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Research Article

Off-Pump *versus* On-Pump Complete Coronary Revascularization: Comparison of the Effects on the Renal Damage in Patients with Non- Dialysis Dependent Renal Dysfunction

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Keywords On and off-pump coronary revascularization; Coronary artery bypass grafting; Renal insufficiency; Requiring dialysis; Surgical complications

Abstract

Objective: We aimed to compare off-pump technique with on-pump technique on renal function in patients with non-dialysis-dependent renal dysfunction who underwent CABG.

Introduction: Preoperative non-dialysis-dependent renal dysfunction is a predictor of renal failure in patients undergoing CABG with CPB. Off-pump coronary revascularization has been shown to be less deleterious than on-pump bypass in patients.

Methods: The 94 patients with renal dysfunction undergoing isolated coronary artery bypass grafting were retrospectively analyzed. No patient was receiving dialysis. Patients were randomly assigned to conventional revascularization with CPB and beating heart. Both groups were compared in terms of renal dysfunction parameters and dialysis requirement. The logistic regression models were constructed to identify risk factors associated with dialysis requirement.

Discussion: Renal dysfunction requiring dialysis developed in 9 patients in the on-pump group. The measures analysis of variance was performed on the data that showed worsening of renal function in the on-pump group compared with the off-pump group. CPB is significant as independent predictor for the development of postoperative dialysis.

Conclusion: These results suggest that off-pump coronary revascularization offers a superior renal protection and has a significantly lower risk for renal complications in patients with non-dialysis-dependent renal dysfunction when compared with conventional coronary revascularization with CPB.

Introduction

Despite improvements in surgical techniques, postoperative renal dysfunction remains a serious complication of coronary revascularization surgery and is associated with significant increases in morbidity and mortality, whether it is dialysis-dependent or not. It has been reported that acute renal failure requiring dialysis develops in 2-7% of cardiac surgery patients [1-6]. Although the cause is multifactorial and depends on the patient's clinical status, cardiopulmonary bypass (CPB)-related events, hypotension, renal hypoperfusion, hypothermia, microemboli events in the renal vasculature, non-pulsatile flow, hemolysis, stimulation of the inflammatory response, and increased levels of circulating catecholamines, cytokines, and free hemoglobin may contribute significantly to this condition [7,8]. Furthermore, the use of aortic cross-clamping and cardioplegic arrest can result in myocardial dysfunction, which can lead to renal perfusion defects and subsequent renal impairment [9,10]. However, the explicit contribution of these factors still remains unclear and needs to be fully elucidated.

These effects result in damage to glomerular as well as tubular structures that, in turn, can produce renal dysfunction especially in the presence of additional risk factors. The renal risk associated with CPB may be avoided by a new surgical technique, off-pump coronary revascularization, which is performed on the beating heart and hence does not use CPB [11].

Off-pump coronary revascularization is known to eliminate several CPB-linked non-physiological conditions. Due to the fact that off-pump coronary revascularization eliminates the use of CPB and cardioplegia, the CPB- and cardioplegia associated morbidity and mortality risks are significantly reduced compared to patients undergoing conventional on-pump coronary revascularization. Recently, the benefits of off-pump coronary revascularization have been well established, and several studies have revealed that off-pump coronary revascularization has better outcomes in patients with renal dysfunction than conventional on-pump coronary revascularization

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[12-14]. However, studies conducted previously in this field have provided conflicting evidence to support this hypothesis, and the data on this topic remain contradictory [8,15-18].

This randomized study was to assess the impact of the off-pump coronary revascularization technique on the incidence and severity of renal dysfunction according to on-pump coronary revascularization technique in patients with preoperative non–dialysis-dependent renal insufficiency. The renal functions have been defined according to the levels of serum blood urea nitrogen, creatinine, creatinine clearance and glomerular filtration rate called glomerular filtration markers. Besides, independent risk factors associated with requiring dialysis were identified.

Materials and Methods

This study was designed to compare the effect of off-pump and on-pump coronary artery bypass grafting (CABG) techniques on renal function in patients with non–dialysis-dependent renal insufficiency. In this retrospective study, from May 2014 through June 2015, 94 consecutive patients with preoperative non–dialysis-dependent renal insufficiency was performed primary, isolated, nonemergent coronary surgery. Patients were prospectively randomized on the day before their operation into two groups by card allocation. Group on the pump (n=48) had conventional myocardial revascularization with CPB and cardioplegic arrest of the heart, whereas group off the pump (n=46) had to beat heart revascularization. Each on-pump and off-pump coronary revascularization was performed with the goal of achieving complete surgical revascularization. Patients were assigned to one of the surgical techniques according to clinical indications as well as to the surgeon's decision to use the off-pump or the conventional on-pump approach.

The preoperative demographics, operative variables, operative morbidity and mortality, short-term survival, cardiac-related event, postoperative renal parameters, requiring dialysis and postoperative data were compared between the 2 groups. The preoperative data and values indicating the preoperative renal dysfunction were shown in Table 1. Factors looked at were considered to be good predictors of postoperative renal complications as postoperative Blood Urea Nitrogen (BUN), creatinine, creatinine clearance, Glomerular Filtration Rate (GFR) and requiring dialysis. After comparing renal dysfunction associated with parameters and requiring dialysis between groups, risk factors associated with requiring dialysis were determined by logistic regression analysis.

In our study, data was collected from patients' case notes in the Medical Records Office. The data were prospectively collected and recorded by clinical cardiology and cardiac surgeon. The study was approved by the Erzurum Regional Training and Research Hospital Ethics Committee. The local institutional review board approved this study and waived the need for informed consent. The study is in accordance with the declaration of Helsinki.

Data definition

BUN is an indication of renal kidney health. The reference range of the BUN level is 10-50 mg/dL. Individual laboratories may have different reference ranges, since the procedure may vary. BUN levels of >50 mg/dL or least a 20 % increase without requiring dialysis was considered renal dysfunction. The reference ranges of serum creatinine in our laboratory were 0.4-1.1mg/dl. Creatinine levels of >1.5 mg/dL or least a 20 % increase without requiring dialysis was considered renal dysfunction. Creatinine clearance was calculated using the Cockcroft and Gault Formula: (140-age) x kg / serum creatinine (mg/dL) x 72), and reference ranges of serum creatinine clearance in our laboratory were 80-120ml/min^{-1}/1.48m^{-2}. Creatinine clearance ≤ 60mL/dk/1.73 m^{2} or decreases of 50 % or higher without requiring dialysis was considered renal dysfunction. The GFR was measured with the MDRD equation (mL/min-1/1.73m^{-2}). The variables included were age, sex, height in centimeters, and weight in kilograms for body surface area calculation, BUN, serum creatinine, and serum albumin. The formula used is as follows.

170 x (Cr) $^{-0.999}$ x (Age) $^{-0.716}$ x (BUN) $^{-0.070}$ x (Alb) $^{+0.318}$ for male patients

170 x (Cr) $^{-0.999}$ x (Age) $^{-0.716}$ x (BUN) $^{-0.070}$ x (Alb) $^{+0.318}$ x (0.762) for female patients. These stages are defined by a GFR greater than or equal to 90 (stage 1), 60 to 89 (stage 2), 30 to 59 (stage 3), 15 to 29 (stage 4), and less than 15 (stage 5). Generally, decreases of 50% or higher in the GFR was considered renal dysfunction. These parameters were measured postoperatively at day 7 and confirmed in at least two measurements.

Non-requiring dialysis renal dysfunction: BUN levels; 30- 60 mg/dL, median GFR; stage I, creatinine levels; 1.3-1.7 mg/dL, creatinine clearance; 40-70 mL/min.

Requiring dialysis: Acute renal dysfunction was classified on the basis of RIFLE (Risk, injury, failure, loss, ESRD) criteria [19]. Postoperative dialysis was indicated if they had diuretics-resistant oliguria associated with volume overload or hyperkalemia. Postoperative renal failure was defined as either a requirement of hemodialysis to support renal function, an increase in serum creatinine greater than 1.5 mg/dl postoperatively, or an occurrence of oliguria (<0.5ml/kg^{-1}/min^{-1}) for more than 6h.

Postoperatively, all patients were admitted to the Intensive Care Unit (ICU), and received standardized treatment. Anesthesia was maintained in all patients with propofol (100 mg/h) for no longer than 24 h postoperatively. When longer anesthesia was required, propofol was switched to sufentanil (0.02 mg/h) and midazolam (5 mg/h). The fluid substitution was adjusted to a central venous pressure of 12 mmHg. The target level for the mean arterial pressure was ≥ 70 mmHg. Crystalloid fluids and inotropes were administered in the case of lower mean arterial pressure according to the specific clinical situation. In the absence of hemorrhage, intravenous heparin was applied for 2 h and 500 mg of intravenous acetylsalicylic acid 4 h after arrival on the ICU. In-hospital outcomes were collected from the medical records. Post discharge outcomes were collected from the medical records and telephone interviews. These data were complete for all patients until discharge from hospital or death.

Exclusion criteria

Patients who underwent combined procedures were excluded. Exclusion criteria were patients with mechanical complications of myocardial infarction such as ventricular septum defect, papillary muscle rupture, mitral valve regurgitation, and patients with cardiogenic shock persisting for a length of 24 hours. Besides, it included impaired left ventricular function as assessed by angiography (ejection fraction <30%), patients with requiring chronic dialysis patients, oliguria and anuria, high serum creatinine level (≥ 2.5 mg/dl), emergency surgery or reoperation, respiratory impairment, and coagulopathy. All patients in both groups received 600 mg of N-acetylcysteine orally once daily immediately before revascularization and for the first 5 postoperative days. None of the patients received amino glycosides or nonsteroidal anti-inflammatory agent's perioperatively.

Anesthesia

Anesthetic technique was standardized for all patients and consisted of intravenous anesthesia with propofol infusion at 3 mg/kg per hour combined with remifentanil infusion at 0.5 to 1 mg/kg per minute. Neuromuscular blockade was achieved by using 0.1-0.15 mg/kg pancuronium bromide or vecuronium, and the lungs were ventilated to normocapnia with air and oxygen (45% to 50%) without positive end-expiratory pressure. Off-pump surgery was performed at a mean arterial pressure between 70 and 100 mmHg. Deviations beyond this range were corrected with phenylephrine or nitroglycerine. If necessary, esmolol hydrochloride (11 mg/kg) was used to maintain a heart rate less than 70 beats per minute.

Surgical techniques

All patients underwent surgical revascularization through a median sternotomy. Conduits were harvested and prepared. The arterial conduit (internal mammalian artery) was harvested with pedicle preparation technique using surgical electrocautery for left anterior descending artery anastomosis. Saphenous vein grafts were harvested with the open method using fine scissors, and they were used generally other cardiac coronary anastomosis. Two surgeons completed all procedures. The daily operation schedule, which established the order of all surgical procedures and scheduled the surgeons to these procedures, assigned patients to one of the two surgeons and by this means to either the off-pump or on-pump technique. A deep posterior pericardiotomy was carried out to allow for rigorous exposure of the heart without hemodynamic compromise. In both groups, a minimal dose of catecholamines was used to maintain a cardiac index of greater than $2.0L/min^{-1}/m^{-2}$ and systolic blood pressure of greater than 80mmHg after surgery. Intravenous diltiazem and nitroglycerin were administered routinely in the ICU.

Conventional CABG

Before CPB was initiated, heparin sodium was administered at an initial dose of 300 IU/kg. Additional heparin was administered if the ACT became less than 500s. CPB was instituted by using ascending aortic cannulation and a two-stage venous cannulation in the right atrium. The aorta was cross-clamped, and myocardial protection was achieved with intermittent antegrade and retrograde blood cardioplegia. A standard circuit was used, including a Bard tubing set, which included a 40-m filter, a roller pump, and a hollow fiber membrane oxygenator. During CPB, the hematocrit was maintained between 18% and 25%, perfusion flows were kept between 2.2 and $2.8L/min^{-1}/m^{-2}$, and mean arterial pressure was maintained between 50 and 70 mmHg. A 1000-mL cold cardioplegic solution (Custodiol®, Alsbach-Hahnlein, Germany) was infused through the aortic root to achieve cardioplegia during aortic cross-clamping. The nonpulsatile flow was used. Antegrade and/or retrograde cold blood cardioplegia was used to induce cardiac arrest, which was maintained by serial administration of additional aliquots at 15-min intervals. The systemic temperature was maintained between 30 and 34°C. Once all distal anastomoses were completed, the aortic cross-clamp was removed and the proximal anastomosis performed with partial clamping. The distal anastomoses were constructed with running sutures of 7-0 or 8-0 polypropylene, and the proximal anastomoses were connected to the ascending aorta with 5-0 or 6-0 polypropylene sutures during a single cross clamping period. After the patient was weaned from CPB and decannulated, heparin was completely neutralized using protamine (1/1.5 rate; Valeant, Eschborn, Germany). Epicardial pacemaker wires were inserted on the surface of the right ventricle for the heart rate manipulations, then the heart was filled with volume adequately and the table broke for variable "head down" Trendelenburg position manipulations.

Off- pump beating-heart technique

After cardiac stabilization, the operation was continued with the assisted beating heart. The temperature of patients was kept approximately 36°C without cooling (normothermic). After mediastinal entry, deep pericardial sutures were placed to lift the myocardial apex and facilitate exposure to the posterior and lateral aspects of the myocardium. The distal anastomoses were constructed before the proximal anastomoses. The left anterior descending artery was revascularized first with the internal mammalian artery, followed by the circumflex and right coronary arteries. Stabilization during distal anastomosis was performed using the Octopus® stabilizing system (Medtronic Inc, Minneapolis, MN, USA), and if found necessary by the surgeon, Starfish heart suction stabilizer of the same manufacturer was used for additional traction and stabilization, prominently for the exposure of the circumflex region. Silicon suture applied proximally and distally to the site selected for the anastomosis and a surgical blower humidifier (Visu-Flow, Research Medical, Midvale, UT, USA) were used for visualization of the surgical field. Systolic arterial pressures were maintained at a minimum of 70 mm Hg during distal anastomoses using venous volume regulation, rate control, inotropic agents, or vasoconstrictors. Distal anastomoses were made with running sutures of 7-0 or 8-0 polypropylene. Intracoronary shunts were not used routinely during the distal anastomoses. In compliance with international experience, ischemia or hypotension was addressed by volume, heart rate, inotrope or beta-blocker-based manipulations and short release of too vigorous exposure and torsion. After each distal anastomoses, perfusion was maintained with warm blood through the pump by using anastomosed saphenous veins. Proximal anastomoses were performed with a side-biting aortic clamp, with systemic pressures that were dictated by individual surgeon preference. These patients received heparin sodium (150 IU/kg) before the anastomosis and the elite-activated clotting time was maintained at more than 300 s. Normothermia was maintained by using warm intravenous fluids, a heating mattress, and a humidified airway, in addition to maintaining a warm operating theater. Postoperatively, whole blood or packed red blood cells were transfused to all patients whose hemoglobin value was less than 9 mg/dL.

Statistical Analysis

Values of continuous variables are expressed as mean ± standard deviation (SD). Student's t-test and Mann-Whitney test were used to analyze continuous variables. The categorical or dichotomous data were presented in percentages (%) and compared by the Chi-square or Fisher's exact test, and p values of 0.05 or less were considered significant.

A univariate logistic regression analysis was performed to identify significant predictors associated with preoperative factors. Besides, the multivariable logistic regression analysis was used to identify independent risk factors for requiring dialysis. The results of the logistic regression analysis were presented as Odds ratios (OR) and 95% confidence intervals (CI). Statistically, significant differences were noted for each analysis, with statistical significance based on a p value of< 0.05. Statistical analysis was performed with SPSS version 11.5J (SPSS, Inc, Chicago, IL).

Results

The study consisted of 49 men and 45 women. The mean age was 49 ± 3.1 years for the off-pump group and 51 ± 2.5 years for the on-pump group. Pre- and intraoperative demographics characteristics of the 46 patients operated by the off-pump and the 48 patients operated by the on-pump technique are shown in Tables 1 and 2, respectively. There were no major differences between patients with regard to gender, age, severity of coronary disease, prevalence of diabetes, hypertension, hypercholesterolaemia, ejection fraction, New York Heart Association functional class, and surgical data such as number of distal anastomoses, and there was no statistically significant difference in preoperative serum creatinine, BUN, creatinine clearance, and GFR levels between the two groups. Conversion from off-pump to on-pump did not occur for any patients. All patients had an uneventful operation and postoperative stay.

Five patients in the on-pump group and 4 in the off-pump group were unstable, in-hospital patients treated with inotropic treatment and Intra-Aortic Balloon Pump (IABP). The severities of coronary heart diseasedid not differ between both cohorts as indicated by similar rates of left main, two- and three-vessel diseases. There was no statistically significant difference in the index of completeness of revascularization (Table 1).

Preoperative furosemide usage and total requirements of intravenous catecholamines and trinitrate during the first 48 h after surgery didn't found significant differences (Tables 1 and 2).

The cross-clamp time in the on-pump group was 56 ± 12 minutes and the perfusion time was 73 ± 13 minutes. Operation time was shortening in an off-pump group than the on-pump group (Table 2). This different was significant statistically (p= 0.012).

Preoperative renal function parameters are shown in Table 1; there was no significant difference between groups. Although there were renal function disorders in both groups, none of them had no indication of dialysis (Table 1). Postoperative data showed that impaired renal function parameters were less in the off-pump group. The increase in postoperative creatinine and BUN levels compared to the preoperative value was markedly higher in the on-pump group (p=0.006 and p=0.007). The decreases in the GFR and the creatinine clearance levels were higher in the on-pump group as opposed to the off-pump group (p=0.002, p=0.004) at postoperative days 7 (Table 3). Nine patients in the on-pump group had required dialysis, whereas only 1 patients in the off-pump group had required dialysis (p=0.0001). Consequently, it was deduced that renal dysfunction was higher in the on-pump group than in the off-pump group after cardiac surgery.

By using stepwise logistic regression analysis 12 variables were identified as independent predictors of postoperative requiring dialysis, and were presented in Table 4. The use of cardiopulmonary

Table 1: Preoperative patient characteristics among groups.

Variables	Off-pump (n=46)	On-pump (n=48)	P Value
Median age	49 ± 3.1	51 ± 2.5	0.76
Sex			0.88
Male	24(52.1%)	25 (52%)	
Female	22(47.9%)	23(48%)	
BMI (kg/m^2)	29.5 ± 3.8	30.2 ± 3.1	0.207
Hypercolesterolemi	28 (60.8%)	30 (62.5%)	0.421
DM	33 (71.7%)	35 (72.9%)	0.528
CVD	2 (4.3%)	1 (2%)	0.442
COPD	18 (39.1%)	20 (41.6%)	0.338
Smoking	121 (65%)	118(65.5%)	0.289
Hypertension	34 (73.9%)	33 (68.8%)	<0.05
PAD	9 (19.5%)	11 (22.9%)	0.19
Left main disease	9	11	0.189
Three vessel disease	19	21	0.237
Two vessels disease	18	16	0.304
Hematocrit	44 ± 2	45 ± 3	0.777
NYHA	3.3 ± 0.45	3.2 ± 0.6	0.589
Preop AF	2 (4.3%)	2 (4.1%)	
Preoperative IABP	4 (8.7%)	5 (10.4%)	0.144
History of MI	37 (80.4%)	39 (81.2%)	0.25
LVEF			
0.30-0.40	16	14	0.87
40-50	14	18	0.777
>0.50	16	16	0.651
Renal dysfunction not requiring dialysis			
BUN levels (mg/dL)	45 ± 12 (range; 30-59)	48±10 (range; 35-61)	0.399
Creatinin levels (mg/dL)	1.5 ±0.2 (range; 1.3-1.7)	1.5±0.3 (range; 1.3-1.6)	0.557
CCL (mL/min.)	59 ± 7 (range; 41-72)	61 ± 8 (range; 40-75)	0.902
Median GFR (Stage I)	77 ± 12 (range; 52-89)	76 ± 3 (range; 51-90)	0.766
Use of Diuretics	9 (19.5%)	10 (20.8%)	0.221

BMI: Body mass index; DM: Diabetes Mellitus; CVD: Cerebro-vascular disease; COPD: Chronic obstructive pulmonary disease; PAD: Peripheral arterial disease; UAP: Unstable angina pectoris; NYHA: New York Heart Association; AF: Atrial fibrillation; IABP: intra-aortic balloon pump; MI: Myocard infarction; LVEF: left ventricular ejection fraction; BUN: Blood urea nitrogen; CCL: Creatinin clearance; GFR: Glomerular filtration rate.

Table 2: Operative data.

Data	Off-pump (n=46)	On-pump (n=48)	p value
XCL time (min.)	0	56 ± 12	0.0001
CPB time (min.)	0	73 ± 13	0.0001
Operating time (h)	3.6 ± 1.2	5.1 ± 1.4	0.012
Number of distal anastomosis	3.0 ± 0.3	3.1 ± 0.4	0.409
LAD by pass	46	48	0.307
Diagonal branches	18	15	0.855
Cx by pass	13	12	0.652
RCA by pass	14	16	0.318
Complett revascularization	45 (97.8%)	48 (100%)	0.212
Coronary endarterectomy	7 (15.2%)	8 (16.6%)	0.327
Cumulative regional ischemic times (min.)	6.1 ± 4.2	7.2 ± 3.3	0.844
Postoperative IABP	3 (6.5%)	4 (8.3%)	0.307
IMA usage	44 (95.6%)	46 (95.8%)	0.855
Sequentional graft	2 (4.3%)	3 (6.2%)	0.652
Use of inotropes	11 (23.9%)	10 (20.8%)	0.318
Use of trinitrat	7 (15.2%)	9 (18.7%)	0.402
Hemodynamic data			
Mean BP (mmHg)	48±9	51±11	0.112
Mean heart rate (min.)	53±13	0 (cross clamping)	0.0001

XCL: Cross clamping; CPB: Cardiopulmonary bypass; IMA: Internal mammalian artery; LAD: Left anterior descending artery; Cx: Circumflex artery; RCA: Right coronary artery; BP: Blood pressure; IABP: Intra-aortic balloon pump.

bypass and increasing age were a significant factor on the univariate logistic regression analysis (OR: 2.91, 95% CI: 1.65-4.11, p= 0.0001 and OR: 0.71, 95% CI: 0.55-1.16, p= 0.002, respectively). Besides, operating time (OR: 1.09, 95% CI: 0.98–2.44, p= 0.038),hypertension (OR: 2.52, 95% CI: 1.26–5.18, p= 0.008), diabetes (OR: 2.90, 95% CI: 2.05–3.15, p= 0.001), smoking (OR: 1.99, 95% CI: 1.02–3.18, p= 0.022), multiple vessels disease (OR: 1.45, 95% CI: 0.17–3.10, p= 0.040), preoperative IABP (OR: 5.9, 95% CI: 4.66-12.01, p= 0.011), preoperative left ventricle ejection fraction (LVEF)< 40 (OR: 4.66, 95% CI: 2.01-9.62, p= 0.002), preoperative increased creatinine and BUN levels (OR: 0.85, 95% CI: 0.66–1.98, p= 0.001), preoperative deceased creatinine clearance and GFR levels (OR: 0.91, 95% CI: 0.73–2.02, p= 0.0001), and having had a previous myocardial infarction (OR: 0.41,

Table 3: Renal functions in the postoperative term.

Parameters associated with renal dysfunctions	Off-pump (n=46)	On-pump (n=48)	P value
BUN levels (mg/dL)	51 ± 18 (range; 35-72)	66 ± 19 (range; 42-88)	0.006
Creatinin levels (mg/dL)	1.6 ± 0.4 (range; 1.4-2.0)	1.9 ± 0.4 (range; 1.7-2.4)	0.007
CCL (ml/dk/1,73m²)	55 ± 9 (range; 40-65)	35 ± 8 (range; 22-52)	0.002
Median GFR	75 ± 11 (range; 50-88)	52 ± 15 (range; 35-67)	0.004
Requiring dialysis	1 (2.17%)	9 (18.75%)	0.0001

BUN: Blood urea nitrogen; CCL: Creatinin clearance; GFR: Glomerular filtration rate

Table 4: Results of Univariate Logistic Regression Analysis for Risk Factors Associated with requiring dialysis.

	Odds Ratio	95% CI	p value
Age > 70	0.71	0.55-1.16	0.002
Sex	4.66	2.01-9.62	0.521
Male			
Female			
Median weight (kg)	0.8	0.66-1.19	0.075
Cardiopulmonary bypass usage	2.91	1.65-4.11	0.0001
Operating time (h)	1.09	0.98-2.44	0.038
Cumulative regional ischemic times (min.)	0.11	0.08-2.13	0.52
Complete revascularization	0.41	0.35-0.60	0.075
Coronary endarterectomy	0.37	0.22-0.72	0.102
COPD	2.7	2.3-3.1	0.902
Multiple vessels disease	1.45	0.17-3.10	0.04
Smoking	1.99	1.02-3.18	0.022
PAD	1.19	1.01-1.33	0.521
History of MI	0.41	0.35-0.06	0.025
Hematocrit	3.79	2.41-6.88	0.101
Preoperative ACE inhibitors	0.49	0.22-4.16	0.209
Preoperative LVEF < 40	4.66	2.01-9.62	0.002
Diabetes mellitus	2.9	2.05-3.15	0.001
Hypertension	2.52	1.26-5.18	0.008
Use of diuretics	0.77	0.81-2.80	0.87
Preoperative increased Cr and BUN levels	0.85	0.66-1.98	0.0001
Preoperative decreased CrCL and GFR levels	0.91	0.73-2.02	0.0001
Preoperative IABP	5.9	4.66-12.01	0.011

ACE: Angiotensin converting enzyme; CPB: Cardiopulmonary bypass; CCL: Creatinine clearance; ICU: Intensive care unit; GFR: glomerular filtration rate; COPD:chronic obstructive pulmonary disease; PAD: Peripheral arterial disease; IABP: intra-aortic balloon pump; LVEF: left ventricular ejection fraction; CI: Cardiac index; PAP: Pulmonary artery pressure; CVP: Central venous pressure; BP: Blood pressure

95% CI: 0.35-1.06, p= 0.025) also showed a significant association with requiring dialysis.

A multivariate ordered logistic regression analysis (with propensity adjustment) was performed to compare the occurrence of requiring dialysis between patients having on-pump and patients having off-pump. The most significant contributor toward the occurrence of post-operative dialysis was the use of cardiopulmonary bypass with OR: 2.51, 95% CI: 1.33-3.77, p= 0.0001. Besides, diabetes mellitus and hypertension (OR: 3.10, 95% CI: 2.66–3.49, p= 0.001 and (OR: 2.52, 95% CI: 1.51-4.90, p= 0.008, respectively) significantly increased the risk of requiring dialysis. Other independent predictors of postoperative dialysis were ejection fraction < 40%, multiple vessels disease, the excess of preoperative creatinine and BUN levels, the lack of preoperative of creatinine clearance and GFR rates, and age > 70 were determined to be among other risk factors. These variables are summarized in Table 5, with their regression coefficient, adjusted odds ratios, and p values.

Table 5: Multivariate Logistic Regression Analysis for Risk Factors Associated with requiring dialysis.

	Odds Ratio	95% CI	P value
Age > 70	0.82	0.61-1.33	0.001
Cardiopulmonary bypass	2.51	1.33-3.77	0.0001
Preoperative LVEF < 40	4.11	2.99-8.88	0.002
Diabetes mellitus	3.1	2.66-3.49	0.001
Hypertension	2.52	1.51-4.90	0.008
Multiple vessels disease	1.1	0.85-2.76	0.04
Preoperative increased Cr and BUN levels	0.78	0.54-1.18	0.0001
Preoperative desceased CrCL and GFR levels	0.82	0.63-1.86	0.0001

Table 6: The clinical results after cardiac surgery.

	Off-pump (n=46)	On-pump (n=48)	p value
Early Results			
Extubation time (h)	4.1 ± 2.1	3.1 ± 2.3	0.701
Surgical revision for bleeding	2 (4.3%)	9 (18.7%)	0.001
Postoperative bleeding > 1000 mL	7 (15.2%)	18 (37.5%)	0.008
Blood transfusion (unite/patients)	0.87 ± 0.66	1.22 ± 0.77	0.002
Chest tube drainage (ml/day)	310 ± 125	588 ± 140	0.007
Operative mortality (first 24 hours)	0 (0%)	0 (0%)	-
Postop MI	0 (0%)	0 (0%)	-
Postop term LCOS	2 (4.3%)	1 (2.08%)	0.902
Postop term IABP	4 (8.7%)	5 (10.4%)	0.751
Postop term AF	3 (6.5%)	4 (8.3%)	0.666
Stroke	0 (0%)	0 (0%)	-
Prolonged intibation	3 (6.5%)	3 (6.2%)	0.282
Duration of inotropic support (days)	7.2 ± 4.3	3.1 ± 4.1	0.188
Late results			
Cardiac arrhthmia	4 (8.7%)	3 (6.2%)	0.247
Postop EF %			
>50	34 (73.9%)	37 (77.1%)	0.225
<50	12 (26%)	11 (22.9%)	0.578
Sternal infection	1 (2.2%)	1 (2.1%)	0.689
Nosocomial infection	1 (2.2%)	4 (8.3%)	0.048
Multiple organ dysfunction	0 (0%)	2 (4.2%)	0.033
Neurological dysfunction	0(0%)	1 (2.1%)	0.677
Hepatic dysfunction	2 (4.3%)	3 (6.2%)	0.566
Pulmonary dysfunction	1 (2.2%)	3 (6.2%)	0.509
Urinary tract infection	2 (4.3%)	2 (4.2%)	0.902
Pneumonia	4 (8.7%)	6 (12.5%)	0.098
Hospital Death	2(4.3%)	6(12.5%)	0.003
ICU stay	2.5 ± 1.2	5.1 ± 1.1	0.005
Hospital stay	7.1 ± 1.2	14.4 ± 3.4	0.006
Charges			
> 5000 Dollar	7 (15.2%)	28 (58.3%)	0.001
< 5000 Dollar	39 (84.7%)	20 (41.6%)	0.001

The postoperative clinical data are given in Table 6. There was no significant difference between the two groups with respect to complications, such as lung infections, stroke, or transient ischemic attacks. The incidence of low-output syndrome, perioperative myocardial infarction, stroke, mediastinitis, superficial would complication, and atrial fibrillation was similar in two groups.

Patients in the on-pump group showed a higher requirement blood transfusion. Blood loss was higher in the on-pump group than in the off-pump group. In the off-pump group, postoperative bleeding > 1000 mL, surgical revision for bleeding, chest tube drainage and blood transfusion amount less than the on-pump group. This difference was statistically significant (Table 6). Nosocomial infection and multiple organ dysfunctions were more frequently observed in the on-pump group (p=0.048 and p=0.033). The incidence of in-hospital mortality following isolated off-pump patients was 4.3 %, compared to 12.5 % for patients with on-pump (p=0.003). Mean follow-up ranged from 6 to 24 months. No significant difference in long-term survival at 2 years was absorbed between the two groups of hospital survivors.

There was an important difference between the groups in terms of durations of ICU and hospital stay. Patients in the on-pump group had a significantly longer ICU stay as well as total hospital stay as those undergoing off-pump surgery (p=0.005 and p=0.006). Because ICU and hospital stay, postoperative bleeding and surgical revision and nosocomial infections were less in patients off-pump than patients on-pump, the hospital costs were significantly lower for off-pump (p=0.001) (Table 6).

Discussion

Renal dysfunction is a well-recognized complication following CABG and has been associated with increased morbidity, mortality, intensive care unit stay, and hospital fees particularly [10,20]. A significant proportion of conventional CABG had a degree of renal dysfunction develop postoperatively [21,22]. Besides, preoperative renal dysfunction is a predictor of renal failure in patients undergoing conventional CABG. Coronary revascularization without CPB has been shown to minimize renal injury in patients with normal preoperative renal function who undergo elective procedures, but the effect of coronary revascularization without CPB in patients with preoperative non-dialysis-dependent renal insufficiency is still controversial, and it has been shown in many studies that preoperative non-dialysis-dependent renal dysfunction have a further deterioration in renal function leading to postoperative renal injury [4,5,17,23-25]. Kidney parenchyma is more sensitive for postoperative renal failure after cardiac surgery, and it can occur as a result of the drop in renal perfusion pressure during CPB or during mechanical lifting of the heart in off-pump surgery.

We investigated the results of patients with non-dialysis renal dysfunction after on-pump and off-pump coronary surgery and risk factors that may cause postoperative dialysis in this study. Both effects of surgical intervention associated with coronary surgery and risk factors requiring dialysis are important determinants of postoperative renal dysfunction. This concept is the basis of our study. Display of renal tubular damage is used many parameters by some authors over the years such as creatinine clearance, fractional excretion of sodium, microalbuminuria, free hemoglobin, free water clearance and N-acetyl-glucosaminidase activity in patients undergoing off-pump as compared with conventional CABG patients [10,16]. This study examined serum creatinine, blood urea nitrogen concentration and serum creatinine clearance and GFR levels in both groups.

The potential reduction of renal risk and its association with morbidity and mortality may have a significant role in the choice of operative technique. The on-pump and off-pump techniques after cardiac surgery were compared in terms of creation of renal damage over the years, and morbidity and mortality rate were examined [16,26-28]. Although it has been reported that off-pump may minimize renal injury in elective patients with normal and impaired preoperative renal function and in high-risk patients [14,16,27,29,30], other studies have failed to show such benefit [15,17,31,32]. Meta-analysis of the literature has shown that off-pump surgery may result in improved short-term and midterm outcomes, and glomerular filtration was significantly worse with off-pump than with off-pump. Off-pump reduced the likelihood of acute renal failure in patients with preoperative non dialysis-dependent renal insufficiency [14,16,33]. In contrast, another studies [26,28] observed no difference in glomerular or tubular function between off-pump and on-pump techniques, and no difference in the requirement for dialysis between on-pump and off-pump was detected in patients with preoperative non dialysis-dependent renal insufficiency.

Previous retrospective analyses have failed to demonstrate a significant renoprotective benefit from using off-pump techniques, although the studies by Gamoso [17] and Zamvar [31] had relatively small numbers of off pump patients in them. The study reported by Wallace and colleagues [34] in Ohio was of comparable size to our study and indicated rates of acute renal failure of 12% and 6%, respectively, for on-pump and off-pump surgery. However, the on-pump group had a higher percentage of high-risk patients, such as diabetics, patients with poor left ventricular function, and reoperations [34]. In our study, there were no significant differences between the risk factors of the on-pump and off-pump.

The cause of renal dysfunction after the cardiac operation is multifactorial and usually attributed to several factors, such as the use of CPB, perioperative cardiovascular compromise, or toxic insults to the kidneys [35-37]. Free plasma hemoglobin, elastase, and endothelin, and free radicals including superoxide, hydrogen peroxide, and the hydroxyl radicals can be generated during CPB and can induce injury in the renal brush-border membrane [36]. Nonpulsatile flow, renal hypoperfusion, hypothermia, and duration of CPB are also thought to have adverse effects on renal function [36,38,39]. There is no uniting mechanism explaining renal failure associated with cardiac surgery [24,40-42]. Previous work has used algorithms to stratify individual risk and has described clinical variables as exerting their effects in four areas. First, there are factors relating to occult renal ischemia caused largely by arteriosclerosis and exacerbated by perioperative reduction of cardiac output, hypotension, and resultant hypoperfusion. Second, the kidneys may be damaged by exogenous nephrotoxins such as aminoglycoside antibiotics, diuretics, or radiologic contrast media. Third, endogenous nephrotoxins may be released (eg, myoglobin, free radicals, or proinflammatory cytokines such as interleukin-8, interleukin-1, and tumor necrosis factor). Last, there may be a background of reduced renal reserve as assessed by preoperative estimates of creatinine clearance. The effect, in turn, can produce renal dysfunction, especially in the presence of additional risk factors like pre-existing renal dysfunction, diabetes, and hypertension [43]. Avoiding CPB is beneficial even in patients with an existing preoperative renal insufficiency undergoing CABG as confirmed in this study [14,22]. This benefit may be due to the avoidance of nonpulsatile flow, renal hypoperfusion, hypothermia, and prolonged duration of CPB for all of them thought to have adverse effects on renal function in patients undergoing off-pump coronary artery bypass grafting. With the resurgence of interest in CABG without the use of CPB, there were a few observational comparative studies published on CABG with or without using CPB in patients with preoperative non–dialysis-dependent renal insufficiency. All these studies showed that off-pump reduces in-hospital morbidity and the likelihood of renal failure in patients with preoperative non–dialysis-dependent renal insufficiency [14,16,27,29,30]. Yet other nonrandomized studies failed to show the renoprotective effect of the off-pump technique in non–dialysis-dependent renal insufficiency [15,17,31,32] as previously mentioned above.

The off-pump technique for coronary revascularization was popularized in the early 1990s and led to an investigation as to whether the avoidance of CPB altogether would minimize postoperative renal injury and/or insufficiency. Use of beating heart techniques means the maintenance of pulsatile flow and no exposure to an extracorporeal circuit, with an anticipated reduction in the inflammatory cytokine response that this would entail. It also means normothermia and a decreased requirement for vasoconstrictor administration to maintain target mean arterial pressures [17,42]. Off-pump CABG surgery eliminates several of the physiologic perturbations associated with CPB that have been implicated in the development of postoperative renal dysfunction. Off-pump may, therefore, be the preferred technique for patients with multiple preoperative risk factors for renal dysfunction. In the present study, we used beating heart operations in elective patients who needed myocardial revascularization to clarify the impact of this procedure on renal function as part of a prospective randomized study. In several previous studies, lower prevalence of postoperative complications (eg, cerebral deficits [stroke or postoperative delirium] or renal insufficiency), and a lower mortality rate have been documented for patients undergoing beating heart surgery as compared with patients undergoing conventional CABG [22,44-47].

In most previous studies investigating the efficacy of off-pump in patients with renal dysfunction, the number of grafts in off-pump was significantly less than that of conventional CABG [4,13,14,48]. Sabik and associates [27] have reported increased occurrence of incomplete revascularization in off-pump that could be harmful to late results. In this study, the number of grafts was similar between groups and complete revascularization carried out and there was no different statistically both groups. However, off-pump techniques are more technically demanding, there has been previous concern over anastomotic quality, and the contortion of the heart for the lateral and posterior vessels may cause outflow tract obstruction and low cardiac output [49]. Off-pump contributes superior functional renal preventing that higher mean arterial pressures are usually maintained during off-pump surgery and may have a renoprotective effect. We mention that systolic arterial pressures were maintained at a minimum of 70 mm Hg during distal anastomoses when performing off-pump, especially in the circumflex territory. Besides, Starfish (Medronic Inc) or the Guidant Vortex Vacuum Assist ensure that higher systemic pressures are maintained when stabilizers are used to facilitate suturing. In a comparable manner, the beneficial effect on functional renal outcome seen with off-pump may be a reflection of the maintenance of higher systemic blood pressures during off-pump [50,51]. In our study, the difference in terms of complete revascularization could not be determined. In addition, hemodynamic problems not encountered to on-pump from off-pump turn during operation.

The patient's age is one of the most reported preoperative risk factors for postoperative renal requiring dialysis [17,23,24,52]. This finding was confirmed in this series as an age of 70 years or older and has been found to be significantly associated with postoperative renal failure. The effect of diabetes mellitus on postoperative renal failure may be the result of renal parenchymal disease, such as glomerulonephritis or glomerulosclerosis [22]. In our study, diabetes was found to be a risk factor relation to requiring dialysis.

The prominent finding in our study is that off-pump surgery preserves renal function. Also, off-pump seems to reduce postoperative bleeding, nosocomial infection, multiorgan dysfunction, ICU and hospital stay, hospital charges, and mortality [53-60]. The incidence of respiratory failure and postoperative bleeding tended to be more frequent in patients with renal dysfunction than those with normal renal function although there was no significant difference [61]. Tabata et al suggest that off-pump does not reduce the requirement of blood transfusion in patients with renal dysfunction [61]. The current study also showed a significantly higher blood loss and transfusion requirement in the off-pump group. Furthermore, these losses concur with other recently published data [62,63]. With regard to the clinical outcomes, the off-pump group had a significantly shorter duration of ICU and hospital stay and hospital charges compared with the on-pump group. These results are in keeping with those from a previous multicenter trial in which early clinical outcomes were compared between off-pump and on-pump CABG in a randomized fashion [64].

Postoperative renal dysfunction in patients undergoing CABG has been associated with high morbidity and mortality [10,20,35,65]. Operative mortalities of conventional CABG have been reported to range from 5.9% to 14.3% in patients with chronic dialysis [66-68] and from 7.0% to 11.0% in patients with non dialysis-dependent renal dysfunction [4-6,13,14,25]. However, our results agree with the findings of Ascione's research group [58]. In their study, they have clearly proven a benefit on cardiac outcome after off-pump surgery. Some studies have reported better outcomes, however, they are much smaller studies [12,48]. Operative mortalities of off-pump have been recently reported to range from 0% to 6.7% in patients with chronic dialysis [12,13,48] and to range from 5.9% to 6.3% in patients with non dialysis-dependent renal dysfunction [4,14]. In this study, the in-hospital mortality rate was 12.5% in patients with the on-pump group. These patients had unstable angina and severe diffuse triple-vessel disease associated with diabetes, mediastinitis, peripheral vascular disease, and low ejection fraction.

Although serum creatinine and blood urea nitrogen are the most widely used assay to measure the presence and progression of kidney disease, equations based on serum creatinine level, age, sex, and other variables are more sensitive at predicting changes in renal function [69]. Recently some parameters were developed such as creatinine clearance and GFR to assess renal function [70-72], and are widely used today. Loganathan et al. show that there were no major differences in any of the renal function associated parameters such as creatinine and blood urea nitrogen blood levels between their off-pump and on-pump groups [8]. In contrast to our study, other studies have suggested serum creatinine levels be a compelling parameter for renal dysfunction after cardiac surgery [32] as agree with our study. Postoperatively, especially serum creatinine and urea levels revealed a significant increase in the classical CABG group compared to the off-pump group. Further, this study showed a significant rise in serum creatinine and BUN levels at postoperative day 7 in the on-pump group compared with the off-pump group and a statistically significant fall in GFR and creatinine clearance in the on-pump group compared with the off-pump group. The decreases in creatinine clearance and glomerular filtration rate were more in on-pump groups compared to off-pump. The increases in serum creatinine and BUN level significantly less in patient's off-pump postoperatively in 7 days. In the present study, marked decreases in the creatinine clearance and GRF values were found early after operation in on-pump groups, which is in accordance with previous studies in which renal function was evaluated in patients undergoing CPB.

In agreement with previous reports [36,73], this study found a marked improvement in creatinine clearance, a reliable indicator of glomerular filtration rate, during CPB in the on-pump group. Nevertheless, at 24 and 48 hours postoperatively the creatinine clearance values decreased significantly in the on-pump group, reaching levels markedly lower than preoperative levels. Conversely, in the off-pump group rising in creatinine clearance was less. Functional alteration of the glomerular and tubular parts of the nephron can be evaluated further by assessing microalbuminuria and NAG activity, respectively. More recently, urinary NAG activity has emerged as the most widely assayed urinary enzyme for detection of renal damage because of its stability in urine, its relative molecular mass which precludes filtration by the glomerulus, and its presence in high activity in the tubular lysosomes. The marked increases in urinary albumin-to-creatinine ratio and NAG activity levels in the current study confirm the potential deleterious effect of the CPB on renal function. Randomized controlled trials in this area have looked beyond serum urea, creatinine, creatinine clearance, and GFR to more sensitive biochemical markers of renal function. These have been associated with decreases in measured creatinine clearance and GFR have been demonstrated to occur with both on the pump and off-pump surgery. But, this decrease was statistically more in on-pump patients.

In the present study, nonsimilar to a previous one [64], the prevalence of postoperative renal failure, defined as either requiring hemodialysis, an increase in serum creatinine and BUN, or decrease in GFR and creatinine clearance did not differ between the groups. Ascione and associates [14] demonstrated higher postoperative serum creatinine and urea levels in patients with preoperative non dialysis-dependent renal insufficiency undergoing on-pump CABG with a significant difference at 12 hours postoperatively as compared with those undergoing OPCAB surgery. Hayashida and associates [7] found a significantly less increase in creatinine levels and a greater creatinine clearance in off-pump patients as compared with the CABG group. In contrast to these findings, in a recent study by Gamoso and associates [17] including 690 patients, no significant reduction of perioperative renal dysfunction in off-pump patients could be found.

In our study, logistic regression model analysis showed the use of CPB is significantly associated with adverse renal outcome. In addition, the effects of the presence of diabetes mellitus, age > 70, hypertension, multiple vessels disease, preoperative increased creatinine and BUN levels, preoperative decreased creatinine clearance and GFR levels and preoperative LVEF < 40 had independent predictors for postoperative renal failure requiring. Some parameters as congestive heart failure, preoperative cardiogenic shock, urgent operations, increasing body mass index, peripheral vascular disease, intraoperative low cardiac output, high transfusion requirement, the use of non-left internal mammary arterial conduits and persistent low cardiac output states has found associated with postoperative dialysis-requiring in reported other series [22,42,50] in addition to the findings of our study.

Conclusion

To the best of our knowledge, there has been no randomized study published comparing the effect of off-pump and on-pump CABG in patients with non–dialysis dependent renal insufficiency defined by GFR as well as serum creatinine, blood urea nitrogen, creatinine clearance and requiring dialysis. These findings suggest that the off-pump technique is more renoprotective in patients with non–dialysis dependent renal insufficiency.

Multivariate stepwise logistic regression confirmed the use of CPB as an independent risk factor for the development of requiring dialysis. In summary, the off-pump technique preserved the glomerular filtration rate and prevented an increase in creatinine concentration during the early postoperative period. The technique also resulted in shorter ICU stay and mortality and fewer complications and requirement for transfusion. The results suggested that off-pump ensures an earlier patient recovery and gives superior renal protection than conventional CABG in patients with nondialysis renal dysfunction. Although baseline measurements of parameters of glomerular and tubular damage were the same in both groups, disorder for these parameters was less in the off-pump patients in the postoperative period in 7 days.

Limitations of the Study

First, there are only a limited number of large comparative studies between on-pump and off-pump focusing on renal outcome and matched for number of coronary grafts.

Furthermore, this study is retrospective, observational and limited to a single institution. All data were entered into the database as part of patient management. One of the important limitations of this study is that we did not investigate late outcomes. Several studies have revealed poor late outcomes of conventional CABG in patients with renal dysfunction. 5-year actuarial survival rates of dialysis patients have been reported to range from 32.0% to 55.8% [2,3,67].

Using the levels of serum creatinine, BUN, creatinine clearance and GFR as the sole marker of renal function can be also a limitation. Although measurements of patients' urinary microalbumin, retinal-binding protein, or n-acetylglucosaminidase might give a more detailed picture of renal insult, in a study of this size it is largely unrealistic.

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