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Renal Failure after Coronary Bypass Surgery and the Associated Risk Factors

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ABSTRACT

Objective: We aimed to evaluate the risk factors associated with acute renal failure in patients who underwent coronary artery bypass surgery.

Methods: One hundred and six patients who developed renal failure after coronary artery bypass grafting (CABG) constituted the study group (RF group), while 110 patients who did not develop renal failure served as a control group (C group). In addition, the RF group was divided into two subgroups: patients that were treated with conservative methods without the need for hemodialysis (NH group) and patients that required hemodialysis (HR group). Risk factors associated with renal failure were investigated.

Results: Among the 106 patients that developed renal failure (RF), 80 patients were treated with conservative methods without any need for hemodialysis (NH group); while 26 patients required hemodialysis in the postoperative period (HR group). The multivariate analysis showed that diabetes mellitus and the postoperative use of positive inotropes and adrenaline were significant risk factors associated with development of renal failure. In addition, carotid stenosis and postoperative use of adrenaline were found to be significant risk factors associated with hemodialysis-dependent renal failure ($P < .05$). The mortality in the RF group was determined as 13.2%, while the mortality rate in patients who did not require hemodialysis and those who required hemodialysis was 6.2% and 34%, respectively.

Conclusion: Renal failure requiring hemodialysis after CABG often results in high morbidity and mortality. Factors affecting microcirculation and atherosclerosis, like diabetes mellitus, carotid artery stenosis, and postoperative vasopressor use remain the major risk factors for the development of renal failure.

INTRODUCTION

Acute renal failure after coronary artery bypass surgery (CABG) increases morbidity and mortality [Bahar 2005; Conlon 1999; Fischer 2002; Hirose 2001; Bove 2004; Santos 2004; Rodrigues 2009; Kim 2011; Durmaz 2003; Durmaz 1999]. The incidence of renal failure after open-heart surgery ranges from 1-30%, while the incidence of renal failure requiring hemodialysis has been reported to vary between 1-5% [Bahar 2005; Fischer 2002; Bove 2004; Santos 2004; Kim 2011; Provenchere 2003; Ascione 2001; Suen 1998; Osterman 2000; Stallwood 2004]. Reported underlying causes of renal failure included low cardiac output (LCO), renovascular emboli and thrombi, nephrotoxic agents and drugs (anesthetics, antibiotics, analgesics, diuretics, contrast agents), diabetes mellitus (DM), hypertension (HT), and cardiopulmonary bypass (CPB) [Bahar 2005; Conlon 1999; Fischer 2002; Bove 2004; Santos 2004; Ascione 2001; Behrend 1999; Weerasinghe 2001]. Kidney failure after CABG can usually be treated with conservative methods (diuretics, volume replacement, and positive inotropic support). Often, it may lead to severe conditions such as multiple organ failure [Bahar 2005]. In this study, we aimed to evaluate the risk factors associated with renal failure that develop after coronary bypass surgery.

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PATIENTS AND METHODS

The patients who underwent coronary bypass surgery between 2008 and 2012 were reviewed retrospectively. The control group included 110 patients, while the study group included 106 individuals who developed renal failure (RF group). Of the 106 patients in the RF group, 80 were treated with conservative methods without hemodialysis (NH group) and 26 patients required hemodialysis in the postoperative period (HR group).

The criteria for renal failure were an oliguric period of at least 6 hours (0.5 cc/kg/hour urine output) and twice the amount of creatinine detected during the preoperative period, despite fluid replacement and diuretic infusions. The criteria for hemodialysis requirement were signs of volume overload, potassium levels >6 mEq/L, metabolic acidosis (pH <7.1), blood urea nitrogen (BUN) >200mg/dL, and oliguria <200 mL/12 hours. Patients who underwent valve surgeries, off-pump procedures, and patients with preoperative renal insufficiency (above normal creatinine values) were excluded from the study.

Demographic characteristics, the time between angiography and surgery (effect of intravenous contrast material), diabetes mellitus, hypertension, smoking, left ventricular ejection fraction (LVEF), and preoperative biochemical parameters (urea, creatinine, sedimentation) were evaluated retrospectively. The cardiopulmonary bypass and X-clamp times, use of positive inotrope, blood transfusion, intra-aortic balloon pump (IABP) use, amount of bleeding, duration of mechanical

Table 1. Patient Demographics

	Control Group (n = 110)	RF Group (n = 106)	RF NH Group (n = 80)	RF HR Group (n = 26)
Mean age, y	58.0	66.1	64.9	69.6
Female	21	36	29	7
Time between angiography and operation, d	6.5	8.4	8.2	9.0
Preoperative ejection fraction, %	49.1	48.6	48.9	47.8
Diabetes mellitus, n	29	62	46	16
Hypertension, n	66	84	64	20
Peripheral artery disease, n	9	15	7	8
Chronic obstructive pulmonary disease, n	57	29	22	7
Redo surgery, n	0	2	0	2
Carotid stenosis, n	8	18	6	12
Sedimentation rate	31.6	43.9	43.7	44.3
Preoperative inotrope use (dopamine, dobutamine)	2	8	6	2
Cardiopulmonary bypass time, min	72.9	78.6	79.3	76.2
X-Clamp duration, min	45.6	47.9	47.4	49.5
Postoperative inotrope use (dopamine, dobutamine)	25	78	60	18
Postoperative adrenalin use	2	24	14	10
Intensive care unit stay, d	1.38	3.8	2.9	6.5
Hospital stay, d	6.2	8.5	8.0	10
Mortality	2 (1.8%)	14 (13.2%)	5 (6.2%)	9 (34%)

RF group indicates renal failure group; NH group, patients treated without hemodialysis; HR group, patients required hemodialysis.

ventilation, and the duration of stay in the intensive care unit and the overall stay at the hospital were evaluated during intraoperative and postoperative periods (Table 1).

Surgical Procedure

In all patients, induction of anesthesia was achieved with midazolam, fentanyl, and vecuronium bromide. Patients were monitored with radial artery and jugular vein cannulation. Preoperative antibiotic prophylaxis was achieved with cefazolin. Following the cannulation, heparinization was performed to attain an activated clotting time (ACT) of higher than 450 seconds. The CBP was accomplished by using a pulsatile membrane oxygenator at moderate hypothermia (28-32°C) and a mean arterial pressure above 50 mmHg.

Statistical Analysis

Statistical analyses were performed using computer software. *P* values of less than .05 were considered significant. The frequency and percentage values of categorical variables and the mean, average, and standard deviation values of continuous variables were determined. Patient characteristics and hospital outcomes were compared using a t test for continuous variables and χ^2 or Fisher exact tests for categorical variables. Patients were classified as having a particular variable or not. Differences between preoperative and postoperative symptom status were compared using linear trend analyses. Risk factors affecting postoperative symptom development were analyzed using multivariate stepwise logistic regression analysis.

RESULTS

Among the 106 patients who developed renal failure following the coronary bypass surgery (RF group), 80 patients did not need hemodialysis (NH group), while 26 patients required hemodialysis (HR group). The mean age of the control group was 58.0 years, while that of the RF group was 66.1 years. The preoperative LVEF values were similar in both groups (control group 49.1%, RF group 48.6%). There was no significant difference between the groups in terms of CPB and X-clamp times (Table 1). Preoperative diabetes mellitus history, postoperative positive inotropic (dopamine, dobutamine) use, and adrenaline use were significantly higher in patients with renal insufficiency (Table 1).

Table 2. Univariate Analysis of Factors Affecting Renal Failure

	RF Group	Control Group	*P*
Advanced age (>70 y)	45 (42%)	17 (15.4%)	<.001
Female	36 (33.9%)	21 (19.0%)	<.013
Diabetes mellitus	62 (58.4%)	29 (26.3%)	<.001
Hypertension	84 (79.2%)	66 (0.6%)	<.002
Chronic obstructive pulmonary disease	29 (27.3%)	57 (51.8%)	<.001
Carotid stenosis	18 (16.9%)	8 (7.2%)	<.028
Increased sedimentation rate (>20)	86 (81.1%)	69 (62.7%)	<.003
Preoperative inotrope use	8 (7.5%)	2 (1.8%)	<.045
X-Clamp duration >60 min	27 (25.4%)	17 (15.4%)	<.048
Postoperative adrenalin use	24 (22.6%)	2 (1.8%)	<.000
Postoperative inotrope use (dopamine, dobutamine)	78 (73.5%)	25 (22.7%)	<.008

RF group indicates renal failure group.

Table 3. Multivariate Analysis of Factors Affecting Renal Failure

	OR	95% CI	*P*
Diabetes mellitus	0.543	1.698-7.393	.001
Postoperative adrenalin use	5.588	1.130-27.635	.035
Postoperative inotrope use (dopamine, dobutamine)	5.788	2.696-12.430	.000

Mortality was 1.8% in the control group (2 patients) and 13.2% (14 patients) in the renal failure group. In patients who developed renal failure but did not need hemodialysis (NH group), the mortality rate was 6.2% (5 patients). Conversely, in patients who required hemodialysis (HR group), the mortality rate was 34% (9 patients) (Table 1).

The univariate analysis that assessed preoperative variables revealed that the following variables were significant: advanced age (>70 years), female sex, diabetes mellitus, hypertension, smoking, the presence of carotid stenosis, high sedimentation rate, preoperative inotrope (dopamine, dobutamine) usage, postoperative adrenaline usage, postoperative inotrope use, and X-clamp time for more than 60 minutes ($P < .1$) (Table 2). Furthermore, the variables that had a P value of greater than .1 in the univariate analysis were further analyzed using multivariate analysis. The multivariate analysis of the variables showed that diabetes mellitus, postoperative use of inotropes, and adrenaline were statistically significant factors ($P < .05$) (Table 3).

The univariate analysis that compared patients with and without hemodialysis showed that advanced age (>70 years), peripheral artery disease, carotid stenosis, redo surgery, and postoperative use of adrenaline were significant factors ($P < .1$) (Table 4). Moreover, carotid stenosis and postoperative use of adrenaline were found to be statistically significant in the multivariate analysis as well ($P < .05$) (Table 5).

Table 4. Univariate Analysis of Factors Affecting Renal Failure That Required Hemodialysis

	NH Group	HR Group	*P*
Advanced age (>70 y)	29 (36.2%)	16 (61.5%)	<.023
Peripheral artery disease	7 (8%)	8 (30.7%)	<.009
Redo surgery	0	2 (7.6%)	<.050
Carotid stenosis	6 (7.5%)	12 (46.1%)	<.000
Adrenalin use	14 (17.5%)	10 (38.4%)	<.027

NH group indicates patients treated without hemodialysis; HR group, patients required hemodialysis.

Table 5. Multivariate Analysis of Factors Affecting Renal Failure That Required Hemodialysis

	OR	95% CI	*P*
Carotid stenosis	9.810	2.162-44.517	.003
Postoperative adrenalin use	4.605	1.307-16.222	.017

DISCUSSION

Despite advances in open-heart surgery, developing renal failure after cardiopulmonary bypass still remains one of the foremost complications. Even though serious complications that require postoperative hemodialysis still occur after cardiac surgery, various methods (such as low-dose dopamine, mannitol infusion, high and pulsatile pressure during CPB, perioperative ultrafiltration, off-pump surgery, strict monitoring of fluid and electrolyte balance, and preoperative prophylactic hemodialysis implementation) have been applied to decrease this risk [Durmaz 2003; Boldt 2003]. Adverse effects of cardiopulmonary bypass, as well as very close interactions between cardiac and renal physiology, are responsible for occurrence of these problems [Durmaz 2003]. The kidneys play an important part in the regulation of extracellular volume and peripheral vascular resistance and, therefore, are crucial in the progression of congestive heart failure and low cardiac output.

Apart from the existing cardiac problems, extra-cardiac risk factors often caused by atherosclerosis and adverse effects of cardiopulmonary bypass on renal perfusion play an important role in patients with coronary artery disease. The renal insufficiency is triggered by the start of the cardiopulmonary bypass and increases with prolonged duration of CPB. Moreover, it was reported that CPB-induced hypothermia, vasoconstriction, microemboli, and decreased renal flow increases the damage [Bahar 2005]. The glomerular filtration rate (GFR) decreases by 30% during CPB and, with prolonged duration of CBP (especially after 60 minutes), the risk of renal failure increases approximately 10-15 times due to developing cortical and medullary edema and tubular necrosis [Bahar 2005]. The use of vasopressor and nephrotoxic drugs after coming off CPB in the postoperative period aggravates renal damage. Therefore, studies focusing on efforts to reduce the occurrence of renal damage due to CBP often have concentrated on CPB time and on the adverse effects of CPB perfusion [Fischer 2002; Boldt 2003]. Boldt et al reported that CPB duration of more than 90 minutes was a risk factor for renal injury, while the CPB duration of less than 70 minutes was safe [Boldt 2003]. Moreover, Suen et al indicated that CPB duration of more than 140 minutes was a significant risk factor for postoperative renal insufficiency and emphasized that during the CPB, perfusion pressure should be above 50 mmHg (60 mmHg in patients with occlusive vascular diseases) [Suen 1998]. In the same study, the authors reported that hypotension was also critical in the postoperative period and that the pressure above 90 mmHg in postoperative follow-up was important for renal perfusion. Although prolonged CPB time was not identified as a significant factor in our study, the extended X-clamp time has emerged as one.

In many studies, it has been reported that off-pump coronary artery bypass (OPCAP) surgery performed instead of CPB (to avoid the negative effects of CBP) has reduced the risk of renal failure [Kim 2011; Ascione 2001]. Hitoshi et al evaluated hemodialysis-independent patients who had high creatinine levels and reported that OPCAP surgeries result in a more rapid recovery during the postoperative period [Hirose 2001]. In our study, the patients who underwent the OPCAP surgery were excluded in order to preserve homogeneity of the study group.

Similar studies have focused on the extra-cardiac factors and investigated the effects of preoperative use of intravenous contrast material [Kim 2011, Provenchere 2003, Mehta 2011]. Provenchere et al determined that intake of contrast material 48 hours before the operation is a risk factor for renal failure in patients undergoing normothermic cardiopulmonary bypass surgery [Provenchere 2003]. In a similar study, Kim et al determined that there was a significant relationship between contrast material intake 7 days prior to the operation and renal failure [Kim 2011]. Mehta et al reported this interval as 24-hours [Mehta 2011]. In our study, we evaluated the time between the angiography and the operation as a means of investigating the effect of contrast material. We did not detect any significant effect of the time between angiography and operation on renal failure.

In our study, the most important factors affecting the development of postoperative renal failure were use of inotropes, DM, and carotid stenosis. This indicated that there were two important aspects in the development of renal failure: (1) vascular cause associated with atherosclerosis, and (2) perfusion disturbances. Studies in the literature regarding this issue revealed that the main cause of renal failure after cardiac surgery is hypoperfusion, i.e. renal ischemia [Bahar 2005; Fischer 2002; Kim 2011; Durmaz 1999; Suen 1998]; while in the perioperative period, hypoperfusion occurs due to CPB-dependent causes. In the postoperative period, it often occurs due to low cardiac output, which in turn develops as a result of postoperative use of vasopressor drugs. Particularly, the use of adrenaline plays an important role in renal damage. In our study, positive inotropic support and the use of adrenaline emerged as important risk factors in the RF group as well as in RF-HR group. Similar to our study, Santos et al also reported that the use of positive inotropic agents was a significant risk factor [Santos 2004]. Likewise, Ascione et al found that inotropic agent and IABP use were risk factors in on-pump surgery [Ascione 2001].

Another risk factor identified in our study was carotid stenosis. Carotid artery stenosis is a significant preoperative parameter, because it is an important quantitative parameter that, along with coronary artery disease, identifies the presence of preoperative atherosclerosis during the routine preparation for cardiac surgery. Conlon et al investigated causes of hemodialysis-dependent renal failure and identified carotid stenosis as an important factor [Conlon 1999]. Similarly, Rodrigues et al determined that the presence of peripheral artery disease after cardiac surgery was significant in the development of renal failure [Rodrigues 2009].

Renal failure following CPB causes an increase in morbidity and the increasing length of hospital stay also leads to increased mortality [Fischer 2002; Gaudino 2005]. This increase has been reported to be higher in the hemodialysis-dependent renal failure group [Provenchere 2003; Ascione 2001; Behrend 1999]. The mortality in patients with renal failure ranges from 7-38%; while in patients who required dialysis this rate has been reported to be as high as 40-90% [Bahar 2005; Ascione 2001; Osterman 2000; Stallwood 2004; Behrend 1999]. In our study, the mortality rate was higher in patients requiring dialysis (34%), which is consistent with other studies.

In addition to hospital morbidity and mortality, development of renal failure also affects medium and long-term follow-ups. Gaudino et al conducted a study to identify risk factors that cause renal failure after cardiac surgery and evaluated the profiles of patients who developed renal failure. They divided patients into two groups: the first group had preoperative creatinine values >2.0, while the second group's preoperative creatinine values were <2.0. The authors reported that patients with high creatinine values had worse mid-term follow-up, while patients with creatinine value under 2.0 had better mid-term follow-ups. This demonstrated that factors that lead to renal failure in patients undergoing cardiac surgery are interrelated and that this process is multifactorial [Gaudino 2005]. In a similar study, Bahar et al observed hemodialysis-dependent renal failure patients and determined a hospital mortality rate as high as 79.7% and 58.6% in a survey after 10-year follow-up [Bahar 2005].

In conclusion, acute renal failure is a very commonly observed complication of coronary bypass surgery. It is associated with high mortality, prolonged hospital stay, and increased cost. The DM and postoperative use of inotropes were found to be significant causes of renal failure, while carotid stenosis and postoperative use of adrenalin were determined to be important causes of hemodialysis-dependent renal failure. After taking all the risk factors into consideration, we conclude and propose that hypoperfusion is the main cause of renal failure after cardiac surgery. Therefore, avoiding hypotension and the unnecessary use of vasopressors during the perioperative CPB and during the postoperative period is important for the prevention of renal failure in patients undergoing cardiac surgery.

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