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Effect of Pre-Operative Anti-Platelets Therapy on Perioperative Bleeding and Blood Transfusion in Patients Undergoing Elective Cardiac Surgery

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Abstract:

Background: Hemorrhage during the operative period is a widespread occurrence in cases undergoing cardiac operations. Hemorrhaging can range from being insignificant and not needing treatment to being severe and potentially fatal.

Aim: To evaluate pre-operative anti-platelet therapy as an independent risk factor for perioperative bleeding & blood transfusion.

Patients and methods: This prospective controlled randomized clinical trial has been carried out on 32 adult cases who underwent elective surgeries on bypass cardiac surgery at the operative theatre of Suez-Canal University Teaching Hospital from October 2019 to July 2022.

Results: There was statistically insignificant variation among the CABG and non-CABG patients in the amount of products of blood transfused either post-bypass or in the first twenty-four hours post-operatively in the ROTEM group and in the classic group. In the ROTEM group, there was a statistically significant reduction in non-CABG patients in terms of blood loss post-operatively (P 0.013). A statistically insignificant distinction has been observed among non-CABG and CABG patients regarding the amount of blood loss post-operatively in the classical group.

Conclusion: Anti-platelet therapy may be an independent risk factor for postoperative blood loss, but not for blood product transfusion, and this variable could require future research with a larger sample size..

Keywords:Anti-platelets therapy, perioperative bleeding, blood transfusion

1. Introduction

Perioperative bleeding is a frequent occurrence in cases who undergo cardiac surgery. Nevertheless, there is no definition for hemorrhaging during surgery and it lacks standardization. To correctly define and measure bleeding during adult cardiac operations, we suggest the use of a universal definition for hemorrhage during operation (UDPB). This will assist in dealing with the challenges associated with this difficult clinical problem and allow further research concerning it **(1)**. The absence of a widely recognized definition for perioperative hemorrhaging following cardiac operations is a difficulty in conducting research on case blood management **(2)**. In their study, Colson PH et al. (2016) defined blood loss as 1.5 milliliters per kilogram per hour over a six-hour duration or the need for early reoperation. The total incidence of this occurrence was found to be 2.6 percent **(3)**. Nevertheless, the rate of PRBC transfusion may not provide a precise estimate of bleeding since the technique for transfusion can differ significantly among different medical centers **(4)**. Recent investigations have included blood loss from chest drains as a direct measure of bleeding. However, these investigations used an established and extended observation period without considering the case's body weight **(5)**. Coagulation system abnormalities in cardiac procedures might pose problems, as there are various ways in which disruptions in coagulation can develop. Coagulopathy arises from platelet dysfunction, hemodilution, depletion of coagulation factors, activation of the fibrinolytic system, & the presence of residual heparin and/or excessive protamine **(6)**.

Activated clotting time (ACT) is frequently assessed throughout and at the end of cardiopulmonary bypass (CPB) to determine the appropriate dosage of heparin or protamine. ACT values are influenced not only by the concentration of heparin but also by factors such as hemodilution, low fibrinogen levels, a low platelet count, and even an excess of protamine **(7)**.

The purpose of this investigation was to assess pre-operative anti-platelet therapy as an independent risk factor for perioperative bleeding and transfusion.

Patients and methods

This prospective controlled randomized clinical investigation has been carried out on 32 adult cases who underwent elective surgeries on bypass cardiac surgery at the operative theatre of Suez-Canal University Teaching Hospital from October 2019 to July 2022.

Inclusion criteria: male and women cases more than eighteen years of age, cases undergoing elective primary cardiac surgery on cardiopulmonary bypass (valve replacement, coronary artery bypass graft, or coronary artery bypass graft with valve replacement, and ASA II and ASA III)

Exclusion criteria: Emergent cardiac surgeries, Re-do cardiac surgeries, patients who take oral anticoagulants (warfarin and direct oral anticoagulants, e.g., rivaroxaban and apixaban) within five days of operation or low molecular weight heparin until the day of operation, cases with congenital or acquired coagulopathy, patients with impaired liver function (elevated liver enzymes) or impaired renal function (serum creatinine more than milligrams per deciliter) and body mass index less than eighteen kilograms per square meteror more than thirty-five kilograms per square meter

Methods:

Pre-operative assessment: medical history, detailed medical history, physical examination, and investigations**.**

Heparinization was started before cardiopulmonary bypass with an initial bolus dose of three hundred international units per kilogram to achieve an activated clotting time value of above 400 seconds. If the target activated clotting time value is not reached, an additional 70 IU per kg of heparin will be given to achieve the target ACT. Activated clotting time was done using an activated clotting time device (Actalyke® MINI II).

Cardiopulmonary bypass details:

Priming:

According to the local protocol of the hospital, the cardiopulmonary bypass machine has been primed with 1500 milliliters of ringer acetate, 150 ml of mannitol and 15000 IU of heparin. Following termination of cardiopulmonary bypass, heparin has been reversed by protamine hydrochloride (one milligram protamine per one hundred international unit of the initial dose of heparin).

Packed red blood cell transfusion:

Both groups received packed red blood cell transfusions according to the Dutch transfusion guidelines. **(8)** Hemoglobin values below 9.7 grams per deciliter are observed in ASA IV cases, as well as in cases of heart failure, symptomatic cerebrovascular disease, or severe pulmonary illness. If a normovolemic ASA II case over the age of sixty has acute blood loss from a single bleeding source, resulting in a hemoglobin level below 8.1 grams per deciliter, or if they develop a fever or follow a cardiac operation, 1 unit of red blood cells will increase hemoglobin one gram per deciliter and hematocrit two to three percent. **(9)**

Ethical considerations: Prior to the surgical procedure, all cases will be needed to provide written consent prior to participating in the investigation. The steps of the investigation, including the objectives, potential benefits, and dangers, will be reviewed. Cases have been informed of any atypical findings from procedures and tests conducted, and they have been given suitable guidance and treatment. Cases have the right to decline involvement or quit the investigation at any time. All data and test results pertaining to the investigation population are kept confidential.

Statistical Analysis

The computer has received data and conducted analysis utilizing the IBM SPSS software program version 20.0 (Armonk, NY: IBM Corp.). Quantitative data has been applied to represent qualitative information. The normality of the distribution has been verified through the utilization of the Shapiro-Wilk test. Quantitative data has been described using range (minimum & maximum), SD, median, and mean. The results were evaluated using a significant level of five percent. The following statistical tests were utilized: the chi-square test, Fisher's exact test or Monte Carlo correction, paired t-test, Mann-Whitney test, student t-test, & Wilcoxon signed rank test.

Results

Table (1): Patients characteristics

Demographic data	ROTEM (number = sixteen)	Classic (number = sixteen)	p
Age (years)			
Mean ± SD.	50.56 ± 12.38	52.06 ± 12.90	0.740
Sex			
Male	10 (62.5%)	13 (81.3%)	
Female	6 (37.5%)	3 (18.8%)	0.433
ASA Status			
II	13 (81.3 %)	14 (87.5 %)	
III	3 (18.7 %)	2 (12.5 %)	0.626
BMI (kg/m^2)			
Mean ± SD.	28.40 ± 3.51	26.76 ± 3.14	0.172

SD: Standard deviation, p: p value for comparing between the two studied groups, *: Statistically significant at $p \leq 0.05$, ASA: American society of anesthesiologist.

There statistically insignificant variance has been among both groups concerning sex, age and BMI (Table 1)

Table (2): Types of cardiac surgeries in both studied groups

Type of surgery	ROTEM (n = 16)		Classic (n = 16)		p
	No.	%	No.	%	
CABG	8	50.0	9	56.3	
AVR	3	18.8	1	6.3	
ASD closure	1	6.3	0	0.0	0.771
Atrial myxoma	0	0.0	1	6.3	
MVR	4	25.0	5	31.3	

CABG: coronary artery bypass graft, AVR: Aortic Valve, Replacement, MVR: Mitral Valve Replacement, ASD: atrial septal defect.

There statistically insignificant variance has been observed among both groups regarding types of surgeries. (Table 2)

Table (3): Blood products (units) requirements in Non-CABG and CABG patients in ROTEM group.

		Non-CABG (n = 8)	CABG (n = 8)	p
RBCS (units)	**Post bypass** Mean ± standard deviation	0.5 ± 0.93	0.75 ± 0.89	0.574
	Median	0 (0 – 2)	0.5 (0– 2)	
	1st 24 hours Mean ± standard deviation.	0 ± 0	0 ± 0	1.000
	Median	0(0 – 0)	0 (0 – 0)	
FFP (units)	**Post bypass** Mean ± standard deviation.	3.13 ± 2.70	5.25 ± 0.71	0.130
	Median	4 (0 – 6)	5 (4 – 6)	
	1st 24 hours Mean ± standard deviation.	0 ± 0	0.38 ± 1.06	0.721
	Median	0 (0 – 0)	0 (0 – 3)	
PLT (units)	**Post bypass** Mean ± standard deviation.	0 ± 0	0.75 ± 2.12	0.721
	Median	0 (0 – 0)	0 (0 – 6)	
	1st 24 hours Mean ± standard deviation.	0 ± 0	0 ± 0	1.000
	Median	0(0 – 0)	0 (0 – 0)	

Median: (Min. – Max.), p: p value for comparing betweenNon-CABG and CABG, CABG: coronary artery bypass graft

There statistically insignificant distinction has been observed among the CABG and the non-CABG cases in the amount of blood products transfused either post-bypass or in the first twenty-four hours following operation in the ROTEM group. (Table 3)

Table (4): Blood products(units) requirements in the Non-CABG and CABG patients in the classic group.

		Non-CABG (n = 7)	CABG (n = 9)	p
RBCS (units)	**Post bypass**			
	Mean ± standard deviation.	1.29 ± 1.25	0.67 ± 1.0	0.351
	Median	2.0 (0 – 3.0)	0 (0 – 2.0)	
	1st 24 hours			
	Mean ± standard deviation.	0.14 ± 0.38	0.11 ± 0.33	0.918
	Median	0 (0.0 – 1.0)	0 (0 – 1.0)	
FFP (units)	**Post bypass**			
	Mean ± standard deviation.	4.86 ± 1.07	5.78 ± 1.56	0.299
	Median	4.0 (4.0 – 6.0)	6.0 (4.0 – 8.0)	
	1st 24 hours			
	Mean ± standard deviation.	5.57 ± 2.30	5.44 ± 1.33	0.758
	Median	6.0 (2.0 – 8.0)	6.0 (3.0 – 7.0)	
PLT (units)	**Post bypass**			
	Mean ± standard deviation.	5.14 ± 2.27	5.33 ± 4.69	1.000
	Median	6.0 (0 – 6.0)	6.0 (0.0 – 12.0)	
	1st 24 hours			
	Mean ± standard deviation.	0 ± 0	2.67 ± 4.36	0.299
	Median	0(0 – 0)	0 (0 – 12.0)	

There statistically insignificant variance has been observed among the CABG and the non-CABG patients in the amount of blood products transfused either post-bypass or in the first twenty-four hours following operation in the classic group. (Table 4)

Table (5):Amount of blood loss (ml) in Non-CABG and CABG patients in both groups.

Blood loss (ml)	Non-CABG	CABG	p
ROTEM	**(n = 8)**	**(n = 8)**	
Mean ± SD.	325.0 ±160.4	562.5 ±174.7	0.013*
Median	350.0 (100.0 –500.0)	525.0 (300.0 –800.0)	
CLASSIC	**(n = 7)**	**(n = 9)**	
Mean ± SD.	592.9 ±402.5	550.0 ±237.2	0.793
Median	500.0 (200.0 –1250.0)	450.0 (350.0 –1050.0)	

There was a statistically significant decline in non-CABG patients regarding amount of blood loss post-operatively in ROTEM group (P 0.013). There was statistically insignificant distinction among non-CABG and CABG cases regarding amount of blood loss post-operatively in classical group. (Table 5)

Discussion

Perioperative hemorrhage is a complex surgical complication that can be related to various factors. Typically identified by localized bleeding that is limited to the surgical site **(10),** The frequent administration of anticoagulant & antiplatelet medications before surgery increases the risk of developing hemostasis disorders that necessitate the use of blood-derived products & hemostatic agents.

Multiple approaches are utilized to decrease hemorrhaging and minimize the utilization of blood products, thereby reducing the severe consequences related to their usage **(11)**. Standard plasma coagulation tests don't provide an overview of the hemostatic process, often resulting in an empirical and unsuitable utilization of blood products. In addition, there is no evidence from randomized controlled trials to support the efficiency of these conventional tests in guiding hemostatic treatment **(12)**.

A statistically insignificant distinction has been observed among both groups as regards sex, body mass index, age, and types of surgeries. Moreover, statistically insignificant variance has been observed among the CABG and non-CABG cases in the amount of blood products transfused either post-bypass or in the first twenty-four hours following surgery in the ROTEM group & in the classic group. There a statistically significant decrease has been observed in non-CABG patients regarding the amount of blood loss post-operatively in the ROTEM group (P 0.013). There a statistically insignificant distinction has been observed among non-CABG and CABG cases regarding the amount of blood loss post-operatively in the classical group.

Girdauskas et al. (13) discovered that using thromboelastometrically to guide transfusion leads to a decline in the utilization of allogenic blood units and a lower occurrence of large transfusions in cases of aortic surgery with circulatory arrest. The administration of blood from a

different case significantly decreased has been observed in the thromboelastometry group (P = 0.02). A significant reduction was observed in the utilization of fresh-frozen plasma (P = 0.005).

Mittermayr et al. (14) discovered that computed tomography measurement utilizing the ROTEM approach seems to be an effective tool for heparin-protamine control.

Mittermayr et al. (7) found that ROTEM could be a useful instrument for excluding any remaining heparin in cases where the activated clotting time is provided. The INTEM-CT: HEPTEM-CT ratio accurately recognized fifty-six out of fifty-eight samples as not containing any remaining heparin. It also correctly detected residual heparin in three of the six samples that showed high anti-factor Xa values following CPB.

Kjellberg et al. (15) found that ADP-TEM showed below-normal AUC values before cardiopulmonary bypass, although treatment was stopped before surgery. With a statistically significant variance among ADP-TEM values prior to and following CBP, the ADP-TEM median AUC was 48 before bypass, which was reduced to 32 with a p value <.001.

Conclusion

Anti-platelet therapy may be an independent risk factor for postoperative blood loss but not for blood product transfusion and this variable could need future research with a larger sample size.

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