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Original Article

Evaluation of Mortality and Morbidity in Off-pump Coronary Artery Bypass Grafting Versus Coronary Artery Bypass Grafting with Cardiopulmonary Bypass in Diabetic Patient Study at NICVD.

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Keywords:
IHD, CABG, Cardiopulmonary bypass, Diabetes mellitus.

Abstract:

Background*: Cardiopulmonary bypass is associated with increased incidence of hyperglycemia. Many studies have shown that diabetes is associated with increased morbidity and mortality in coronary artery bypass (CABG) surgery. We reviewed the outcome of on-pump versus off pump CABG in diabetic patients.*

Methods*- 80 Adult diabetic patients undergoing isolated CABG both on-pump and OPCAB were divided into 2 groups – 40 patients in each group. To evaluate both preoperative, perioperative and postoperative out come and to compare their in hospital outcome mortality and morbidity.*

Results*: Diabetic patients undergoing coronary artery bypass grafting without cardiopulmonary bypass had fewer complications, including neurological dysfunction (7.5% vs. 10.0%, p=0.1), and reduced incidence of prolonged ventilation (7.5% vs. 12.5%, p = 0.709), atrial fibrillation (15.0% vs. 20.0%, p = 0.002), and renal dysfunction (10.0% vs. 17.5%, p=0.556). In postoperative period, 70% patients in OPCAB group did not experience any cardiac events whereas 30% patients developed myocardial infarction, 5% had cardiac arrest and 7.5% had low output syndrome. . In on pump group 65% patients had no cardiac events whereas 35% patients developed one or more cardiac events. Of them 20% patients developed atrial fibrillation, 2.5% developed myocardial infarction, 2.5% develop cardiac arrest and 10% had low output syndrome. 2.5% patient developed both atrial fibrillation and low output.*

Conclusion*: Diabetic patients undergoing CABG without cardiopulmonary bypass compared with those having coronary artery bypass grafting with cardiopulmonary bypass had higher mean predicted mortality and morbidity.*

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Introduction:

Diabetes mellitus (DM) is an established risk factor for the development of coronary artery disease. Coronary artery disease is not only more prevalent in diabetic patients compared with nondiabetic patients, but also tends to be more extensive, involving multiple vessels, and rapidly progressive5 R.M Jacoby and R.W Nesto, Acute myocardial infarction in the diabetic patient pathophysiology, clinical course and prognosis, J Am Coll Cardiol **20** (1992), pp. 726–744.. Accordingly, diabetic patients represent a large proportion of patients requiring myocardial revascularization. Unfortunately, diabetes is also a significant risk factor for adverse early and late outcomes after surgical revascularization.[1] Symptoms of hyperglycemia and a random plasma glucose >200 mg/dl (11.1mmol/L) defines DM.[2] Patients with

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diabetes mellitus who undergo CABG surgery have increased perioperative mortality and morbidity, significantly reduced long-term survival, and less freedom from recurrent episodes of angina.[3-6]

During CPB hyperglycemia in preexisting diabetes mellitus is exacerbated by hormonal stress response to surgery, impaired insulin production and peripheral insulin resistance resulting from elevated levels of the counteregulatory hormones, including cortisol, epinephrine and growth hormone. Even in non - diabetes, the same mechanisms lead to hyperglycemia.[6,7]

Hyperglycemia (DM) interferes with monocyte and neutrophil function, affects endothelial function and induces the expression of pro-inflammatory cytokines. These events might be responsible for a directly negative effect of hyperglycemia, including the facilitation of wound infection or sepsis with or without multiorgan failure indirectly, hyperglycemia might be a surrogate parameter for insulin resistance. [8]

Lazar et al. has shown that maintaining serum glucose ≤200 mg/dL using a modified GIK solution in diabetic patients decreases perioperative morbidity, enhances sur-vival, and diminishes recurrent ischemic events.[9] A 20 mg/dl increase in blood glucose level was associated with more than 30% increase in adverse effects.[10] Patients with diabetes mellitus who undergo CABG sur-gery have increased perioperative mortality and morbid-ity, significantly reduced long-term survival, and less free-dom from recurrent episodes of angina. The poorer outcomes in these patients have been attributed to a higher incidence of left ventricular dysfunction, altered endothelial function, more diffuse coronary disease, abnormal fibrino-lytic and platelet function, and impaired glucose utilization.[10-12]

Every operation result in hyperglycemia due to the stress response associated with them. CPB is associated with increased incidence of hyperglycemia. Many studies have shown that diabetes is associated with increased morbidity and mortality in CABG surgery. We reviewed CABG experience to determine the impact of cardiopulmonary bypass in diabetic patients undergoing CABG surgery.

Methods:

This is a prospective, non-randomized, observational study conducted from January 2008 to December 2010 in the Department of Cardiac Surgery of National institute of cardiovascular diseases, Dhaka. 80 Adult diabetic patients undergoing isolated CABG were divided into 2 groups – 40 patients in each group, Off-pump CABG with diabetes (n=40) group –A, On –pump CABG with diabetes (n=40) group-B. Diabetic patients undergoing CABG having left ventricular EF <35% were excluded. We followed the treatment protocol for diabetic patients. In diabetic patients taking oral hypoglycemic agents discontinued after admission into the hospital and converted into insulin (subcutaneous). Those diabetic patients taking insulin was also continued and adjusted insulin dose after measuring blood glucose level. Their dose was held at the morning before surgery. Following protocol was followed-

If blood glucose level is

>10 mmol/L -Start with a bolus of 2 U, followed by insulin infusion at 2 units/hour.

Repeat blood glucose measurement every 30 minutes.

>10 mmol/L- Increase infusion by 2 U/h.

>6 and <10 mmol/l.- Maintain current infusion rate

<6.0 mmol/L= Stop insulin infusion

<4.0 mmol/L- Stop insulin infusion; administer 25 mL of 50% dextrose

Maximum insulin infusion, 20 U/h.

Postoperative hyperglycemia protocol for CABG surgery patients:

Goal was to maintain blood sugar (BS) between 110 mg/dl and 180 mg/dL after surgery. Check glucometer Blood Sugar 2 hourly; increase to hourly during rapidly changing conditions and decrease to 4 hourly if no changes in insulin drip rate for 6 h and serum Blood Sugar <180 mg/dl on 3 consecutive measurements. Correlate glucometer Blood Sugar to serum Blood Sugar daily. Serum potassium was maintained >4 mEq/L.

Measures of variables: Age (years), Sex, Dyslipidemia, Hypertension, Smoking. Oral

hypoglycemic agents, insulin use, Pre-operative serum glucose level, Left ventricular EF, Coronary artery pathology, Per-operative measures Serum glucose level, Total operative time, Number of graft, total grafting time. Post-operative out comes- Ventilation time in hours (prolonged ventilation time > 48 (hours), ICU stay (hours), CVD (Neurological dysfunction), reoperation for bleeding, renal impairment, wound infection, myocardial infraction, cardiac arrest , LOS (Low output syndrome), atrial fibrillation, length of hospital stay, mortality (operative and post-operative), immediate post- operative blood glucose measurement. Follow up at one month was done by clinical evaluation, Echocardiographic evaluation, ECG, Blood sugar evaluation.

Results:

Age were 55.25±5.1 years and 54.75±5.2 years respectively (p = 0.510). In this study among 40 patients in off-pump CABG 3 (7.5%) patients were female and in on-pump CABG 1(2.5%) patients were female (p>0.05).

Table-I

Preoperative risk factors among the study population (n=80).

Risk Factors	Off-pump CABG freq. (%)	On-pump CABG freq. (%)	p value
Smoking	22 (55%)	21 (51.5%)	0.792
Hypertension	30(75%)	27(67.5%)	0.785
Hyperlipidemia	29(72.5%)	26 (63%)	0.176

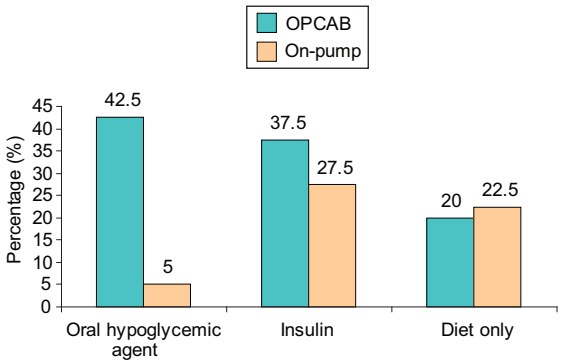

Fig-1: *Antidiabetic therapy of both groups.*

Table-II

Preoperative random blood glucose level

Group	Mean(±SD) (mmol/L)	p value
Group A (OPCAB)	8.86(±1.56)	0.684
Group B (On -pump)	8.72(±1.50)	

Number of coronary arteries involved were compare between the groups. In Off-pump group, 42.5% patients had double coronary artery involvements and rest 50% and 7.5% had triple coronary artery and Single coronary involvements. In On-pump group, double and triple vessel coronary artery involvements were found in47.5% and 52.5% patients respectively. The LM involvements both groups were 15% and 17.5% (p value > .05).

Number in parenthesis indicate percentage. P value >.05, but number of incidences differ in both group Major post-operative Complications.

In postoperative period, 28 (70%) patients in OPCAB group did not experience any cardiac events whereas 12 (30%) patients developed different cardiac events. Among them AF were 6 (15%), myocardial infarction 1 (2.5%), 2 (5%) had cardiac arrest and 3 (7.5%) had low output syndrome.

In On-pump group, 26 (65%) had no post-operative cardiac events. whereas 14 (35%) patients developed one or more cardiac events. Of them 8 (20%) patients developed atrial fibrillation, 1(2.5%) developed myocardial infarction, 1(2.5%) develop cardiac arrest and 4 (10%) had low output syndrome. 1(2.5%) patient developed both atrial fibrillation and low output in postoperative period.

The mortality was found 2(5%) in Off-pump group one due to per-operative ventricular fibrillation and one postoperative LOS, 3(7.5%) in On-pump, one due to failure to wean from cardiopulmonary bypass one due to low output syndrome and one due to postoperative cardiac arrest. A total of 5 patients died out of eighty CABG in this series, mortality percentage being 6.66%. difference was not be stated as statically significant p=.608(P>0.05). The mean difference of LVEF from pre-operative period to Post operatively after 1 months between Off-pump was 8.78±8.0 (%) and On-pump CABG was 7.78±3.4 (%). The improvement of LVEF between Off-pump and On-pump was not statistically insignificant (p>0.05) in unpaired students' t-test.

Table-III

ICU events among the study population (n=80).

Findings	Off-pump CABG (Mean±SD)	On-pump CABG (Mean±SD)	p-value
Period of mechanical ventilation (hours)	7.5±2.7	12.5±3.7	0.001
ICU Stay (hours)	30.1±6.6	36.6±7.6	0.002
Total post- operative hospital stays (days)	6.3±0.8	8.7±2.1	0.001

S=Significance; P-value<0.05 was considered significant. (Student t Test),

Table-IV

Postoperative events among the study population (n=80).

Major post-operative Complications	Off-pump CABG freq. (%) (n=40)	On-pump CABG freq. (%) (n=40)	p value
Neurological dysfunction	1 (2.5%)	3 (7.5%)	0.608
Renal dysfunction	2 (5%)	3 (7.5%)	0.055
Prolonged ventilation>48 hours	3 (7.5%)	5 (12.5%)	0.709
Sternal wound infection	2 (5%)	2 (5%)	0.050
Requirements-operation for bleeding	1 (2.5%)	3(7.5%)	0.608

Table-V

Showing types of postoperative cardiac events.

			Group		p value
			OPCAB	On-pump	
Cardiac events	Absent	No cardiac event	28(70)	26(65)	0.633
	Present	Atrial fibrillation	6(15)	8(20)	0.556
		Myocardial infarction	1(2.5)	1(2.5)	1.00
		cardiac arrest	2(5)	1(2.5)	1.00
		Low output syndrome	3(7.5)	4(10)	1.00
		Myocardial infarction + Low output syndrome		0	-
		Atrial fibrillation + Low output syndrome	0	1(2.5)	-
Total	40(100)	40(100)			

Number in parenthesis indicate percentage. p value >.05, but number of incidences differ in both groups.

Discussion:

NICVD is one of the best referral hospitals for CABG operation. The first CABG (on-pump) surgery was done at NICVD, Bangladesh, in 1985. OPCAB surgery is being performed since 1997 in NICVD then subsequently in other cardiac centers in Bangladesh.

The mean age was 67 years for the off pump and 68 years for the on-pump groups in the study of Yokoyama et al.[13] A study by Calafiore et al.[14] had a mean age of 64.4±9.6 years for OPCAB patient and 63.3±9.7 years for on pump CABG patients. This study mean ages of off-pump and On-pump group of patients were 54.75±5.2, 55.25 years respectively. In this study among 40 patients in off-pump CABG 3 (7.5%) patients were female and in on-pump CABG 1(2.5%) patients were female.

In a study by Calafiore et al.[14] found 2 vessel disease and 3 vessel disease were 36.8% and 63.2% in OPCAB and 23.9% and 76.1% in on pump CABG group respectively. Chamberlain et al.[15] reported double vessel affected and 3 vessels affected were 28.2% and 60.4% in off pump and 18.9% and 77.3% in on pump CABG group respectively. In the observation of Hernandez et al. [16] 2 diseased vessels were 35.6% and 35.3% and 3 diseased vessels were 39% and 44.7%.in OPCAB and CCAB

respectively. Our study, in off-pump group 42.5% cases had double vessel disease and 50% case had triple and 7.5% had single vessel disease. In On-pump group, 47.5% patients had double vessel disease and 52.5% patients had triple vessel disease. Hernandez et al study was near to similar our study

In a study of Arom et al. [17] smoker was 22% and 18.8% in off-pump and on-pump group, diabetes was 33.3% in off-pump and 33.8% in on-pump. Hypertension was 66.7% and 53.4% in off-pump and on-pump patient.

A study on 1570 high risk patients by Chamberlain et al. [15] reported hypertension was 60.7% and 61.9% in off-pump and on-pump group respectively, hypercholesterolemia 75.2% and 68.3% in off-pump and on-pump group and smoker was 74.7% and 77% in off-pump and on-pump patient respectively. In this study the pre-operative risk factors smoking, hypertension and Hyperlipidemia were the predominance risk factor in both groups (55% vs. 51.5% and 75.7% vs. 67% and 72.5% vs. 635 in off-pump vs. on-pump CABG respectively. Chamberlain et al.[15] study was similar to our study, but no significant difference exists in between groups. Both groups were almost comparable regarding other risk factors.

The length of operation time Mean±SD was 213±56.7 (min) and 252.1±80.8 (min) in OPCAB vs. CABG in the study of. Arom et al.[17] reported that total operation time was 175 min and 235 min in off pump and on pump group respectively. In a study by Shennib et al. [18] observed that total operation time was 192.1±42.2 min and 199.8±42.2 in off pump and on pump respectively. Czerny et al. [19] in a study reported duration of operation in OPCAB and CCAB were 178±49 min and 254±64 min respectively. Compare to our study shows in per-operative finding between groups demonstrates that total operative time in off-pump group (165.3±20.9 min) is significantly less than that of on-pump group (205.3±48.4 min) in this study, the average number of grafts in off-pump group was 2.9±0.7 and in on- pump group (3.2±0.8) were comparable.

Several post-operative out-come have been compared between groups, In a study by Czerny et al.[19] reported intubations time (hours) was 4.8±2.9 in OPCAB and 17.7±24.4 in on pump CABG, mean ICU stay (days) was 1.2±0.3 day in OPCAB and 2.0±2.8 days in on pump, in hospital stay was 13.5±8.2 in OPCAB and 12.6±7.3 in on pump. Shennib et al.[18] found in a study intubations time (hours) was 16.5±22.4 in off pump and 22.2±32.5 in on pump, ICU length of stay (hours) was 45.5±52.2 in off pump and 57±67.6 in on pump, postoperative length of stay (days) was 9.3±9.2 in off pump and 11.1±11.5 in on pump.

Arom et al.[17] observed in a study intubations time (hours) was 23.5 (67.7) in off pump and 33.2 (118.6) in on pump, ICU hours mean (SD) was 60.5 (83.9) in off pump and 58 (94.1) in on pump and postoperative hospital stay (days) mean (SD) was 8.2(4.7) in off pump and 7.9 (5.7) in on pump groups. Calafiore et al. [14] showed in a study ICU stay (hours) was 13.5±16.6 in off pump and 16.2±15.3 in on pump, in hospital stay (day) 4.2±2.8 in off pump and 4.9±2.7 in on pump. Boyd et al. (1999)[20] reported ventilation time (hour) was 7.9±5.2 in off pump and 16.3±9.7 in on pump, ICU stay (hour) 24±10.9 in off pump and 36.6±33.5 in on pump and hospital stay (days) was 6.3±1.8 in OPCAB and 7.7±3.9 in on pump groups.

In this study mean (Mean±SD) ventilation period in off-pump group was 7.5±2.7 hours and that in on-pump group was 12.5±3.7 hours. This shows that ventilation time was significantly higher in on-pump group. But this is much lower than that in the series of Shennib et al.[18] suggesting a trend towards early extubation in our institution (NICVD). Total ICU stay (hours) 30.1±3.6 vs. 36.6±3.7 and total postoperative stay in hospital averaged 6.3±0.8 days in off-pump group of patients and 8.7±2.1 days in both group of patients. Thus, the mean period of mechanical ventilation, ICU-stay period, total post-operative stay in hospital all were significantly greater in on-pump group as opposed to off-pump group.

All these reflect definite clinical advantage as well as favorable economic outcome associated with off-pump group of patients. Yokoyama et al.[13] in a study on off pump vs. on pump coronary bypass in high risk subgroup showed renal complication was 3.3% in off pump and 5.4% in on pump, prolonged ventilation > 72 hours 3.7% in off pump and 6.6% in on pump, neurological complication 3.3% in off pump and 5% in on pump CABG. Bull et al.[21] in a study showed that renal failure was 3% off pump

mediastinitis was 5%. In this study on pump CABG patients experienced higher postoperative morbidity than off pump CABG especially renal dysfunction (5% vs. 7.5%), prolonged ventilation more than 48 hours (7.5% vs. 12.5%) and deep sternal wound infection (5% vs. 5%). Neurological dysfunction was 2.5% vs. 7.5%. All were similar above mention study.

Ascione et al.[22] reported in a study mortality was 5.9% in off pump and 7.9% in on pump. Ahmed et al. (1988) observed mortality was; 12.5% in beating heart CABG and 25% in on pump CABG. Arom et al.[15] in a study showed operative modality was 4.4% in off pump and 7.5% in on pump groups.

In this study 30 days operative mortality was higher in on pump CABG group (7.5%) than off pump CABG group (5%) but statistically not significant due to small sample size. But the study was correlate to the other study.

During follow up evaluation improvement is statistically significant. In echocardiographic evaluation in off pump CABG mean difference of LVIDd and LVIDs (51,32±6.98 vs. 47.47±7.81 and 42.02 ±6.75 vs. 36.54±8.08 mm) was statistically significant ($p<0.05$) in after.1-month postoperative period compare to preoperative period. During the preoperative period LVEF was 45±8% and 1 months postoperatively LVEF was 53±7 which was significantly higher? compared to per-operative period. In on pump CABG mean difference of LVIDd and LVIDS (49.67±4.85 mm vs. 47.56±4. 78 mm and 40.22±4.53mm vs. 36.71±4.13 mm) was statistically significant in after 1 month's postoperative period compare to preoperative period. LVEF also improved from 47±6% to 54±5% after 1-month postoperative period compare to preoperative period.

The mean difference of LVEF from preoperative period to postoperatively after 1 months between off pump was 8.78±3.0% and on pump CABG was 7.78±3.4%. The improvement of LVEF between off pump and on pump was statistically insignificant ($p> 0.05$).

Arnese et al.[23] in a study on prediction of improvement of regional left ventricular function after surgical revascularization reported postoperative improvement occurred in 79% of severe hypokinetic segment of ventricular wall.

In this study in off pump CABG 95% patients showed improvement of wall motion abnormality after 1 month postoperatively compared to preoperative period and in on pump CABG 88.9% patients showed normal wall motion after 3 months postoperatively compared to preoperative period. Both these findings conclusively demonstrated functional improvement and effectiveness of revascularization in both off pump CABG and on pump CABG.

But Mean±SD difference between preoperative to postoperative areas was 5.7±2.1 in off pump and on pump CABG was 7.8±8.6. The Mean±SD difference of ejection fraction was 8.5±2.5 in off pump and on pump CABG was 8.9±7.5.

Above these findings indicate functional improvement of treatment group in diabetic CABG patients tending towards a favorable impact on OPCAB CABG outcome in compare to on pump CABG group.

Conclusion

Off-pump CABG has gained increasing popularity due to its potential to avoid induced myocardial damage by CPB. From this study we concluded that Off-pump CABG provides a significant survival advantage in compare to On-pump CABG in diabetic patients in association with a significant reduction in morbidity. Additional studies including larger number of diabetic patients for prospective randomization is needed to confirm these conclusions.

Study Limitations

We recognize that there are a number of important limitations with our data and our results. All operations were not performed by the same surgeon and sample size was small.

Conflict of Interest - None.

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