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## Original article

# Off-Pump Versus On-Pump Coronary Artery Bypass Surgery in Ischemic Heart Disease Patients with Impaired Contractility and Renal Dysfunction: A Comparative Study

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## ABSTRACT

**Background:** Coronary artery bypass surgery using cardiopulmonary bypass [CPB] carries the risk of renal impairment, which cannot be attributed to a single factor. This study compared the off-pump technique with the on-pump technique on kidney function in ischemic heart disease patients.

**Aim of the work:** The study aimed to compare off-pump with on-pump technique on kidney and heart functions in patients with renal impairment with no need for dialysis but with impaired Ejection fraction [EF].

**Patients and methods:** This prospective non-randomized study included 60 patients who presented with symptoms of ischemic heart disease and subsequently underwent myocardial revascularization with preoperative serum creatinine levels between 1.6 to 2.5 mg/dl and EF below 45%. Patients were as following: Group A patients [on-pump]: included those who underwent surgery on cardiopulmonary bypass. Group B patients [off-pump]: included those who underwent off-pump surgery. Both groups were compared in terms of renal impairment markers and needed for dialysis and early postoperative outcome.

**Results:** Renal impairment needs management by dialysis was developed in nine patients [30%] in the pump group [group I] and two patients [7.67%] in the off-pump group, with a significant difference. Group [I] showed a significant increase of transfused blood, blood urea nitrogen, serum creatinine, acute kidney injury [13 patients], reopening for bleeding, postoperative renal impairment, need for renal dialysis, total intensive care unit stay, and the total duration of hospital admission. However, it had a significant reduction in hemoglobin and creatinine clearance.

**Conclusion:** Off-pump coronary revascularization offers a better kidney function preservation and has a decreased risk for kidney dysfunction in patients with renal impairment without dialysis compared with coronary revascularization with cardiopulmonary bypass.

**Keywords:** Coronary artery; On Pump; Coronary revascularization; Renal insufficiency; Dialysis.

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\* Main subject and any subcategories have been classified according to the research topic.

## INTRODUCTION

Myocardial revascularization has been considered the mainstay in coronary artery disease management for the last 50 years. Coronary artery bypass grafting [CABG], since the 1960s, is the most intensively studied surgical intervention ever undertaken<sup>[1]</sup>.

Coronary artery bypass grafting [CABG] performed using cardiopulmonary bypass [CPB] has been the ideal treatment for patients with ischemic heart disease. However, there has been increasing evidence that CPB may be responsible for part of the morbidity associated with CABG surgery<sup>[2]</sup>.

Recently, CPB was considered a crucial factor for creating a perfect vascular anastomosis. Because of CPB's many undesired effects, especially in elderly and risky candidates being taken up for CABG, off-pump coronary artery bypass surgery [OPCAB] is gaining importance<sup>[3]</sup>.

Beating heart surgery is becoming a safe alternative to conventional myocardial revascularization. It is thought to be a more physiological method with the possibility of reducing mortality and morbidity<sup>[4]</sup>.

Patients with low EF and impaired renal functions preoperatively have significant intraoperative and postoperative complications and mortality and require an efficient preoperative assessment to verify surgical indication and optimum intervention modalities to decrease these consequences<sup>[2]</sup>.

Perioperative renal impairment is the main determinant of operative and long-term mortality following surgery. Even patients with mild renal dysfunction before surgery are more prone to experience acute kidney insult [AKI] afterward with a compromised outcome<sup>[5]</sup>.

## AIM OF THE WORK

The current work aimed to evaluate practice with coronary artery bypass surgery in patients with impaired kidney functions with preoperative serum creatinine 1.6 to 2.5 mg/dl and impaired cardiac function with preoperative EF [25% up to

40%]. The two interventions surgery using off-pump technique or using cardiopulmonary bypass technique in a trial to reach a conclusion about which technique may be safer regarding preserving kidney and heart function and associated morbidities in these patients.

## PATIENTS AND METHODS

### Study design:

This prospective non-randomized study included 60 patients who had symptoms of coronary artery disease [CAD] and so underwent myocardial revascularization with preoperative serum creatinine levels between 1.6 to 2.5 mg/dl and EF below 45% at Kasr El-Aini, Banysuef University Hospital, and Al-Azhar University Hospitals [Centers for both on and off-pump coronary artery bypass grafting surgery]. Patients were divided into two groups according to the surgeon's practice choice and his experience as following: Group [A] included patients [on-pump] included those who had myocardial revascularization using cardiopulmonary bypass, and Group [B] included patients [off-pump]: included those who had off-pump myocardial revascularization. Each patient's written informed consent was obtained preoperatively for data collection and use.

### Inclusion and exclusion criteria

The study **included** any patient submitted to CABG with preoperative serum creatinine levels between 1.6 to 2.5 mg/dl [level who do not need maintenance dialysis] and poor or LVEF < 45%.

The **excluded** patients were: those who underwent combined surgery, for example, CABG alongside valve surgery, patients on regular dialysis, urgent cases, patients planned for off pump CABG and reverted to on pump due to hemodynamic instability and finally patients for redo CABG.

### Management protocol

#### Preoperatively:

Assessed preoperative items were age, gender, smoking, hypertension, diabetes mellitus, routine preoperative laboratory investigations

[complete blood count [CBC], renal function tests, estimated glomerular filtration rate preoperatively [Glomerular Filtration Rate [GFR] calculated by Cockcroft and Gault's formula, resting 12-lead electrocardiogram [ECG], plain chest X-ray, cardiac catheterization, and pre-operative baseline transthoracic echocardiography [TTE].

#### **Intraoperative:**

The analyzed operative items included intraoperative mortality, aortic cross-clamping [ischemic] time, cardiopulmonary bypass [CPB] time, hemodynamics, inotropic support demand, and blood transfusion, and need for intra-aortic balloon counterpulsation.

#### **Postoperatively:**

All patients were followed-up during ICU stay for hemodynamic status, blood transfusion, blood glucose level, the need and duration of inotropic support, daily laboratory investigations, and total ICU stay. All patients were followed-up during a postoperative hospital stay for postoperative adverse complications [ low cardiac output syndrome, hemorrhagic complications, acute kidney injury], the total duration of hospital stay, and routine postoperative TTE. Perioperative mortality was considered as death occurring during the 30 days postoperatively. Hemorrhagic complications were defined by re-operation to control bleeding or relieve cardiac tamponade. Acute kidney injury was defined as an increase in the creatinine level [absolute  $\geq 0.3$  mg/dl, percentage  $\geq 50\%$ ] needing treatment or dialysis.

#### **Statistical analysis:**

All patients' data were tabulated and processed using SPSS V13.0 [SPSS Inc., Chicago, IL] for Windows 2007. Quantitative variables were expressed using mean and standard deviation and were compared using the t-student test. Qualitative variables were compared using the Chi-square test or Fischer's exact test when appropriate. Correlation between parameters was performed using Spearman's rank correlation coefficient. In all tests, the p-value was considered significant when

$p < 0.05$ , highly significant when  $p < 0.01$ , and extremely significant when  $p < 0.001$ .

**Sample size justification:** A sample size calculation was performed depend on MedCalc® version 12.3.0.0 program "Ostend, Belgium," and calculation of statistical calculator based on 95% confidence interval and power of the study 95 % with  $\alpha$  error of 5%. The sample size was 60 patients; 30 patients in each group.

## **RESULTS**

Between April 2017 and March 2019, 60 documented ischemic heart disease patients necessitating coronary artery bypass grafting were used. Patients were divided into two groups according to the surgical preference of performing surgery using cardiopulmonary bypass or off-pump.

#### **Preoperative data:**

The study populations were 48 [80%] males and 12 [20%] females whose ages ranged from 33 to 72 years with a median age of 52.7 years. Further interpretation of the preoperative patients' characteristics of the 2 groups is summarized in [Table 1].

#### **Operative data:**

All patients of the 2 groups were submitted for CABG. No intraoperative mortality occurred. Group [I] showed statistically significant results in total operative time. [Table 2] illustrates the analyzed operative data.

#### **Postoperative data:**

All the patients were discharged to the ICU mechanically ventilated and discharged to a regular room after stabilization. Group [I] showed a statistically significant increase in blood transfusion, blood urea nitrogen, creatinine, acute kidney injury, reopening for bleeding, postoperative renal impairment, need for renal dialysis, total ICU stay, and the total duration of hospital admission. But, it had a significant reduction of hemoglobin concentration and creatinine clearance. Postoperative data are expressed in [Table 3].

**Table [1]:** Patients' preoperative characteristics

	Group [I] [n=30]	Group [II] [n= 30]	P-value	Significance
Age [years]	52.40 ± 20.38	51.66 ± 24.43	>0.05	NS
Female/male	5/25 [16.29%]	7/23[23.88%]	>0.05	NS
Dyslipidemia	90 [83.33%]	28 [77.77%]	>0.05	NS
Smoking	8 [25.92%]	9 [30.22%]	>0.05	NS
HTN	27 [90.11%]	24 [80.66%]	>0.05	NS
Previous M.I	14 [46.25%]	12 [41.11%]	>0.05	NS
Diabetes mellitus [DM]	18 [60.55%]	19 [58.11%]	>0.05	NS
Angina pectoris as main symptom	23 [75.41%]	21 [70.55%]	>0.05	NS
Shortness of breath as main symptom	7 [25.03%]	9 [30.88%]	>0.05	NS
Heart rate preoperative	88.37 ± 9.72	72.65 ± 11.03	<0.05	Significant
LVEDD [cm]	6.01 ± 0.5	5.69 ± 0.7	>0.05	NS
F.S [%]	24.10 ± 6	22 ± 5	>0.05	NS
EF [%]	32.7 ± 13.1	34.3 ± 9.5	>0.05	NS
Hemoglobin [gm/dl]	11.5 ± 1.6	11.4 ± 1.3	>0.05	NS
B.U.N [mg/dl]	35.5 ± 17.7	31.5 ± 12.9	>0.05	NS
Creatinine clearance [mg/dl]	41.46 ± 8.45	40.47 ± 9.38	>0.05	NS
Creatinine [mg/dl]	1.87 ± 0.34	1.85 ± 0.25	>0.05	NS
FBG	127.8 ± 31.1	123.3 ± 19.1	>0.05	NS

HTN: Hypertension, LVEDD: Left Ventricular End-Diastolic Diameter, FS: fraction shortening, EF: Ejection fraction, ALT: Alanine transaminase, AST: Aspartate transaminase, FBG: Fasting blood glucose.

**Table [2]:** Intraoperative data

	Group [A] [n= 30]	Group [B] [n= 30]	p-value	Significance
Total operation time [min]	344.60 ± 57.54	273.77 ± 43.07	<0.05	Significant
Total CPB time [min]	112.40 ± 37.8	-	-	-
Total cross clamp time [min]	67.50 ± 24.18	-	-	-
Number of distal anastomoses	3± 0.5	3.23±1.1	>0.05	NS
Need for DC shock	10 [ 33.3 %]	12 [37.12]	>0.05	NS
Need for IABP	7 [23.3 %]	5 [16.6]	>0.05	NS
Need for inotropic support	29 [96.67%]	27 [90%]	>0.05	NS

CPB: Cardiopulmonary bypass, DC shock direct current cardio version, IABP intra-aortic balloon counter pulsations.

**Table [3]:** Postoperative data

	Group [A] [n= 30]	Group [B] [n= 30]	p-value	Significance
Inotropic support [hrs]	24 [72 %]	20[ 66%]	>0.05	NS
Reoperation for bleeding	7 [ 22.78]	2 [6.67%]	<0.05	Significant
Blood transfusion	935.33±495.71	580±238.90	<0.05	Significant
Creatinine [mg/dl]	2.62±0.87	1.98±0.66	<0.05	Significant
BUN	49±15.36	32.5±15.43	<0.05	Significant
Creatinine clearance	30.87±11.04	39.84±13.68	<0.05	Significant
Hemoglobin	9.42±1.10	10.35±0.89	<0.05	Significant
Postoperative renal dysfunction	13/30 [43.33 %]	-	<0.05	Significant
Total ICU stay [days]	3.67±3.33	2.70±2.15	<0.05	Significant
Postoperative M.I	3/10 [10 %]	3/30 [ 10 %]	>0.05	NS
Postoperative E.F	28±7	32±5	>0.05	NS
Postoperative F.S	26±5	24±5	>0.05	NS
Postoperative LVEDD	6±0.5	5.8±0.5	>0.05	NS

BUN; Blood urea nitrogen, MI; Myocardial infarction, EF; Ejection fraction, FS; fraction shortening, LVEDD; Left ventricular end diastolic diameter ICU: Intensive care unit.



## DISCUSSION

This work documented the early outcome of isolated CABG, using cardiopulmonary bypass and off-pump, for patients with basal serum creatinine [1.6 to 2.5 mg/dl] who do not need maintenance hemodialysis and who have low EF. We examined if off-pump coronary revascularization offers better kidney preservation and early postoperative outcome in general when compared with the standard on-pump technique.

The aim to decrease kidney injury and an associated complication is an essential item that may control the decision to perform CABG without CPB<sup>[6]</sup>. Results indicate that CPB avoidance by using current off-pump techniques significantly reduces the risk for postoperative kidney injury after CABG.

In this study, the mean age in the two groups was relatively younger than in other studies. **Ueki et al.**<sup>[6]</sup> and **Elmahrouk et al.**<sup>[7]</sup> stated that the mean age was above 60 years. This study's younger mean age may be due to higher risk factors, especially smoking, dyslipidemia, and sedentary lifestyle, which are common in most developing countries, including Egypt. For example, **Mahmoud et al.**<sup>[8]</sup> reported that, in the on-pump group, 56 % of patients had diabetes, 70% were hypertensive, 48.5% had a history of myocardial infarction [MI], 65.5% were smokers, and 48.5% had dyslipidemia. In the OPCAB group, 51.5% of candidates had diabetes, 68% were hypertensive, 41.5 % had a history of myocardial infarction, 70 % were smokers, and 41.5 % had dyslipidemia. No statistical significance regarding the comorbidities, which was nearly comparable to our study. Otherwise, **Dalén et al.**<sup>[9]</sup> Keeps risk factors constant.

The mean EF was 30% in the two groups. It is comparable to the mean EF in other studies; **Li S et al.**<sup>[10]</sup> for example, reported EF of 37% in the two groups; while **Mahmoud et al.**<sup>[8]</sup> reported EF of 30% in both groups, as in the current study.

Although the EF is a good indicator for the

outcome of surgery; yet some patients with no increase in the EF have still better follow up; low EF is not an obstacle to surgery, especially with the new advents in the anesthetic, surgical techniques, medications, machines and advanced technology in ICU<sup>[8]</sup>

In patients with low EF, OPCAB was associated with a significant reduction of reoperation, perioperative transfusion, prolonged ICU, and hospital stay.

These results are not different than the largest retrospective study of OPCAB in patients with low cardiac function, which showed the clinical impact of OPCAB<sup>[11]</sup>, but that was not the case with the large randomized controlled trials [the ROOBY and CORONARY trials] did not show improved mortality in the OPCAB groups.

However, in both studies, patients with an EF<0.35 comprised only a small portion of the entire cohort. In the ROOBY trial, patients with impaired EF accounted for only 5.7% of the entire cohort, whereas in the CORONARY trial, patients with a low EF accounted for only 5.4% of the OPCAB group and 5.6% of the ONCAB group. Therefore, these trials could not reach definite conclusions about the best surgical coronary revascularization technique in low-EF patients<sup>[12,13]</sup>.

In this issue, large retrospective studies using suitable risk-adjustment tools are still needed to consider an appropriate management modality for candidates with a low cardiac function undergoing CABG.

Avoidance of transfusion is considered among the most important benefits of eliminating extracorporeal circulation. Many studies have shown the relation of OPCAB with decreased need for transfusion in patients with a low EF<sup>[14-16]</sup>; especially, Puskas and colleagues' well-designed randomized trial showed that OPCAB decreased the occurrence of coagulopathy. Other recent studies have shown that perioperative blood transfusion requirement was significantly associated with increased CABG complications.

This finding points that a decrease in transfusion requirement could explain the lower mortality in our OPCAB group<sup>[17-18]</sup>.

There was no significant difference in mean early post-operative EF between on and off-pump patients, unlike other studies like **Mahmoud et al.**<sup>[8]</sup> that was  $[28.1 \pm 5.2. \%]$  in the on-pump group and  $[31.4 \pm 11\%]$  in the off-pump group and **Li S et al.**<sup>[10]</sup> that was  $[29.2 \pm 6.5\%]$  in the on-pump group and  $[33.6 \pm 7.12\%]$  in the off-pump group. In other studies, the EF increased slowly in the first 3 months, so the judgment of whether this patient will have an improvement in EF or not after CABG is not an early one<sup>[19]</sup>

Preoperative renal function, which is one of the strongest prognostic factors, should also be considered when interpreting the less risk-benefit of OPCAB that we have demonstrated in this study. We have [13] patients in the pump group [43%] Vs. [3] patients in the off-pump group [10%] who had impaired postoperative kidney functions. In the on-pump group, there were [9] patients who required dialysis [30%], and they were among the group of [13] patients who were diagnosed as postoperative renal dysfunction, while in the off-pump group [2] patients required dialysis [6.76%] and they were among the [3] patients who had postoperative renal dysfunction. Comparing that to other studies as following **Mahmoud et al.**<sup>[8]</sup> that shows [27%] of patients in pump group who had impaired postoperative renal dysfunction and [7%] of those had needed renal dialysis while in the off-pump group [6%] of patients had impaired postoperative renal functions and [2.3%] of those needed hemodialysis and also **Arslan et al.**<sup>[20]</sup> that shows [18.75 %] of patients in the pump group who needed renal dialysis while in the off-pump group [2.77%] only needed renal dialysis.

From 13 patients who developed postoperative renal impairment, nine patients needed dialysis, analysis of risk factors showed that 5 were older than 70 years and all patients were hypertensive and had EF below 35% and had preoperative renal impairment; 3 patients had previous MI and pump time > 3 hours, and three patients were reopened

for surgical bleeding. The off-pump group revised the data showed that two patients were hypertensive, diabetic, had previous MI, EF below 35%, and impaired preoperative kidney functions and reopened post-operative for bleeding.

From this, we found that there is statistical significance for an elevated level of creatinine postoperatively between the off-pump group and on-pump group, and this reflected the role of CPB in elevating the postoperative level of creatinine. Statistical significance was found for post-operative renal dialysis events for the two groups [30% required dialysis in on-pump versus 6.66% in the off-pump group]. The systemic inflammatory response related to CPB has been claimed to affect multiple organ systems, including the kidney, adversely. CPB was recognized as an independent cause of acute renal failure. Performing CABG without CPB can prevent renal function affection by avoiding non-pulsatile flow, interactions between the inflammatory, coagulation, and fibrinolytic cascades. This could cause a positive impact, particularly in high-risk patients<sup>[21]</sup>.

More recently, CORONARY multicenter study showed a significant reduction in the incidence of acute kidney injury in the OPCAB population.<sup>[13]</sup> In most of the reviewed studies, including ours, renal function is better preserved in patients undergoing off-pump CABG than those undergoing on-pump CABG. Today, despite the appearance of techniques related to anesthesia and CPB, the incidence of postoperative kidney injury varies from 2.5% to 31% and is still associated with an overall mortality rate of 67%<sup>[11]</sup>

This study indicates that avoidance of CPB by using current off-pump techniques significantly reduces the risk for postoperative kidney injury after CABG. Also, it is notable that, in this study, there is a higher percentage of candidates who developed postoperative renal dysfunction requiring dialysis postoperatively than in the other different studies, especially in the pump group, but this is expected as the small number of patients in our study. The inclusion criteria for all patients



were patients with preoperative renal impairment [serum creatinine 1.6-2.5 mg/dl], but so many of these studies included patients with normal kidney functions preoperatively and measured the affection beyond normal renal function.

**Study limitations:** The most important limitations in this study is the small number of patients. Lack of randomization also subjected it to selection bias. Limiting the study to a limited period of early postoperative time did not allow us to reach a meaningful conclusion of the benefits of the off-pump over on-pump technique. Socioeconomic obstacles precluded performing more accurate patient assessment regarding graft patency and perfusion studies, which can add a lot of important data in the follow-up period.

**Conclusion:** Many patients with ischemic heart disease and marked left ventricular dysfunction and impaired kidney function, and so many surgeons try to find the perfect technique for revascularization of this high-risk group. General Measures to prevent kidney injury after Cardiac Surgery should be utilized in patients with special attention to those with preoperative impaired kidney function. Renal function is better preserved in patients who underwent off-pump CABG than those undergoing on-pump CABG. CPB was found to have a higher risk for PRD, and this injury is associated further with complications and mortality. Based on previous data, off-pump CABG can be recommended as a safe option in patients with impaired renal functions and marked left ventricular dysfunction with better results than on-pump CABG regarding postoperative renal impairment.

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**Study registration and ethical aspects:** Al-Azhar University Research Centre Ethical Committee approved the study; informed consent was obtained from each patient before participation in the study after a full explanation of the study protocol

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