Original article

The Outcome of Patients with Renal Dysfunction, after Coronary Artery Bypass Grafting (CABG). Comparison Between the two Methods, On-Pump and Off-Pump CABG

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Abstract: *Background. Renal dysfunction is known to be a major predictor of in-hospital and remote mortality among patients with coronary artery disease (CAD), who undergo coronary artery bypass grafting (CABG). The aim of this study was to investigate the outcome of patients with non-dialysis-dependent renal dysfunction, who underwent on - pump and off-pump CABG. Methods. Between October 1, 1996 and September 30, 2000, a total of 1723 consecutive patients underwent isolated CABG. Fifty-nine of 1723 patients with CAD had also renal dysfunction (serum creatinine ≥2 mg/dl). On-pump CABG was performed in 43/59 and off-pump CABG in 16/59 patients. The causes of renal dysfunction were diabetes mellitus (49,2%), hypertension (18,6%), atherosclerosis (13,6%), chronic glomerulonephritis (8,5%) and others (10,1%) of unknown etiology. In on-pump CABG we maintained the perfusion pressure above 60mmHg. Furocemide or mannitol were given during the heart surgery. Off-pump CABG was performed using initially a compression type of coronary stabilizer and after mid-1999 a suction type of stabilizer. Results. The hospital mortality rate was 3/43 (7,0%) in on-pump and 1/16 (6,3%) in off-pump group. The Intensive Care Unit (ICU) stay was significantly shorter in off-pump group than the on-pump group (p<0,05), and the length of postoperative stay was two-thirds of that in the on-pump group. No significant differences were found in terms of the long-term survival of cardiac event-free rate between the two groups. Postoperative hemodialysis was performed in 8/59 patients. Conclusions. Patients with renal dysfunction carry significant operative risks and require prolonged hospital care. Off-pump CABG strategy in these patients is safe and contributes to the improvement of both postoperative and remote results. The long-term results were not different between the two groups in this study. Hippokratia 2006; 10(2): 75-79*

Key words: *Renal dysfunction, on-pump, off pump coronary artery bypass grafting (CABG), preoperative risk factors, surgical results, postoperative results, survival*

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Introduction

Renal dysfunction is known to be a major predictor of in-hospital and remote mortality among patients who undergo coronary artery bypass grafting (CABG)[1]. The negative effects of cardiopulmonary bypass (CPB) on renal function are well studied and may be due to several factors, such as non-pulsative flow, inadequate renal perfusion and free plasma hemoglobin[2,3]. However, CABG without CPB (off-pump) is recent worldwide growing surgical technique, with good short-term results in high-risk patients[3]. Beginning in October 1996 and supported by the initial good short-term results of off-pump CABG, we have the last three years more patients with renal dysfunction referred to off-pump CABG.

The prognosis of patients with renal dysfuntion independent from hemodialysis is not well studied and there are few reports on these patients[2,4]. This study investigated the outcomes of patients with renal dysfunction (serum creatinine ≥2mg/dl), who underwent on-pump and off-pump CABG.

Patients and Methods

Between October 1, 1996 and September 30, 2000, a total of 1723 consecutive patients undrewent isolated CABG in AHEPA University Hospital of Thessaloniki. Among them, there were 59 (3,4%) with renal dysfunction, as it was defined by serum creatinine ≥2 mg/dl. Serum creatinine was chosen for the detection of renal dysfunction because of the simplicity of its measurement. Patients on either hemodialysis or peritoneal dialysis were excluded from this study. These 59 patients were divided into two groups: On-pump CABG was performed in 43 patients (group A) and off-pump CABG in 16 patients (group B). The outcomes of these two groups of patients were compared.

Group A consisted of 43 patients (35 male and 8 female with mean age of 66.8 ± 8.3 years) and Group B consisted of 16 patients (13 males and 3 females with a mean age of 65.8 ± 7.9 years).

The preoperative data are shown in Table 1. The causes of renal dysfunction were diabetic nephropathy in 29 (42,9%), hypertension in 11 (18,6%), atherosclerosis in 8 (13,6%), glomerulonephritis in 5 (8,5%), and unknown etiology in 6 (10,1%). Angiographic profiles in Group A and B were similar.

Patients' demographics, operative data, postoperative

Table 1. ***Preoperative risk factors.***

On pump CABG vs. off pump CABG					
	Group A, on-pump		**Group B, off-pump**		**p**
	n=43		n=16		
Clinical Characteristics					
Age (years)	66.8±8.3	range 31-77	65.8±7.9	range 52-79	NS*
Age over 70 (years)	7	16.2%	4	25.5%	NS
Female	8	18.5%	3	18.8%	NS
Cardiac profile					
Previous myocardial infarction	34	79.1%	11	68.8%	NS
Poor ejection fraction (< 40%)	6	14.0%	2	12.5%	NS
Redo surgery	2	4.7%	0	0.0%	NS
Emergency surgery	6	14.0%	3	18.8%	NS
Angiographic profile					
Left main disease	5	11.6%	3	18.8%	NS
Number of diseased vessels	2.6±0.5	range 1-3	2.4±0.7	range 1-3	NS
Three vessel disease	16	37.2%	9	563%	NS
Coronary risk factors					
Hypertension	24	55.8%	14	87.5%	<0.05
Diabetes melitus	23	53.5%	6	37.5%	NS
Insulin user	13	30.2%	3	18.8%	NS
Co-morbidity					
Cerebral vascular accident	6	14.0%	3	18.8%	NS
Calcified ascending aorta	8	18.6%	2	12.5%	NS
Chronic pulmonary obstructive disease	3	7.0%	2	12.5%	NS
Renal function					
Preoperative serum creatinine (mg/dl)	2.7±0.9	range 2.0-5.8	2.6±0.6	range 2.0-4.9	NS
NS*: not significant					

complications and remote results were collected. Hospital mortality included death occuring within 30 days of the operation or during the same hospitalization. Remote cardiac events included: recurrence of angina (symptomatic angina or positive treadmill test), percutaneous transluminal coronary angioplasty (PTCA), redo CABG, congestive heart failure (CHF), arrhythmia requiring hospital admission and sudden death. Remote results were collected by correspondence with patients or reports from the private physicians.

Statistical analysis was performed using Student's t-test for continuous variables. Results were expressed as the mean ± standard deviation. Postoperative patient survival rate was constructed by the Kaplan - Meier method, and compared using Mantel-Cox's log-rank tests. A p-value less than 0.05 was considered significant.

Surgical Technique

On - pump CABG was performed under cardioplegic arrest using St. Thomas solution, supported with CPB at normothermia (36^0C). In October 1996, off-pump CABG under the beating heart was introduced and selected patients underwent off-pump CABG. Off-pump CABG was performed through a median sternotomy incision, using initially a compression type of coronary stabilizer and, after mid-1999, a suction type of stabilizer.

Our strategy of CABG was complete revascularization using arterial conduits if possible. In our practice, usually the left anterior descending artery (LAD) was bypassed with the left internal thoracic artery (LITA), the right coronary artery (RCA), if possible, with the right internal thoracic artery (RITA) and the circumflex artery with the saphenous vein. The use of bilateral internal thoracic arteries was avoided for the patients with uncontrolled diabetes due to the risk of postoperative sternal wound complication. Since hemodialysis blood access is usually established in the radial artery, the radial artery was not selected as a graft conduit if the patient had elevated serum creatinine.

In on - pump CABG for patients with renal dysfunction, we maintained the perfusion pressure above 60 mmHg, preferably above 70 mmHg to preserve renal perfusion. Furosemide and mannitol were given in order to increase urine output. Ultrafiltration was added to remove excess water during CPB. Hyperkalemia and acidemia were the indications for use the intraoperative hemodialysis.

Results

Operative results

Operative data are shown in Table 2. Both internal thoracic arteries, if possible, and the saphenous vein were used for myocardial revascularization. Harvesting of the radial artery was avoided intentionally, since future induction of hemodialysis was anticipated. The number of distal anastomosis performed by off-pump

Table 2. ***Surgical results.***

On pump CABG vs. off pump CABG					
	Group A, on-pump		**Group B, off-pump**		**p**
n	43		16		
n			16	100%	
MIDCAB			2	12.5%	
Number of distal anastomosis	3.5±1.3	2-7	2.1±0.6	1-3	<0.0005
Bilateral internal thoracic arteries	12	27.9%	6	37.5%	NS
Total arterial bypass	6	14.0%	10	62.5%	NS
Complete revascularization	38	88.4%	10	62.5%	<0.05
Aorta clamp time (min)	38±14	38-216			
Pump time (min)	68±36	22-122			
Average coronary clamp time					
(off-pump CABG)			13.3±2.8	9.5-19	
Grafts					
Left intrernal thoracic artery	41	95.3%	16	100%	NS
Right internal thoracic artery	12	27.9%	8	50.0%	NS
Saphenous vein	35	81.4%	4	25.0%	<0.0005
Blood transfusion	29	67.4%	5	31.3%	<0.05

CABG was significantly lower ($p<0.0005$) than in on-pump CABG. The frequency of the arterial grafts was not significantly different between the off-pump and on-pump groups; however, the frequency of use of saphenous vein graft was significantly lower ($p<0.0005$) in the off-pump group.

Requirement of blood transfusion was markedly lower in the off-pump group.

The hospital mortality rate was 7.0% (3/43 patients) in group A and 6.3% (1/16 patients) in group B. The causes of the in-hospital deaths were pneumonia in two, cardiac related in one, and mediastinitis in one.

than in the on-pump group. The ICU stay for patients who underwent off-pump CABG was less than half of that of patients who underwent on-pump CABG, and the length of postoperative stay was two thirds that of the on-pump group. No postoperative stroke, perioperative myocardial infarction, low-output syndrome, or re-exploration for bleeding occurred in the off-pump group.

During the mean follow-up of 1.5 years in the off-pump group, two episodes of CHF including one death were observed. Although the length of follow-up in both groups was limited, no significant differences were identified in terms of the long-term survival or cardiac event-free rate between the two groups. Postoperative hemodialysis

Table 3. ***Postoperative outcomes.***

On-pump CABG vs. off-pump CABG					
	Group A, on-pump		**Group B, off-pump**		**p**
n	43		16		
Intubation (h)	16.0 ± 29.9	3-184	15.3±32.1	1-95	NS
ICU stay (days)	5.1 ± 5.3	1-31	2.2 ± 1.5	1-7	<0,05
Postoperative stay (days)	22.6 ± 13.3	10-71	15.1 ± 7,4	5-32	<0,05
Major complication (patients)	14	32.6%	3	18.8%	NS
Low output syndrome	3	7.0%	0	0.0%	NS
Postoperative myocardial infarction	0	0.0%	0	0.0%	NS
Cerebral vascular accident	2	4.7%	0	0.0%	NS
Mediastinitis	0	0.0%	1	6.3%	NS
Re-exploration for bleeding	0	0.0%	0	0.0%	NS
Postoperative hemodialysis	6	14.0%	2	12.5%	NS
In - hospital death	3	7.0%	1	6.3%	NS

Postoperative results

The postoperative results are shown in Table 3. The intubation period was not significantly different between the on-pump and off-pump groups; however, the Intensive Care Unit (ICU) stay and postoperative stay were ($p<0.05$) significantly shorter in the off-pump group

was performed in eight (8/59) patients (13.6%). Among them, one patient required long-term maintenance hemodialysis, and the others were supported with hemodialysis in the immediate postoperative period only.

Long - term results

The collection of long-term data, excluding the 4

Table 4. *Long term results.*

On pump CABG vs. off pump CABG			
	Group A	**Group B**	**p**
Number of patients followed (53/55)	39		
Follow up period (years)	2.5 ± 1.9	2.3 ± 1.9	NS
Permanent dialysis	6 (15.4%)	2 (14.3%)	NS
Total outpatient cardiac events			
Angina	1 (2.6%)	0 (0.0%)	NS
Congestive heart failure	8 (20.5%)	2 (14.3%)	NS
Sudden death	1 (2.6%)	0 (0.0%)	NS
Distant death	10 (25.6%)	3 (21.4%)	NS
Cardiac	3 (7,7%)	2 (14,3%)	NS
Non - cardiac	6 (15.4%)	2 (14.3%)	NS
Related with renal dysfunction	1 (2.6%)	1 (7.1%)	NS
1 year survival rate	92.1%	92.3%	NS
2 year survival rate	83.6%	84,0%	NS
3 year survival rate	73.8%	74.9%	NS
5 year survival rate	70.4%	74.3%	NS

hospital deaths, was completed in 96.4% of patients with renal dysfunction with a mean follow-up period of 2.5±1.9 years in group A and 2.3±1.9 years in group B. The long-term results are listed in Table 4. Analysis of the late cardiac events revealed that CHF occurred more frequently in group A than in B, but that the recurrence of angina was less frequent in both groups. Eight patients (15.0%), 6 in group A and 2 in group B, required chronic hemodialysis.

Late death was observed in 13 patients (24.5%) 10 in group A and 3 in group B. Cardiac death was observed in five patients (9.4%). Among the 10 non-cardiac deaths in these groups, two deaths were directly related to renal dysfunction. The survival curve is shown in

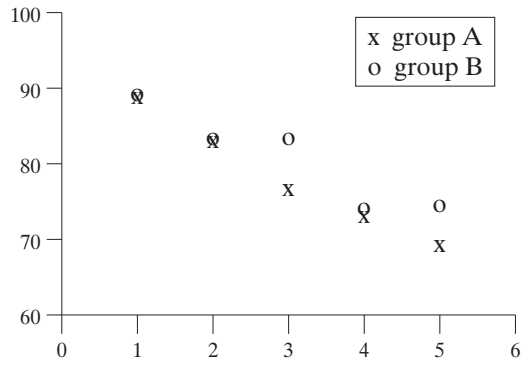

Figure 1. ***The five year survival curve of group A and B.***

Figure 1. The actuarial 1-, 2-, 3-, 4-, and 5-year survival rates (Kaplan-Meier analysis) were 92.1, 83.6, 77.1, 73.8 and 70.4% in group A and 92.3, 84.0, 84.0, 74.9 and 74.9 in group B (non-significantly different by Log rank test). Although the length of follow-up in both groups was limited, no significant differences were indentified in terms of long-term survival or cardiac event free rate between the two groups.

Discussion

The development of multiple clinical and subclinical deleterious effects of CPB on renal function has been well recognized[1,5]. However, off-pump CABG demonstrated earlier recovery and other benefits, compared to the patients who underwent on-pump CABG[5,6]. After 1999, supported by the initial good results, 69,6% (16 out of 23) of our renal patients were referred to off-pump CABG, and only patients with contraindications for off-pump CABG, such as intramuscularly coronary artery or severely calcified coronary artery, underwent on-pump CABG.

The results of our study showed that patients who underwent off-pump CABG demonstrated early recovery, compared to the patients who underwent on-pump CABG. In off- pump bypass, the perfusion pressure is physiological and is much higher than the pressure created by CPB. Since renal perfusion pressure was well maintained during the entire operation, urine output would be preserved as well. Dilutional anemia when using CPB does not occur in off-pump bypass and the frequency of blood transfusion was much lower than in on-pump CABG[7,8]. Calcified aorta, frequently observed in patients with renal dysfunction, was considered to be the risk factor of postoperative stroke[9]. Off-pump CABG successfully contributed to reduce the length of stay to a level similar to that of patients with normal renal function. Thus, we considered that off-pump CABG successfully contributed to the reduction of the length of stay.

The number of distal anastomosis in the off-pump group was significantly smaller than that in the on-pump CABG group. However, after mid-1999 the suction type of stabilizer allowed us to perform multivessel revascularization including the posterior wall of the heart. The number of distal anastomosis in off-pump CABG was increased from 1.9 ± 0.4 with the compression device to 2.4 ± 0.7 with the suction device. The percentage of complete revascularization also increased from 44.4%

in the early phase using the compression device to 85.7% in the late phase using the suction device.

Due to impaired water clearance, postoperative hypoxia secondary to pulmonary congestion was often observed. The metabolism of anesthetic medication in patients with renal dysfunction is delayed and the effect of anesthesia might be prolonged[9]. These two factors might result in a delay in extubation and a delay in tranfer out of ICU. Postoperative hemodialysis was indicated if the patient developed anuria, which was refractory to diuretics or inotropic support, and / or if the patient had elevated serum potassium. Three out of 6 patients who required prolonged ventilator support in our study were supported with hemodialysis in ICU. If hemodynamics were well preserved during hemodialysis, the patient's urine output eventually increased and the patients were then independent of hemodialysis. However, patients with unstable hemodynamics due to low output syndrome and hemodialysis-dependent patients all died in ICU. Preoperative serum creatinine in patients who received postoperative hemodialysis was 5.8 ± 1.4 mg/dl, and it was significantly higher than in patients with renal dysfunction who were not hemodialyzed postoperatively (2.5 ± 0.7 mg/dl, $p<0.001$).

Diabetes mellitus is known to influence long-term mortality. Patients with diabetic nephropathy are reported more likely to develop cardiovascular complications than those whose renal dysfunction is due to other causes[10]. Among the 8 patients of this study with postoperative permanent dialysis, 3 were with diabetic nephropathy.

The reported mortality rates in patients with non-dialysis-dependent renal dysfunction were between 5.3% [10] and 19.3%[11]. Thakar et al[12] reported recently that the mortality rate was 5.9% among patients who developed 30% or greater decline in postoperative GFR not requiring dialysis versus 0.4% among those with less of 30% decline of GFR. Our hospital mortality rate was comparable to these previous reports.

Even after surgical revascularization, late cardiac events occurred and would be a problem in patients with renal dysfunction[13]. CABG controlled angina recurrence and the incidence of remote PTCA adequately. However, CHF occurred more frequently in patients with renal dysfunction, which may be related to poor water clearance due to renal disease.

Long-term survival was poor in both groups and renal dysfunction was identified as an isolated predictor of remote death[13]. However, the long-term survival after CABG in patients with non-dialysis-dependent renal dysfunction has been poorly studied[11-14]. Durmaz et al [11] followed non-dialysis-dependent patients with various degrees of renal function and reported a 3-year survival rate of 96% in patients with creatinine between 1.6 mg/dl and 2.5 mg/dl and 57% in patients with creatinine > 2.5 mg/dl. The 3-year survival rate of the patients in our study was 77.1% in on-pump group and 84.0 in off-pump group and the preoperative serum creatinine ≥ 2 mg/dl was an independent predictor of late death. Both cardiac and non-cardiac deaths were frequent in patients with renal dysfunction. Four out of 5 cardiac deaths, 3 in group A and 1 in group B were due to CHF. Once CHF occurs after CABG in patients' with decreased renal function, it may be fatal and special care should be taken.

In conclusion, patients with decreased renal function carry significant operative risks and require prolonged hospital care. Changes in the strategy of CABG, such as the induction of off-pump CABG, influenced both postoperative and remote results. Off-pump CABG for patients with renal dysfunction is safe and contributes to shorten the patients recovery period; however, the long-term results were not different between the two groups in this study.

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