

## ORIGINAL ARTICLE

# Post Operative Complications Associated with Preoperative use of Clopidogrel in Patients Undergoing Coronary Artery Bypass Surgery

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## ABSTRACT

**Background:** Majority of the patients presenting for coronary artery bypass surgery are preoperatively on clopidogrel and aspirin i.e., Dual antiplatelets therapy (DAPT) because of high incidence of left main stem disease, acute coronary syndrome and diffuse coronary artery disease. Preceding coronary stenting and coming from far flung areas even from other countries with poor socioeconomic status contributes to continuation of DAPT till surgery.

The main objective of the study was to evaluate hospital complications like chest tube output, re-explorations, blood, and blood product administration and in-hospital mortality in patients who continued DAPT till 48 hours prior to surgery versus those who continued DAPT until 48 to 120 hours before surgery.

**Methods:** Preoperative history, perioperative and postoperative data of patients was gathered retrospectively from 1<sup>st</sup> July to 31<sup>st</sup> December 2019 in a tertiary care hospital of Peshawar. Total patients undergoing CABG Surgery were 223. From those 223 patients 192 patients were on DAPT. We then divided the 192 patients into two groups, Group A and Group B. 102 patients (Group A) received clopidogrel plus aspirin until 48 hours before surgery, and 89 patients (Group B) continued clopidogrel 48 to 120 hours prior to surgery. Chest tube output, need for exploration, in-hospital mortality, and blood or products transfusions among both groups were compared.

**Results:** In terms of bleeding complications no significant difference between the both groups with similar chest drainage in the first 24 hours (602 ml and 609ml). In group A 33 patients received blood transfusion compared to 25 patients from group B. There was no significant difference in the amount of platelets given to group A (0.63 L) and to group B was (0.60 L). On the other hand, Group, A received 1.08 L fresh frozen plasma (FFPs) transfusion and group B 1.10 L respectively. Re-exploration was observed in Group A and B as (3 vs 2). Mortality was observed in 7 patients from group A and 2 from Group B.

**Conclusions:** Usage of Dual antiplatelets therapy (DAPT) before surgery was an effective treatment method for postoperative complication of bleeding. It was suggested that with proper management with DAPT before surgery was planned is an effective and safe treatment method.

**Keywords:** Cardiopulmonary surgery, Coronary bypass grafting, hemoglobin, platelets, bleeding.

## INTRODUCTION

One of the top leading causes of mortality among world is cardiovascular diseases. According to these diseases coronary artery diseases are considered to be the one of the most common leading reason of mortality in different age group (1-3).

Recently with breakthroughs in medicine and technology coronary artery bypass graft (CABG) surgery has become the standard for the treatment of coronary artery diseases (4, 5). Dr. René G. Favaloro, an Argentine on May 9<sup>th</sup>, 1967 was the first person who perform the first CABG surgery (6). Clopidogrel holds its reputation as a potent irreversible thrombocyte aggregation inhibitor. It is an acetate derivative of ticlopidine, with greater potency in terms of its antiaggregant effect along with a much faster onset of action. (7, 8) Additionally, clopidogrel has a minimum side effects ratio and therefore is much better tolerated as compared to its parent drug. (9)

The dual antiplatelet therapy (DAPT) that is combination of aspirin and clopidogrel as has been established by existing literature as the recent treatment method for the prevention of thrombosis in coronary stent placements. (9, 10) Most of the time it is not feasible before surgery to stop taking these kind of drugs. However, persistent use of such drugs preoperatively has increased risk of bleeding perioperative in patients with acute coronary syndrome who require (CABG). (11) Post-operative bleeding and reopening as a result of bleeding leads to persistent use of blood products and as well as blood which further put patients in different complications (12). Platelets do not have the ability to synthesize protein and adequate aggregation can only be restored with new platelets. The life expectancy of platelets is 8 to 10 days it needs around 5 days for the reload the pool of platelets

(13). Before major procedures this reveals the side effect of clopidogrel treatment and increased risk of postoperative bleeding in surgical patients. In the results of bleeding anemia and need of blood transfusion, both of which are life threatening complications after major cardiac surgery especially post CABG (14).

Due to such postoperative complications, several studies have shown to recommend a washout period before CABG. (15) Alternatively, some studies have shown a reduced risk of reoperation and complications in patients that were administered preoperative clopidogrel in the setting of better surgical techniques and more effective management. (16) Despite this, there is great variation in existing literature with regards to the duration of such a washout period prior to CABG. (17, 18) The usage of preoperative clopidogrel should be avoided so that major complications like thrombosis after post-stenting and post-CABG bleeding. The objective of the current study was to evaluate during hospital complications and mortality in patients who continued DAPT till 48 hours prior to surgery versus those who continued DAPT until 48 to 120 hours before surgery, and thereby further highlight the degree of risks of CABG-related bleeding under DAPT therapy prior to CABG surgery.

## MATERIAL AND METHODS

The 192 patients who underwent CABG were randomly selected at Rahman Medical Institute (RMI) were included. Ethical approval of current study was obtained from the hospital ethical committee. 102 patients had a history of taking DAPT within 48 hours prior to surgery and the other 89 patients stopped DAPT from 48 to 120 hours before surgery. Under the management of same surgical

and anesthesiology team all the operations were conducted to remove biasness.

The perioperative data was collected from the time of admission and discharge. Total blood loss was calculated by the first and second postoperative days blood loss with the help of total chest tube drainage. If the blood loss > 400ml in first hour, .300ml for two consecutive hours or >200 ml for four consecutive hours was considered as surgical re openings. The primary cut off point was defined as amalgam of red blood cell transfusion of >1000ml, chest drainage of >2000ml and bleeding requiring surgical re exploration. During the hospital stay rate and number of allogeneic blood products (platelets, FFPs) transfused was also compared.

Standardization of surgical technique and postoperative management was maintained for all patients. A median sternotomy followed cardiopulmonary bypass was instituted with the application of ascending aorta cannulation and two stage venous cannulation of right atrium. The membrane oxygenator was primed with 1000ml of Hartman's crystalloid, 500 ml of gelosusine, 0.5 mg/kg of mannitol, 7ml of 10% calcium glucometer and 6000IU heparin. Systemic temperature was kept between 36 and 32 c and myocardial protection was accomplished with intermittent cold hyperkalemia cardioplegia. Patients were at the end of transferred to cardiac intensive care unit.

## RESULTS

In current study total 192 patients were included who underwent CABG. Patients were divided into two groups (A= 102, B= 89). Prior to surgery, Patients in Group A stopped taking DAPT before 48 hours of surgery and Group B before 48 to 120 hours.

Table 1: Difference between Preoperative data among groups

Variables	Clopidogrel stop in 48hr (n=102)	Clopidogrel stop in 120hr (n=89)	p-Value
Age (year)	56.34	56.44	0.777
Gender, Male (n%)	75(72.8)	61(68.5)	0.516
Risk profile			
Diabetes Mellitus	43(41.7)	41(46.1)	0.547
Hypertension	94(91.3)	73(82)	0.05
MI	96(93.2)	78(87.6)	0.18
NYHA I,II	3(2.9)	7(7.9)	0.124
NYHA III,IV	100(97.1)	82(92.1)	0.124

Group A= Clopidogrel stop in 48hr      Group B= Clopidogrel stop in 120hr

Table 1, represent the baseline data of patients in both groups. There was no statistically significant difference in gender, age, diabetes mellitus, hypertension and NYHA classification between the both groups.

Table 2 illustrates that the Euro score was same for both the groups. Preoperative left ventricular ejection fraction and hemoglobin were similar among both groups.

Table 2: Comparison of Preoperative variables among both Groups

Variables	Group A Clopidogrel stop in 48hr (n=103) %	Group B Clopidogrel stop in 120hr (n=89) %	p-Value
Euroscore	2.84	2.74	0.268
LV ejection fraction (%)	55.90	53.47	0.804
Hemoglobin (gr/dl)	12.09	12.68	0.639

Table 3 shows the outcome data in this study. The average chest-drain in both the groups were same (602 vs. 609ml). In group A 33 patients received blood transfusion compared to 25 patients from group B. There was no significant difference in the platelets count given to group both groups (0.63 vs. 0.60). On the other hand, Group A received 1.08 L FFPs transfusion and group B 1.10L respectively. Re-exploration was observed in Group A and B as (3(2.9%) vs 2(1.1%)). Mortality was observed (7(6.8%) vs 2(2.2%)) in seven patients from group A and 2 from Group B.

Table 3 Outcome data

Variables	Group A Clopidogrel stop in 48hr (n=103) %	Group B Clopidogrel stop in 120hr (n=89) %	p-Value
Chest drain	602.28ml	609.87ml	0.796
IABP (n, %)	3(2.9)	1(1.1)	0.387
Blood transfusion (n, %)	33(32)	25(28.1)	.552
Blood products infused units			
Platelets	0.63	0.60	0.734
Frozen plasma	1.08	1.10	0.807
Complications (n, %)			
Reopen	3(2.9)	1(1.1)	0.387
Mortality	7(6.8)	2(2.2)	.137

## DISCUSSION

The most common cardiac Surgery performed in United States was CABG. In initial CABG surgery exploration due to bleeding is 2.3% and patients who have 2nd CABG surgery were 3.1% (19). The reason behind bleeding after CABG surgery was multifactorial. A study reveals that the actual reason behind bleeding was hemostasis, coagulation disorders, platelet dysfunction. (20). For surgical bleeding in ACS patients, DAPT was considered as effective treatment method. The use of preoperative DAPT can distress homeostasis and can lead to excessive bleeding. The patients who underwent CABG surgery have chances of exploration which can further lead to increased mortality and morbidity. (19, 21).

Over the period of time different studies showed different result of using DAPT in ACS. Variation in these results can be evaluated in different surgical indications like difference in surgical and anesthesiologist teams, preoperative management, comorbidities etc. Certainly, many different studies reported that prior to surgery preoperative administration clopidogrel increases postoperative bleeding, accelerates chances of re-exploration, blood transfusion and long hospital stay (12, 22-24).

A retrospective study conducted by Berger et al. reported that prior to CABG surgery the patients who receives clopidogrel < 5 days have increased risk of reexploratin, bleeding and long hospital stay. The preoperative outcome shows that patients have more chances of cerebrovascular accidents, myocardial infarction urgent surgical revascularizations and previous percutaneous coronary intervention (PCI). IN terms of mortality there was in significant difference was observed. (23). Similar results were also reported by Yende et al that the usage of DAPT within 5 days of surgical procedure increases exploration rate. (12). In another study it was reported that within 7 days of surgery patients experience more transfusions, exploration, chest tube drainage and bleeding. (22) a study was conducted on 55 patients who were preoperatively clopidogrel showed increased incidence of bleeding and requirmnt of blood transfusion (25). For the prevention of Recurrent Events trial (CURE) A subgroup analysis was performed by using Clopidogrel. Total 192 patients were included in study who had emitted use of clopidogrel within 5 days of CABG. The results of the study revealed that bleeding complications in patients ha increased which leads to major bleeding. (26). A recent study reported that there was not significant association of preoperative use clopidogrel with increased transfusion of RBC. (27).

In current study, all procedures were carried out by the same surgical and anesthesia teams. The study elaborates that the patients who underwent CABG surgery DAPT were not significantly associated with bleeding complications. It was suggested that it may be safer option to continue DAPT and not stop it before CABG surgery.

## CONCLUSION

Bleeding complication in CABG surgery with the administration of DAPT doesn't increase the risk. The Risk of bleeding in both groups was same. Although Prior to CABG surgery risk of bleeding under DAPT should be investigated by conducted more studies.

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