Clinical Trial/Experimental Study

Medicine®

OPEN

Off-pump versus on-pump complete coronary artery bypass grafting

Comparison of the effects on the renal damage in patients with renal dysfunction

Umit Arslan, MD[a], Eyupserhat Calik, MD[a], Ali Ihsan Tekin, MD[b], Bilgehan Erkut, MD[a,*]

Abstract

Background: We aimed to compare off-pump technique with on-pump technique on renal function in patients with nondialysis-dependent renal dysfunction who underwent coronary artery bypass grafting.

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 cardiopulmonary bypass 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.

Results: 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. Cardiopulmonary bypass 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 nondialysis-dependent renal dysfunction when compared with conventional coronary revascularization with cardiopulmonary bypass.

Abbreviations: BUN = blood urea nitrogen, CABG = coronary artery bypass grafting, CIs = confidence intervals, CPB = cardiopulmonary bypass, GFR = glomerular filtration rate, IABP = intra-aortic balloon pump, ICU = intensive care unit, MDRD = modification of diet in renal disease, NAG = N-acetyl-glucosaminidase, ORs = odds ratios, SD = standard deviation.

Keywords: coronary artery bypass grafting, on- and off-pump coronary revascularization, renal insufficiency, requiring dialysis, surgical complications

1. 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 dialysis-dependent or not. Acute renal failure requiring dialysis develops in 2% to 7% of cardiac surgery patients.[1–3] Although the cause of this renal failure 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, nonpulsatile flow, hemolysis, stimulation of the inflammatory response, and increased levels of circulating catecholamines, cytokines, and free hemoglobin may contribute significantly to this condition.[4,5] Furthermore, the use of aortic cross-clamping and cardioplegic arrest can result in myocardial dysfunction that may lead to renal perfusion defects and subsequent renal impairment.[6,7] However, the explicit contribution of these factors remains unclear and must be fully clarified.

Off-pump coronary revascularization removes the nonphysiologic condition associated with CPB. Because 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 those of patients undergoing conventional on-pump coronary revascularization. Recently, the benefits of off-pump coronary revascularization have been established, and several studies have revealed that off-pump coronary revascularization results in better outcomes for patients with renal dysfunction than conventional, on-pump coronary revascularization.[8–10] However, studies conducted previously in this field have provided conflicting evidence to support this hypothesis, and the data on this topic remain contradictory.[5,11–14]

The randomized study discussed in this study assessed the impact of the off-pump coronary revascularization technique on the incidence and severity of renal dysfunction according to the on-pump coronary revascularization technique in patients with preoperative nondialysis-dependent renal insufficiency. The renal

Editor: Yan Li.

The authors have no funding and conflicts of interest to disclose.

[a] Department of Cardiovascular Surgery, Atatürk University, Erzurum, [b] Department of Cardiovascular Surgery, Health Science University, Kayseri Training and Research Hospital, Kayseri, Turkey.

[*] Correspondence: Bilgehan Erkut, Department of Cardiovascular Surgery, Atatürk University, Erzurum 25100, Turkey (e-mail: bilgehanerkut@yahoo.com).

Medicine (2018) 97:35(e12146)

Received: 16 May 2018 / Accepted: 8 August 2018

http://dx.doi.org/10.1097/MD.0000000000012146

functions were defined according to the levels of serum blood urea nitrogen (BUN), creatinine, creatinine clearance, and the glomerular filtration rate called glomerular filtration markers. Several independent risk factors associated with requiring dialysis were also identified.

2. Materials and methods

This study was designed to compare the effect of off- and on-pump coronary artery bypass grafting (CABG) techniques on renal function in patients with nondialysis-dependent renal insufficiency. This retrospective study utilizes data from 94 consecutive patients with preoperative, nondialysis-dependent renal insufficiency who underwent primary, isolated, non-emergent coronary surgery between May 2014 and June 2015. The patients were divided into 2 groups, the on-pump group (n=48; cardioplegic arrest and CPB) and the off-pump group (n=46; beating heart surgery). In both groups, complete coronary revascularization was attempted.

The preoperative demographics, operative variables, operative morbidity and mortality, short-term survival, cardiac-related events, postoperative data, and postoperative renal parameters, requiring dialysis were compared between the 2 groups. The preoperative data and values indicating the preoperative renal dysfunction are shown in Table 1. Several factors considered good indicators of postoperative renal complications were evaluated, including postoperative BUN, creatinine, clearance of creatinine, and the glomerular filtration rate (GFR) levels. In addition to comparing the renal dysfunction and dialysis requirements associated with these parameters, the risk factors associated with needing dialysis were determined by logistic regression analysis.

In this study, data were collected from patients' case notes in the Medical Records Office and recorded by clinical cardiologies and cardiac surgeons. This study was approved by the Erzurum Regional Training and Research Hospital Ethics Committee. The local institutional review board approved this work and an informed consent form was signed by the patients. The study is in accordance with the declaration of Helsinki.

2.1. Data definition

The BUN (10–50 mg/dL) is an indication of renal kidney health. BUN levels of >50 mg/dL without requiring dialysis were considered renal dysfunction. The reference ranges of serum creatinine in the laboratory were 0.4 to 1.1 mg/dL. Creatinine levels of >1.5 mg/dL or at least a 20% increase without requiring dialysis was considered renal dysfunction. Creatinine clearance was calculated using the Cockcroft and Gault formula: ([140age] × kg/serum creatinine [mg/dL] × 72). The reference ranges of serum creatinine clearance in the laboratory were 80 to 120 mL/min 1/1.48 m^2. Creatinine clearance ≤60 mL/dk/1.73 m^2 without requiring dialysis was considered renal dysfunction. The GFR was measured using the modification of diet in renal disease (MDRD) equation (mL/min/1.73 m^2). GFR is divided into 5 stages: ≥90 (stage I), 60 to 89 (stage II), 30 to 59 (stage III), 15 to 29 (stage IV), and at least 15 (stage V). Generally, decreases of 50% or more in the GFR were considered renal dysfunction. These parameters were measured postoperatively at day 7 and confirmed by at least 2 measurements.

Nondialysis renal dysfunction: BUN levels between 30 and 60 mg/dL; stage I GFR; creatinine levels between 1.3 and 1.7 mg/dL and creatinine clearance levels between 40 and 70 mL/min.

Requiring dialysis: Acute renal dysfunction was classified on the basis of RIFLE (Risk, injury, failure, loss, end-stage renal disease) criteria.[14–16] Postoperative dialysis was indicated if they had diuretics-resistant oliguria associated with volume overload or hyperkalemia. Postoperative renal failure was defined as either requiring hemodialysis to support renal function, an increase in serum creatinine >1.5 mg/dL postoperatively, or an occurrence of oliguria (<0.5 mL/kg/h) for more than 6 hours.

For our patients, the end point for renal disease is dialysis or death in the follow-up period. After the patient data were collected and compared, the patients were removed from follow-up.

Postoperatively, all patients were admitted to the intensive care unit (ICU) and received standardized treatment. 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, unfractioned heparin was started according to the height of the patient (1.5 mg/kg/24 h), and on the second postoperative day, 300 mg of aspirin was given to all patients. In-hospital and postdischarge outcomes were collected from medical records and telephone interviews. These data were completed for all patients until their discharge from the hospital or their death.

2.2. Exclusion criteria

Patients with mechanical complications of myocardial infarction, such as a ventricular septum defect, papillary muscle rupture, and mitral valve regurgitation, and patients with cardiogenic shock persisting for a length of 24 hours were excluded from this study. Besides, combined procedures, impaired left ventricular function as assessed by angiography (ejection fraction < 30%), patients requiring chronic dialysis, oliguria and anuria, a high-serum creatinine level (≥2.5 mg/dL), emergency surgery or reoperation, respiratory impairment, and coagulopathy not included in the study. 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 aminoglycosides or nonsteroidal anti-inflammatory agents perioperatively.

2.3. Surgical techniques

All patients underwent surgical revascularization through a median sternotomy. The arterial conduit (internal mammalian artery) was harvested with the pedicle preparation technique using surgical electrocautery for the left anterior descending artery anastomosis. Saphenous vein grafts were harvested with the open method using fine scissors, and these vessels were used for other coronary anastomoses. 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 >2.0 L/min/m^2 and systolic blood pressure of >80 mm Hg after surgery. Intravenous diltiazem and nitroglycerin were administered routinely in the ICU.

2.4. Conventional CABG

Before CPB was initiated, heparin sodium was administered at an initial dose of 300 IU/kg. CPB was instituted by using ascending aortic cannulation and a 2-stage venous cannulation in the right atrium. The aorta was cross-clamped, and myocardial protection was achieved with intermittent antegrade and retrograde blood

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	.760
Sex			.880
Male	24 (52.1%)	25 (52%)	
Female	22 (47.9%)	23 (48%)	
BMI, kg/m^2	29.5±3.8	30.2±3.1	.207
Hypercholesterolemia	28 (60.8%)	30 (62.5%)	.421
DM	33 (71.7%)	35 (72.9%)	.528
CVD	2 (4.3%)	1 (2%)	.442
COPD	18 (39.1%)	20 (41.6%)	.338
Smoking	121 (65%)	118 (65.5%)	.289
Hypertension	34 (73.9%)	33 (68.8%)	<.05
PAD	9 (19.5%)	11 (22.9%)	.190
Left main disease	9	11	.189
Three vessel disease	19	21	.237
Two vessels disease	18	16	.304
Hematocrit	44±2	45±3	.777
NYHA	3.3±0.45	3.2±0.6	.589
Preop AF	2 (4.3%)	2 (4.1%)	
Preoperative IABP	4 (8.7%)	5 (10.4%)	.144
History of MI	37 (80.4%)	39 (81.2%)	.250
LVEF			
0.30–0.40	16	14	.870
40–50	14	18	.777
>0.50	16	16	.651
Renal dysfunction not requiring dialysis			
BUN levels, mg/dL	45±12 (range: 30–59)	48±10 (range: 35–61)	.399
Creatinine levels, mg/dL	1.5±0.2 (range: 1.3–1.7)	1.5±0.3 (range: 1.3–1.6)	.557
CCL, mL/min	59±7 (range: 41–72)	61±8 (range: 40–75)	.902
Median GFR (Stage I)	77±12 (range: 52–89)	76±13 (range: 51–90)	.766
Use of diuretics	9 (19.5%)	10 (20.8%)	.221

AF=atrial fibrillation, BMI=body mass index, BUN=blood urea nitrogen, CCL=creatinine clearance, COPD=chronic obstructive pulmonary disease, CVD=cerebro-vascular disease, DM=diabetes mellitus, GFR=glomerular filtration rate, IABP=intra-aortic balloon pump, LVEF=left ventricular ejection fraction, MI=myocard infarction, NYHA=New York Heart Association, PAD=peripheral arterial disease, UAP=unstable angina pectoris.

cardioplegia (Custodiol, Alsbach-Hahnlein, Germany). Mean arterial pressure was maintained between 50 and 70 mm Hg. The nonpulsatile flow was used. The systemic temperature was maintained between 30°C and 34°C. Once all distal anastomoses were completed, the aortic cross-clamp was removed, and the proximal anastomosis was performed with partial clamping. After the patient was weaned from CPB and decannulated, the heparin was completely neutralized using protamine (1/1.5 rate; Valeant, Eschborn, Germany).

2.5. Off-pump beating-heart technique

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 for beating-heart technique surgery. Stabilization during distal anastomosis was performed using the Octopus stabilizing system (Medtronic Inc, Minneapolis, MN). These patients received heparin sodium (150 IU/kg) before the anastomosis, and the elite-activated clotting time was maintained at more than 300 seconds. 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. 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. After each distal anastomoses, perfusion was maintained with warm blood through the pump by using anastomosed saphenous veins, then the proximal anastomoses were performed.

2.6. Statistical analysis

The values of continuous variables are expressed as mean ± standard deviation (SD). The Student *t* test and Mann–Whitney *U* test were used to analyze these continuous variables. The categorical or dichotomous data were presented in percentages (%) and compared using the Chi-squared method or Fisher exact test, and *P*-values of .05 or fewer were considered significant.

Univariate logistic regression analysis was performed to identify significant predictors associated with preoperative factors. Multivariable logistic regression analysis was used to identify independent risk factors related to requiring dialysis. The results of the logistic regression analysis were presented as odds ratio (OR) and 95% confidence intervals (CIs). Statistically significant differences were noted for each analysis, with statistical significance based on a *P*-value of <.05. Statistical analysis was performed using SPSS version 11.5J (SPSS, Inc, Chicago, IL).

3. Results

The study included 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. The pre- and intraoperative demographics

Table 2

Operative data.

Data	Off-pump (n=46)	On-pump (n=48)	*P*-value
XCL time, min	0	56±12	.001
CPB time, min	0	73±13	.001
Operating time, h	3.6±1.2	5.1±1.4	.012
Number of distal anastomosis	3.0±0.3	3.1±0.4	.409
LAD by pass	46	48	.307
Diagonal branches	18	15	.855
Cx by pass	13	12	.652
RCA by pass	14	16	.318
Complete revascularization	45 (97.8%)	48 (100%)	.212
Coronary endarterectomy	7 (15.2%)	8 (16.6%)	.327
Cumulative regional ischemic times, min	6.1±4.2	7.2±3.3	.844
Postoperative IABP	3 (6.5%)	4 (8.3%)	.307
IMA usage	44 (95.6%)	46 (95.8%)	.855
Sequential graft	2 (4.3%)	3 (6.2%)	.652
Use of inotropes	11 (23.9%)	10 (20.8%)	.318
Use of trinitrate	7 (15.2%)	9 (18.7%)	.402
Hemodynamic data			
Mean BP, mm Hg	48±9	51±11	.112
Mean heart rate, min	53±13	0 (cross clamping)	.0001

BP=blood pressure, CPB=cardiopulmonary bypass, Cx=circumflex artery, IABP=intra-aortic balloon pump, IMA=internal mammalian artery, LAD=left anterior descending artery, RCA=right coronary artery, XCL=cross clamping.

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)	.004
Creatinine levels, mg/dL	1.6±0.4 (range: 1.4–2.0)	1.9±0.4 (range: 1.7–2.4)	.007
CCL, mL/dk/1.73 m^2	55±9 (range: 40–65)	35±8 (range: 22–52)	.001
Median GFR	75±11 (range: 50–88)	52±15 (range; 35–67)	.003
Requiring dialysis	1 (2.17%)	9 (18.75%)	.0001

BUN=blood urea nitrogen, CCL=creatinine clearance, GFR=glomerular filtration rate.

characteristics of the 46 patients in the off-pump group and the 48 patients in the on-pump group are shown in Tables 1 and 2, respectively. There was no statistical difference between the groups in terms of preoperative and operative data. Conversion from off- to on-pump did not occur for any patients. All patients had uneventful operations and postoperative stays.

Five patients in the on-pump group and 4 in the off-pump group were unstable, in-hospital patients treated with inotropic treatments and intra-aortic balloon pumps (IABPs). The severity of the coronary heart disease did not differ between both cohorts, as indicated by similar rates of left main, 2- and 3-vessel diseases. There was no statistically significant difference in the index of revascularization completeness (Table 1). No significant differences were found in preoperative furosemide usage and the total requirement of intravenous catecholamines and trinitrates during the first 48 hours after surgery (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 (*P*=.001). The operation time was shorter in the off-pump group than the on-pump group (Table 2). This difference was statistically significant (*P*=.012).

Postoperative data showed that impaired renal function parameters were fewer in the off-pump group. The increases in the postoperative creatinine and BUN levels compared to the preoperative values were markedly higher in the on-pump group (*P*=.004 and *P*=.007). The decreases in the GFR and the creatinine clearance levels were higher in the on-pump group compared with the off-pump group (*P*=.001, *P*=.003) at postoperative day 7 (Table 3). Nine patients in the on-pump group required dialysis, whereas only 1 patient in the off-pump group required dialysis (*P*=.0001). Consequently, renal dysfunction was higher in the on-pump group than in the off-pump group after CABG surgery.

By using stepwise logistic regression analysis, 12 variables were identified as independent predictors of postoperative requiring dialysis, and are presented in Table 4. The use of CPB and increasing age were a significant factor on the univariate logistic regression analysis (OR: 1.01, 95% CI: 0.65–2.11, *P*=.0001 and OR: 0.51, 95% CI: 0.55–0.91, *P*=.012, respectively). Besides, operating time (OR: 0.52, 95% CI: 0.48–0.90, *P*=.018), hypertension (OR: 2.52, 95% CI: 1.26–5.18, *P*=.008), diabetes (OR: 0.90, 95% CI: 0.75–0.99, *P*=.001), smoking (OR: 1.99, 95% CI: 1.02–3.18, *P*=.022), multiple vessels disease (OR: 0.78, 95% CI: 0.51–0.80, *P*=.033), preoperative IABP (OR: 5.9, 95% CI: 4.66–12.01, *P*=.011), preoperative left ventricle ejection fraction (LVEF)< 40 (OR: 4.66, 95% CI: 2.01–9.62, *P*=.002), preoperative increased creatinine and BUN levels (OR: 0.75, 95% CI: 0.56–0.88, *P*=.0001), preoperative deceased creatinine clearance and GFR levels (OR: 0.61, 95% CI: 0.43–0.93, *P*=.0001), and having had a previous myocardial infarction (OR: 0.31, 95% CI: 0.05–0.48, *P*=.055) 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 postoperative dialysis was the use of CPB with OR: 0.51, 95% CI: 0.33–1.01, *P*=.0001. Besides, diabetes mellitus and hypertension (OR: 1.10, 95% CI: 0.66–1.49, *P*=.001) and (OR: 2.52, 95% CI: 1.51–4.90, *P*=.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 OR, and *P*-values.

The postoperative clinical data are given in Table 6. There was no significant difference between the 2 groups. Patients in the on-pump group showed a higher blood transfusion requirement. In the off-pump group, postoperative bleeding >1000 mL, surgical revision for bleeding, chest tube drainage, and blood transfusion amounts were 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*=.037 and *P*=.031). The incidence of in-hospital mortality for off-pump patients was 4.3%, compared to 12.5% for on-pump patients (*P*=.003). The mean follow-up ranged from 6 to 24 months. No significant difference in long-term survival at 2 years was noted between the 2 groups of survivors.

Table 4

Results of univariate logistic regression analysis for risk factors associated with requiring dialysis.

	Odds ratio	95% CI	*P*-value
Age > 70	0.51	0.55–0.91	.012
Sex	4.66	2.01–9.62	.521
Male			
Female			
Median weight, kg	0.8	0.66–1.19	.075
Cardiopulmonary bypass usage	1.01	0.65–2.11	.0001
Operating time, h	0.52	0.48–0.90	.018
Cumulative regional ischemic times, min	0.11	0.08–2.13	.520
Complete revascularization	0.41	0.35–0.60	.075
Coronary endarterectomy	0.37	0.22–0.72	.102
COPD	2.7	2.3–3.1	.902
Multiple vessels disease	0.78	0.51–0.80	.033
Smoking	1.99	1.02–3.18	.022
PAD	1.19	1.01–1.33	.521
History of MI	0.31	0.05–0.48	.055
Hematocrit	3.79	2.41–6.88	.101
Preoperative ACE inhibitors	0.49	0.22–4.16	.209
Preoperative LVEF < 40	4.66	2.01–9.62	.002
Diabetes mellitus	0.90	0.75–0.99	.001
Hypertension	2.52	1.26–5.18	.008
Use of diuretics	0.77	0.81–2.80	.870
Preoperative increased Cr and BUN levels	0.75	0.56–0.88	.0001
Preoperative decreased CrCL and GFR levels	0.61	0.43–0.93	.0001
Preoperative IABP	5.9	4.66–12.01	.011

ACE = angiotensin converting enzyme, BP = blood pressure, CCL = creatinine clearance, CI = cardiac index, COPD = chronic obstructive pulmonary disease, CPB = cardiopulmonary bypass, CVP = central venous pressure, GFR = glomerular filtration rate, IABP = intra-aortic balloon pump, ICU = intensive care unit, LVEF = left ventricular ejection fraction, PAD = peripheral arterial disease, PAP = pulmonary artery pressure.

There was an important difference between the groups in terms of their ICU duration and the length of their hospital stay. Patients in the on-pump group had a significantly longer ICU and total hospital stay compared with those in the off-pump group (*P* = .005 and *P* = .006). Because the ICU and hospital stays were longer and the postoperative bleeding, surgical revision, and nosocomial infections were less in off-pump patients compared with on-pump patients, the hospital costs were significantly lower for off-pump patients (*P* = .001) (Table 6).

4. Discussion

Renal dysfunction is a well-recognized complication following CABG and has been associated with increased morbidity, mortality, ICU stay, and hospital fees, particularly.[7,13] A significant proportion of conventional patients with CABG had a degree of renal dysfunction develop postoperatively.[15–17] Preoperative renal dysfunction is a predictor of renal failure in patients undergoing conventional CABG. Coronary revascularization without CPB minimizes 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 nondialysis-dependent renal insufficiency is still controversial. Many studies indicate that patients with preoperative nondialysis-dependent renal dysfunction show a further deterioration in renal function leading to postoperative renal injury.[18–20] This study compared the effects of on-pump and off-pump coronary surgeries with respect to renal function in patients with impaired renal function without indications for dialysis. Several authors have used parameters related to the display of renal tubular damage, 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 patients with CABG.[7,12] In this study, serum creatinine, BUN, serum creatinine clearance, and GFR levels were evaluated in terms of impairment in renal function criteria and dialysis indications in both groups. The findings suggest that the

Table 5

Multivariate logistic regression analysis for risk factors associated with requiring dialysis.

	Odds ratio	95% CI	*P*-value
Age > 70	0.77	0.61–0.95	.001
Cardiopulmonary bypass	0.51	0.33–1.01	.0001
Preoperative LVEF < 40	4.11	2.99–8.88	.002
Diabetes mellitus	1.10	0.66–1.49	.001
Hypertension	2.52	1.51–4.90	.008
Multiple vessels disease	0.88	0.65–0.99	.025
Preoperative increased Cr and BUN levels	0.58	0.44–0.71	.001
Preoperative deceased CrCL and GFR levels	0.62	0.53–0.81	.001

BUN = blood urea nitrogen, Cr = creatinine, CrCL = creatinine clearance, GFR = glomerular filtration rate, LVEF = left ventricle ejection fraction.

Table 6

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	.701
Surgical revision for bleeding	2 (4.3%)	9 (18.7%)	**.01**
Postoperative bleeding > 1000 mL	7 (15.2%)	18 (37.5%)	.011
Blood transfusion (unite/patients)	0.87 ± 0.66	1.22 ± 0.77	.037
Chest tube drainage, mL/d	310 ± 125	588 ± 140	.022
Operative mortality (first 24 h)	0 (0%)	0 (0%)	–
Postop MI	0 (0%)	0 (0%)	–
Postop term LCOS	2 (4.3%)	1 (2.08%)	.902
Postop term IABP	4 (8.7%)	5 (10.4%)	.751
Postop term AF	3 (6.5%)	4 (8.3%)	.666
Stroke	0 (0%)	0 (0%)	–
Prolonged intubation	3 (6.5%)	3 (6.2%)	.282
Duration of inotropic support (days)	7.2 ± 4.3	3.1 ± 4.1	.188
Late results			
Cardiac arrhythmia	4 (8.7%)	3 (6.2%)	.247
Postop EF			
>50	34 (73.9%)	37 (77.1%)	.225
<50	12 (26%)	11 (22.9%)	.578
Sternal infection	1 (2.2%)	1 (2.1%)	.689
Nosocomial infection	1 (2.2%)	4 (8.3%)	.037
Multiple organ dysfunction	0 (0%)	2 (4.2%)	.031
Neurologic dysfunction	0 (0%)	1 (2.1%)	.677
Hepatic dysfunction	2 (4.3%)	3 (6.2%)	.566
Pulmonary dysfunction	1 (2.2%)	3 (6.2%)	.509
Urinary tract infection	2 (4.3%)	2 (4.2%)	.902
Pneumonia	4 (8.7%)	6 (12.5%)	.098
Hospital Death	2 (4.3%)	6 (12.5%)	.003
ICU stay	2.5 ± 1.2	5.1 ± 1.1	.006
Hospital stay	7.1 ± 1.2	14.4 ± 3.4	.008
Charges			
>5000 Dollar	7 (15.2%)	28 (58.3%)	.001
<5000 Dollar	39 (84.7%)	20 (41.6%)	.001

AF = atrial fibrillation, EF = ejection fraction, IABP = intra-aortic balloon pump, ICU = intensive care unit, LCOS = low cardiac output syndrome, MI = myocard infarction.

off-pump technique is more renoprotective in patients with nondialysis-dependent renal insufficiency.

The potential reduction of renal risk and its association with morbidity and mortality may play a significant role in choosing an operative technique. The on-pump and off-pump techniques after cardiac surgery were compared in terms of renal damage creation over the years, and morbidity and mortality rates were examined.[12,21–23] Although some research indicates that off-pump surgery may minimize renal injury in elective patients with normal and impaired preoperative renal function and in high-risk patients,[10,12,22,24,25] other studies have failed to show such benefits.[11,26–28] Meta-analysis of the literature has shown that off-pump surgery may result in improved short-term and mid-term outcomes, and that glomerular filtration was significantly worse in on-pump surgery compared with off-pump surgery.

The causes of renal dysfunction after a cardiac operation are multifactorial and usually attributed to several factors, such as the use of CPB, perioperative cardiovascular compromise, or toxic insults to the kidneys.[28,29] Free plasma hemoglobin, elastase, 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.[29] Nonpulsatile flow, renal hypoperfusion, hypothermia, and the duration of CPB are also thought to have adverse effects on renal function.[29,30] There is no uniting mechanism explaining renal failure associated with cardiac surgery.[19,31–37] These effects can produce renal dysfunction, especially in the presence of additional risk factors like preexisting renal dysfunction, diabetes, and hypertension.[34] The present study confirms that avoiding CPB is beneficial even in patients with an existing preoperative renal insufficiency undergoing CABG.[10,17] This benefit may be due to the avoidance of nonpulsatile flow, renal hypoperfusion, hypothermia, and prolonged duration of CPB. These studies showed that off-pump surgery reduces in-hospital morbidity and the likelihood of renal failure in patients with preoperative nondialysis-dependent renal insufficiency.[10,12,22,24,25]

The off-pump technique for coronary revascularization was popularized in the early 1990s, leading investigations about whether avoiding CPB altogether would minimize postoperative renal injury and/or insufficiency. Use of beating-heart surgery techniques means maintaining pulsatile flow with no exposure to an extracorporeal circuit; this technique entails an anticipated reduction in the inflammatory cytokine response. The technique also results in normothermia and a decreased requirement for vasoconstrictor administration to maintain target mean arterial pressures.[32,33] 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 surgery may, therefore, be the preferred technique for patients with multiple preoperative risk factors for renal dysfunction.

The patient's age is one of the most reported preoperative risk factors for postoperative renal function requiring dialysis.[18,19,38] The present study confirmed this finding, as an age of 70 years or older was 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.[17] In this study, diabetes was found to be a risk factor related to requiring postoperative dialysis.

Off-pump surgery appears to reduce nosocomial infection, multiorgan dysfunction, the length of ICU and hospital stays, hospital charges, and mortality.[39–43] 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 no significant difference was noted.[44] Tabata et al suggested that off-pump surgery does not reduce blood transfusion requirements in patients with renal dysfunction.[44] The current study also showed significantly higher blood loss and transfusion requirements in the off-pump group. Furthermore, these findings concur with other data.[45,46] With regard to the clinical outcomes, the off-pump group had a significantly shorter duration in the ICU and hospital, and the hospital charges were less when compared with the on-pump group. These results align with those from a previous multicenter trial, in which early clinical outcomes were compared between off- and on-pump CABG in a randomized fashion.[47]

Postoperative renal dysfunction in patients undergoing CABG has been associated with high morbidity and mortality.[7,15,48,49] Operative mortalities of conventional CABG range from 5.9% to 14.3% in patients with chronic dialysis[15,48–50] and from 7.0% to 11.0% in patients with nondialysis-dependent renal dysfunction.[3,9,10,20] However, this study's results agree with the findings of Ascione research group.[39] 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.[11,40] Recent studies indicate that the operative mortalities of off-pump surgeries range from 0% to 6.7% in patients with chronic dialysis[8,9] and 5.9% to 6.3% in patients with nondialysis-dependent renal dysfunction.[1,10] In the present study, the in-hospital mortality rate was 12.5% in on-pump patients. These patients had unstable angina and severe diffuse triple-vessel disease associated with diabetes, mediastinitis, peripheral vascular disease, and a low ejection fraction.

Although serum creatinine and BUN 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 more sensitively predict changes in renal function.[15] Recently, additional parameters, such as creatinine clearance and GFR, were developed to assess renal function[50–52]; they are now widely used. Loganathan et al show that there were no major differences in any of the renal-function-associated parameters, such as creatinine and BUN blood levels, between their off-pump and on-pump groups.[5] The another study showed that serum creatinine levels are a compelling parameter for monitoring renal dysfunction after cardiac surgery[25] as agree with our study. Postoperatively, serum creatinine and urea levels revealed a significant increase in the on-pump CABG group compared with the off-pump group. Furthermore, 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 noted a statistically significant fall in GFR and creatinine clearance in the on-pump group compared with the off-pump group. The creatinine clearance and glomerular filtration rates decreased more in the on-pump groups compared to the off-pump groups. The serum creatinine and BUN levels were significantly less in off-pump patients on postoperative day 7. In the present study, marked decreases in the creatinine clearance and GRF values were found soon after the operation in the on-pump group, which agrees with the previous studies where renal function was evaluated in patients undergoing CPB. In agreement with previous reports,[29,53,54] 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 postoperative, the creatinine clearance values decreased significantly in the on-pump group, reaching levels markedly lower than the preoperative levels. Conversely, the off-pump group saw less of a rise in creatinine clearance. Functional alteration of the glomerular and tubular parts of the nephron may be evaluated further by assessing the microalbuminuria and N-acetylglucosaminidase (NAG) activity, respectively. More recently, urinary NAG activity has emerged as the most widely assayed urinary enzyme for detecting renal damage because of its stability in urine, its relative molecular mass that precludes filtration by the glomerulus, and its high activity presence in the tubular lysosomes. The marked increases in the urinary albumin-to-creatinine ratio and NAG activity levels in the present 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.[52–54] These have been associated with decreases in measured creatinine clearance and GFR and have occurred in both on-pump and off-pump surgeries. This decrease was statistically higher in on-pump patients.

In the present study, logistic regression model analysis showed that the use of CPB is significantly associated with adverse renal outcomes. In addition, the effects of diabetes mellitus, age >70, hypertension, multiple vessels disease, preoperative increased creatinine and BUN levels, preoperative decreased creatinine clearance and GFR levels, and a preoperative left ventricle ejection fraction <40 were independent predictors for postoperative renal failure requiring dialysis. Some parameters, such as congestive heart failure, preoperative cardiogenic shock, urgent operations, increased body mass index, peripheral vascular disease, intraoperative low cardiac output, high blood transfusion requirements, the use of nonleft internal mammary arterial conduits, and persistent low cardiac output states were associated with postoperative dialysis requirements in other studies,[19,37,40] and were confirmed by the findings of this study.

5. Conclusion

An examination of the previous literature did not reveal any comparisons of the effects of on-pump and off-pump coronary bypass surgery on renal function in patients with nondialysis-dependent renal dysfunction. The present study indicates that the off-pump technique is more renoprotective in patients with nondialysis-dependent renal insufficiency.

The results support that off-pump coronary revascularization leads to earlier patient improvement and provides superior renal protection for patients with nondialysis-dependent renal dysfunction than conventional CABG does. Additionally, this technique resulted in a shorter duration of intensive care, fewer complications associated with surgery, and lower hospital fees.

5.1. Limitations of the study

This study is retrospective, observational, and limited to a single institution. All data were entered into the database as a part of patient management. One important limitation of this study is that the researchers did not investigate late outcomes. Several studies have revealed poor late outcomes of conventional CABG in patients with renal dysfunction. Five-year actuarial survival rates of dialysis patients range from 32% to 55.8%.[2,3,54]

Using the levels of serum creatinine, BUN, creatinine clearance, and GFR as the sole markers of renal function may also be considered a limitation. Although measuring patients' urinary, the microalbuminuria, retinal binding protein, or NAG might give a more detailed picture of renal damage; in our work, we could not use these parameters due to economic and technical deficiencies.

Author contributions

Conceptualization: Bilgehan Erkut.
Data curation: Umit Arslan, Ali Ihsan Tekin, Bilgehan Erkut.
Formal analysis: Umit Arslan, Bilgehan Erkut.
Funding acquisition: Eyupserhat Calik.
Investigation: Eyupserhat Calik, Bilgehan Erkut.
Methodology: Eyupserhat Calik, Bilgehan Erkut.
Project administration: Bilgehan Erkut.
Resources: Umit Arslan, Bilgehan Erkut.
Software: Bilgehan Erkut.
Supervision: Umit Arslan, Eyupserhat Calik, Bilgehan Erkut.
Validation: Bilgehan Erkut.
Visualization: Eyupserhat Calik, Bilgehan Erkut.
Writing – original draft: Eyupserhat Calik, Ali Ihsan Tekin, Bilgehan Erkut.
Writing – review & editing: Ali Ihsan Tekin, Bilgehan Erkut.

References

[1] Hayashida N, Chihara S, Tayama E, et al. Coronary artery bypass grafting in patients with mild renal insufficiency. Jpn Circ J 2001;65:28–32.
[2] Franga DL, Kratz JM, Crumbley AJ, et al. Early and long-term results of coronary artery bypass grafting in dialysis patients. Ann Thorac Surg 2000;70:813–9.
[3] Nakayama Y, Sakata R, Ura M, et al. Long-term results of coronary artery bypasses grafting in patients with renal insufficiency. Ann Thorac Surg 2003;75:496–500.
[4] Hayashida N, Teshima H, Chihara S, et al. Does off-pump coronary artery bypass grafting really preserve renal function? Circ J 2002; 66:921–5.
[5] Loganathan S, Nieh CC, Emmert MY, et al. Off-pump versus on-pump coronary artery bypass procedures: postoperative renal complications in an Asian population. Ann Acad Med Singapore 2010;39:112–6.
[6] Massoudy P, Wagner S, Thielmann M, et al. Coronary artery bypass surgery and acute kidney injury - impact of the off-pump technique. Nephrol Dial Transplant 2008;23:2853–60.
[7] Loef BG, Epema AH, Navis G, et al. Off-pump coronary revascularization attenuates transient renal damage compared with on-pump coronaryrevascularization. Chest 2002;121:1190–4.
[8] Tashiro T, Nakamura K, Morishige N, et al. Off-pump coronary artery bypass grafting in patients with end-stage renal disease on hemodialysis. J Card Surg 2002;17:377–82.
[9] Hirose H, Amano A, Takahashi A. Efficacy of off-pump coronary artery bypass grafting for the patients on chronic hemodialysis. Jpn J Thorac Cardiovasc Surg 2001;49:693–9.
[10] Ascione R, Nason G, Al-Ruzzeh S, et al. Coronary revascularization with or without cardiopulmonary bypass in patients with preoperative nondialysisdependent renal insufficiency. Ann Thorac Surg 2001;72: 2020–5.
[11] Schwann NM, Horrow JC, Strong MD3rd, et al. Does off-pump coronary artery bypass reduce the incidence of clinically evident renal dysfunction after multivessel myocardial revascularization? Anesth Analg 2004;99:959–64.
[12] Ascione R, Lloyd CT, Underwood MJ, et al. On-pump versus off-pump coronary revascularisation: evaluation of renal function. Ann Thorac Surg 1999;68:493–8.
[13] Khilji SA, Khan AH. Acute renal failure after cardiopulmonary bypass surgery. J Ayub Med Coll Abbottabad 2004;16:25–8.
[14] Mehta RL, Chertow GM. Acute renal failure definitions and classification: time for change? J Am Soc Nephrol 2003;14:2178–87.
[15] Sirivella S, Gielchinksy I, Parsonnet V. Mannitol, furosemide, and dopamine infusion in postoperative renal failure complicating cardiac surgery. Ann Thorac Surg 2000;69:501–6.
[16] Corwin HL, Sprague SM, DeLaria GA, et al. Acute renal failure associated with cardiac operations. A case control study. J Thorac Cardiovasc Surg 1989;98:1107–12.

[17] Bucerius J, Gummert JF, Walther T, et al. On-pump versus off-pump coronary artery bypass grafting: impact on postoperative renal failure requiring renal replacement therapy. Ann Thorac Surg 2004;77:1250–6.

[18] Suen WS, Mok CK, Chiu SW, et al. Risk factors for development of acute renal failure (ARF) requiring dialysis in patients undergoing cardiac surgery. Angiology 1998;49:789–800.

[19] Chertow GM, Lazarus JM, Christiansen CL, et al. Preoperative renal risk stratification. Circulation 1997;95:878–84.

[20] Rao V, Weisel RD, Buth KJ, et al. Coronary artery bypass grafting in patients with non-dialysis-dependent renal insufficiency. Circulation 1997;96:38–45.

[21] Meharwal ZS, Mishra YK, Kohli V, et al. Off-pump multivessel coronary artery surgery in high-risk patients. Ann Thorac Surg 2002;74:1353–7.

[22] Sabik JF, Gillinov AM, Blackstone EH, et al. Does off-pump coronary surgery reduce morbidity and mortality? J Thorac Cardiovasc Surg 2002;124:698–707.

[23] Tang AT, Knott J, Nanson J, et al. A prospective randomised study to evaluate the renoprotective action of beating heart coronary surgery in low risk patients. Eur J Cardiothorac Surg 2003;22:118–23.

[24] Puskas JD, Cheng D, Knight J, et al. Off-pump versus conventional coronary artery bypass grafting: a meta-analysis and consensus statement from the 2004 ISMICS consensis conference. Innovation 2005;1:3–27.

[25] Arom KV, Flavin TF, Emery RW, et al. Safety and efficacy of off-pump coronary artery bypass grafting. Ann Thorac Surg 2000;69:704–10.

[26] Chukwuemeka A, Weisel A, Maganti M, et al. Renal dysfunction in high-risk patients after on-pump and off-pump coronary artery bypass surgery: a propensity score analysis. Ann Thorac Surg 2005;80:2148–53.

[27] Reston JT, Tregear SJ, Turkelson CM. Meta-analysis of short-term and mid-term outcomes following off-pump coronary artery bypass grafting. Ann Thorac Surg 2003;76:1510–5.

[28] Hiberman M, Derby GC, Spencer RJ, et al. Sequential pathophysiological changes characterizing the progression from renal dysfunction to acute failure following cardiac operation. J Thorac Cardiovasc Surg 1980;79:838–44.

[29] Regragui IA, Izzat MB, Birdi I, et al. Cardiopulmonary bypass perfusion temperature does not influence perioperative renal function. Ann Thorac Surg 1995;60:160–4.

[30] Bhat JG, Gluck MC, Lowenstein J, et al. Renal failure after heart surgery. Ann Intern Med 1976;84:677–82.

[31] Mangano CM, Diamondstone LS, Ramsay JG, et al. Renal dysfunction after myocardial revascularization: risk factors, adverse outcomes, and hospital resource utilization. The Multicenter Study of Perioperative Ischaemia Research Group. Ann Intern Med 1998;128:194–203.

[32] Corwin HL, Sprague SM, DeLaria GA, et al. Acute renal failure associated with cardiac operations: a case control study. J Thorac Cardiovasc Surg 1989;98:1107–12.

[33] Stallwood MI, Grayson AD, Mills K, et al. Acute renal failure in coronary artery bypasses surgery: independent effect of cardiopulmonary bypass. Ann Thorac Surg 2004;77:968–72.

[34] Hilberman M, Myer BD, Carrie BJ, et al. Acute renal failure following cardiac surgery. J Thorac Cardiovasc Surg 1979;77:880–8.

[35] Murkin JM, Boyd WD, Ganapathy S, et al. Beating heart surgery: why expect less central nervous system morbidity? Ann Thorac Surg 1999;68:1498–501.

[36] Kshettry VE, Flavin TF, Emery RW, et al. Does multi-vessel off-pump coronary artery bypass (OPCABG) reduce postoperative morbidity? Ann Thorac Surg 2000;69:1725–30.

[37] Bull DA, Neumayer LA, Stringham JC, et al. Coronary artery bypass grafting with cardiopulmonary bypass versus off-pump cardiopulmonary bypass grafting: does eliminating the pump reduce morbidity and cost? Ann Thorac Surg 2001;71:170–5.

[38] Mangos GJ, Brown MA, Chan WY, et al. Acute renal failure following cardiac surgery: incidence, outcomes, and risk factors. Aust N Z J Med 1995;25:284–9.

[39] Buffolo E, de Andrade CS, Branco JN, et al. Coronary artery bypasses grafting without cardiopulmonary bypass. Ann Thorac Surg 1996; 61:63–6.

[40] Mack M, Bachand D, Acuff T, et al. Improved outcomes in coronary artery bypass grafting with beating-heart techniques. J Thorac Cardiovasc Surg 2002;124:598–607.

[41] Cleveland JCJr, Shroyer AL, Chen AY, et al. Off-pump coronary artery bypass grafting decreases risk-adjusted mortality and morbidity. Ann Thorac Surg 2001;72:1282–8.

[42] Hart JC, Spooner TH, Pym J, et al. A review of 1,582 consecutive Octopus off-pump coronary bypass patients. Ann Thorac Surg 2000;70:1017–20.

[43] Zamvar V, Williams D, Hall J, et al. Assessment of neurocognitive impairment after off-pump and on-pump techniques for coronary artery bypass graft surgery: prospective randomized controlled trial. BMJ 2002;325:1268.

[44] Tabata M, Takanashi S, Fukui T, et al. Off-pump coronary artery bypass grafting in patients with renal dysfunction. Ann Thorac Surg 2004;78: 2044–9.

[45] Lemmer JH, Dilling EW, Morton JR, et al. Aprotinin for primary coronary artery bypass grafting: a multicenter trial of three dose regimens. Ann Thorac Surg 1996;62:1659–68.

[46] Bouchard D, Cartier R. Off-pump revascularization of multivessel coronary artery disease has a decreased myocardial infarction rate. Eur J Cardiothorac Surg 1998;14:S20–4.

[47] van Dijk D, Nierich AP, Jansen EW, et al. Early outcome after off-pump coronary bypass surgery: results from a randomized study. Circulation 2001;104:1761–6.

[48] Hilberman M, Derby GC, Spencer RJ, et al. Sequential pathophysiological changes characterizing the progression from renal dysfunction to acute renal failure following cardiac operation. J Thorac Cardiovasc Surg 1980;79:838–44.

[49] Zanardo G, Michielon P, Paccagnella A, et al. Acute renal failure in the patients undergoing cardiac operation: prevalence, mortality rate, and main risk factors. J Thorac Cardiovasc Surg 1994;107: 489–95.

[50] Liu JY, Birkmeyer NJ, Sanders JH, et al. Risks of morbidity and mortality in dialysis patients undergoing coronary artery bypass surgery. Northern New England Cardiovascular Disease Study Group. Circulation 2000; 102:2973–7.

[51] Labrousse L, de Vincentiis C, Madonna F, et al. Early and long-term results of coronary artery bypass grafts in patients with dialysis-dependent renal failure. Eur J Cardiothorac Surg 1999;15:691–6.

[52] Khaitan L, Sutter FP, Goldman SM. Coronary artery bypass grafting in patients who require long-term dialysis. Ann Thorac Surg 2000; 69:1135–9.

[53] Weinstein GS, Rao PS, Vretakis G, et al. Serial changes in renal function in cardiac surgical patients. Ann Thorac Surg 1989;48:72–6.

[54] Gamoso MG, Phillips-Bute B, Landolfo KP, et al. Off-pump versus on-pump coronary artery bypass surgery and post-operative renal dysfunction. Anaesth Analg 2000;91:1080–4.