ACUTE RENAL FAILURE AFTER CARDIAC SURGERY

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Abstract- Acute renal failure (ARF) following cardiac surgery occurs in 1 to 10% of patients. Patients who develop ARF have higher rates of mortality. This study was undertaken to estimate the role of perioperative variables in predicting of post cardiac surgery ARF. We studied a cohort of 398 adult patients who underwent cardiac surgery at our institution from February 2004 to February 2006. Adult patients who were scheduled for cardiac valvular surgery, coronary artery bypass grafting (CABG) or both, with or without cardiopulmonary bypass (CPB) were included. Exclusion criteria were death within two days of operation (n= 8), incomplete patient data, and preexisting renal dysfunction and dialysis requirement or a baseline serum creatinine > 4 mg/dl. Age, sex, left ventricular ejection fraction, diabetes, preoperative, presence of proteinuria (on dipstick), type of surgery, use of CPB and duration of surgery were recorded. A logistic regression analysis was performed to assess independent contribution of variables in the risk of ARF. A binary logistic regression revealed age was an independent predictor of ARF ($P < 0.05$). When both preoperative and intraoperative variables were included in a multinominal logistic regression model, preoperative proteinuria independently predicted ARF (Odds ratio= 3.91, 95% CI: 1.55-9.91, $P = 0.004$). Our results revealed that special considerations should be given to elderly and patients with proteinuria when managing post cardiac surgery ARF.

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Key words: Acute renal failure, cardiac surgery, proteinuria

INTRODUCTION

Acute renal failure (ARF) after cardiac surgery is a well recognized complication that generally occurs in 1 to 10% of patients (1). Patients who develop ARF have higher rates of mortality and resource utilization, with the worst values seen in dialyzed patients. Emerging evidence suggests that even small changes in creatinine after cardiac surgery are associated with significant effects on mortality (2).

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Whether ARF directly causes adverse outcomes is not entirely clear; however, an increase in infection and new-onset sepsis, congestive heart failure, and fluid overload may be contributory (3). The aetiology of renal insufficiency following cardiac surgery is poorly understood, but it is believed that ischemic injury of the kidney, resulting from inadequate perfusion, is a major factor, although renal injury by exotoxins (*e.g.* antibiotics, anaesthetic agents, contrast media, diuretics) and endotoxins (*e.g.* myoglobin) may also be involved (4).

This study was undertaken to evaluate the value of perioperative variables in predicting of developing ARF after cardiac surgery. In an effort to address this issue, we prospectively studied a cohort of 398 adult patients who underwent cardiac surgery at our institution from 2004 to 2006.

MATERIALS AND METHODS

From February 1, 2004 to February 1, 2006, we prospectively studied 430 consecutive adult patients who underwent open-heart surgery at the Department of Cardiac Surgery, Tabriz University of Medical Science. The study was approved by Ethics Committee of Tabriz University of Medical Sciences. Written informed consent was obtained from all subjects.

We included adult patients (> 18 yr) who were scheduled for cardiac valvular surgery, coronary artery bypass grafting (CABG) or both, with or without cardiopulmonary bypass (CPB). The following interventions were not included: transplant surgery, scheduled insertion of a cardiac assist device, operation on the descending aorta, thromboendarterectomy of the pulmonary arteries, and congenital heart disease. Exclusion criteria were death within 48 h after the operation (n= 8), incomplete patient data (n= 14), and preexisting renal dysfunction requiring renal replacement therapy (n= 4) or a baseline serum creatinine > 4 mg/dl (n= 10).

Baseline variables included age, sex, ventricular dysfunction assessed by echocardiography, diabetes on oral therapy or insulin, preoperative proteinuria defined as 1+ or more protein in preoperative urine sample by urinary dipstick test. Intraoperative variables measured were type of surgery (CABG, valvular, combined CABG and valvular) and CPB time.

For the purposes of this analysis, ARF defined as a rise of more than 50% above baseline in serum creatinine on the postoperative day 3 or 5. The association between baseline and intraoperative variables and the development of ARF was assessed by logistic regression. Variables measured at baseline included: age, sex, presence of diabetes, LV ejection fraction, presence of preoperative proteinuria, serum creatinine. In addition, the relationship between the following intraoperative variables and the development of ARF was assessed: duration of CPB and type of surgery (CABG, valvular, combined CABG and valvular). Variables that were significantly associated (at the 0.1 level of significance) with the development of ARF were also included in a multivariate logistic model. Backward variable selection was used serially to remove non-significant factors, until only significant ($P < 0.05$) factors remained in the model.

RESULTS

During the period of study, 211 of the 398 patients included in this analysis underwent coronary artery bypass surgery only and 187 underwent valvular surgery with or without coronary artery bypass. ARF developed in 44 patients (11.05%): 8% of patients undergoing CABG-only surgery and 11% of patients undergoing valvular surgery with or without CABG developed ARF.

Table 1 display the baseline and intraoperative variables according to development of ARF after cardiac surgery. Preoperative variables that were associated with the development of ARF included increased age, valvular surgery and preoperative proteinuria. When both preoperative and intraoperative variables (Table 2) were included in a multivariate model, preoperative proteinuria (Odds ratio= 3.91, 95% CI: 1.55-9.91, $P = 0.004$) was independently associated with ARF.

DISCUSSION

This study confirms that ARF is one of the major complications of cardiac surgery and its incidence is in accordance with previous reports (5). The risk of ARF after cardiac surgery ranges from 1% to 30%, depending on the criteria used to define this complication.

Table 1. Baseline and intraoperative variables associated with the development of ARF following cardiac surgery

Variable	OR (95% CI)	*P*
Age	-	0.058
Sex	1.062 (0.56-2.008)	0.853
Diabetes	0.59 (0.20-1.73)	0.335
Ejection fraction	-	0.247
Preoperative proteinuria	4/41 (1.78-10.92)	0.001
Bypass time	-	0.759
Type of surgery	2.39 (1.24-4.62)	0.008
CABG (on and off pump)	0.49 (0.054-4.49)	0.521

Abbreviations: ARF, acute renal failure; CI, confidence interval; CABG, coronary artery bypass grafting.

Table 2. Multivariate analysis of risk factors associated with the development of ARF following cardiac surgery

	OR (95% CI)	*P*
Age	1.01 (0.994-1.03)	0.182
Preoperative proteinuria	3.95 (1.56-9.99)	0.004
Type of surgery	1.89 (0.89-3.85)	0.095

Abbreviations: ARF, acute renal failure; CI, confidence interval.

The incidence of acute renal failure has decreased after cardiac surgery due to clinicians' awareness of its pathophysiology and preoperative management strategies. Previous studies have attempted to identify predictors of ARF after cardiac surgery. Age, emergency surgery, low ejection fraction, intra-aortic balloon pump (IABP) device, diabetes, mitral valve surgery, cardiopulmonary bypass (CBP) duration and preoperative renal disease were independently associated with acute renal failure at a multivariate analysis (6).

Novel finding of in this study, an unexpected interesting data compared with previous studies, was a significant correlation between presence of preoperative proteinuria and the development of ARF after cardiac surgery in multivariate logistic regression analysis. Although the major concern of this finding is that although a 1+ proteinuria detected by dipstick can occur in normal physiological conditions such as fever, exercise, orthostatic position, pregnancy and hyperbilirubinemia, it has been shown that in healthy patients a trivial proteinuria there is evidence of abnormality in nitric oxide dependent macrovascular generalized endothelial dysfunction remote from the kidney and of low grade chronic inflammation that is associated with microvascular endothelial dysfunction (7). The endothelium is not just a permeability barrier, but is increasingly recognized as a mediator in pathogenesis of cardiovascular and renal disease (8). The integrity of the endothelium has been recognized to control intrarenal hemodynamics by releasing endothelium-derived vasoactive substances (9). Thus, it is conceivable that changes in endothelial function subsequently may modulate vascular resistance and kidney function. Hence, we speculate that proteinuria that is an indicator of a generalized and microcirculatory endothelial dysfunction discloses a group of patients that are more vulnerable to ARF (10). This finding could provide the basis for a therapeutic approach of improving endothelial dysfunction and the course of ARF in proteinuric patients after cardiac surgery.

Age and valvular type surgery were significantly associated with the development of ARF in univariate, but not in multivariate analysis. Age is still controversial risk factor; a number of studies reported that ARF is more likely to develop in older patients (6), but some other studies did not confirm it (11). Elderly patients are susceptible to many forms of ARF, especially ischemic injury, because the aging kidney loses functional reserve and the ability to withstand acute insults is compromised. Studies using blood oxygenation level dependent magnetic resonance imaging in nine female volunteers between 59 and 79 years of age showed inability to improve medullary oxygenation with water diuresis, compared to younger subjects, suggesting a possible predisposition to hypoxic renal injury in older patients (12). Some have suggested that disposing to ischemic ARF may be due to increased renal generation of oxygen free radicals (13, 14) or altered renal endothelial nitric oxide production in aged kidney (13,15).

While the benefits of performing cardiac surgery to improve survival have been clearly demonstrated, the continued poor outcomes associated with ARF after cardiac surgeries reinforce the importance of identify high risk patients preoperatively to allow appropriate interventions.

Conflict of interests

The authors declare that they have no competing interests.

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