

# Coronary artery bypass grafting in patients with dialysis-dependent renal failure: ten-year results

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**Key words:**  
Coronary artery bypass graft; Dialysis; End-stage renal disease.

**Background.** Coronary artery disease has been reported to be accelerated in patients with chronic renal failure on maintenance dialysis. Coronary artery bypass grafting (CABG) in patients on long-term dialysis is still a debated issue.

**Methods.** We retrospectively reviewed 19 patients (12 men, 7 women, mean age  $64 \pm 11.2$  years) with end-stage renal disease who underwent CABG between 1990 and 2000. Operative procedures were CABG alone in 15 (78.9%) patients and CABG associated with valve procedures in 4 (21.1%) patients.

**Results.** The early (30-day) mortality rate was 10.5% (2 of 19 patients). Non-fatal complications occurred in 6 patients (31.5%). Four delayed deaths occurred; the actuarial survivals at 1, 2, 5 and 10 years were  $0.86 \pm 0.14$ ,  $0.78 \pm 0.10$ ,  $0.68 \pm 0.13$  and  $0.54 \pm 0.15$  respectively. Among 13 survivors the mean Canadian Cardiovascular Society class was  $1.3 \pm 0.3$  ( $p < 0.001$  vs preoperatively). ANOVA procedures showed age ( $p = 0.01$ ), Canadian Cardiovascular Society class  $\geq$  III ( $p < 0.001$ ), urgent/emergency operation ( $p < 0.001$ ), left ventricular ejection fraction  $< 0.50$  ( $p < 0.001$ ), a prior myocardial infarction ( $p = 0.01$ ), a preoperative mean creatinine level  $\geq 5$  mg/dl ( $p = 0.02$ ) and a duration of dialysis  $\geq 60$  months ( $p = 0.03$ ) to be strongly related to early and delayed mortality.

**Conclusions.** CABG in patients with dialysis-dependent chronic renal failure is associated with acceptable results. Accurate patient selection, early referral to surgery, and adequate perioperative management are advisable.

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## Introduction

Coronary artery disease (CAD) has been reported to be accelerated in patients with chronic renal failure on maintenance dialysis<sup>1</sup>. The higher incidence of CAD in this patient population can be attributed to such factors as hyperlipidemia, hypertension, renal anemia, fluid overload by artero-venous shunts, platelet dysfunction, heterotopic calcification due to secondary hyperparathyroidism and hypercalcemia<sup>2</sup>.

The number of patients requiring dialysis for end-stage renal disease is increasing at a rate of approximately 10% per year, predominantly in patients over 65 years of age<sup>3</sup>, and coronary artery bypass grafting (CABG) has become the standard treatment for CAD in patients on maintenance dialysis, since its superiority over percutaneous transluminal coronary angioplasty (PTCA) in terms of overall and angina-free survival has been demonstrated<sup>4</sup>.

CABG is associated with an increased perioperative risk<sup>5-8</sup> and since it was first performed in a patient with chronic renal failure by Menzoian et al.<sup>9</sup> in 1974, its real benefit and feasibility are still controversial.

The aim of this study was to examine our 10-year experience with myocardial revascularization in patients on maintenance dialysis.

## Methods

**Patient characteristics.** Between January 1990 and January 2000, 19 consecutive patients with end-stage renal disease maintained on chronic dialysis underwent CABG at our Institution. Twelve (63.1%) were male and 7 (36.9%) were female. The mean age at the time of surgery was  $64 \pm 11.2$  years (range 43-80 years). Preoperatively, 13 (68.4%) patients were on hemodialysis and 6 (31.6%) on peritoneal dialysis; the duration

of dialysis ranged from 3 to 97 months (mean  $34.2 \pm 21.5$  months). The cause of renal failure was chronic glomerulonephritis in 9 patients (47.3%), diabetic nephropathy in 5 (26.3%), vascular nephropathy in 2 (10.5%), rapidly progressive glomerulonephritis in 1 (5.3%), systemic lupus erythematosus in 1 (5.3%) and unknown in 1 patient (5.3%). The mean preoperative serum creatinine level was  $9.8 \pm 2.1$  mg/dl (range 3.5 to 12 mg/dl) and the hemoglobin concentration ranged from 8 to 12 g/dl (mean  $10.2 \pm 1.1$  g/dl). At the time of surgery the mean left ventricular ejection fraction (LVEF) was  $46.1 \pm 10.8\%$  and 7 patients (36.8%) had moderate or severe left ventricular dysfunction (LVEF < 50%). Preoperative symptoms of CAD included Canadian Cardiovascular Society (CCS) class IV angina in 7 (36.9%) patients, class III angina in 11 (57.8%) and class II angina in 1 patient (5.3%). Preoperative angina patterns were characterized as stable in 3 patients (15.7%), unstable in 13 (68.6%) and postinfarction in 3 (15.7%) patients. Five patients (26.3%) had dyspnea (2 at rest) and 4 (21%) had symptoms of congestive heart failure.

Four (21%) patients had previously documented myocardial infarction, 1 (5.3%) had previous PTCA and none had a previous CABG.

Cardiac catheterization revealed left main coronary disease in 5 patients (26.3%), three-vessel disease in 6 (31.5%), two-vessel disease in 5 (26.3%) and one-vessel disease in 1 patient (5.3%). Associated cardiac pathologies included: mitral regurgitation in 1 patient (5.3%), severe aortic stenosis in 2 (10.5%) and aortic incompetence in 1 patient (5.3%). Associated, co-morbid diseases included hypertension (42.1%), diabetes mellitus (31.5%), hypercholesterolemia (21%), chronic obstructive pulmonary disease (36.9%) and cerebrovascular disease (5.3%). Seven patients (36.9%) reported a history of tobacco smoking within 1 year before CABG and 10 (52.6%) had a familial history of CAD.

**Surgical procedures.** Details of the operative procedures are given in table I. Patients received a mean of  $2.1 \pm 0.8$  grafts. The left internal thoracic artery was used in 14 (73.6%) and the radial artery in 2 patients (10.5%); all other grafts were constructed using the saphenous vein. Globally, the percentage of patients with at least one arterial graft was 73%. Surgery was elective in 12 (63.2%) patients, urgent in 5 (26.3%) and performed in emergency conditions in 2 (10.5%) patients. Two patients (10.5%) underwent off-pump CABG while in 17 patients (89.5%) surgery was performed using a cardiopulmonary bypass and moderate systemic hypothermia (25 to 32°C).

In 14 patients (73.6%) double venous cannulation, caval tourniquets and atrial drainage were employed to avoid hyperkalemia due to the cardioplegic solution, while in the other 3 (15.3%) patients, single two-stage venous cannulation was used. Myocardial protection was enhanced by infusion of a hypothermic crystalloid cardioplegic solution, delivered either in an antegrade

**Table I.** Myocardial revascularization in patients with chronic renal failure.

Case	Age (years)	Sex	Procedure
1	68	F	SVG → LAD; SVG → CCA
2	80	M	SVG → LAD; AVR*
3	44	M	LIMA → LAD; SVG → CCA; SVG → RCA
4	59	M	LIMA → LAD; MVR*
5	74	F	SVG → LAD; SVG → CCA; SVG → DB
6	72	M	SVG → LAD; SVG → CCA; SVG → RCA
7	47	M	LIMA → LAD; SVG → CCA
8	71	M	LIMA → LAD; SVG → CCA; SVG → RCA
9	64	F	LIMA → LAD; SVG → CCA; SVG → RCA
10	67	F	LIMA → LAD; SVG → CCA
11	78	M	LIMA → LAD; SVG → CCA; SVG → DB
12	43	M	LIMA → LAD; SVG → CCA; SVG → RCA
13	61	F	LIMA → LAD; SVG → RCA; AVR*
14	63	F	LIMA → LAD; SVG → CCA; SVG → RCA
15	69	F	LIMA → LAD**
16	71	M	LIMA → LAD**
17	56	M	LIMA → LAD; RA → MB
18	53	M	LIMA → LAD; RA → MB; AVR*
19	76	M	SVG → LAD

AVR = aortic valve replacement; CCA = circumflex coronary artery; DB = diagonal branch; LAD = left anterior descending coronary artery; LIMA = left internal mammary artery graft; MB = marginal branch; MVR = mitral valve replacement; RA = radial artery graft; RCA = right coronary artery; SVG = saphenous vein graft. \* associated cardiac procedures; \*\* off-pump coronary artery bypass grafting.

fashion (16 patients) or in a retrograde fashion through the coronary sinus (1 patient). The mean cross-clamp time and mean cardiopulmonary bypass time were  $128 \pm 38.2$  and  $70 \pm 25.6$  min respectively. All patients were submitted to dialysis the day before surgery.

Intraoperatively, 2 patients underwent dialysis and 15 had intraoperative ultrafiltration. The mean ultrafiltered volume was  $1680 \pm 560$  ml. The serum potassium levels before and after cardiopulmonary bypass were  $4.2 \pm 0.4$  and  $5.1 \pm 0.6$  mmol/l respectively (p = NS). The hematocrit values before and after cardiopulmonary bypass were  $22.1 \pm 6.0$  and  $22.5 \pm 6.2\%$  respectively (p = NS). A mean of  $1.3 \pm 0.3$  units of packed red blood cells and  $2.3 \pm 0.4$  units of fresh frozen plasma were administered intraoperatively.

Data were collected during outpatient clinic appointments or by telephone interviews to patients or their physicians. The mean follow-up time was  $60.3 \pm 12.6$  months (range 1-120 months). No patient was lost to follow-up.

**Statistical analysis.** Continuous variables were expressed as means  $\pm$  SD. Discrete variables were presented as percentages. Data were compared using the  $\chi^2$  or the Fisher's exact test for categorical variables. Continuous data were analyzed using the paired and unpaired Student's t-test. One-way ANOVA analysis of variance was performed, where appropriate, to define the sig-

nificance of individual factors which might influence early and delayed survival. A total of 34 variables were studied: 17 were preoperative (age, gender, body surface area, presence of hypertension, diabetes, cerebrovascular disease, chronic obstructive pulmonary disease, peripheral vascular disease, prior myocardial infarction, CCS class, dyspnea at rest, angina at rest, unstable angina, LVEF < 0.50, preoperative creatinine levels  $\geq$  5 mg/dl, duration of dialysis, hemodialysis/peritoneal dialysis), 9 were operative (urgent-emergency/elective surgery, coronary artery bypass surgery, valvular surgery, combined surgery, off-pump/cardiopulmonary bypass surgery, cardiopulmonary bypass time, cross-clamping time, mono or double cannulation, use of whole blood or blood derivatives), and 8 were postoperative (bleeding, arrhythmias, low cardiac output, neurological complications, pulmonary complications, postoperative creatinine levels, postoperative potassium levels, postoperative infections). The strength of analyses was reduced by the small number of patients.

Death and event-free survival estimates were calculated by the product-limit method of Kaplan and Meier<sup>10</sup>, reported using 95% confidence limits and expressed as  $\pm$  SEM. SPSS for Windows release 8.0 (SPSS, Inc., Chicago, IL, USA) was used to perform data analyses.

In all cases a p value of < 0.05 was considered statistically significant.

## Results

In 16 patients dialysis treatment was resumed on the second postoperative day. The remaining 3 patients required dialysis during the first 24 postoperative hours because of volume overload. The mean duration of mechanical ventilation was  $22.6 \pm 12.4$  hours (range 12-41 hours) and the mean duration of permanence within the Intensive Care Unit (ICU) was  $36 \pm 21$  hours (range 10-74 hours).

There were two in-hospital deaths (defined as occurring within 30 days of surgery) and, thus, the early-mortality rate was 10.5%. A 62-year old female, urgently submitted to CABG, died of a low cardiac output syndrome on the first postoperative day. The second death occurred in a 68-year-old man who had been urgently submitted to CABG. He developed septic shock 2 weeks after surgery.

Non-fatal complications occurred in 6 patients (31.5%). Details are given in table II. There were four delayed deaths and thus, the delayed mortality rate was 23.5%. The mean interval between surgery and death was  $26 \pm 5$  months. The causes of delayed deaths were: acute myocardial infarction, a cerebrovascular accident, sudden death and unknown.

The actuarial survivals at 1, 2, 5 and 10 years were  $0.86 \pm 0.14$ ,  $0.78 \pm 0.10$ ,  $0.68 \pm 0.13$  and  $0.54 \pm 0.15$  respectively.

**Table II.** Non-fatal complications after coronary artery bypass grafting in dialysis-dependent patients.

None	13 (68.3%)
Bleeding	2 (10.5%)
Arrhythmias	1 (5.3%)
Low cardiac output	1 (5.3%)
Neurological	1 (5.3%)
Pneumonia	1 (5.3%)

Among survivors an overall improvement of the functional status was observed and the mean postoperative CCS class was  $1.3 \pm 0.3$  ( $p < 0.001$  vs preoperatively).

No patient showed any signs of improved renal function. Postoperative creatinine levels ranged from 3.4 to 12 mg/dl (mean  $7.6 \pm 1.4$  mg/dl,  $p = \text{NS}$  vs preoperatively).

The mean hemoglobin concentration was  $10.8 \pm 1.3$  g/dl (range 9.0-12.1 g/dl,  $p = \text{NS}$  vs preoperatively), and serum potassium levels ranged from 4.0 to 4.7 mmol/l (mean  $4.1 \pm 0.2$  mmol/l,  $p = \text{NS}$  vs preoperatively).

Among variables studied, age ( $67 \pm 10.4$  vs  $60 \pm 7.2$ ,  $p = 0.03$ ), CCS angina class ( $3.4 \pm 0.3$  vs  $2.7 \pm 0.2$ ,  $p < 0.001$ ) and LVEF ( $38 \pm 10.7$  vs  $51 \pm 10.1$ ,  $p < 0.001$ ) significantly differed between non-survivors and survivors respectively.

ANOVA procedures showed that age ( $p = 0.01$ ), a CCS class  $\geq$  III ( $p < 0.001$ ), urgent/emergency surgery ( $p < 0.001$ ), a LVEF < 0.50 ( $p < 0.001$ ), a prior myocardial infarction ( $p = 0.01$ ), a preoperative mean creatinine level  $\geq$  5 mg/dl ( $p = 0.02$ ), and a duration of dialysis  $\geq$  60 months ( $p = 0.03$ ) were variables which were strongly related to early and delayed mortality.

## Discussion

It is well known that cardiac disease is the leading cause of death in dialysis patients; according to the latest renal database<sup>11</sup> it accounts for 47% of deaths in end-stage renal disease patients on maintenance dialysis. The higher incidence of CAD in this patient population can be attributed to the presence of co-morbid conditions including hypertension, hyperlipidemia and abnormal carbohydrate metabolism leading to accelerated atherosclerosis<sup>12-14</sup>. In the last 10 years the number of candidates requiring coronary intervention has increased and although PTCA in chronic dialysis patients is technically feasible and provides relief of angina, aggressive restenosis limits its long-term benefit and thus CABG remains the preferred therapy in such patients<sup>4-15</sup>.

Even though many reviews regarding CABG in end-stage renal disease patients have been reported, its benefit and feasibility in terms of myocardial revascularization are still debated<sup>16</sup>. In fact, some groups have shown improved survival and improved quality of life<sup>17-19</sup>, oth-

er studies have demonstrated the opposite<sup>7-20</sup>, and yet more studies have shown an improved quality of life but no improvement in survival<sup>6-21</sup>.

More recently Labrousse et al.<sup>22</sup> demonstrated an improvement of functional status in 31 survivors among 82 dialysis patients undergoing CABG; Khaitan et al.<sup>23</sup> reported that CABG performed in 70 dialysis patients was associated with high morbidity and mortality risks vs the limited long-term resolution of angina and ultimate survival. Franga et al.<sup>24</sup> found that in 44 end-stage renal disease patients on chronic dialysis myocardial revascularization was feasible. Operative mortality was acceptable and surgery resulted in good symptomatic relief of angina and heart failure.

In this study we presented a small series of patients with dialysis-dependent chronic renal failure undergoing CABG. Our operative (30-day) mortality rate was 10.5% and it fits within the widely variable range of previous reports (0 to 31%, Table III)<sup>4,6,7,16-24</sup>.

The complication rate in the present study was 31.5%, comparable to that reported in the literature<sup>7,23</sup> and very close to the overall frequency of complications according to the Society of Thoracic Surgeons database (33%)<sup>25</sup>. An overview of the available literature of the last 12 years shows that the delayed mortality rate ranges from 10.5 to 55.7%; in our series the delayed mortality rate was 23.5%. Considering that from 1977 to 1995, the survival for dialysis patients experiencing myocardial infarction is reported to be 41% at 1 year and 27% at 2 years<sup>25</sup> early and long-term risks of these patients, although higher than in the general CABG population, are still better than that of general dialysis patients.

At follow-up, among 15 survivors, the mean CCS class was 1.3 ± 0.3 (p < 0.001 vs preoperatively) which demonstrates improved functional status and quality of life and confirms the benefit of CABG in our series.

Among the variables analyzed we found the preoperative patient's clinical situation to have a strong impact on mortality. Particularly, compromised left ventricular function, advanced CCS functional class and surgery performed in emergency conditions were found to contribute to the higher rates of early and delayed mortality.

In conclusion end-stage renal disease patients on chronic dialysis requiring CABG still constitute a surgical challenge. CABG can be performed in selected patients with increased but acceptable risks of perioperative morbidity and mortality. These patients are expected to have improved functional status with relief of angina. Thus, we believe that patients with chronic renal failure should not be denied surgery since, in such patients, medical treatment or PTCA are associated with a worse long-term outcome. Accurate patient selection based on the identification of risk factors and early referral to surgery (before the onset of congestive heart failure) are recommended.

Furthermore an adequate perioperative management is advisable. It should comprise:

**Table III.** Literature review of coronary artery bypass grafting in dialysis-dependent patients.

Author	No. patients	Early deaths (≤ 30 days)	Delayed deaths
Rostand et al. <sup>16</sup> , 1988	20	4 (20%)	5 (31.2%)
Opsahl et al. <sup>17</sup> , 1988	39	1 (2.6%)	11 (28.9%)
Deutsch et al. <sup>20</sup> , 1989	16	1 (6%)	Not reported
Batiuk et al. <sup>18</sup> , 1991	25	5 (20%)	4 (20%)
Owen et al. <sup>6</sup> , 1994	21	2 (9.5%)	2 (10.5%)
Blum et al. <sup>19</sup> , 1994	40	6 (15%)	11 (27.5%)
Samuels et al. <sup>7</sup> , 1996	13	4 (31%)	2 (19.3%)
Koyanagi et al. <sup>4</sup> , 1996	23	0	4 (17.3%)
Jahangiri et al. <sup>21</sup> , 1997	14	1 (7.1%)	4 (30.7%)
Labrousse et al. <sup>22</sup> , 1999	82	12 (14.6%)	39 (55.7%)
Khaitan et al. <sup>23</sup> , 2000	70	10 (14.3%)	27 (45%)
Franga et al. <sup>24</sup> , 2000	44	5 (11.4%)	13 (33.3%)
Current study	19	2 (10.5%)	4 (23.5%)

- the identification of conditions associated with chronic renal failure such as chronic anemia, coagulation defects and platelet dysfunction that expose these patients to postoperative complications;
- the prevention of infections which are more common because of decreased chemiotaxis, lymphopenia, decreased cell-mediated immunity, reduction of interferon and reduced monocyte function;
- the surveillance of fluid and electrolyte balance;
- the maintenance of an adequate red cell mass;
- the control of perioperative bleeding;
- care in administering fluids, with preference for albumin and plasma;
- intraoperative ultrafiltration;
- care in timing and deciding the route of perioperative dialysis.

Finally, in selected cases, off-pump CABG may be an optimal approach for end-stage renal disease patients on chronic dialysis because it allows complications associated with cardiopulmonary bypass (bleeding, fluid overload, cerebrovascular accident) to be avoided.

**Limitations of the study.** Our study presents some limitations that have to be pointed out: 1) the small number of patients; 2) the retrospective nature of the study; 3) the small number of postoperative events that limits the strength of statistical analyses.

In conclusion, although CABG in dialysis patients is associated with a high early and delayed mortality, long-term survival of these patients is still better than that of general dialysis patients. Surgery should be the preferred treatment in selected patients.

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