Original Research Article

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Off - pump coronary artery bypass grafting on patients with preoperative dual antiplatelets: our centre experience

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ABSTRACT

Background: With the advances in percutaneous intervention techniques, the majority of patients referred for coronary artery bypass grafting (CABG) are on aspirin and clopidogrel. Standard guidelines suggest to stop clopidogrel 5 days and continue aspirin before surgery. We aim to report our centre experience on effects of continuation of preoperative clopidogrel on postoperative bleeding and use of blood products after off- pump CABG (OP-CABG).

Methods: This retrospective study included 120 consecutive patients who underwent isolated OP-CABG operation between Nov 2019 and March 2021 in our centre. Data was obtained from hospital records. Patients were divided into two groups: Group-1: this group consists of 86 patients. All patients included were elective CABG cases with preoperative Clopidogrel 75 mg discontinued 3-5 days before surgery. Group-2: this group consists of 34 patients. All patients included were urgent CABG cases with preoperative Clopidogrel 75 mg discontinued 24 hours before surgery. Aspirin 75 mg was continued in both groups till surgery. Preoperative, intraoperative and postoperative data was recorded.

Results: 120 patients were enrolled in the study. There was no statistical significance in postoperative bleeding, reexploration and use of blood products between the two groups. However, use of total arterial vascularisation and operative time was significant among the groups. The postoperative outcome was similar in both the groups.

Conclusions: OP-CABG can be done safely in patients requiring urgent surgery. However, clopidogrel should be stopped 3-5 days in patients undergoing elective surgeries as it influences graft selection, prolongs operative time and exposes the patients to unnecessary risks.

Keywords: Dual antiplatelet therapy, Off-pump coronary artery bypass grafting, Clopidogrel, Aspirin, Bleeding

INTRODUCTION

There has been a dramatic decrease in numbers of coronary artery bypass grafting (CABG) in last few years due to significant advances in percutaneous intervention (PCI) techniques by interventional cardiologists.^{1,2} Now cardiologists successfully perform PCI in ostial coronary artery disease, left main coronary artery disease and other complex coronary lesions, though studies have clearly indicated advantages of CABG in these subsets of patients.^{3,4} The patients with acute MI are subjected to staged angioplasties. Because of this the spectrum of patients referred for coronary artery bypass grafting today has entirely changed. Majority of patients are stent restenosis with or without angina, stent thrombosis in one or major arteries with patent stent in other arteries, critical ostial left main with or without triple vessel disease, severe left ventricular dysfunction and severe diffuse disease of coronary arteries.5 Hence majority of patients referred for coronary artery bypass grafting (CABG) are on dual antiplatelet therapy (DAPT) with aspirin and clopidogrel.6 The use of DAPT in patients with above mentioned profiles is like a double-edged sword for surgeons, which on the one hand is protective for patients from ischemia but on the other hand, increases the risk of surgical bleeding. The risk of bleeding following the aspirin or clopidogrel intake increases by up to 20%, and after combination therapy, it increases by up to 50%.7,8 There are still significant controversies regarding the timing of discontinuation of DAPT treatment in patients undergoing CABG. Several retrospective studies have shown that clopidogrel in association with aspirin given less than 5 days before surgery is associated with more blood products, reexplorations for bleeding and an increase in chest drain blood loss. 9,10 The CURE (Clopidogrel in Unstable angina to prevent Recurrent ischaemic Events) and Acute Catheterization and Urgent Intervention Triage strategy (ACUITY) trials have suggested that patients undergoing CABG after clopidogrel and aspirin benefit from adverse anti-ischaemic effects without an increase in life threatening bleeding. 11,12 We report our centre experience of preoperative administration of clopidogrel and aspirin postoperative bleeding, blood transfusion requirements, re-exploration rate and other adverse postoperative events in patients undergoing off-pump CABG (OP-CABG).

METHODS

This retrospective study included 120 patients who underwent isolated OP-CABG surgery consecutively between November 2019 and March 2021 in our centre. De-identifying data was obtained from hospital records. Patients were divided into two groups: Group-1: This group consists of 86 patients. All patients included were elective CABG cases with preoperative Clopidogrel 75 mg discontinued 3-5 days before surgery. Group-2: This group consists of 34 patients. All patients included were urgent CABG cases with preoperative Clopidogrel 75 mg discontinued 24 hours before surgery. Urgent CABG patients were defined as those requiring surgery during the current admission and cannot be discharged without definitive therapy. Aspirin 75 mg was continued till surgery in patients of both the groups. The following data was recorded: standard demographics, comorbidities, coronary angiographic profile, left ventricle ejection fraction, intraoperative surgical data, amount of blood loss after sternal closure from chest drains in next 48 hours, any re-exploration, total intra and postoperative usage of blood and blood products, any cardiac, renal or neurologic adverse events.

Exclusion criteria

Cases with additional surgical procedures, patients who had received loading doses of antiplatelet drugs within 72 hours, redo surgeries, preoperative haemoglobin less than 10 mg/dl, preoperative coagulation disorders, emergency surgeries, patients on IABP, patients on preoperative drugs like warfarin sodium, heparin infusions, platelet

glycoprotein IIb/IIIa inhibitors or thrombolytics were excluded from the study.

Methodology

All of the operations were conducted by the same surgical and anaesthesiology teams. All patients underwent standard OP-CABG with routine anaesthetic techniques. Systemic heparinisation during anastomosis was achieved with 2 mg/kg of heparin with additional doses to maintain activated clotting time more than 300 during surgery. On completion of anastomosis, heparin was neutralised with protamine sulphate in ratio of 1:1. Blood or blood products whenever required in operation theatre were given after protamine administration. Patients' nasopharyngeal temperature was maintained between 350 centigrade and 370 centigrade. None of the patients received antifibrinolytic agents. Platelet transfusion and or fresh frozen plasma was given in operation theatre if there was significant visible blood loss (two large laparotomy sponge getting soaked within 15 to 30 minutes) with normal ACT values and no identifiable surgical cause of bleeding.

The clinical criterion for postoperative platelet and fresh frozen plasma (FFP) transfusion in intensive care unit (ICU) was excessive bleeding (more than 200 ml /hour for 2 consecutive hours) despite normal value of activated clotting time (ACT). The criteria for packed red blood cell transfusion were haemoglobin below 9 mg/dl in ICU and less than 8 mg/dl in operation theatre. The decision for re-exploration was based on the Kirklin and Barratt-Boyes criteria: drainage greater than 500 mL during the first hour, greater than 400 mL for 2 consecutive hours, greater than 300 mL for three consecutive hours, more than 1200ml in total during first 5 hours, sudden increase in drainage greater than 300 ml / hour that has been small in the first few postoperative hours and acute cardiac tamponade. This threshold value was decreased in case patient becomes hemodynamic unstable. The late reexploration was indicated when there was echocardiographic evidence of pericardial effusion greater than 1.5 cm or cardiac tamponade.

Definitions

Unstable angina was defined as new onset of chest pain at rest or increase in episodes of chest pain that takes longer to resolve and an increase in the severity of symptoms.

Statistical analysis

Statistical package for social sciences (SPSS) version 21.0 was used for statistical analysis. Categorical variables were summarized using frequency and percentage and continuous variable using mean and standard deviation. The statistical differences between categorical variables between two groups were done using Chi-square test and for continuous variable independent sample t test was used. All tests were two

tailed and the results were considered significant when p<0.05.

RESULTS

The preoperative characteristics of patients is shown in Table 1. The intra-operative and postoperative data is depicted in Table 2. The use of blood transfusion requirements is shown in Table 3.

Table 1: Preoperative characteristics.

	Group-1 (n=86)	Group-2 (n=34)	P value
Age (years±SD)	58.8±8.68	63.5±8.40	0.008
Males, n (%)	78 (91)	33 (97)	0.25
Females, n (%)	8 (9)	1 (3)	0.25
Hypertension, n (%)	34 (40)	17 (50)	0.32
Diabetes Mellitus, n (%)	33 (38)	18 (53)	0.13
Serum creatinine >2.0, n (%)	4 (5)	3 (9)	0.41
Acute MI, n (%)	5 (6)	11 (32)	0.002
Unstable angina, n (%)	12 (14)	21 (62)	0.0001
Active Smoker, n (%)	35 (41)	9 (26)	0.12
History of stroke, n (%)	5 (6)	0	0.14
Coronary angio	graphy n (%	o)	
SVD	0	1 (3)	0.10
DVD	20 (23)	1 (3)	0.009
TVD	66 (77)	32 (94)	0.03
Left main >80%	15 (17)	13 (38)	0.014
LVEF, n (%)			
<30	13 (15)	4 (12)	0.67
30-50	45 (52)	18 (53)	0.92
>50	28 (33)	12 (35)	0.83
Post PTCA with patent stents in one or more coronary arteries, n (%)	24 (28)	12(35)	0.45
77.1) harm

^a Values are either mean <u>+</u> SD or number (percentage). ^b SVD: single vessel disease. ^c DVD: Double vessel disease. ^d TVD: triple vessel disease. ^e LVEF: left ventricular ejection fraction. ^f PTCA: percutaneous transluminal coronary angioplasty.

Table 2: Operative and postoperative data.

	Group-1	Group-2	P		
- a	(n=86)	(n=34)	value		
Left Internal Mammary artery, n (%)	75 (87)	28 (82)	0.49		
Right Internal Mammary artery, n (%)	16 (19)	0	0.006		
Radial artery, n	7 (8)	0	0.09		
Number of distal anastomosis n (%)					
>3	12 (14)	5 (15)	0.88		
3	54 (63)	21 (62)	0.91		
2	18 (21)	7 (20)	0.90		
1	2 (2)	1 (3)	0.74		
Operative time (min±SD)	250.76±49.88	272.64±47.24	0.03		
Chest tube drainage in 48 hours (ml + SD)	578±146	610±190	0.32		
Re- exploration, n (%)	0	1 (3)	0.10		
Postop MI, n (%)	0	0	-		
Stroke, n (%)	0	1 (3)	0.10		
Rise in serum creatinine greater than 1 from preoperative value, n (%)	1 (1)	2 (6)	0.10		
Death, n (%)	1 (1)	1 (3)	0.42		

 a Values are either mean \pm SD or number (percentage). b MI: myocardial infarction

There were no statistically significant differences in preoperative characteristics between the two groups except for age, acute MI, unstable angina and angiographic profile. The patients in group 2 had a higher percentage of acute MI and unstable angina patients. The angiographic profile of patients in group 2 mainly consisted of Left main coronary with critical triple or double vessel disease. Two groups showed significant difference in use of right internal mammary artery and radial artery grafts. The operative time in both the groups was also statistically significant. No significant difference

was detected in chest tube drainage, re-exploration and use of blood products between two groups. One patient in group 2 underwent surgical re-exploration because of hemodynamic instability due to continuous ventricular tachycardia (VT). Re-exploration in this patient revealed severe poor contractions of left ventricle. Cardiopulmonary bypass was instituted in this patient but unfortunately patient could not be saved. There were 2 deaths in the study. 1 patient as highlighted above had history of acute MI, unstable angina with LVEF of 40 %. He developed refractory VT postoperatively. 2nd patient of group 1, died had severe LV dysfunction (LVEF 20%) low cardiac output developed syndrome postoperatively.

Table 3: Blood transfusion requirements.

Characteristi	Group n (%)		P value#			
cs	1	2	P value"			
PRBC units consumed						
0	71 (82.6)	22 (64.7)	0.09			
1	8 (9.3)	7 (20.6)				
2	7 (8.1)	4 (11.8)				
3	0	1 (2.9)				
FFP units consumed						
0	71 (82.6)	23 (67.8)				
1	7 (8.1)	4 (11.8)	0.17			
2	8 (9.3)	7 (20.6)				
RDP units consumed						
0	73 (84.9)	24 (70.6)	0.07			
2	13 (15.1)	10 (29.4)				

p value based on Chi-square test. a PRBC: packed RBCs. b FFP: Fresh frozen plasma. c RDP: Random donor platelets.d 1 unit of PRBC is 250 ml. e 1 unit of RDPC is 50 ml. f 1 unit of FFP is 200-250 ml

DISCUSSION

Currently the majority of patients referred for CABG are usually with coronary artery disease not amenable to angioplasty and are receiving DAPT (clopidogrel and aspirin) therapy. 13,6 DAPT is protective for coronary artery disease patients in preventing ischemia and stent thrombosis. 11,12 Latest trends have witnessed a surge in urgent and decrease in emergent CABG cases. 13 As these patients have been on clopidogrel and aspirin medications the potential risk of increased postoperative bleeding, reexploration along with transfusion of blood products is a matter of great concern for the surgeons. It's practically very difficult to stop clopidogrel more than 5 days before surgery as per standard guidelines, in these new emerging subsets of patients with critical coronary disease and sometimes it's a big economic burden on the patient.¹⁴ Because of the conflicting guidelines and lack of reliable recommendations in current scenario, the decision of preoperative antiplatelet drug regime relies more on preference rather than evidence-based approach. Though there are recommendations on continuing clopidogrel in patients with drug eluting stents

subjected to CABG, timing of discontinuation is missing other subset of patients.¹⁵ OP-CABG revolutionised the coronary artery surgery by decreasing cardiopulmonary bypass related complications and attaining complete revascularisation in a safe and effective ways thus reducing the incidence of postoperative bleeding and its associated complications. 16,17 Even studies doing CABG on cardiopulmonary bypass have reported that use of DAPT is not associated with increased haemostatic reexploration and use of blood products.18

The results of the present study show that off pump CABG on patients continuing preoperative clopidogrel was not associated with statistically significant increased amount of postoperative blood losses, re-exploration and blood transfusions. However, there was significant difference in operative time and use of total arterial revascularisation between the two groups. The increase in operative time in group 2 was due to maintaining thorough haemostasis. The surgeons did not use bilateral internal mammary artery (BIMA) in group 2 patients as patients in this group were sicker, advanced age and on preoperative clopidogrel. The bleeding complications are enhanced by use of BIMA. 19 However, a recent study has concluded that BIMA can be safely used in sick patients without prolonging operative time and bleeding complications.²⁰ The mean chest tube drainage in 48 hours was not significant between two groups. The bleeding is also dependent on other factors like age, gender, diabetes, renal dysfunction, poor LVEF, emergency surgery, platelet abnormalities and number of anastomoses.^{17,21} Hypothermia being an important factor for postoperative bleeding, the core temperature of patients was maintained between 35 degrees to 37 degrees centigrade both intraoperatively postoperatively in this study.²² There is an individual variability in efficacy of aspirin and clopidogrel among patients, with some patients having tendency of increased bleeding postoperatively even on routine doses of aspirin.

The mean chest drainage volumes were similar with no statistical significance in rate of blood transfusion in the study comparing the effects on postoperative bleeding and use of blood products after elective on-pump CABG in patients with aspirin alone and with DAPT. A recent meta-analysis concluded use of DAPT with aspirin and clopidogrel in patients with acute coronary syndrome (ACS) before CABG for better graft function despite increase in chest drainage. The DAPT therapy may also be beneficial in the hypercoagulable state associated with OP-CABG and help in improving long term graft patency often questionable in OP-CABG as compared to on-pump CABG. A compared to on-pump CABG.

Limitations of our study

This was a single centre retrospective observational study with a small sample size. A multicentre prospective

randomized controlled studies with large sample size is required to confirm our data.

CONCLUSION

In conclusion OP-CABG can be done safely in patients continuing clopidogrel requiring urgent CABG. However, clopidogrel should be stopped 3-5 days in patients undergoing elective surgeries as it influences graft selection strategy, prolongs operative time and exposes the patients to avoidable risks.

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Institutional Ethics Committee

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