Comparison of Early Outcome of Off-pump and Conventional Coronary Artery Bypass Graft Surgery in Patients with Multivessel Coronary Artery Disease and Left Ventricular Dysfunction

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Abstract:

Introduction: Left ventricular dysfunction is an important predictor of in-hospital mortality. Due to the theoretical and practical advantages to avoid the harmful effects of cardiopulmonary bypass (CPB), many cardiac surgeons are using Off-pump Coronary Artery Bypass (OPCAB)as an effective alternative to conventional CABG (CCAB) even in patients with reduced left ventricular (LV)ejection fraction.

Objectives: This study performed in the National Institute of Cardiovascular Diseases (NICVD) evaluated the early outcomes of OPCAB in terms of mortality and major post-operative morbidities and compared them with that of CCAB in patients with multivessel coronary artery diseases and reduced left ventricular (LV) function.

Methods: Total 120 patients with multivessel coronary artery disease with reduced left ventricular ejection fraction (d"50%)were allocated into two groups: a) 60 patients who underwent OPCAB and b) another 60 patients who underwent conventional CABG between January 2013 and December 2015. Pre-operative, peroperative and early post-operative variables were recorded, compiled and compared.

Results: All risk factors and co-morbidities were homogenously distributed between the two groups. Majority of the patients had triple vessel disease. Nearly three-quarter (73.3%) of patients in OPCAB group and 80% in CCAB group received 3 grafts (p=0.470). The mean total operative time (268.5 \pm 33.5vs. 296.3 \pm 34.8minutes, p < 0.001), intubation times(8.6 \pm 0.3 vs. 12.3 \pm 0.5 hours, p<0.001), blood losses (377.8378 \pm 45 ml vs. 602 \pm 60 ml, p < 0.001); requirements for blood and blood products (689.7 \pm 21.1 vs. 1199.3 \pm 34.5 ml, p < 0.0010), intensive care unit stays (31.7 \pm 0.9 hours versus 41.6 \pm 1.5 hours; p<0.001) and hospital stays (8.2 \pm 0.2days vs.10.3 \pm 0.3days, p < 0.001)were all significantly lower in the OPCAB group.

Conclusion: OPCAB is a safe and effective operative revascularization procedure for patients with multivessel coronary artery disease and left ventricular dysfunction and is associated with reduced morbidity. However, a larger and omized trial with long-term follow-up may show the real benefits of OPCAB.

Key Words: OPCAB, CCAB, Multivessel Coronary Artery Disease, Left Ventricular Dysfunction.

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Introduction:

Jones et al¹examined seven large datasets, with more than 172,000 patients undergoing isolated CABG, to assess the predictive power of certain preoperative values on operative mortality. Seven variables were found to be predictive of mortality in all datasets. These seven core variables included urgency of operation, age, prior heart surgery, gender, left ventricular ejection fraction (LVEF), and percentage of stenosis of the left main coronary artery and number of major coronary arteries with 70% stenosis.¹

CABG with cardioplegia has been considered the gold standard operation for coronary revascularization. The introduction of the heart-lung machine created optimal operative conditions of bloodless, motionless operative field and allowed CABG to be done consistently with generally good results in most patients.² However, this technique is linked to several side effects mostly due to use of aortic cross clamp, cardioplegia, and cardiopulmonary bypass. High risk patients are extremely sensitive to cardioplegic arrest and have higher intra-operative and post-operative risk.³

Atrial fibrillation occurs in 20-40% of patients who had CABG with cardiopulmonary bypass and is associated with higher risk of cerebrovascular accidents. The higher incidence of post-operative IABP insertion, renal hemodialysis, mechanical ventilation and/or reintubation or tracheostomy could be responsible for the significant higher rate of readmission for CPB patients.

The invention of Off-pump Coronary Artery Bypass (OPCAB) is often attributed to Kolessov in 1967.6 In the mid-1990s interest in beating-heart techniques experienced resurgence in an attempt to decrease the morbidity associated with CABG without jeopardizing the benefits⁶. Although the initial experience with OPCAB was limited to single or double vessel disease with preserved left ventricular function, 7,8 the availability of modern retractor-stabilizers, heart positioning devices, techniques of exposure of all surfaces of heart, intracoronary shunts, and adequate surgeon experience, similar completeness of revascularization and graft patency can be achieved with OPCAB even in patients with multivessel disease and reduced left ventricular function.9,10,11 Now OPCAB is widely accepted and considered to be safe for myocardial revascularization specially for high risk patients. 12

The rapidly increasing incidence of diabetes mellitus, hypertension, and hypercholesterolemia in most communities has given rise to more severe and diffuse coronary artery disease. ¹³As a result of improvement in

invasive cardiology most patients referred for CABG have diffuse disease and poor ventricles. The global ischemia caused by conventional CABG (CCAB) could be detrimental to them. The OPCAB technique was developed with specific purpose of reducing mortality and morbidity in high risk patients.⁶

The shorter operating time in OPCAB group is probably because of the shorter time required for hemostasis and no time spent on cannulation, managing cardiac arrest and rewarming from hypothermia during CPB. There is also less intra-operative and post-operative blood loss, a lower incidence of re-exploration for bleeding, a smaller transfusion volume and lower incidence of transfusion.¹⁴

The shorter ICU stay and ventilation time in the OPCAB group may be related to lack of the pulmonary dysfunction that occurs after CPB. Glomerular filtration rate and renal tubular function are better protected by OPCAB group than by conventional CABG.¹⁴

There are also potential economic benefits including reduced postoperative patient instability and faster recovery rate, reduced use of vasoactive drugs, less need for blood products and cost effective resource utilization.¹⁵

Materials and Methods:

This was prospective non-randomized clinical study was done in National Institute of Cardiovascular Diseases (NICVD) from January 2013 and December 2015. Among the 120 patients with multivessel coronary artery disease with reduced left ventricular ejection fraction (d"50%) 60 patients underwent OPCAB (Group: A) and the rest 60 underwent conventional CABG (Group: B).

Anesthesia and Monitoring

Patients were premedicated with morphine (0.1 mg/kg) and bromazepam (3mg). Induction and maintenance was done according to local protocol. All patients had a radial artery cannula, a central venous catheter, ECG leads and nasopharyngeal temperature probe for monitoring. Femoral artery cannulation was performed in patients with poor ventricular function (left ventricular ejection fraction <35%) in the event that urgent institution of an intra-aortic balloon pump was required. Arterial blood gases and activated clotting time (ACT) were monitored every 30 minutes. The patient's temperature was maintained close to 36°C for OPCAB and 32-34°C for CCAB.

Technique of OPCAB

All patients were operated through a median sternotomy. The internal thoracic artery, the radial artery, and the saphenous vein were harvested as appropriate with

standard techniques. Then intravenous heparin (100IU/ kg) was given to maintain an ACT of 300 second before starting distal anastomoses. Regional myocardial immobilization was achieved with a suction stabilizer (Octopus) and apical suction device (Star Fish). Intracoronary shunts were used in most patients to maintain coronary flow, thereby reducing myocardial ischemia and at the sametime minimizing bleeding from the coronary arteriotomy. The left anterior descending (LAD) artery was revascularized first using left internal mammary/ thoracic artery (LIMA/ LITA). Proximal anastomoses were performed on the partially clamped ascending aorta using 6-0 continuous Prolene suture. Distal anastomoses were performed with continuous 7-0 or 8-0 polypropylene (Prolene)monofilament suture. After the procedure, heparin therapy was reversed with protamine sulfate in a 1:1 ratio. The leg, forearm, and chest wounds were closed and the patients were shifted to ICU. Total operation time and number of grafts were recorded.

Technique of Conventional CABG

After median sternotomy conduits were harvested and prepared and the patients were heparinized with an initial dose of 300 IU/kg heparin to achieve a target activated clotting time greater than 450 second. CPB was established with ascending aortic and two-stage venous cannulation. The blood pressure was maintained within 50 to 70 mm Hg. The aorta was cross-clumped, and myocardial protection was achieved with intermittent antegrade cold blood cardioplegia according to a standard protocol. On completion of all the distal anastomoses aortic clamp was released and the proximal anastomoses were performed with partial clamping of the ascending aorta during rewarming. Then the patients were gradually weaned from cardiopulmonary bypass (CPB). Heparin neutralization was done by protamine in 1:1 ratio at the end of the procedure. The leg, forearm, and chest wounds were closed and the patients were shifted to ICU. Total operation time and number of grafts were recorded.

Postoperative Management

After surgery, all patients were transferred to the intensive care unit (ICU). Cardiac, respiratory, renal function and hourly blood loss were monitored meticulously. Extubation was done as early as possible while the patients fulfill the extubation criteria. Arterial blood gas, serum electrolytes and hematocrit estimation were done as per standard protocol. Haemodynamic and other parameters were managed according to standard protocol. Pre-operative medications continued as per protocol. Patients were encouraged to intensive spirometry and early mobilization. Then the patients were shifted to general wards and subsequently discharged

according to unit protocol. Antibiotic administration was continued until the patient hadcentrallines or chest drains (normally 24-48 hours).

Data collection:

All data were collected from each patient using predesigned questionnaire and collection form. Data were analyzed and verified with statistical program for social sciences (SPSS) using student's t test, fisher's exact test, chi-square test, where appropriate. The descriptive statistics used here were frequency, mean and standard deviation (SD) and compared using student's t test. Categorical data were expressed as percentages and evaluated using Chi-square or Fischer's exact probability test. The level of significant was 0.05. Any p-value <0.05 was considered as significant.

Results:

Patient characteristics are shown in the Table-1. The mean ages of the study sample were61.4±9.56 years for the OPCAB group and 59.2±5.87 years for CCAB group with no significant difference (p=0.4090; >0.05) in age distribution. In the study both sexes were homogenously distributed between the two groups but with clear male predominance (90% in OPCAB vs. 86.7%). Overweight and obese patients were higher among CCAB group than that in OPCAB group (43.3% vs. 33.3%). However, the mean BMI were almost similar (28.1±2.38vs. 27.7 ± 3.4 kg/m², p = 0.955; >0.05).In our study, the commonest co-morbid factor was smoking in both groups (66.7% in OPCAB vs. 63.3% in CCAB group). It was followed by dyslipidemia (63.3% vs. 53.3%), hypertension (53.3% vs. 50%) and diabetes mellitus (33.3% in both groups). Other co-morbid factors were family history of CAD (10% vs. 13.3%), past history of CVA (6.7% vs. 10%), COPD (10% vs. 10%), history of MI (20% vs. 23.3%), PVD (10% vs. 10%) and renal dysfunction (6.7% vs. 3.3%). All were almost identically distributed between the groups (p > 0.05). In the study the mean left ventricular ejection fraction (LVEF) was almost similar in both groups $(39.5 \pm 3.6\% \text{ vs. } 38.65 \pm 2.7, p = 0.1461)$. Preoperative angiographic study demonstrated that majority of the patients had triple vessel disease (TVD) in each group (70% and 83.3% respectively). The rest had double vessel disease (DVD). The operating time was significantly higher in CCAB group (296.3 ± 34.8vs. 268.5 ± 33.5minutes, p < 0.001). The mean cardiopulmonary bypass (CPB) time was 110.3 ± 23.9 minutes in conventional CABG group. Most of the patients of both groups (73.3% and 80%respectively, p = 0.470) required 3 grafts. 2(6.7%) CCAB and 1(3.3%) OPCAB patients had 4 distal anastomoses. Among the post-operative variables the mean ventilation time was significantly higher in the CCAB group than those in OPCAB group (12.3±0.5 vs. 8.6±0.3 hours, p<0.001). In NICVD there is a trend to use inotropic support to almost all post-CABG patients unless otherwise specified. So, we used

prolonged post-operative inotropic support (>24 hours) or use of IABP as post-operative outcome variables. In our study 4(6.7%) CCAB patient required prolonged inotropic support. Among them 2 (3.3%) required IABP support. On the other hand, one (1.67%) of the OPCAB patients received prolonged inotropic support and one (1.67%) required IABP.

Total post-operative bleeding was significantly lower in OPCAB (378 \pm 45 ml vs. 602 \pm 60 ml, p < 0.001) group. Blood product requirement was also significantly lower in OPCAB group(690 \pm 30 vs.1085 \pm 45 ml, p < 0.0010).In this study, the average ICU-stay (34.7 \pm 0.9hours vs. 43.6 \pm 1.5hours, p<0.001) and total postoperative hospital stay was also shorter in OPCAB group (8.2 \pm 0.2days vs.10.3 \pm 0.3days, p < 0.001).

One patient (1.67%) of OPCAB group and two (3.3%) of CCAB group (p=1.000) died within 30days of operation. In the immediate postoperative period, 2(3.3%) of the CCAB patients and 1(1.67%) of the OPCAB patients developed new Q-wave myocardial infarction (MI). Other patients with post-operative myocardial infarction recovered with conservative management. One patient of CCAB group having LVEF of 30% required IABP during weaning from CPB. The only death of OPCAB group was

due to cardiac temponade from mediastinal bleeding. Re-exploration was done and bleeding was secured. But he died later due to multi-organ dysfunction from prolonged low output syndrome. The other patient of CCAB group died of pulmonary complication (pneumonia) requiring re-intubation. The mean period of mechanical ventilation, amount of blood products needed, length of ICU stay and hospital stay during the early post-operative period- all were significantly greater in CCAB group. Three (6.7%) patients of CCAB group and one (1.67%) of OPCAB group required re-exploration for bleeding (p=0.6186). Two (3.3%) of CCAB patients and one 1(1.67%) of OPCAB group developed stroke (p=1.000). New postoperative arrhythmias were developed in 12 (20%) CCAB and6 (10%) OPCAB patients (p=0.236). In most (14 patients) of them there were atrial arrhythmia and the remaining (4 patients) had ventricular tachycardia.

LOS (6.7% vs. 1.67%), pulmonary complications (10 vs. 6.7%), infective complications (10 % vs. 4%), and renal dysfunction(10 % vs. 4%), were also more common in CCAB group. Thus, postoperative complications were relatively less common in OPCAB group although statistically not significant. But this might be significant if larger sample would have been taken.

 Table-I

 Patient characteristics of multivessel coronary artery disease

Variables	OPCAB group(n=60)	CCAB group(n=60)	p Value
Age, years#	61.4±9.56*	59.2±5.87*	0.4090 ^{ns}
Male, n (%) [¥]	54(90)	52(86.7)	0.500 ^{ns}
Female, n (%) [¥]	6 (10)	8(13.3)	0.500 ^{ns}
BMI(kg/m²) [#]	28.1±2.38*	27.7±3.4*	0.4568 ^{ns}
Hypertension, n (%) [¥]	32(53.3)	30(50.0)	0.796 ^{ns}
Diabetes mellitus, n (%)¥	20(33.3)	20(33.3)	0.608 ^{ns}
Smoking, n (%) [¥]	40(66.7)	38(63.3)	0.787 ^{ns}
Dyslipidemia, n (%) [¥]	38(63.3)	32(53.3)	0.432 ^{ns}
Family H/O CAD, n (%) [¥]	6(10.0)	8(13.3)	0.500 ^{ns}
Past H/O CVA, n (%)¶	4(6.7)	6(10.0)	0.500 ^{ns}
COPD, n (%) [¥]	6(10.0)	6(10.0)	0.665 ^{ns}
History of MI, n (%) [¥]	12(20.0)	14(23.3)	0.754 ^{ns}
PVD, n (%) [¥]	6(10.0)	6(10.0)	0.665 ^{ns}
Renal dysfunction, n (%)¶	4(6.7)	2(3.3)	0.500 ^{ns}
Arrhythmia, n (%)¶	4(6.7)	4(6.7)	0.694 ^{ns}
LVEF (%)#	39.5 ± 3.6*	38.65± 2.7*	0.1461 ^{ns}
NYHA class III or IV, n (%)¥	10(16.67%)	8(13.33%)	0.952 ^{ns}
CCS angina class III or IV, n (%)¥	26(43.33%)	32(53.33)	0.757 ^{ns}
DVD¥	18(30.0)	10(16.7)	0.222 ^{ns}
TVD¥	42(70.0)	50(83.3)	0.222 ^{ns}

^{*}Data are presented as the mean ± SD for continuous variable.

[#] Student's t-Test, ¥ Chi-square (Ç2) Test, ¶ Fisher's Exact Test, ns= Non-significant

OPCAB: Off-Pump Coronary Artery Bypass; CCAB: Conventional Coronary Artery Bypass; COPD: Chronic Obstructive Pulmonary Disease; CVA:Cerebrovascular Accident; MI: Myocardial Infarction; NYHA: New York Heart Association; CCS: Canadian Cardiovascular Society Angina Class; PVD: Peripheral Vascular Disease.

Table-IIIntraoperative Variables

Variables	OPCAB group	CCAB group	p Value
	(n=60)	(n=60)	
Conversion to CPB, n (%)	2(3.33%)		
CPB time, minutes		110.3 ± 23.9	
Total operating time, minutes#	268.5 ± 33.5*	296.3 ± 34.8*	<0.0001s
Conduit used¥			
LIMA, n (%)	60(100%)	60(100%)	0.694 ^{ns}
Radial artery, n (%)	8(13.33%)	6(10%)	0.500 ^{ns}
SVG, n (%)	60(100%)	60(100%)	0.694 ^{ns}
Graft distribution¥			
LAD territory, n (%)	60(100%)	60(100%)	0.694 ^{ns}
Circumflex territory, n (%)	56(93.33%)	60(100%)	0.246 ^{ns}
RCA territory, n (%)	51(85%)	50(83.33%)	0.083 ^{ns}
Intraoperative IABP¶	0(0%)	2(3.3%)	0.500 ^{ns}

 $^{^{\}star}$ Data are presented as the mean \pm SD for continuous variable.

OPCAB: Off-Pump Coronary Artery Bypass; CCAB: Conventional Coronary Artery Bypass; CPB: Cardiopulmonary Bypass; IABP: Intra-AorticBalloon Pump; LAD: Left Anterior Descending Artery; RCA: Right Coronary Artery; LIMA: Left Internal Mammary Artery; RIMA: Right Internal Mammary Artery; SVG: Saphenous Vein Graft.

Table-III

Comparison of post-operative outcome between groups

Variables	OPCAB group	CCAB group (n=60)	p Value
	(n=60)		
30 days mortality, n (%)¶	1(1.67)	2(3.3)	1.000 ^{ns}
Ventilation time, hours#	8.6±0.3*	12.3±0.5*	<0.0001s
LOS or Prolonged inotropic support [¶]	1(1.67)	4(6.7)	0.3644 ^{ns}
Postoperative IABP¶	0(00)	2(3.3)	0.4958 ^{ns}
Total bleeding (ml) #	$378 \pm 45^*$	$602 \pm 60^*$	<0.0001 s
Amount of blood products needed (ml) #	690 ± 30 [*]	1085 ± 45 [*]	<0.0001 ^s
Length of ICU stay(hours) #	$34.7 \pm 0.9^*$	43.6 ± 1.5*	<0.0001 s
Length of post-operative hospital stay(days) #	$8.2 \pm 0.2^*$	$10.3 \pm 0.3^*$	<0.0001 s
Re-exploration for bleeding [¶]	1(1.67)	3(5)	0.6186 ^{ns}
Stroke [¶]	1(1.67)	2(3.3)	1.000 ^{ns}
Pulmonary complication	4(6.7)	6(10.0)	0.500 ^{ns}
Perioperative MI [¶]	1(1.67)	2(3.3)	1.000 ^{ns}
Arrhythmia [¥]	6(10.0)	12(20)	0.236 ^{ns}
Surgical site infection [¶]	4(6.7)	6(10.0)	0.500 ^{ns}
Renal dysfunction¶	4(6.7)	6(10.0)	0.500 ^{ns}

^{*} Data are presented as the mean \pm SD for continuous variable. # Student's t-Test, \pm Chi-square (ζ^2) Test, \P Fisher's Exact Test ns=Non-significant; \pm Significant

LOS= Low Output Syndrome

Discussion:

In the present study, we analyzed our experience with OPCAB in patients having multivessel disease with reduced left ventricular ejection fraction (d"50%). Although OPCAB approach has fewer short-term complications

than conventional CABG, incomplete revascularization is more common with off-pump approach, which led to more complications and repeat revascularization.¹⁶ Complete revascularization is believed to be important in producing a re-intervention-free result following

[#] Student's t-Test, Υ Chi-square (χ^2) Test, \P Fisher's Exact Test ns=Non-significant; s = Significant

OPCAB.¹⁷Meharwal et al. showed the average numbers of grafts were 3.0±0.7 for OPCAB group and 3.2±0.8 for on-pump group. 18 Shroyer et al. showed the average numbers of grafts were 2.9±0.9 for OPCAB group and 3.0±1.0 for on-pump group. 19 Youn et al. demonstrated in their study that patients with conventional CABG tended to have more grafts, but there was no significant difference in number of distal anastomoses and complete revascularization between the groups.²⁰Technical improvement and experience have led some surgeons to perform off-pump total arterial grafting using two internal thoracic arteries (ITA) or one ITA and radial artery for multivessel coronary artery disease in regular basis.²¹We have used intracoronary shunts in all patients during distal coronary anastomoses. Positioning and stabilization of the heart in OPCAB, specially during circumflex and posterior descending artery anastomosis, are associated with significant haemodynamic changes.²² These changes may be further exacerbated by the snaring of the coronary arteries. Several studies have shown the effectiveness of intracoronary shunts for maintaining myocardial perfusion to avoid ischemia of target vessels during OPCAB, although the use of shunts is not widespread and remains controversial.²³We have found intracoronary shunts useful.

The mean period of mechanical ventilation, amount of blood products needed, length of ICU stay and hospitalstay during the early post-operative period- all were significantly lower in OPCAB group. All these reflect definite clinical advantage as well as favorable economic outcome associated with OPCAB group of patients. Transmission of viral infections, induction of immunologic transfusion reactions, and suppression of the immune system remain important risks related to the transfusion of blood and blood products despite improvements in donor-screening methods.²⁴

OPCAB has been shown to be associated with decreased morbidity and mortality in high- risk patients, including the elderly, patients with poor left ventricular function, renal dysfunction, left main stenosis, or chronic obstructive pulmonary disease, and patients with prior neurologic dysfunction.²⁵As in many studies, our hospital mortalities for OPCAB and CCAB done on patients with multivessel disease with reduced left ventricular ejection fraction (d"50%)were comparable. Meharwal et al. reported that the operative mortality was higher in CCAB group (1.86% vs. 0.97%, p<.001).¹⁸ Ruzzeh et al. in amulti-centre comparative analysis showed similar result (1.4% vs. 2.9%)⁵. But, Sajja et al. (2.8% vs.3.9%, p=0.746) showed a bit different results.²⁶

Study Limitations:

The present study has several limitations and those are as follows:

- Sample size was small and patients were selected purposefully.
- 2. They were not randomly assigned to either group.
- The surgical procedure either OPCAB or CCAB was determined by the surgeon. Therefore selection bias may affect our findings.
- The duration of follow up of this study was limited. Clinical outcomes were restricted to 30-days mortality. No data beyond three months follow-up were available. Nothing was mentioned about the quality of life after CABG.
- As a single institutional study the conclusions may not be applicable in general because of differences in practice patterns of other centres.
- Other factors such as variations in surgical skill, patient difference in extent or distribution of coronary artery disease and echocardiography reports although unavoidable should also are considered.

Recommendations:

OPCAB surgery can yield better outcome in terms of shorter recovery time and less adverse effects than CCAB. We recommend OPCAB as a safe and effective surgical strategy for the patients with multivessel coronary artery disease with reduced left ventricular ejection fraction (d"50%). A prospective large scale multi-institutional randomized trial along with long term follow up and evaluation of graftpatency are necessary to confirm our findings and to define the long term clinical and functional results of both on-pump and off-pump CABG.

Development of well-trained cardiac surgical and anesthetic team, establishment of cardiac surgical centres equipped with modern devices, adequate logistic support and research of ischemic heart disease are needed to ensure up to date service and to widen the future prospects of revascularization procedures.

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Disclosure of Interests:

I have no potential conflict of interest with respect to the research, authorship, and/or publication of this article.

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