monitoring was done using the radial artery cannulation. An 18G peripheral intravenous cannula was established. Baseline vitals which include, arterial blood gas (ABG), heart rate, blood oxygen saturation (SpO_2), blood pressure (both invasive and non-invasive) were documented.

After three minutes of preoxygenation with 100% oxygen, general anaesthesia (GA) was induced with injection fentanyl 5mcg/kg, injection propofol 0.5mg/kg and endotracheal intubation was performed after administering muscle relaxant - injection pancuronium 0.1mg/kg. Anaesthesia was maintained with isoflurane of 1%, and air-oxygen mixture to maintain a FiO_2 of 0.5.

Intraoperatively following parameters were noted and documented according to the proforma: (No antithrombolytic agents was used eg. Tranexemic acid)

Total amount of anticoagulant (heparin) used, activated clotting time (ACT) after 3 minutes of anticoagulation, total duration of graft harvest (time from start of first graft harvesting to end of last graft harvest), total number of grafts taken, total duration for anastamoses (time from start of anastamosis to end of last graft anastamosis), were noted.

The total amount of blood loss was calculated by two methods. First method was by calculation of blood loss from mops (100% soaked and dripping=100ml, 100% soaked=75ml, 75% soaked= 50ml, 50% soaked= 25ml) and from gauze pieces (100% soaked=25ml, 50% soaked=10 to 15ml) and total amount of blood in suction apparatus, substracting the total amount of saline used. The second method was, the modification of the Gross formula[11] which calculates the ABL as the following.

ABL = BV [Hct (i) - Hct (f)]/ Hct (m)

Blood volume is calculated from the Body Weight from the below formula.

Blood Volume = Body Weight (Kgs) x 70 ml/ kg

Hct (i)- initial hematocrit, Hct (f) – final hematocrit, and Hct (m) -mean hematocrit of the two.

Total amount of blood product transfused (blood transfusion is carried out as per Institutional Transfusion Guideline Protocol): cryoprecipitate, packed red blood cells (PRBC), platelet rich concentrate (PRC), fresh frozen plasma(FFP) and total quantity of reversal of anticoagulation (with protamine) used and activated clotting time (ACT) after reversal, intraoperative complications, intraoperative Intra Aortic Balloon Pump (IABP) insertion, total duration of surgery (till the last suture of sternotomy closure) and total duration of anaesthesia (from start of administration of induction agent to shift to ITU) were noted. After the sternotomy closure patient was shifted to Intensive Treatment Unit (ITU) for postoperative monitoring.

Postoperatively, following parameters were noted and documented as per the proforma: Haemoglobin (Hb) and haematocrit (PCV), total amount of blood product transfused: packed red blood cells (PRBC), platelet rich concentrate (PRC), fresh frozen plasma (FFP) and cryoprecipitate, total amount of blood loss for first 24 hours, postoperative complications (such are cardiac arrhythmias, re-explorations), postoperative Intra Aortic Balloon Pump use (IABP), total duration of intensive treatment unit (ITU) stay (from time of entry to ITU to time of exit from ITU or shift toward), total duration of ventilator support (the time from resuming mechanical ventilation in ITU to the time of extubation), total duration of hospital stay were noted and documented.

2.1. Statistical methods

Statistical analysis was performed by STATA 11.2 (College Station TX USA). The demographic variables were expressed as Frequency/percentages of mean ± SD. Shapiro Wilk Test was used to check the normality. For comparison of mean values, student t-test was used. Bivariate analysis using Fisher Exact test or Chi-Square was applied for categorical variables. Binary logistic regression analysis was performed for factors associated with blood transfusion. Initially univariate analysis was used to detect significant predictors, followed by multivariate regression analysis. Only the significant factors in the univariate analysis were considered to build the multivariate analysis model. $P<0.05$ was taken as statistically significant.

3. Result

Totally 196 participants were enrolled for the study and were monitored for the hemodynamic changes and blood transfusion reactions if any. 178 of the participants (90.81%) were males while the rest 18 (9.19%) were females. 105 required blood transfusion (53.57%). 31 (15.82%) were transfused intraoperatively while 96 (48.98%) required postoperatively.

Age of the study participants, BMI, Euro Score II, LVEF percentage were more or less similar between both the groups before the start of the study. Mean difference between both groups was significant with respect to preoperative hemoglobin, total intraoperative heparin administered, activated clotting time after heparin administration, total intraoperative protamine administered, activated clotting time after heparin administration, Total intraoperative protamine administered, Duration of graft anastomoses, Duration of surgery, Duration of anesthesia, intra operative blood loss, post-operative blood loss, duration of ventilator support. Hemoglobin levels were less and all other parameters were high in patients who received blood transfusion. There was no statistical mean

difference between activated clotting time after protamine administration, dur harvest time duration, ITU stay duration and duration of hospital stay. (Table 1)

Table 2 shows the association between both the groups with various parameters. Nearly 95% of females received blood transfusion. The need for blood transfusion was high among ASA IV(42% vs 24%, P=0.009). The need for intra aortic balloon pump insertion was high among those who received blood transfusion either intraoperatively or postoperatively.

Around two third of those who had LMCA involvement needed blood transfusion (Table 3). There is no association between number of vessels involved and need for blood transfusion. (Table 4) As the number of grafts increases, the need for blood transfusion also increases and the results are statistically significant.(Table 5) There is no significant relationship between need for blood transfusion and complications intraoperative/postoperative. Multiple logistic regression shows that Male gender, Preoperative anaemia and number of grafts for anastomoses were significantly associated with need for blood transfusion. (Table 6)

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4. Discussion

Cautious administration of blood and blood products are emphasized nowadays due to the various adverse effects following blood transfusion, especially in cardiac surgeries. There are high chances of renal failure, atrial fibrillation, infections and respiratory problems.[12] Increase in cardiac events and complications due to infections have also been reported.[13] Hence identifying the potential predictive factors for blood and blood transfusion will help in prior planning and reducing the blood requirements thereby preventing the complications arising out of blood transfusion.[14,15]

The present study was conducted among 196 participants in a tertiary care hospital in Bangalore to determine the factors influencing the blood and blood products transfusion during off pump coronary artery bypass graft. Significant difference was appreciated on mean scores in age of the study participants, BMI, Euro Score II and LVEF percentage between both the groups before the start of the study signifying that there was an equal representation in both the groups.

The overall blood and blood products transfusion rate was 53.57% (intra operative transfusion rate was 15.82% and post operative transfusion rate was 48.98%). Elmistekawy et al[5] their study observed a transfusion rate of 67.6% and Scott et al.[15] observed a transfusion rate of 47.5%. Inspite of various guidelines and strategies to limit the blood transfusion, the blood transfusion rates are still high.[14,16]

Nearly 95% of females received blood transfusion. Female gender had an odds of 17.38 in univariate analysis and 29.48 odds in multivariate analysis. Similar results were observed in results from other studies.[8,17,18] Low hematocrit value was attributed as a contributory factor for blood transfusion among female gender by Utley et al.[19] Few authors have observed that transfusion rates are higher in females even when both genders had similar preoperative condition.[19–22]

Preoperative anaemia (HB less than 13 for males and 12 for females) is associated with increased need for blood transfusion. Similar results were observed in many other studies.[5,9,23,24] Lim C et al[24] demonstrated that the need for blood transfusion could be reduced by pre-operative iron supplementation.

Involvement of left main coronary artery was a significant risk factor for blood transfusion. Similar results were observed by studies done by other authors.[25–29] Preoperative administration of unfractionated heparin increases the risk of blood transfusion. Excessive blood loss

Table 1: Comparison of mean parameters between those who received blood transfusion and those who did not

Parameter	Patients who received blood transfusion (%)	Patients who did not receive blood transfusion (%)	p value
Age (years)	56.94 ± 8.61	56.61 ± 8.72	0.792
BMI(kg/m2)	24.26 ± 3.52	25.17 ± 3.58	0.077
EuroSCORE II	1.33 ± 0.59	1.32 ± 0.72	0.883
LVEF (%)	50.74 ± 8.82	50.08 ± 9.10	0.604
Preoperative haemoglobin	12.71 ± 1.81	13.54 ± 1.41	0.001
Total intraoperative heparin administered	284.98 ± 104.24	225.93 ± 83.10	<0.001
Activated clotting time after heparin adminstration (minutes)	494.14 ± 132.01	451.04 ± 104.33	0.012
Total intraoperative protamine administered	187.71 ± 58.93	158.85 ± 56.61	0.001
Activated clotting time after protamine adminstration (minutes)	157.69 ± 23.87	159.38 ± 34.43	0.686
Duration of graft harvest time (minutes)	88.81 ± 34.20	80.35 ± 33.76	0.084
Duration of graft anastomoses (minutes)	127.12 ± 70.84	96.49 ± 43.42	<0.001
Duration of surgery (minutes)	342.48 ± 131.62	262.27 ± 100.13	<0.001
Duration of anesthesia (minutes)	407.62 ± 143.25	329.42 ± 109.43	<0.001
Intraoperative blood loss (milliliter)	348.98 ± 132.01	272.43 ± 145.39	0.037
Postoperative blood loss (millilitre)	449.46 ± 223.88	354.20 ± 120.12	0.006
Duration of ventilator support (minutes)	978.97 ± 158.84	662.42 ± 218.43	<0.001
Duration of ITU stay (days)	2.92 ± 1.73	2.70 ± 1.89	0.134
Duration of hospital stay (days)	12.32 ± 4.93	12.46 ± 5.23	0.849

Table 2: Association between both groups with various parameters studied

Comorbidity	Patients who received blood transfusion (%)	Patients who did not receive blood transfusion (%)	p value
Male	88 (84%)	90 (99%)	0.0026
ASA IV	44 (42%)	22 (24%)	0.009
Diabetes mellitus (DM)	66 (63%)	51 (56%)	0.332
Hypertension (HTN)	68 (65%)	54 (59%)	0.435
Chronic kidney disease (CKD)	4 (4%)	1 (1%)	0.23
Hypothyroid	10 (10%)	8 (8%)	0.859
Bronchial asthma (BA)	5 (5%)	2 (2%)	0.335
Preooperative Anaemia	50 (48%)	30 (33%)	0.037
RWMA	55 (52%)	52 (57%)	0.504
LMCA (left main cornary artery) involvement	33 (86.8%)	15 (88.2%)	0.886
Preoperative clopidogrel	89 (85%)	69 (76%)	0.095
Preoperative low molecular weight heparin (LMWH)	15 (14%)	21 (23%)	0.113
Preoperative unfractionated heparin	12 (11%)	20 (22%)	0.046
Intraoperative Intra Aortic Balloon Pump (IABP) insertion	5(4.76%)	0(0)	0.035
Postoperative IABP (Intra Aortic Balloon Pump) insertion	6 (6%)	3 (3%)	0.011

Table 3: Association between coronary artery involvement and blood transfusion

Coronary artery	Patients who received blood transfusion (%)	Patients who did not receive blood transfusion (%)	Total	p value
LMCA (left main coronary artery)	37 (35%)	18 (20%)	55	0.016
LAD (left anterior descending artery)	103 (98%)	89 (98%)	192	0.885
RCA (right coronary artery)	94 (90%)	76 (84%)	170	0.216
Circumflex artery	85 (81%)	77 (76%)	162	0.409

Table 4: Association between Blood transfusion and number of vessels involved

Coronary artery involved	Patients who received blood transfusion (%)	Patients who did not receive blood transfusion (%)	Total	p value
Single	6 (6%)	6 (7%)	12	
Double	16 (15%)	26 (29%)	42	0.065
Triple	83 (79%)	59 (65%)	142	
Total	105	91	196	

Table 5: Association between transfusion and total number of grafts used for anastamoses

Number of grafts	Patients who received blood transfusion (%)	Patients who did not receive blood transfusion (%)	p value
1	10 (9.3%)	24 (15.9%)	
2	60 (50%)	50 (63.6%)	
3	34 (39.8%)	15 (18.2%)	0.009
4	1 (0.9%)	2 (2.3%)	
Total	105	91	

Table 6: Multiple logistic regression analysis for factor associated with blood transfusion

	Univariate analysis			Multivariate analysis		
Variables	**Odds ratio**	**95% C.I**	**p-value**	**Odds ratio**	**95% C.I**	**p-value**
Age	1	0.97 – 1.04	0.791	0.99	0.95 – 1.03	0.734
Female gender	17.38	2.26-133.45	0.006	29.48	3.68 – 236.48	0.001
LMCA	1.01	1.00 – 1.02	0.047	1	0.98 – 1.02	0.781
Total intraoperative heparin used	1.01	1.00 – 1.01	<0.001	1	0.99 – 1.01	0.191
Total intraoperative protamine used	1.01	1.00 – 1.01	0.001	1	0.99– 1.01	0.829
Duration of surgery	1.01	1.00 – 1.01	<0.001	1	1.00 – 1.01	0.024
Preoperative anaemia	1.85	1.03 – 3.31	0.038	1.88	0.92- 3.84	0.043
Number of grafts for anastamoses	1.98	1.26 – 3.11	0.009	1.58	0.91 – 2.74	0.104
ASA grade IV	0.44	0.23 – 0.82	0.009	0.6	0.20 – 1.74	0.345

due to the anticoagulant effect necessitates the need for blood transfusion. Similar results were attributed by other authors.[16,28,30]

The need for blood transfusion is directly proportional to the number of grafts, duration of anastomoses, total duration of surgery. Studies done by other authors[5,9,23] in different places also revealed similar results

Intra Aortic Baloon Pump(IABP) insertion is used to support failing heart to augment cardiac output during the surgical procedure.[31] It is associated with increased use of heparin to prevent thromboembolic complication. As a negative effect, heparin induces more blood loss, there by necessitating blood transfusion.[32] Frank et al[28] also documented the necessity of increased blood transfusion with the use of heparin for IABP insertion. Kogan et al[33] in his study demonstrated the reduced need for blood transfusion by minimizing the need for heparin in IABP insertion.

5. Conclusion

The preoperative predictors were male gender, preoperative anaemia, ASA grade III or more, left main coronary artery (LMCA) involvement. The major intraoperative

predisposing factors include total intraoperative heparin used, total number of grafts used for anastomoses, total duration of graft anastomoses, total duration of surgery, total intraoperative blood loss and insertion of intraoperative IABP. The postoperative factors are total amount of postoperative blood loss and postoperative insertion of IABP. Hence we can predict the need for blood transfusion with the forementioned factors and thereby appropriate measures can be applied to minimize the requirement for blood transfusion and also to plan ahead the need for blood transfusion.

6. Source of Funding

None.

7. Conflict of Interest

The author declares no conflict of interest.

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