Relation Between Preoperative Plasma Fibrinogen Level And Postoperative Bleeding Following Off-Pump Coronary Artery Bypass Surgery

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Abstract

Background: Bleeding is a major concern after cardiac surgery and also a significant cause of morbidity and mortality. Fibrinogen is a key factor in the coagulation cascade and seems to be the most fundamental hemostatic risk factor following OPCAB. **Objective:** The objective of the study was to evaluate the relation between preoperative plasma fibrinogen level with postoperative bleeding following OPCAB. **Methods:** This comparative cross-sectional study was carried out at the Department of Cardiac Surgery in BSMMU hospital from March, 2017 to August, 2019. The study population was 60, with 2 (two) groups having 30 patients in each. Preoperative quantitative determination of plasma fibrinogen levels were measured by the Clauss method. Grouping of patients were done with respect to a preset cutoff value for plasma fibrinogen level (Plasma fibrinogen level above and below the cutoff value in group A and group B respectively). Patients from both the groups underwent OPCAB. The total amount of drainage blood from chest tubes within 1st 24 hours was recorded after termination of operation. Statistical analysis of different characteristics between the patients of both groups was done to draw a conclusion. **Results:** There was inverse relationship between preoperative plasma fibrinogen level and postoperative bleeding following OPCAB. The incidence of low preoperative plasma fibrinogen and postoperative bleeding were more common in old age. Platelet count was significantly lower in low preoperative plasma fibrinogen group. Blood transfusion, ICU stay and Hospital stay were more in low preoperative plasma fibrinogen group. There were no postoperative thromboembolic events, cardiac ischemic incidents, re-exploration and mortality. Multivariate logistic regression analysis was done to assess the predictive value of preoperative plasma fibrinogen level, age and platelet count. Among these, preoperative plasma fibrinogen level was the most valuable predictor for increased postoperative bleeding after OPCAB. **Conclusion:** Low preoperative plasma fibrinogen concentration level was associated with increased postoperative bleeding in patients undergoing off-pump coronary artery bypass grafting.

Keywords: Coronary Artery Bypass, Fibrinogen, Blood Transfusion, Mortality.

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I Introduction

Coronary artery disease (CAD) is one of the most scrutinized diseases in medical science and coronary revascularization is the most studied intervention. Coronary artery disease (CAD) results from narrowing of the coronary arteries. The narrowing is caused by thickening and loss of elasticity of arterial walls. When this narrowing is sufficiently severe, it limits blood flow to the myocardium. At primary stage, the disease limits only coronary flow reserve (increase inflow that normally accompanies increased myocardial oxygen demands) but when sufficiently advanced, CAD reduces blood flow through the affected artery even at rest. In its most severe form, atherosclerotic CAD occludes the coronary artery [1]. Initially, for revascularization of the coronary arteries in CAD, coronary artery bypass surgeries were performed using cardiopulmonary bypass with cardioplegic arrest [2]. To reduce postoperative complications caused by systemic inflammation, off-pump coronary artery bypass (OPCAB) was introduced into clinical practice in the early 1990s [3]. During off-pump surgery, the coronary artery grafts are placed on coronary arteries of a beating heart using intra-coronary shunts, thereby avoiding aortic cross clamping and CPB. Benefits of OPCAB are early extubation, reduced perioperative blood transfusion, hospital stay and mortality [4]. In spite of having several advantages, OPCAB is still accompanied with a risk of complications such as bleeding, infections, stroke, myocardial infarction with heart failure, renal insufficiency and pulmonary dysfunction [5]. Bleeding is a common and severe complication after cardiac surgery. It may be caused by surgical factors or disturbed hemostasis or combination of both. Disturbed postoperative hemostasis may be related to impaired coagulation, increased fibrinolysis or platelet dysfunction [6]. Fibrinogen is a key protein in hemostasis synthesized by the liver. It is also known as clotting factor I (one) and it circulates in plasma at a concentration of 2.0-4.5 gm/L. In healthy human adults, about 2-5 gm of fibrinogen is synthesized daily and the same amount is catabolized. The plasma half-life of fibrinogen in normal humans has been estimated to be 3-5 days. Fibrinogen is converted in plasma by thrombin into fibrin, which under the influence of factor XIII is formed into a meshwork at the site of tissue damage to minimize blood loss and stimulate tissue repair. Fibrinogen is the final clotting factor activated in the coagulation cascade during hemostasis [7]. Fibrinogen binds to the specific platelet receptor, which is important for incorporating platelet aggregation [8]. Thus, in primary hemostasis it supports formation of platelet plug and in secondary hemostasis the formation of insoluble fibrin clot. Fibrinogen and fibrin also interact with other adhesive glycoproteins, hemostatic factors and blood cells forming a complex system that constitutes the process of hemostasis. So, preoperative fibrinogen levels are associated with the amount of 24-hours mediastinal blood loss, even when levels are above the lower limit of reference range [9]. An increasing number of studies indicate that fibrinogen plays a more important role to achieve adequate hemostasis than what previously was thought in patients suffering from major bleeding. Effect of preoperative fibrinogen infusion on CABG patients showed that prophylactic fibrinogen infusion reduced postoperative bleeding by approximately 30% and maintained postoperative hemoglobin at a higher level in patients who were randomized to fibrinogen infusion compared with the control group. Therapeutic fibrinogen substitution is based on products derived from human plasma, such as fresh-frozen plasma (about 2-3 mg/ml), cryoprecipitate (about 200-250 mg/unit) or fibrinogen concentrate (dose: 70mg/kg body weight). However, there were significant inverse correlation between postoperative bleeding and preoperative fibrinogen levels [10]. So, further studies are still required in this matter. This study was conducted to evaluate the relation between preoperative plasma fibrinogen level and postoperative bleeding in patients undergoing OPCAB.

II Objectives of the Study

General objective:

1. To evaluate the relation between preoperative plasma fibrinogen level with postoperative bleeding following OPCAB.

Specific objectives

2. To determine the preoperative plasma fibrinogen level of patients undergoing OPCAB.

3. To measure postoperative bleeding of patients from chest tube drainage hourly for 24 hours following OPCAB.

4. To assess the relationship between post operative bleeding following OPCAB with preoperative plasma fibrinogen level.

III Materials & Methods

This comparative cross-sectional study was carried out at the Department of Cardiac Surgery in BSMMU hospital from March, 2017 to August, 2019. The study population was 60, with 2 (two) groups having 30 patients in each. Preoperative quantitative determination of plasma fibrinogen levels were measured by the Clauss method. Grouping of patients were done with respect to a preset cutoff value for plasma fibrinogen level (Plasma fibrinogen level above and below the cutoff value in group A and group B respectively). Patients from both the groups underwent OPCAB. The total amount of drainage blood from chest tubes within 1st 24 hours was recorded after termination of operation. Statistical analysis of different characteristics between the patients of both groups was done to draw a conclusion.

Selection Criteria

Inclusion Criteria:

1. All patients with coronary artery disease admitted for off pump coronary artery bypass surgery (OPCAB) except the following exclusion criteria.

Exclusion Criteria:

2. Patients having known bleeding disorder.

3. Patients receiving un-fractionated or low molecular weight heparin.

4. Patients with hepatic impairment.

5. Patients with renal impairment.

6. Patients having congestive cardiac failure.

7. Patients needing valve surgery along with CABG.

8. Patients needing conversion to On-pump CABG.

9. Patients operated on emergency basis or redo surgery.

All Data Collection: All patients admitted in Cardiac Surgery Department, BSMMU with coronary artery disease scheduled for OPCAB were considered as study population (without exclusion criteria). Patient who fulfilled the inclusion criteria and willing to enroll in the study was included in the study after receiving the proper consent. Preoperative plasma fibrinogen level was measured in each subject in Hematology laboratory, BSMMU, the day before surgery. Venous blood sample for plasma fibrinogen level was taken 24 hours before the scheduled date of surgery. Preoperative plasma fibrinogen level was measured according to Clauss Method. The specimen was platelet-free plasma or platelet poor plasma. Amount of specimen needed from each subject is 1 ml of plasma. To obtain this, after all aseptic precaution, venous blood sample was collected from each study subject in a disposable plastic syringe and immediately transferred to a sterile 2.7 ml blue-top (3.2% sodium citrate) tube. Then, the tube was gently moved upside down for several times to mix the whole blood with 3.2% sodium citrate. Blood was not drawn from a heparinized line. To avoid contamination of the sample with tissue thromboplastin or heparin, venipuncture was done very carefully to avoid any trauma. In case blood was drawn from an indwelling catheter, it was flushed with 5 ml of saline and the first 5 ml of blood collected was discarded. If drawn with a butterfly setup, a discard was made first to remove air from tubing. Tubes were labeled with patients name, ID number & collection date and sent to BSMMU Hematology laboratory immediately for centrifugation & further procedure. Plasma fibrinogen level was determined from venous blood sample using fully automated coagulation analyzer (SYSMEX CS1600, USA) and reagent (Thrombin reagent) according to Clauss method. Patients who had preoperative plasma fibrinogen level more than 3.1gm/L were included in group A and who had preoperative plasma fibrinogen level equal or less than 3.1gm/L were included in group B. Detailed history, clinical examination and relevant investigation reports of all patients were recorded in the data collection sheet pre-operatively. According to schedule, patients were taken to the operating room. Peripheral venous catheterization and central venous catheterization (in the internal jugular vein) and arterial line were done aseptically. Standard anesthetic techniques of induction and maintenance were followed for all procedures. All patients were operated through a median sternotomy approach. Left internal mammary artery (LIMA) was harvested. Great saphenous vein was also harvested. Target coronary arteries were stabilized using tissue stabilizing system, appropriate sized intracoronary shunts were used in all cases to maintain distal perfusion and to achieve bloodless operative field. After completion of surgery all patients were transferred to intensive care unit (ICU) intubated and ventilated. Postoperative blood loss was recorded hourly for 24 (twenty four) hours after OPCAB and then amount of total drain output in each subject. All patients received ionotrope support and other medication as per hospital protocol. Patients were extubated as soon as they met the standard criteria. Then the patients were transferred to the SDU (Step Down Unit) and then to post-operative ward whenever appropriate, according to the consultant’s judgment. After meeting the discharge criteria, the patients were discharged from the hospital.

Data Analysis: Statistical analysis was conducted using Statistical Package for Social Science (SPSS) version 23.0 for windows software. Comparisons between groups were made with Student’s t-test, Chi-Square test and Fisher’s exact test. The results were presented in tables. Observations were recorded as statistically significant if a p-value is ≤ 0.05.

IV Results

Total sixty (60) patients who underwent off-pump coronary artery bypass graft surgery were evaluated in this study as per the inclusion and exclusion criteria. Venous blood samples to determine plasma fibrinogen level was collected a day before surgery. Based on the pre-fixed cutoff value, the patients were grouped into group A and B. OPCAB were performed in both groups maintaining the standard hospital protocol. Postoperative care at ICU was given to the patients of both groups as per standard hospital protocol. The findings of the study obtained from data analysis presented in the following pages.

Comparison of demographic and anthropometric variables:

Among the study population mean age in group A was 55.43±8.53 years and in group B was 59.63±6.86 years. The difference in age between two groups was statistically significant ($p<0.05$). There was no statistical significance of gender between the two study groups ($p>0.05$). The mean BMI in group A was 24.13±2.49 kg/m² and that in group B was 24.62±3.71 kg/m². The findings were statistically not significant ($p>0.05$) [Table-1].

Table 1: Comparison of demographic and anthropometric variables:

Variables	Group Group A(n=30)	Group B(n=30)	p value*
[a]Age (In years) Mean ± SD Range	55.43±8.53 (42 to 72)	59.63±6.86	0.012[S]
[b] Sex Male Female	23 (76.66%) 07 (23.33%)	18 (60.0%) 12 (40.0%)	0.165[ns]
[a] BMI (kg/m^2) Mean ± SD	24.13±2.49	24.62±3.71	0.548[ns]

Table in the parentheses indicate percentage. Data were analyzed using, [a]Student's t-test and was presented as mean ± SD. [b]Chi-square test (χ^2) was used to measure the level of significance. *p>0.05 was considered not to be significant. n= number of subjects, s= significant, ns= not significant, BMI = Body Mass Index.

Comparison of preoperative risk variables:

[Table 2] shows the distribution of data obtained by evaluating history and major risk factors. The comparison of the presence of breathlessness, chest pain, Hypertension, Diabetes mellitus and COPD in group A and B patients were statistically not significant (p>0.05).

Table 2: Comparison of preoperative risk variables:

Variables	Group Group A(n=30)	Group B(n=30)	p value*
[b] Shortness of Breath	07 (23.33%)	03 (10%)	0.166[ns]
[a] Chest Pain	28 (93.33%)	29 (96.66%)	0.554[ns]
[a] Hypertension	20 (66.7%)	19 (63.3%)	0.787[ns]
[a] Diabetes mellitus	17 (56.7%)	11 (36.7%)	0.121[ns]
[b] COPD	03 (10%)	04 (13.33%)	0.688[ns]

Table in the parentheses indicate percentage. Data were analyzed using, [a]Chi-square test (χ^2) & [b]Fisher's exact test and these were used to measure the level of significance. *p>0.05 was considered not to be significant. n= number of subjects, ns= not significant.COPD = Chronic Obstructive Pulmonary Disease

Comparison of preoperative biochemical and echocardiographic variables:

[Table 3] shows that there were no statistically significant differences in findings between two groups in terms of CRP, serum albumin, serum creatinine, serum calcium and EF(%) (p>0.05).

Table 3: Comparison of preoperative biochemical and echocardiographic variables:

Variables	Group Group A(n=30)	Group B(n=30)	p value*
CRP (mg/L)	2.94±1.02	3.10±1.13	0.580[ns]
Serum albumin (gm/L)	36.16±2.26	36.76±2.83	0.369[ns]
Serum creatinine (mg/dl)	1.19±0.09	1.20±0.11	0.847[ns]
Serum calcium (mg/dl)	9.49±1.07	9.25±0.63	0.287[ns]
EF(%)	52.96±6.19	49.60±7.34	0.060[ns]

Data were analyzed using, Student's t-test and was presented as mean ± SD. *p>0.05 was considered not to be significant. n= number of subjects, ns= not significant, CRP = C-reactive protein, EF = Ejection fraction.

Comparison of preoperative hematological variables:

[Table 4] shows that there were no statistically significant differences in findings between two groups in terms of hemoglobin, prothrombin time and activated partial thromboplastin time (p>0.05). However, lower mean platelet count was observed in group B patients than that of group A which was statistically significant (p<0.05)

Table 4: Comparison of preoperative hematological variables:

Variables	Group Group A(n=30)	Group B(n=30)	p value*
Hb (gm/dl)	12.5±0.9	11.4±0.9	0.855^{ns}
Platelet count (×10^3/cumm of blood)	316.17±45.97	249±42.54	0.021^{s}
PT (sec)	12.29±0.68	12.34±0.65	0.758^{ns}
APTT (sec)	33.83±3.02	33.17±2.70	0.371^{ns}

Data were analyzed using, Student's t-test and was presented as mean ± SD. *p>0.05 was considered not to be significant. n= number of subjects, s= significant, ns= not significant, Hb = Hemoglobin, PT = Prothrombin time, APTT = Activated partial thromboplastin time

Comparison of per operative variables:

[Table 5] shows that mean ACT after heparinization was 357.9±31.26 seconds in group A and 389.1±26.86 seconds in group B. The averages of ACT after heparin neutralization in both groups were 123.27±9.17 seconds and 129.47±8.24 seconds respectively. The difference in ACT after heparinization and ACT after heparin neutralization between the two groups was statistically not significant (p>0.05). The duration of surgery in group A was 4.38±0.57 hours and that in group B was 4.53±0.66 hours, which was statistically not significant (p>0.05). The number of coronary anastomoses performed in group A and B patients were also statistically not significant (p>0.05).

Table 5: Comparison of per operative variables:

Variables	Group Group A(n=30)	Group B(n=30)	p value*
ACT after Heparinization (sec)	357.9±31.26	389.1±26.86	0.142^{ns}
ACT after Heparin neutralization (sec)	123.27±9.17	129.47±8.24	0.332^{ns}
Duration of surgery (hours)	4.38±0.57	4.53±0.66	0.347^{ns}
Number of grafts (Mean ± SD)	2.86±0.77	3.03±0.49	0.324^{ns}

Data were analyzed using, Student's t-test and was presented as mean ± SD. *p>0.05 was considered not to be significant. n= number of subjects, ns= not significant, ACT = Activated Clotting Time.

Comparison of postoperative variables regarding blood loss:

[Table 6] shows the comparison of postoperative variables between group A and B patients. Amount blood loss in 1st 12 hours immediate after surgery in group A and B were 185.67±35.20 ml and 219.67±57.32 ml respectively, which was statistically significant (p<0.05). Amount blood loss in 1st 24 hours after surgery in group A and B were 306.00±73.37 ml and 370.33±69.65 ml respectively, which was also statistically significant (p<0.05). Total drain collection after surgery in group A was 792.33±160.32 and in group B was 905.33±137.03 ml, which was statistically significant (p<0.05).

Table 6: Comparison of postoperative variables regarding blood loss:

Variables	Group Group A(n=30) Group B(n=30)	p value*
Blood loss in 1st 12 hours (ml) Range	185.67±35.20 219.67±57.32 (140-380)	0.008^{S}
Blood loss in 1st 24 hours (ml) Range	306.00±73.37 370.33±69.65 (180-550)	0.001^{S}
Total drain collection (ml) Range	792.33±160.32 905.33±137.03 (530-1700)	0.005^{S}

Data were analyzed using, Student's t-test and was presented as mean ± SD. *p>0.05 was considered not to be significant. n= number of subjects, s= significant.

Comparison of postoperative outcome variables:

[Table 7] shows that among the study population, difference between the postoperative ventilation time of the two groups was not statistically significant (p>0.05). Post operative blood transfusion in group A and B were 2±0.53 units and 2.5±0.68 units respectively, which was statistically significant (p<0.05). Duration of ICU stay following surgery was longer in group B patients (64.37±11.98 hours) compared to group A patients (58.5±9.06 hours), which was statistically significant ($p<0.05$). Difference between the duration of hospital stay of the two groups was also statistically significant ($p<0.05$).

Table 7: Comparison of postoperative outcome variables:

Variables	Group Group A(n=30)	Group B(n=30)	p value*
Postoperative ventilation time (minutes)	401.5±33.84	415.83±47.16	0.181^{ns}
Postoperative blood transfusion (units)	2±0.53	2.5±0.68	0.002^{s}
Duration of ICU stay (hours)	58.5±9.06	64.37±11.98	0.037^{s}
Duration of hospital stay (days)	9.03±0.99	10.97±1.56	0.028^{s}

Data were analyzed using, Student's t-test and was presented as mean ± SD. *p>0.05 was considered not to be significant. n= number of subjects, s= significant, ns= not significant ICU = Intensive Care Unit.

<u>Pearson correlation test for preoperative plasma fibrinogen level and postoperative bleeding in 1st 24 hours after off-pump coronary artery bypass grafting surgery:</u>

The Pearson co-efficient correlation test shows a significant inverse relationship between the preoperative plasma fibrinogen level and post operative bleeding in 1st 24 hours after off pump coronary artery bypass grafting surgery, $r = -0.30$, $p < 0.05$.

Table 8: Pearson correlation test for preoperative plasma fibrinogen level and postoperative bleeding in 1st 24 hours after off-pump coronary artery bypass grafting surgery:

Correlations		Preoperative plasma fibrinogen level	Post operative bleeding in 1st 24 hours after OPCAB
Preoperative plasma fibrinogen level	Pearson Correlation	1	-0.302
	p value*		0.019^{s}
	N	60	60
Post operative bleeding in 1st 24 hours after OPCAB	Pearson Correlation	-0.302	1
	p value*	0.019^{s}	
	N	60	60

*p>0.05 was considered not to be significant.
s= significant

N= number of subjects

<u>Logistic regression analysis:</u>

Analysis of predictors of postoperative bleeding following OPCAB:

The relationship between baseline predictors and post operative bleeding following OPCAB were assessed by the use of logistic regression analysis. Among the variables, the preoperative plasma fibrinogen level was found to be the most valuable predictor (OR 2.96, 95% CI 1.009-8.678, $p<0.05$).

Table 9: Logistic regression analysis of predictors of postoperative bleeding following OPCAB:

Variables	B	p value*	Odds ratio	95% CI for odds ratio	
				Lower	Upper
Preoperative plasma fibrinogen level	1.085	0.048^{s}	2.960	1.009	8.678
Platelet count	0.109	0.844^{ns}	1.116	0.376	3.307
Age	-0.310	0.570^{ns}	0.734	0.252	2.135

*p>0.05 was considered not to be significant. s= significant, ns= not significant.;

V Discussion

This study aimed at finding the association between preoperative plasma fibrinogen level with postoperative bleeding following OPCAB. The study was conducted at BSMMU hospital, Shahbagh, Dhaka, included a total number of 60 patients undergoing OPCAB as per the inclusion and exclusion criteria. The patients were divided into two groups (Group A and Group B; 30 patients in each) on the basis of preoperative plasma fibrinogen level. Alagha and associates found a clear threshold for the preoperative plasma fibrinogen level and postoperative bleeding following OPCAB of 3.1gm/L. Preoperative plasma fibrinogen level of 3.1gm/L or less was detected 1.57 times more frequently in patients with excessive bleeding [11]. According to this, patients with preoperative plasma fibrinogen level with more than 3.1gm/L were included in group A and those with preoperative plasma fibrinogen level equal or less than 3.1gm/L were in group B. OPCAB was performed and postoperative ICU care was given to the patients of both groups as per standard protocol. The demographic variables of the participating patients were recorded and analyzed. The mean age for group A was 55.43±8.53 years and group B was 59.63±6.86 years respectively, the difference was statistically significant (p=0.012). The age range of the patients of this study was from 42 years to 72 years. This study observed that the incidence of low plasma fibrinogen and postoperative bleeding were more common in old age. A similar study showed plasma fibrinogen level and relation to age was statistically significant (p=0.015) which was carried out by Ucar and colleagues [12]. In group A, approximately two third of the population were male 23 (76.66%) and one third 07 (23.33%) were female. In group B, Male were 18 (60%) and 12 (40%) respectively. Male patients were predominant in both the groups. The distribution of gender between the groups were not statistically significant (p=0.16). Ucar and associates also found insignificant (p=0.87) relationship between fibrinogen and gender (male gender=400.7±123.0 versus female gender=395.6±148.1) [12]. A study done by Blome and colleagues in 2005 included ninety-eight (n=98) patients undergoing CABG showed that sex distribution had no significant influence (p=0.389) on postoperative bleeding [13]. When average BMI was compared between the two groups, it was 24.13±2.49 kg/m^2 in Group A and 24.62±3.71 kg/m^2 in Group B. The difference was statistically insignificant (p=0.548). This finding correlates to this study of Kim and colleagues, where they found BMI distribution among the groups was not significant (p=0.096) [14]. Demographic data are listed in Table 1. Presence of diabetes mellitus as a risk factor between two groups were also analyzed statistically but was found to be of no significance (p=0.121). Alagha and associates found distribution of diabetic patients between the two groups were not statistically significant as a risk factor (p=0.07) [11]. Distribution of hypertensive patients between group A and group B was analyzed. Group A had 20 (66.7%) hypertensive patients and group B had 19 (63.3%). This distribution was not statistically significant (p=0.787). The finding of Kim and colleagues correlates with current study, in which p=0.058 for hypertension [14]. In this study, Group A had 03(10%) patients of COPD whereas group B was comprised of 04(13.33%) COPD patients. But, there was no significant relationship of COPD with post operative bleeding following OPCAB (p=0.688) which is similar to the findings of Alagha and associates [11]. The distribution of COPD patients of their study was 51(23%) and 80 (25%) with p-value of 0.54 [11]. Critsinelis and associates stated in their study that, there is significant association of preoperative low serum albumin levels with postoperative adverse outcomes and lower survival rates [15]. So, preoperative serum albumin was observed (36.16±2.26 gm/L and 36.76±2.83gm/L in group A and group B respectively) but it was found that the difference between two groups was not statistically significant (p=0.369). Among the preoperative echocardiographic parameter ejection fraction (EF) were considered for comparison between group A and group B. The difference of EF in between the two groups was not statistically significant (p=0.06). Group A had a mean EF of 52.96±6.19 % and that of group B was 49.60±7.34 %. Alagha and colleagues reported similar findings in their study [11]. The preoperative haemoglobin level and serum calcium were observed. The mean haemoglobin level in two groups were 12.5±0.9 gm/dl and 11.4±0.9 gm/dl and was not significantly associated (p=0.855). This correlates with the study of Walden and associates (p=0.52) [16]. The mean serum calcium was 9.49±1.07 mg/dl in group A and 9.25±0.63 in group B which was also not statistically significant (p=0.287). Preoperatively measured platelet count (316.17±45.97 ×10^3/cumm of blood in group A and 249±42.54 ×10^3/cumm of blood in group B) was found to be significantly associated (p=0.021) with postoperative bleeding following OPCAB, which is similar to the finding reported by Alagha and colleagues. In that study, the mean platelet count of two groups were 264±90 ×10^3/cumm of blood and 240±85 ×10^3/cumm of blood respectively which was statistically significant (p<0.001) [11]. Alagha and associates also stated that commonly used preoperative laboratory tests such as activated partial thromboplastin time (APTT), prothrombin time (PT) were inadequate for estimating postoperative bleeding after cardiac surgery [11]. In current study it was found that, the mean PT of the two groups were 12.29±0.68 seconds and 12.34±0.65 seconds with mean APTT of group A 33.83±3.02 seconds and group B 33.17±2.70 seconds. No significant association was found between PT (p=0.758) and post operative bleeding. The association of APTT was also statistically insignificant (p=0.371). These findings also correlate with the findings of Blome and Colleagues [13]. The difference in ACT after heparinization and ACT after heparin neutralization between the two groups was statistically not significant (p>0.05). Mean ACT after Heparinization was 357.9±31.26 seconds in group A and

389.1±26.86 seconds in group B (p=0.142). The average ACT after Heparin neutralization in both groups were 123.27±9.17 seconds and 129.47±8.24 seconds (p=0.332). Similar findings were observed in the study done by Rosin and Holt [17]. Operative time to perform OPCAB on patients of group A and B were also compared statistically. The mean time taken to complete OPCAB in group A was 4.38±0.57 hours and that of group B was 4.53±0.66 hours, which was statistically not significant (p=0.347). Comparison of number of distal grafts performed on patients of group A and B was also not significant (p=0.324). These findings correspond to the study conducted by Jeppsson and associates [18].

In present study, mean blood loss in 1st 12 hours in group A was 185.67±35.20 ml and 219.67±57.32 ml in group B and the difference was statistically significant (p=0.008). And the difference between mean Blood loss in 1st 24 hours in the two groups was (306±73.37 ml in group A and 370.33±69.65 ml in group B, range 180-550 ml) statistically significant (p=0.001). These findings are also found in the retrospective study done by Alagha and associates. The difference of postoperative bleeding in 1st 24 hours following OPCAB was statistically significant (p=0.01) [11]. Blome and colleagues also found significant (p=0.002) association of preoperative plasma fibrinogen level with postoperative bleeding after cardiac surgery [13]. The difference of total drain collection between two groups in present study was (792.33±160.32 ml in group A and 905.33±137.03 ml in group B, range 530-1700 ml) statistically significant (p=0.005). In the study done by Ucar [12], and associates, chest drainage was a mean of 972 ml (range, 240-2445 ml) and there were negative linear relation between the fibrinogen levels and the postoperative bleeding. This relation was statistically significant (r = –0.897, p<0.001) which correlates with current study [12]. The mean post operative blood transfusion in group A and B were 2±0.53 units and 2.5±0.68 units respectively, which was statistically significant (p<0.05). These findings correspond to the study conducted by Tettey and associates [19]. The distribution of mean postoperative ventilation time in the two groups was not significant (p=0.181). This is comparable to the study conducted by Birla and associates [20]. The mean ICU stay of the patients of group A and group B (58.5±9.06 hours and 64.37±11.98 hours respectively) was observed and longer duration of ICU stay of the group B patients were statistically significant (p=0.037). This finding is similar to the finding (p=0.023) of Kim and colleagues. They found duration of ICU stay to be significantly associated (p=0.023) with preoperative lower plasma fibrinogen and increased postoperative bleeding following OPCAB [14]. The mean hospital stay in group A was 9.03±0.99 days and in group B was 10.97±1.56 days and the difference was statistically significant (p=0.028). The Pearson co-efficient correlation test for preoperative plasma fibrinogen level and postoperative bleeding following OPCAB showed a significant inverse relationship, (r =-0.302, p=0.019). Another study found the similar inverse correlation between postoperative bleeding volume and preoperative fibrinogen concentration (r =-0.53, p<0.001) [10]. Ozolina and colleagues also found a strong inverse relationship between the level of preoperative fibrinogen and the amount of postoperative bleeding in 1st 24 hours (r =-0.35; p<0.001) [21]. A logistic regression analysis was done to assess the predictive value of plasma fibrinogen level, age, platelet count for postoperative bleeding following OPCAB. Among the other variables plasma fibrinogen level was the most valuable predictor of postoperative bleeding following OPCAB (OR 2.960, 95% CI, 1.009-8.678, p=0.048). This is similar to the information provided by Alagha and associates [11]. The prevalence of plasma fibrinogen concentration was inversely proportional to excessive postoperative bleeding in a univariate testing performed in another study done by Walden and colleagues and they concluded that preoperative concentration of plasma fibrinogen is independently associated (OR 0.75, 95% CI, 0.64 to 0.89 per gm/L, p=0.001) with post-operative bleeding following CABG [16]. There were no postoperative thromboembolic events, cardiac ischemic incidents, re-exploration and mortality in present study.

VI Conclusion

Plasma fibrinogen level appears to be a useful predictor of postoperative bleeding in patients undergoing OPCAB. Its preoperative level may indicate us to take necessary steps to prevent postoperative bleeding as well as reduce the rate of ICU stay. This study demonstrated that low preoperative fibrinogen levels are associated with increased postoperative bleeding following OPCAB and preoperative fibrinogen determination may be a useful screening tool to identify individuals at added risk for excessive bleeding after OPCAB.

VII Limitations

This study evaluated a small population of patients for a limited period of time. This analysis was done in a single center of Bangladesh and the sample only represents a small fraction of patients undergoing off pump coronary artery bypass surgery. Duration of the study was short.

VIII Recommendations

Preoperative estimation of plasma fibrinogen level should be done routinely. Plasma fibrinogen level should be corrected before surgery to reduce postoperative bleeding. Preoperative fibrinogen determination should be used as a screening tool to identify patients at added risk for excessive bleeding after OPCAB. Multi center based, larger prospective studies are needed to validate the findings.

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