Nephrol Dial Transplant (1999) 14: 1158–1162

Nephrology
Dialysis
Transplantation

Original Article

Acute renal failure following cardiac surgery

Peter J. Conlon, Mark Stafford-Smith[1], William D. White[1], Mark F. Newman[1], Sally King[1], Michelle P. Winn and Kevin Landolfo[2]

Departments of Medicine, [1]Anesthesia and [3]Surgery, Duke University Medical Center, Durham, NC 27710, USA

Abstract

Background. Acute renal failure requiring dialysis (ARF-D) occurs in 1–5% of patients following cardiac surgery, and remains a cause of major morbidity and mortality. While some preoperative risk factors have been characterized, the influence of preoperative and intraoperative factors on the occurrence of ARF following cardiac surgery is less well understood.

Methods. Preoperative and intraoperative data on 2843 consecutive adult patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) from February 1, 1995 to February 1, 1997 were recorded and entered into a computerized database. Two definitions of renal failure were employed: (i) ARF defined as a rise in serum creatinine (Cr) of 1 mg/dl above baseline; and (ii) ARF-D defined as the development of ARF for which some form of dialytic therapy was required. The association between preoperative and intraoperative variables and the development of ARF was assessed by multivariate logistic regression.

Results. A total of 2672 of the 2844 patients underwent isolated coronary artery bypass grafting (CABG) surgery, the remaining 172 underwent valve surgery with or without bypass grafting. Of the CABG patients 7.9% developed ARF and 0.7% developed ARF-D. The mortality for patients who developed ARF was 14% (OR 15, $P=0.0001$) compared with 1% among those who did not develop ARF. The mortality for CABG patients who developed ARF-D was 28% (OR 20, $P=0.0001$) compared with 1.8% among those who did not require dialysis. Variables that were significantly associated with the development of ARF by multivariate analysis included: increased age, elevated preoperative serum Cr, duration of CPB, presence of a carotid artery bruit, presence of diabetes, reduced cardiac ejection fraction and increased body weight. Variables independently associated with ARF-D included serum Cr, duration of CPB, carotid artery bruit and presence of diabetes. The utility of these models for predicting the development of ARF and ARF-D was confirmed by bootstrapping techniques. Because of the small number of patients who underwent valve surgery, none of these variables were significantly associated with the development of ARF or ARF-D in this group of patients.

Conclusion. The development of ARF or ARF-D is associated with a high mortality following CABG surgery. We have identified perioperative variables, which may be useful in stratifying risk for the development of ARF.

Key words: cardiac surgery; haemodialysis; renal failure

Introduction

Acute renal failure (ARF) remains a frequent and serious complication of cardiac surgery. The incidence of ARF following cardiac surgery has been reported to vary between 1 and 30% [1–6]. When renal failure develops following cardiac surgery and is severe and associated with the need for haemodialysis support, it is associated with increased mortality, hospital stay and cost. Despite steady improvements in the results of cardiac surgery, there has been a trend in operating on higher risk patients, which inevitably leads to increased morbidity and mortality. The aetiology of renal insufficiency following cardiac surgery is poorly understood, but it is believed that ischaemic 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 [7].

This study was undertaken to evaluate the prevalence, in-hospital mortality rate and the main risk factors for the development of ARF. In an effort to address this issue, we prospectively studied a cohort of 2844 patients who underwent cardiac surgery at our institution over the last 2 years.

Patients and methods

From February 1, 1995 to February 1, 1997, we prospectively studied 2848 consecutive adult patients who underwent cardiac surgery with cardiopulmonary bypass (CPB). Four

Correspondence and offprint requests to: Dr Peter J. Conlon MB, Consultant Nephrologist, Beaumont Hospital, Beaumont Road, Dublin 9, Ireland.

patients were maintained on dialysis prior to cardiac surgery and were excluded from subsequent analysis, leaving 2844 patients that are the subject of this analysis.

Demographic data, medical history, physical findings and blood chemistries were entered prospectively into a computerized medical information system prior to cardiac catheterization. Peripheral vascular disease was defined as a history of claudication, previous vascular procedure or physical exam evidence of femoral or abdominal bruits. Symptoms of congestive heart failure were classified in accordance with the New York Heart Association criteria. Chronic obstructive pulmonary disease (COPD) was defined as functional disability and/or hospitalization and/ chronic bronchodilator therapy. Patients were considered to have diabetes if they were taking insulin or oral hypoglycaemic agents at the time of cardiac surgery. Left ventricular (LV) ejection fraction was assessed preoperatively by either contrast ventriculography, radionucleotide ventriculography or echocardiography. Serum creatinine (Cr) concentration was assessed within 48 h of cardiac surgery. Operative mortality was defined as death during the index hospitalization.

Operative procedure

Patients were pre-medicated with oral diazepam or lorazepam and methadone hydrochloride 90 min before anaesthesia induction. Anesthaesia was induced with 75–100 μg/kg midazolam and 5–10 μg/kg fentanyl intravenously. Anaesthesia maintenance consisted of 0.8/μg/kg/min of midazolam and 0.08 μg/kg/min of fentanyl by continuous infusion. Vecuronium was given as required to maintain neuromuscular blockade.

The perfusion apparatus consisted of a Cobe CML oxygenator (Cobe Laboratories, Lakewood, CO), a Sarns 7000 MDX pump (Sarns Inc., Ann Arbor, MI) and a Pall SP 3840 arterial line filter (Pall Biomedical Products Co., Glencove, NY). Non-pulsatile perfusion was used throughout the study, with perfusion maintained between 2 and 2.8 l/min/m^2. The pumps were primed with crystalloid (asanguinous) solution formulated to achieve a haematocrit of 18% or more during extracorporeal circulation. Packed red blood cells were added to achieve the desired haematocrit and as required by the clinical circumstance. Blood oxygen saturation and haematocrit were assessed with an IL482 co-oximeter (Instrumentation Laboratories, Lexington, MA). α-Stat blood gas management was used during CPB, with $PaCO_2$ maintained at 35–40 mmHg and PaO_2 maintained at 150–250 mmHg.

Statistical analysis

For the purposes of this analysis, two definitions of ARF were employed. Firstly ARF, and secondly ARF requiring dialysis (ARF-D). ARF was defined by a rise in serum Cr from baseline of 1.0 mg/dl or greater following cardiac surgery. ARF-D was renal failure that required some form of renal replacement therapy to be instituted, either haemodialysis, peritoneal dialysis or continuous veno-venous haemofiltration. Dialysis therapy was initiated by the attending nephrologist based on the clinical situation rather than any pre-set criteria.

The association between baseline and intraoperative variables and the development of both ARF and ARF-D was assessed by logistic regression. Variables measured at baseline included: age, sex, race, presence of a carotid artery bruit, presence of congestive heart failure, presence of cardiogenic shock, history of previous cerebrovascular accident, presence of diabetes, LV ejection fraction, peripheral arterial disease, serum Cr, body weight and presence of COPD. In addition, the relationship between the following intraoperative variables and the development of ARF and ARF-D was assessed: duration of CPB, number of coronary artery grafts performed, the use of an intraaortic balloon pump to assist in separation from CPB, the lowest CPB inflow temperature and the lowest nasopharyngeal temperature.

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. The model that was derived for the development of ARF was also tested for its capacity to predict ARF-D.

Because of the limitation which the relatively few outcome events imposes on our analysis, we used a bootstrapping technique to explore further the association of the independent variables with the development of ARF and ARF-D. Bootstrapping is a methodology used in regression to adjust for the effect of outliers and to decrease the effect of variability in a given sample. This is done through the creation of multiple sub-samples by random selection of subjects from the original sample. The selected subject is returned immediately to the original sample and thus can be selected more than once into a given sub-sample (i.e. sampling with replacement). The size of each sub-sample is the same as the original one (2673 in our case), therefore, some subjects will be selected into a given sub-sample more than once and others not at all. Repeated samples are then used to examine the relationship between the variables of interest. We generated 100 bootstrap samples on which a multivariable regression analysis was performed using all independent variables (Tables 2 and 4) with the development of ARF and ARF-D. Model cross-validation was also performed using a 100 sample bootstrap analysis. Means are listed as ± 1 standard deviation, and odds ratios (OR) are expressed together with their 95% confidence intervals (CI) and associated *P*-values.

Results

During the period of study, 2672 of the 2844 patients included in this analysis underwent coronary artery bypass surgery (CABG) only and 172 underwent valvular surgery with or without coronary artery bypass.

Eight percent of patients undergoing CABG-only surgery developed ARF and 0.7% developed ARF-D. The mortality of CABG patients who developed ARF was 14% (OR 15.3, $P=0.0001$) compared with 1.0% among those who did not develop ARF. The mortality among CABG patients who developed ARF-D was 28% (OR 20, $P=0.0001$) compared with 1.8% for those who did not develop ARF-D.

Table 1 displays the baseline characteristics for study subjects according to surgery type and the presence or absence of ARF. Preoperative variables that were significantly associated with the development of ARF included increased age, black race, presence of a carotid bruit, presence of congestive heart failure, history of a previous cerebrovascular event, diabetes, decreased LV ejection fraction, increased serum Cr, peripheral arterial disease and increased body weight. The effect of

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

	No renal *failure* ($n=2465$)	Renal *failure* ($n=207$)	OR (95% CI)	*P*
Age[a]	64.4±10.8	66.0±10.8	1.1(1.0–1.2)	0.05
Sex % (male/female)	64%/36%	67%/33%	0.86(0.7–1.0)	0.3
Race (white/black)	89%/11%	80%/20%	1.5(1.3–1.7)	0.008
Carotid bruit	12.6%	20.4%	1.8(1.4–2.1)	0.0022
Congestive heart failure	6.3%	12.1%	2.1(1.7–2.3)	0.0001
Previous CVA	7.2%	12.6%	1.9(1.6–2.3)	0.0003
Diabetes	29%	47%	2(1.7–2.4)	0.0001
Ejection fraction[a]	52.4±15	47.5±14.6	1.1(1.2–1.3)	0.0001
Peripheral arterial disease	15.5%	19%	1.2(1–1.2)	0.2
Weight (kg)[a]	80.4±16	84±16	1.2(1.1–1.3)	0.0002
COPD	8%	8%	0.96(0.84–1.2)	0.8
Serum creatinine	1.1±0.3	1.5±0.8	1.4(1.3–1.4)	0.0001
Bypass time[a]	113.7±48.4	139±81.2	1.07(1.05–1.08)	0.0001
No. of grafts	3±0.29	3±0.87	1(0.9–1.0)	0.7
Intraaortic balloon pump inserted	7%	23%	3.2(2.2–4.7)	0.0021
Inflow temperature	31.5±2.4	30.5±3.2	0.90(0.92–0.96)	0.0046
Nasal temperature	30.9±2.23	30.3±3.1	0.90(0.92–0.96)	0.0012

OR = odds ratio ± 95% confidence interval.
[a]Odds ratio expressed for a 10 unit change.

baseline serum Cr on probability of developing ARF and need for dialysis is depicted graphically in Figure 1. The risk of developing ARF-D for subjects with normal preoperative renal function (Cr < 1.4) was 0.03% and the need for dialysis among patients with moderate renal insufficiency (a serum Cr of between 2.5 and 3.5 mg/dl) was 4%. Intraoperative variables that were significantly associated with the development of ARF included: length of time on CPB, the insertion of an intraaortic balloon pump to assist separation from CPB, increased nasopharyngeal temperature and inflow temperature.

When both preoperative and intraoperative variables (Table 2) were included in a multivariate model, increased age (OR 1.24, $P=0.01$), preoperative serum Cr (OR 1.3, $P=0.0001$), duration of CPB (OR 1.08, $P=0.0001$), presence of a carotid bruit (OR 1.6, $P=0.002$), presence of diabetes (OR 1.7, $P=0.001$), decreased LV ejection fraction (OR 1.1, $P=0.02$) and increased body weight (OR 1.2, $P=0.0001$) were independently associated with ARF.

Model cross-validation using a 100 sample, bootstrap analysis was performed. It can be seen that all the variables were significantly associated with the development of ARF in the majority of samples.

Preoperative variables that were significantly associated with ARF-D included black race, presence of a carotid artery bruit, congestive heart failure, previous cerebrovascular event, diabetes, decreased LV ejection fraction, serum Cr and increased body weight. Intraoperative variables that were significantly associated with the development of ARF-D were the duration of CPB, the insertion of an intraaortic balloon pump to assist separation from CPB, decreased inflow temperature and decreased nasal temperature (Table 3). Using multivariate analysis, preoperative serum Cr (OR 2.2, $P=0.0001$), length of time on bypass (OR 1.09, $P=0.001$), presence of a carotid artery bruit (OR 3.8, $P=0.01$) and diabetes (OR 3.3, $P=0.01$) were independently associated with ARF-D.

Using a 100 sample boot strap analysis, it can be seen that serum Cr, length of time on CPB and carotid

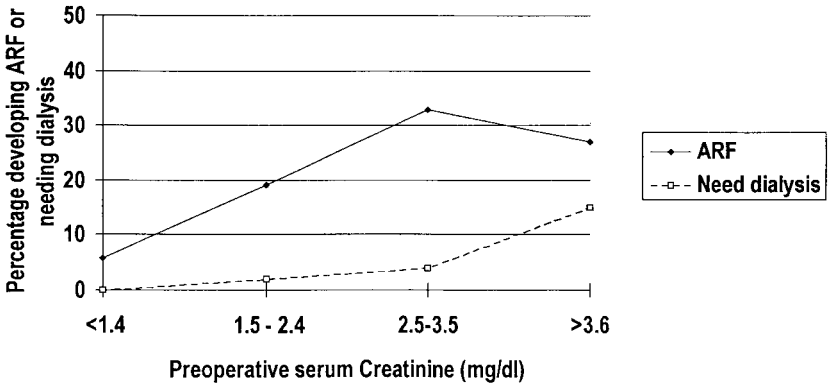

Fig. 1. Probability of developing ARF and ARF-D based on preoperative serum creatinine.

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

	Odds ratio (95% CI)	*P*	Bootstrap
Age (years)[a]	1.24(1.1–1.3)	0.01	75%
Preoperative serum creatinine (mg/dl)	1.3(1.2–1.4)	0.0001	100%
CPB duration (min)[a]	1.08(1.01–1.09)	0.0001	100%
Carotid artery bruit	1.6(1.3–2)	0.002	74%
Diabetes	1.7(1.4–2)	0.001	91%
Ejection fraction (%)	1.1(1–1.2)	0.02	78%
Weight (kg)[a]	1.2(1.1–1.3)	0.0001	99%

Results derived from the bootstrap procedure display the variables most frequently significantly associated with the development of ARF in patients undergoing CABG.
[a]Odds ratio expressed for a 10 unit change.

Table 3. Baseline and intraoperative variables associated with the development of ARF-D following CABG

	No dialysis ($n=2655$)	Dialysis ($n=18$)	OR (95% CI)	*P*
Age[a]	64.5 ± 10.8	67.7 ± 7.4	1.3(1.06–1.7)	0.2
Sex % (male/female)	64%/36%	44%/66%	0.7(0.4–1.1)	0.4
Race (white/black)	86%/14%	83%/17%	0.9(0.5–1.5)	0.8
Carotid bruit	13%	33%	3.2(1.95–5.3)	0.02
Congestive heart failure	25.4%	66%	5.8(3.5–9.7)	0.0004
Previous CVA	12.2%	11.1%	0.89(0.4–1.9)	0.8
Diabetes	30.5%	72%	5.9(3.4–10)	0.0008
Ejection fraction[a]	52.1 ± 15	39.5 ± 18.6	0.63(0.5–0.7)	0.0007
Peripheral arterial disease	15.6%	33.5%	2.6(1.6–4.4)	0.5
Weight (kg)[a]	80.8 ± 16.4	80.8 ± 15.7	1.0(0.8–1.2)	0.98
COPD	12.9%	33%	3.4(2.0–5.5)	0.01
Serum creatinine	1.16 ± 0.5	2.5 ± 1.9	2.5(2.1–2.8)	0.0001
CPB duration[a]	114.9 ± 51.9	60 ± 64	1.04(1.03–1.06)	0.0044
No. of grafts	3.0 ± 1.8	2.8 ± 0.8	0.82(0.6–1.06)	0.4
Intraaortic balloon pump inserted	1.7%	5.5%	3.3(1.2–9.4)	0.2
Inflow temperature	31.02 ± 2.5	30.0 ± 3.4	0.91(0.8–1.03)	0.09
Nasal temperature	30.9 ± 2.3	30.4 ± 2.4	0.94(0.9–1)	0.4

OR = odds ratio ± 95% confidence interval.
[a]Odds ratio expressed for a 10 unit change.

Table 4. Multivariate analysis of risk factors associated with the development of ARF-D following CABG

	Odds ratio (95% CI)	*P*	Bootstrap
Preoperative serum creatinine (mg/dl)	2.2(1.9–2.6)	0.0001	97%
CPB duration (min)[a]	1.09(1.06–1.12)	0.0010	81%
Carotid artery bruit	3.8(2.2–6.5)	0.01	67%
Diabetes	3.3(1.8–6)	0.01	50%

Results derived from the bootstrap procedure display the variables most frequently significantly associated with the development of ARF-D in patients undergoing CABG.
[a]Odds ratio expressed for a 10 unit change.

artery bruit were associated with ARF-D in the majority of the models, while diabetes was significant in 50% of the models (Table 4).

An analysis was also performed to determine if there was a relationship between the length of time between coronary angiography and CABG surgery and the risk of ARF, and this did not appear to be a significant independent risk factor for ARF.

Discussion

The demonstration of a considerable survival benefit of CABG surgery in selected patient populations has seen the application of cardiac surgery to increasingly elderly and debilitated patients. In this study, we have reported the lowest yet recorded incidence of renal dysfunction following cardiac surgery, with 0.7% devel-

oping ARF-D. We have also identified a number of preoperative risk factors that can be used to identify patients at highest risk of this serious complication. In our series, the development of ARF-D following CABG surgery was associated with a 20-fold increase in mortality.

This study demonstrates interesting new data when compared with previous studies. Chertow analysed a very large data set of >43 000 patients undergoing cardiac surgery [6] at 43 Department of Veterans Affairs hospitals. These authors noted the development of ARF-D among 1.1% of these patients, and identified a number of preoperative factors associated with increased risk of developing ARF-D. In contrast to our study, Chertow did not find a significant independent association between presence of a carotid artery bruit, body weight or diabetes, and the development of ARF-D. In addition, Chertow and colleagues were unable to assess the effect of duration of CPB and the development of ARF-D.

Previous authors [8] have observed the association between the use of an intraaortic balloon pump to assist in separation from CPB and the development of ARF. Clearly this device is inserted in order to assist in maintenance of cardiac output in unstable patients. The use of intraaortic balloon devices may also be associated with the development of ARF, if limb ischaemia develops, and rhabdomyolysis [9,10].

Recently, it has been argued that modern CPB is not deleterious to renal function. Pre-operative reductions in creatinine clearance and urine output (from inadequate hydration) have been proposed as the main culprits [11]. Alternatively, it has been suggested that those reductions which do occur are insufficient to influence routine parameters of renal function [12]. However, these conclusions may be biased by the small tightly controlled nature of the studies themselves, in contrast to more realistic prospective and retrospective studies. In this study, we have observed a clear-cut linear relationship between length of time on bypass and risk of ARF and ARF-D.

In summary, the likelihood of developing ARF and ARF-D after cardiac surgery depends on factors associated with poor cardiac performance (particularly when separating from CPB) and with the level of baseline renal insufficiency. While the benefits of performing cardiac surgery to improve survival have been clearly demonstrated, these data may be used to assess risk of developing renal failure following cardiac surgery. In patients at highest risk of ARF-D, the procedure may be tailored to try to reduce the risk of ARF-D, by, for example optimizing cardiac output or trying to shorten the period on bypass.

References

1. Corwin HL, Sprague SM, DeLaria GA, Norusis MJ. Acute renal failure associated with cardiac operations. *J Thorac Cardiovasc Surg* 1989; 98: 1101–1112
2. Frost L, Pedersen RS, Lund O, Hansen OK, Hansen HE. Prognosis and risk factors in acute, dialysis-requiring renal failure after open-heart surgery. *Thorac Cardiovasc Surg* 1991; 25: 161–166
3. Andersson L-G, Ekroth R, Bratteby LE, Hallhagen S, Wesslen O. Acute renal failure after coronary surgery—a study of incidence and risk factors in 2009 consecutive patients. *Thorac Cardiovasc Surg* 1993; 41: 237–241
4. Corwin HL, Sprague SM, DeLaria GA, Norusis MJ. Acute renal failure associated with cardiac operations. A case–control study. *J Thorac Cardiovasc Surg* 1989; 98: 1107–1112
5. Mangos GJ, Brown MA, Chan WYL, Horton D, Trew P, Whitworth JA. Acute renal failure following cardiac surgery: incidence, outcomes and risk factors. *Aust NZ J Med* 1995; 23: 284–289
6. Chertow GM, Lazarus JM, Christiansen CL *et al.* Preoperative renal risk stratification. *Circulation* 1997; 95: 878–884
7. Endre ZH. Post cardiac surgery acute renal failure in the 1990s. *Aust NZ J Med* 1997; 25: 278–279. 1997
8. Zanardo G, Michielon P, Paccagnella A *et al.* Acute renal failure in the patient undergoing cardiac operation. Prevalence, mortality rate, and main risk factors. *J Cardiovasc Anesth* 1993; 7: 711–716
9. Maccario M, Fumagalli C, Dottori V *et al.* The association between rhabdomyolysis and acute renal failure in patients undergoing cardiopulmonary bypass. *J Cardiovasc Surg Torino* 1996; 37: 153–159
10. Maccario M, Fumagalli C, Dottori V. Rhabdomyolytic acute renal failure in cardiac surgery. *Minerva-Anestesiol* 1995; 61: 397–400
11. Weinstein GS, Rao PS, Vretakis G, Tyras DH. Serial changes in renal function in cardiac surgical patients. *Ann Thorac Surg* 1989; 48:72–76
12. Mazzarella V, Galluci T, Tozzo C. Renal function in patients undergoingcardiopulmonary bypass operations. *J Thorac Cardiovasc Surg* 1992; 104: 1625–1627

Received for publication: 31.7.98
Accepted in revised form: 21.12.98