| Original | Article |

Effect of cardiopulmonary bypass on hemostasis in patients undergoing cardiac surgery

Jubayer Ahmad, Redoy Ranjan, Heemel Saha, S. M. G. Saklayen, Masuda Begum and Asit Baran Adhikary

Article Info

Department of Cardiac Surgery, Faculty of Surgery, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh (JA, RR, HS, SMGS, ABA); Department of Hematology, Faculty of Medicine, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh (MB)

For Correspondence:
Asit Baran Adhikary
drasit2005@yahoo.com

Received: 11 February 2018
Accepted: 20 May 2018
Available Online: 28 May 2018

ISSN: 2224-7750 (Online)
2074-2908 (Print)

DOI: 10.3329/bsmmuj.v11i2.35780

Keywords: Cardiac surgery; Cardiopulmonary bypass; Hemostasis

Cite this article:
Ahmad J, Ranjan R, Saha H, Saklayen SMG, Begum M, Adhikary AB. Effect of cardiopulmonary bypass on hemostasis in patients undergoing cardiac surgery. Bangabandhu Sheikh Mujib Med Univ J. 2018; 11: 134-138.

Available at:
www.banglajol.info

A Journal of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Abstract

This study aimed to evaluate the hemostatic derangement in patients undergoing elective cardiac surgery using cardiopulmonary bypass. Total 55 patients of either sex, were divided into three groups: Group A (n=20): Patients selected for elective cardiac surgery without cardiopulmonary bypass; Group B (n=20): Patients who undergone cardiac surgery with cardiopulmonary bypass time <90 min; and Group C (n=15): Patients who undergone cardiac surgery with cardiopulmonary bypass time either 90 min or more. The difference of mean hemoglobin, total count of WBC, and platelet count on immediate post-operative period and at 7 days after surgery were statistically significant among the groups. The mean hematocrit value, fibrinogen level and coagulation profile were statistically significant between the two groups in comparison to pre-operative value. The mean cross-clamp time and bypass time were statistically significant between the two sub-groups of cardiopulmonary bypass population. The mean blood loss was more (1513.3 ± 307.9 mL) where the cardiopulmonary bypass was used for >90 min in comparison to other population. Prolong cardiopulmonary bypass time associated with more hemostatic abnormalities and complications can be minimized by shortening the bypass time.

Introduction

Cardiopulmonary bypass is a technique used to bypass the heart and lungs in order to facilitate heart surgery. It has been reported to be associated with hemostatic defect and activation of the inflammatory system.[1] The consequences of blood cell activation and plasma protein alteration during cardiopulmonary bypass prolong the bleeding time, increase the post-operative blood loss and necessity for massive infusion of blood lead to pulmonary function abnormality.[1, 2] Massive transfusion can cause not only transmission of infection and circulatory overload, but also increase the mortality risk, longer stay in Intensive Care Unit and hospital, and increase the mortality.[3, 4] Cardiopulmonary bypass activates large number of platelets, which then bind to exposed sub-endothelium, to the cardiopulmonary bypass circuit, or to circulating monocytes and neutrophils, potentially causing platelet numbers to decrease beyond what would be expected from hemodilution alone.[5-7] In addition to thrombocytopenia, a qualitative platelet defect during the cardiopulmonary bypass has also been reported. The combination of a decrease in platelet number and altered platelet function are responsible for a major proportion of blood loss associated with cardiopulmonary bypass.[8-10]

Cardiopulmonary bypass has been reported to be associated with hemodilution in order to improve the oxygen delivery and tissue perfusion, and in a typical adult, the onset of cardiopulmonary bypass decreases the hematocrit from 40% to approximately 25%.[11] Additionally, fibrinogen is known to bind extra-corporeal surfaces within minutes when blood passage through the cardiopulmonary bypass circuit. This bounded fibrinogen is conformationally altered in such a way that it is capable of binding to the resting glycoprotein IIb/IIIa receptor on platelets, thus responsible for more decrease in the circulatory platelets and fibrinogen and post-cardiopulmonary bypass bleeding.[10, 11] It has been documented that the tissue factor path-way, the extrinsic pathway of coagulation is also activated during the cardiopulmonary bypass by surgical disruption of the endothelium.[9-11]

However, cardiopulmonary bypass-induced hemostatic defect during and after cardiac surgery is not conclusive and found that cardiopulmonary bypass assisted bypass surgery does not significantly alter hemostasis during and after operation compared to that of off-pump

Table I

Demographic and hemodynamic data of the study population

Variable	Group A (n = 20)	Group B (n = 20)	Group C (n = 15)
Age (years)	51.5 ± 4.7	33.2 ± 10.2	34.2 ± 11.4
Sex			
Male (n)	18	6	6
Female (n)	2	14	9
Hemoglobin (g/dL)			
Pre-operative	12.8 ± 1.4	12.5 ± 2.0	13.2 ± 2.2
On arrival at ICU	12.5 ± 1.1	9.2 ± 0.7	9.5 ± 1.5
48 hours after surgery	12.5 ± 1.0	11.5 ± 0.9	12.6 ± 1.2
7 days after surgery	13.6 ± 0.8	12.5 ± 1.0	13.1 ± 1.4
Total RBC count (10^{12}/L)			
Pre-operative	4.4 ± 0.6	4.6 ± 1.4	4.9 ± 0.8
On arrival at ICU	4.4 ± 0.7	2.9 ± 0.4	2.8 ± 0.8
48 hours after surgery	4.3 ± 0.4	3.7 ± 0.6	3.9 ± 0.8
7 days after surgery	4.7 ± 0.3	4.3 ± 0.4	4.4 ± 0.3
Total WBC count (10^9/L)			
Pre-operative	9.2 ± 2.7	8.0 ± 1.4	9.6 ± 2.7
On arrival at ICU	13.4 ± 3.8	9.1 ± 1.8	12.8 ± 7.0
48 hours after surgery	22.4 ± 5.5	17.8 ± 5.6	18.2 ± 6.4
7 days after surgery	9.9 ± 0.7	9.5 ± 0.9	10.1 ± 1.2
Platelet count (10^9/L)			
Pre-operative	285.5 ± 69.1	265.3 ± 54.2	249.3 ± 68.8
On arrival at ICU	261 ± 52.9	119.0 ± 57.7	68.3 ± 47.2
48 hours after surgery	277.5 ± 55.2	180.5 ± 41.2	119.3 ± 48.9
7 days after surgery	331.5 ± 22.1	225.5 ± 40.2	140.7 ± 31.0
Blood loss (mL)	650.0 ± 280.7	683.5 ± 274.3	1513.3 ± 307.9
Blood transfused (mL)	945.0 ± 316.2	1132.5 ± 341.5	1666.7 ± 318.3

Data are Mean ± SD; ICU- Intensive Care Unit

CABG.[10, 12] As the blood enters into the extra-corporeal circuit, there are various qualitative and quantitative changes in the biochemical, hematological and blood coagulation parameters leading to a significant peri-operative and post-operative risk of both thrombosis and hemorrhage.[12, 13]

Therefore, the present study was designed to evaluate the association between the cardiopulmonary bypass and hemostatic defect in patient undergoing cardiac surgery and the after effect during peri-operative and post-operative period.

Materials and Methods

This prospective interventional study was carried out from July 2014 to April 2016. This study was carried out on patients, aged 18 to 57 years of either sex, and divided into Group A [Control Group (n=20)]: Patients selected for elective cardiac surgery without cardiopulmonary bypass; Group B (n=20): Patients who undergone cardiac surgery with cardiopulmonary bypass time <90 min; and Group C (n=15): Patients who undergone cardiac surgery with cardiopulmonary bypass time either 90 min or more. Patients with following criteria were not included in the present study like the history of diagnosed hemostatic defect, other systemic diseases such as renal impairment, hepatic failure, redocardiac surgery and pregnancy.

The patient prepared for cardiac surgery either with cardiopulmonary bypass or without cardiopulmonary bypass and agree to participate was purposively selected for the present study. Informed written consent was taken in a prescribed form. After selection of patients and enrolment in the present study, the detailed history and clinical examination findings were recorded in the pre-designed data collection sheet pre-operatively. Cardiopulmonary bypass time, aortic cross-clamp time, blood loss and blood transfusion were recorded in the pre-designed data collection sheet at the end of the operation and cardiopulmonary bypass, prothrombin time and fibrinogen level measured by autoanalyzer (Stago - STA Compact Max). Bleeding time measured by the blotting paper and clotting time by the glass pipette.

Statistical analysis

Statistical analyses were carried out using the Statistical Package for Social Sciences (SPSS) software and results were presented in tables.

Results

Total 60% of the patients belonged to the age above 50 years in Group A. The mean age was found 51.5 ± 4.7 years in Group A, 33.2 ± 10.2 years in Group B and 34.2 ± 11.4 years in Group C. The majority of patients were male and the difference of age was statistically significant ($p<0.05$) among the three groups. The difference of post-operative mean hemoglobin and RBC value on arrival at the intensive care unit, at 48 hours and at 7 days after surgery were statistically significant ($p<0.05$) among the three groups. The difference of post-operative mean total count of WBC and platelet were also statistically significant. The mean blood loss was 650.0 ± 280.7 mL in Group A, 683.5 ± 274.3 mL in Group B and 1513.3 ± 307.9 in Group C. Moreover, the difference of mean blood transfused was statistically significant ($p<0.05$) among the three groups (Table I).

In this study, the mean cross-clamp time was statistically significant between the two sub-groups Group B and C. The mean total bypass was found 64.2 ± 16.9 min in Group B and 204.1 ± 85.6 min in Group C, which was also statistically significant

Table II

Peri-operative coagulation profile of study patients

	Group A (n = 20)	Group B (n = 20)	Group C (n = 15)
Cross-clamp time (min)	-	31.5 ± 10.6	123.5 ± 44.5
Total bypass time (min)	-	64.2 ± 16.9	204.1 ± 85.6
Fibrinogen (mg/dL)			
Pre-operative	256.0 ± 29.3	258.5 ± 27.6	248.7 ± 31.9
On arrival at ICU	525.0 ± 83.6	556.0 ± 50.7	662.8 ± 58.0
48 hours after surgery	517.5 ± 55.4	510.2 ± 49.8	564.7 ± 55.7
7 days after surgery	257.0 ± 42.8	351.0 ± 56.9	345.7 ± 92.6
Bleeding time (min)			
Pre-operative	3.3 ± 1.0	3.0 ± 0.6	3.3 ± 0.6
On arrival at ICU	4.7 ± 1.1	7.0 ± 0.8	8.8 ± 1.2
48 hours after surgery	4.0 ± 1.0	6.1 ± 0.9	7.3 ± 1.6
7 days after surgery	3.4 ± 0.6	4.7 ± 0.9	6.3 ± 1.6
Clotting time (min)			
Pre-operative	5.6 ± 0.8	6.1 ± 0.7	5.8 ± 0.7
On arrival at ICU	6.9 ± 0.7	9.0 ± 1.2	12.4 ± 1.2
48 hours after surgery	6.5 ± 0.6	7.7 ± 0.9	10.6 ± 1.9
7 days after surgery	5.7 ± 0.9	6.9 ± 0.7	9.2 ± 1.8
Prothrombin time (sec)			
Pre-operative	12.9 ± 1.2	13.6 ± 1.9	14.2 ± 1.4
On arrival at ICU	15.9 ± 1.7	23.8 ± 4.0	25.0 ± 6.0
48 hours after surgery	14.6 ± 1.5	19.3 ± 3.9	18.1 ± 5.2
7 days after surgery	14.0 ± 2.5	16.3 ± 3.0	19.5 ± 4.2

Data are mean ± SD

($p<0.05$) between two groups. However, on arrival at Intensive Care Unit, after 48 hours and at 7 days after surgery, the coagulation profile like mean fibrinogen level, bleeding time, clotting time and prothrombin time were statistically significant ($p<0.05$) among the three groups (Table II).

Discussion

In this study, it was observed that the majority of study patients in Group A were male and the age difference was statistically significant ($p<0.05$) among the three groups. Group A includes mostly ischemic heart diseases patients and we do prefer coronary artery bypass without using cardiopulmonary bypass. The difference of post-operative mean hemoglobin level and RBC value on arrival at Intensive Care Unit, at 48 hours and at 7 days after surgery were statistically significant ($p<0.05$) among the three groups. Moreover, post-operative mean total count of WBC and platelet were also statistically significant. The mean total bypass time and cross-clamp time were statistically significant ($p<0.05$) between the study groups. However, coagulation profile like mean fibrinogen level, bleeding time, clotting time and prothrombin time were statistically significant.

There is scanty of literature where we have compared irrespective of age and sex for this study. However, Roy et al. (2014) found that male was 77.4% in OPCAB group and 69.0% in cardiopulmonary bypass group, which is also discordance to this study.[10] Roy et al. (2014)observed that the mean age was 61.7 ± 7.3 years in OPCAB group and 60.2 ± 6.9 years in cardiopulmonary bypass group and the difference was not statistically significant,[10] which is also supported by Scrascia et al. (2013) who observed that the mean age was 65.1 ± 9.5 years in OPCAB (off pump coronary artery bypass) group and 66.8 ± 8.2 years in cardiopulmonary bypass group in their study.[12] This dissimilarity of present study may be due to involvement of miscellaneous type of patients including cardiopulmonary bypass group whereas in their study they include only CABG patients.[6, 8, 10, 13]

In a study, Ascione et al. (2001) found hemoglobin level decreased more over time in the on-pump group despite this group requiring a significantly higher transfusion of red blood cells during the postoperative period.[13] The findings are consistent with other authors.[10, 14, 15] Mohnle et al. (2005) demonstrate that changes like decreased platelet counts, rise in white blood cell count mainly because of increased neutrophils, and fall in hemoglobin and hematocrit levels, which is concordance to this study findings.[14] Moreover, Moller and Steinbruchel (2003) demonstrated an increase in platelet activation after OPCAB and a temporary platelet dysfunction in the cardiopulmonary bypass group, which is also supported in several published literatures.[5, 10, 12, 15, 16] A limitation of this study was that we did not measure the platelet functions. In another study, Holloway et al. (1988) found that the decrease in platelet count during cardiopulmonary bypass was due to hemodilution for priming the extracorporeal circuit.[16] Several authors also found that platelet count in the on-pump group show the typical time course previously reported during and after operations with cardiopulmonary bypass.[13, 17]

The greater reduction of platelet count throughout the study observed in the on-pump group suggests a depletion caused by contact activation with extracorporeal surfaces, bubble oxygenator, cardiotomy suction, and filters by Weerasinghe and Taylor (1998).[18] However, the decrease of platelet count in the on-pump group was rarely less than the value (50,000-100,000/μL) normally required for hemostasis, suggesting a degree of impaired platelet function resulting bleeding after cardiopulmonary bypass.[18, 19] Lamy et al. (2012) observed post-operative bleeding time was higher in the OPCAB group. These data differ from those of larger trials, in which bleeding time in OPCAB group was lower compared to cardiopulmonary bypass group which is similar to this study.[20] In another study, Puskas et al. (2003) found a significant reduction of post-operative bleeding time in OPCAB group when compared to on-pump group which is similar to other study findings.[10, 15, 21, 22] Weerasinghe and Taylor (1998) found that thrombocytopenia and its relation to post-operative bleeding are well documented in association with cardiopulmonary bypass.[18] In a study, Kumle et al. (2003) found the mean aortic-cross-clamp-time was 64 ± 30 min which correspond to other studies.[23-25]

The decline in the blood hemoglobin level at the end of the operation in the off-pump group might be related to intraoperative blood loss. However, the effects of hemodilution have to be considered because the infusion of colloid or crystalloid solutions is required during off-pump coronary operations to maintain the mean systemic pressure at greater than 60 mm Hg, particularly during the distal anastomoses.

Conclusion

Cardiopulmonary bypass assisted cardiac surgery is associated with hemostatic abnormalities, but shorter cardiopulmonary bypass time minimizes this complication.

Acknowledgement

We express our heartfelt gratitude and indebtedness to Late Prof. Md. Aftab Uddin, Department of Cardiac Surgery, Bangabandhu Sheikh Mujib Medical University.

References

1. Roach GW, Kanchuger M, Mangano CM, Newman M, Nussmeier N, Wolman R. Adverse cerebral outcomes after coronary bypass surgery: Multicenter study of peri-operative ischemia Research Group and Ischemia Research and Education Foundation Investigator. N Engl J Med. 1996; 335: 1857-63.
2. Paparella D, Brister SJ, Buchanan MR. Coagulation disorders of cardiopulmonary bypass: A review. Intensive Care Med. 2004; 30: 1837-81.
3. Engoren MC, Habib RH, Zacharias A, Schwann TA, Riordan CJ, Durham SJ. Effect of blood transfusion on long-term survival after cardiac operation. Ann Thorac Surg. 2002; 74: 1180-86.
4. Murphy GJ, Reeves BC, Rogers CA, Rizvi SI, Culliford L, Angelini GD. Increased mortality, post-operative morbidity, and cost after red blood cell transfusion in patients having cardiac surgery. Circulation 2007; 116: 2544-52.
5. Rinder C, Gaal D, Student L, Smith BR. Platelet-leukocyte activation and modulation of adhesion receptors in pediatric patients with congenital heart disease undergoing cardiopulmonary by-pass. J Thorac Cardiovasc Surg. 1994; 107: 280-88.
6. McKenna T, Bachman F, Whittaker B, Gilson JR, Weinberg M. The hemostatic mechanism after open -heart surgery. II. Frequency of abnormal platelet functions during and after extracorporeal circulation. J Thorac Cardiovasc Surg. 1975; 70: 298-307.
7. Addonizio VP, Strauss JF, Colman RW, Colman RW, Edmunds LH. Thromboxane synthesis and platelet secretion during cardiopulmonary bypass with a bubble oxygenator. J Thorac Cardiovasc Surg. 1980; 79: 91-96.
8. Zill P, Fasol R, Broscurth P, Klepetko W, Reichenspurner H, Wolner E. Blood platelets in CPB operations: Recovery occurs after initial stimulation rather than continual activation. J Thorac Cardiovasc Surg. 1989; 97: 379-88.
9. Rinder CS, Bonan JL, Rinder HM, Mathew J, Hines R, Smith BR. Cardiopulmonary bypass induces leukocyte–platelet adhesion. Blood 1992; 79: 1201-05.
10. Roy S, Saha K, Mukherjee K, Dutta S, Mukhopadhyay D, Das I, Raychaudhuri G. Activation of coagulation and fibrinolysis during coronary artery bypass grafting: A comparison between on-pump and off-pump techniques. Indian J Hematol Blood Transfus. 2014; 30: 333-41.
11. Linden MD. The hemostatic defect of cardiopulmonary bypass. J Thromb Thrombolysis. 2003; 16: 129-47.
12. Scrascia G, Rotunno C, Guida P, Conte M, Amorese L, Margari V, de Luca L, TupputiSchinosa T, Paparella D. Haemostasis alterations in coronary artery bypass grafting: Comparison between the off -pump technique and a closed coated cardiopulmonary bypass system. Interact Cardiovasc Thorac Surg. 2013; 16: 636-42.
13. Ascione R, Williams S, Lloyd CT, Sundaramoorthi T, Pitsis AA, Angelini GD. Reduced post-operative blood loss and transfusion requirement after beating-heart coronary operations: A prospective randomized study. J Thorac Cardiovasc Surg. 2001; 121: 689-96.
14. Mohnle P, Schwann NM, Vaughn WK, Snabes MC, Lau W, Levin J. Perturbations in laboratory values after coronary artery bypass graft surgery with cardiopulmonary bypass. J Cardiothorac Vasc Anesth. 2005; 19: 19-25.
15. Moller CH, Steinbruchel DA. Platelet function after coronary artery bypass grafting: Is there a pro-coagulant activity after off-pump compared with

on-pump surgery? Scand Cardiovasc J. 2003; 37: 149-53.

16. Holloway DS, Summarie L, Sandesara J, Vagher JP, Alexander JC, Caprini JA. Decreased platelet number and function and increased fibrinolysis contribute to post-operative bleeding in cardio-pulmonary bypass patients. Thromb Haemost. 1988; 59: 62-67.
17. Consten ECJ, Henny CP, Eijsman L, Dongelmans DA, Van Oers MHJ. The routine use of fresh frozen plasma in operations with cardiopulmonary bypass is not justified. J Thorac Cardiovasc Surg. 1996; 112: 162-67.
18. Weerasinghe A, Taylor KM. The platelet in cardio-pulmonary bypass. Ann Thorac Surg. 1998; 66: 2145 -52.
19. Oberman HA. Indications and monitoring of use of fresh frozen plasma as a haemostatic agent. Curr Stud Hematol Blood Transfus. 1986; 53: 125-32.
20. Lamy A, Devereaux PJ, Prabhakaran D, Taggart DP, Hu S, Paolasso E, Straka Z, Piegas LS, Akar AR, Jain AR, Noiseux N, Padmanabhan C, Bahamondes JC, Novick RJ, Vaijyanath P, Reddy S, Tao L, Olavegogeascoechea PA, Airan B, Sulling TA, Whitlock RP, Ou Y, Ng J, Chrolavicius S, Yusuf S. Off-pump or on-pump coronary-artery bypass grafting at 30 days. N Engl J Med. 2012; 366: 1489-97.
21. Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E, Lucke JC, Baltz JH, Novitzky D. Veterans affairs Randomized On/Off Bypass (ROOBY) Study Group. On-pump versus off-pump coronary-artery bypass surgery. N Engl J Med. 2009; 361: 1827-37.
22. Puskas JD, Williams WH, Duke PG, Staples JR, Glas KE, Marshall JJ, Leimbach M, Huber P, Garas S, Sammons BH, McCall SA, Petersen RJ, Bailey DE, Chu H, Mahoney EM, Weintraub WS, Guyton RA. Off-pump coronary artery bypass grafting provides complete revascularization with reduced myocardial injury, transfusion requirements, and length of stay: A prospective randomized comparison of two hundred unselected patients undergoing off-pump versus conventional coronary artery bypass grafting. J Thorac Cardiovasc Surg. 2003; 125: 797-808.
23. Kumle B, Boldt J, Suttner SW, Piper SN, Lehmann A, Blone M. Influence of prolonged cardio-pulmonary bypass times on splanchnic perfusion and markers of splanchnic organ function. Ann Thorac Surg. 2003; 75: 1558-64.
24. Aftabuddin M, Rajbhandhari N, Rahman MZ, Islam N, Khan OS. Cardiopulmonary bypass-induced hematological changes in patients undergoing cardiac surgery. Bangladesh Heart J. 2015; 30: 53-57.
25. Hosain SN, Akter SJ, Rasheed H, Maruf F, Ahmed N. Effect of cardiopulmonary bypass on post-operative nutrition of cardiac surgery patients. Bangladesh Med J. 2009; 38: 53-55.