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Institutional report - Cardiac general

Predictors of acute renal failure requiring renal replacement therapy post cardiac surgery in patients with preoperatively normal renal function☆

Kishore Doddakula, Nael Al-Sarraf*, Kathy Gately, Anne Hughes, Michael Tolan, Vincent Young, Eillish McGovern

Department of Cardiothoracic Surgery, St James's Hospital, Dublin 8, Ireland

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Abstract

Acute renal failure requiring continuous renal replacement therapy post cardiac surgery carries a high mortality. Most studies have focused on patients with impaired renal function preoperatively but little is known about predictors of such a complication in patients with preoperatively normal renal function. This is a retrospective review of a prospective collected database. A total of 1609 patients underwent cardiac surgery over a 4-year period. Dialysis was required in 47 patients (2.9%). Univariate analysis identified the following as significant risk factors: age, female gender, chronic obstructive pulmonary disease, congestive cardiac failure, creatinine clearance, Euro, Parsonnet and Cleveland clinic scores, body mass index, non-isolated CABG, cardiopulmonary bypass time, extubation time and pulmonary complications ($P<0.05$). Multivariate analysis identified EuroSCORE, congestive cardiac failure, insulin-dependent diabetes, emergency surgery, post-operative extubation time and pulmonary complications as independent risk factors ($P<0.05$). In-hospital mortality and length of stay ($P<0.0001$) were higher in dialysis group. Acute renal failure requiring dialysis post cardiac surgery is associated with a higher mortality and prolonged hospital stay. By identifying higher risk patients, early planned preventative measures should be readily available to both reduce the incidence of such a complication and improve utilisation of hospital resources.

Keywords: Renal failure; Dialysis; Mortality; Coronary artery bypass

1. Introduction

Acute renal failure (ARF) requiring continuous renal replacement therapy (CRRT) is a devastating complication post cardiac surgery with an estimated incidence of 2–15% and in-hospital mortality >40% [1]. Advances have been achieved in cardiac surgery through improvements in operative techniques, post surgery intensive care and through a safer and more efficient use of cardiopulmonary bypass circuits. Despite all that, renal failure requiring CRRT remains a problem incurring increased morbidity, mortality, hospital bed usage and cost. Current measures to decrease the associated morbidity and mortality following such a complication are limited and the only effective measure remains preventative strategies.

In this paper, we sought to determine predictors of ARF in patients with normal preoperative renal function and by doing so, how dealing with such a devastating complication could be planned in advance leading to potentially better outcome and decreasing its associated mortality and cost.

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*Corresponding author. Tel.: +353-1-4103389; fax: +353-1-4103700.
E-mail address: trinityq8@hotmail.com (N. Al-Sarraf).

2. Materials and methods

2.1. Patients

Between October 2001 and October 2005, 1813 consecutive patients who underwent cardiac surgery in a single institute were retrospectively reviewed. Of those, 204 patients were excluded from the study because of their preoperative dialysis ($n=22$) and preoperatively impaired renal function ($n=182$). A total of 1609 cases were enrolled and divided into two groups. Group 1 included patients who required CRRT post surgery ($n=47$), and group 2 included patients who did not require CRRT post surgery ($n=1562$). All clinical, intensive care and operative data were reviewed retrospectively through the review of patient charts and the use of a prospectively collected departmental patient database. Indications for CRRT were: hyperkalaemia (>6.0 mmol/l) not responding to insulin infusion, metabolic acidosis, anuria or oliguria <20 ml/h for more than 6 h (despite adequate filling and adequate cardiac output). CRRT was commenced largely through nephrologist recommendation. This study was approved by our institutional review board.

Table 1
Factors examined as potential predictors of renal replacement therapy post cardiac surgery

Preoperative factors
1. Age
2. Gender
3. EuroSCORE
4. Parsonnet score
5. Diabetes mellitus
6. Hypertension
7. Creatinine level
8. Presence of extra-cardiac arteriopathy (cerebrovascular disease, carotid artery disease, peripheral vascular disease)
9. Pre-operative ejection fraction (measured by echo/angio)
10. Body mass index (BMI)
11. Operative priority (Emergent vs. non-emergent)
12. Chronic obstructive pulmonary disease (COPD)
13. Congestive cardiac failure (CCF)
14. Intra-aortic balloon pump
15. Cleveland clinic score
Intraoperative factors
1. Cardiac procedure (isolated CABG vs. others)
2. Cardiopulmonary bypass time
3. Aortic cross-clamp time
Early postoperative factors
1. Extubation time post-op
2. Hours ventilated
3. Postoperative pulmonary complication

2.2. Data analysis

The relationship between factors of interest (Table 1) and their distribution among the two groups were analysed using unpaired *t*-test, Fisher's exact test and χ^2 test (univariate analysis). Multivariate analysis was performed using logistic regression backwards stepwise method to identify factors associated with continuous renal replacement therapy. The software package SPSS version 11.0 (SPSS Inc., Chicago, IL) was used to perform the statistical analysis. Results were considered statistically significant when *P*-value was <0.05.

2.3. Definitions

Operative priority was determined by cardiothoracic surgeons according to standard criteria [1]. Emergency/salvage surgery refers to medical factors relating to patient's cardiac disease dictating that surgery should be performed within hours to prevent morbidity or death. Urgent operation means that medical factors require the patient to have an operation during the same admission (i.e. before discharge).

Elective operation means that medical factors indicate the need for an operation through a readmission at a later date. In-hospital mortality refers to all mortalities within the same admission post cardiac surgery regardless of their length of stay.

Creatinine clearance was calculated using Cockcroft-Gault equation as follows: Creatinine clearance (ml/min) $=$ ($140-$age in years)*actual weight (kg)/serum creatinine (μmol/l). This formula is applicable to females, and in the case of males the formula is multiplied by 1.2. Normal range for serum creatinine clearance is >90 ml/min.

2.4. Cardiopulmonary bypass (CPB)

All CABGs were performed through a median sternotomy. Following full anticoagulation with heparin given at a dose of 300 IU/kg to maintain an activated clotting time of 400–600 s, CPB was instituted using ascending aortic cannulation and a two-stage right atrial venous cannulation. A roller pump (jostra HL 20) and hollow-fibre membrane oxygenator (Optima, Cobe Cardiovascular Inc.) were used. The extracorporeal circuit was primed with 1400 ml of Hartmann's solution and 5000 IU heparin. CPB was maintained with non-pulsatile flow with a minimum flow rate of 2.4 l/m²/min at normothermia with temperature allowed to drift to 32 °C.

Arterial line filtration (Sentoy, Cobe Cardiovascular Inc.) was used in all the cases. Shed blood was recycled using cardiotomy suction. Acid-base was managed with alpha stat control. Myocardial protection was achieved with intermittent antegrade cold/tepid blood cardioplegia. On completion of all distal anastomoses, the aortic cross-clamp was removed and the proximal anastomoses performed with partial aortic clamping. Heparin was reversed with protamine at 1:1 ratio on weaning off cardiopulmonary bypass.

3. Results

Incidence of ARF requiring CRRT was 2.9% (47 of 1609). Patient characteristics and factors of interest are summarized in Tables 1 and 2. Univariate analysis of individual risk factors and their relevant *P*-values are summarized in Table 2. Multivariate analysis examining the above factors is summarized in Table 3. In-hospital mortality and length of stay are summarized in Table 4.

Univariate analyses have identified the following as significant predictors of ARF requiring CRRT post cardiac surgery: age ($P=0.0002$), female gender ($P=0.003$), EuroSCORE ($P<0.0001$), Parsonnet score ($P<0.0001$), preoperative creatinine clearance ($P<0.0001$), BMI ($P=0.002$), emergency/salvage surgery ($P=0.006$), chronic obstructive pulmonary disease ($P=0.003$), CCF ($P<0.0001$), Cleveland clinic score ($P<0.0001$), CPB time ($P=0.005$), extubation time ($P<0.0001$), postoperative pulmonary complication ($P<0.0001$) and non-CABG cardiac surgery ($P<0.0001$).

Multivariate analysis has identified the following as significant predictors of patients requiring CRRT: CCF, IDDM, EuroSCORE , urgent surgery, extubation time and postoperative pulmonary complication. Patients who required CRRT post cardiac surgery had higher mortality ($P<0.0001$) and increased length of stay ($P<0.0001$) than control group.

4. Discussion

Acute renal failure post cardiac surgery remains a leading cause of morbidity, mortality, prolonged hospital stay and increased hospital costs [1]. Most of the previously reported studies have focussed on predicting renal failure in patients with impaired renal function preoperatively as either mild-moderate or moderate-severe [2, 3].

Table 2
Patient population and variables of interest in univariate analysis

Variable	RRT group (n=47)	No RRT group (n=1562)	P-value
Age (years)			
Mean±S.D.	68.9±9.1	63.0±10.7	0.0002*
Gender			
Male	24 (51%)	1131 (72%)	0.003*
Female	23 (49%)	431 (28%)	<0.0001*
Pre-op EuroSCORE			
Mean±S.D.	8.0±4.3	4.0±2.9	<0.0001*
Pre-op Parsonnet score			
Mean±S.D.	14.0±8.1	8.0±6.8	0.426
Pre-op DM			
Yes	10 (21%)	259 (17%)	
No	37 (79%)	1303 (83%)	
Pre-op hypertension			
Yes	27 (57%)	800 (51%)	0.459
No	20 (43%)	762 (49%)	
Pre-op creatinine level (μmol/l)			
Mean±S.D.	96.3±15.3	93.1±14.3	0.132
Pre-op creatinine clearance (ml/min)			
<90 ml/min	43 (91%)	1137 (73%)	
≥90 ml/min	4 (9%)	425 (27%)	0.002*
Mean±S.D.	61.6±17.2	77.2±24.8	<0.0001*
Extra-cardiac arteriopathy			
Present	3 (6%)	72 (5%)	0.479
Absent	44 (94%)	1490 (95%)	
Pre-op ejection fraction			
Good (≥50%)	24 (51%)	1016 (65%)	0.062
Fair–poor (<50%)	23 (49%)	546 (35%)	
Operative priority			
Elective/urgent	42 (89%)	1493 (96%)	0.006*
Emergency/salvage	5 (11%)	69 (4%)	
Body mass index (BMI)			
Mean±S.D.	25.8±4.0	27.9±12.2	0.002*
Chronic obstructive pulmonary disease (COPD)			
Yes	3 (6%)	8 (4%)	
No	44 (94%)	1494 (96%)	0.0036*
Congestive cardiac failure			
Yes	22 (47%)	249 (16%)	
No	25 (53%)	1313 (84%)	<0.0001*
Intra-aortic balloon pump			
Yes	1 (2%)	17 (1%)	
No	46 (98%)	1545 (99%)	0.415
Cleveland clinic score			
Mean±S.D.	2.7±1.4	1.4±1.4	<0.0001*
CPB time (min)			
Mean±S.D.	126.4±72.6	95.3±39.3	0.005*
Cross-clamp time (min)			
Mean±S.D.	66.4±44.8	58.4±27.6	0.229
Ex-tubation post-op			
Immediate to 24 h	27 (57%)	1504 (96%)	<0.0001*
>24 h	20 (43%)	58 (4%)	
Hours ventilated			
Mean±S.D.	53.6±99.9	11.3±30.7	0.006*
Post-op pulmonary complications			
None	20 (43%)	1454 (93%)	<0.0001*
Re-intubation/CPAP/tracheostomy	27 (57%)	108 (7%)	
Cardiac procedures			
CABG only	24 (51%)	1152 (74%)	
Valve only	10 (21%)	236 (15%)	<0.0001*
CABG+valve	5 (11%)	122 (8%)	
Aortic/aortic root surgery	6 (13%)	22 (1%)	
Others #	2 (4%)	30 (2%)	

#Include: VSD/ASD repair, Pericardiectomy, excision of atrial myxoma, removal of pacemakers, tamponade evacuation and excision of LV aneurysm. CABG: coronary artery bypass graft; CPAP: continuous positive airway pressure; CPB: cardiopulmonary bypass; DM: Diabetes mellitus; *n:* number of patients; S.D.: standard deviation. *Statistically significant (P-value <0.05).

Table 3
Multivariate analysis of the predictors of RRT post cardiac surgery

Variable	Odds ratio	95% Confidence interval	*P*-value
Pre-op congestive cardiac failure	0.39	0.18–0.83	0.015*
Pre-op IDDM#	0.171	0.048–0.61	0.006*
EuroSCORE	1.34	1.21–1.478	0.000*
Emergent surgery	0.24	0.066–0.864	0.029*
Ventilatory duration	0.138	0.062–0.308	0.000*
Post-op pulmonary complication	0.09	0.043–0.172	0.000*

*Statistically significant (*P*-value <0.05). #IDDM, Insulin-dependent diabetes mellitus.

In this study, we have attempted to correlate and predict factors (preoperative, intraoperative and early postoperative) predisposing to ARF and leading to CRRT. By doing so, one might be able to predict those at high risk and interventional measures might be planned ahead to improve outcome following such a complication.

We have identified that elderly and female patients were associated with a higher risk of ARF requiring CRRT. Presence of hypertension and extra-cardiac arteriopathy does not seem to incur increased risk. Effect of diabetes on ARF post cardiac surgery has been controversial. While some studies have shown increased risk of ARF post surgery among diabetics, others have failed to show such a risk. The difference might be in part due to the prevalence of diabetics among population of interest and the predominant type of diabetes (i.e. diet-controlled, NIDDM, or insulin dependent diabetes) [4]. In our series IDDM patients had higher incidence of postoperative ARF requiring dialysis than non-diabetics ($P=0.006$, odds ratio 0.377).

Cardiac surgery risk scoring systems were developed in order to predict mortality (and to a lesser extent morbidity) [5, 6]. Such scoring systems have also proved useful in predicting direct costs from surgical intervention. In our institute, the two commonly used scoring systems are EuroSCORE [5] and Parsonnet score [6]. Patients who required CRRT post cardiac surgery had a higher mean EuroSCORE (8 vs. 4, respectively, $P<0.0001$) and a higher Parsonnet score (14 vs. 8, respectively, $P<0.0001$) than controls. Applying these scoring systems can be a useful aid in predicting such morbidity and better advanced planning. Cleveland clinic score was developed to predict risk of ARF post cardiac surgery [7]. In our series, patients who required dialysis had a higher mean Cleveland score than controls (2.7 vs. 1.4, respectively, $P<0.0001$). The advantage of this scoring system is that it can be used to predict renal failure based on a defined set of preoperative criteria, but it does not take into account the operative or early postoperative factors (e.g. CPB and cross-clamp time) [7]. In addition, Cleveland score relies on patients with abnormal serum creatinine (both mild renal impairment and severe renal dysfunction). This explains the lower value of our mean as we intentionally excluded patients with preoperatively raised serum creatinine in order to predict ARF among patients with preoperatively normal renal function as dictated by normal serum creatinine.

Table 4
In-hospital mortality in the two groups

Variable	RRT group	No RRT group	*P*-value
Mortality	20 (43%)	26 (2%)	<0.0001*
Post-op length of stay (days)			
Mean ± S.D.	22.2±21.8	7.9±9.3	<0.0001*

S.D.: Standard deviation. *Statistically significant (*P*-value <0.05).

Operative factors that are associated with a higher incidence of CRRT include CBP time, non-isolated CABG surgeries, and emergency/salvage operations. CPB time was significantly higher in the CRRT group (Table 1). Effects of the cardiopulmonary bypass circuits on systemic inflammatory response and endothelial cell-neutrophil adhesion has been well established [8]. These changes promote leucosequestration and adhesions of leucocytes to capillary bed in kidneys with subsequent release of cytokines and oxygen free radicals causing renal injury [8]. These findings are supported by the observation that the incidence of acute renal failure post off-pump CABG is 50% less than that of on-pump CABG [9]. Emergency and salvage operations carry higher risk of worsening renal function necessitating CRRT than elective/urgent cases. Complex cardiac cases including aortic root replacement, aortic surgery and simultaneous CABG with valve replacement carry higher risk of CRRT than CABG alone. This might be in part due to the prolonged CPB, prolonged hypo-perfusion of renal medulla and the increased levels of vasoconstrictors (e.g. catecholamines, aldosterone, angiotensin) [10].

Serum creatinine levels were not significantly different among the dialysis vs. the control group. However, patients requiring dialysis had significant reduction in their creatinine clearance (mean 61 vs. 77, $P<0.0001$). This in turn could be useful in a clinical setting were creatinine clearance could be estimated prior to surgery among high-risk patients as it is a more sensitive indicator of glomerular filtration than serum creatinine alone.

It seems that patients requiring prolonged ventilation post cardiac surgery and those developing pulmonary complications are at an increased risk of developing ARF. It is unclear what the underlying reason is for that among patients with normal renal function preoperatively. It has been reported that patients with preoperative renal failure have a higher risk of prolonged intubation and a higher risk of pulmonary complications following CABG [11]. A similar case seems applicable to our study in relation to postoperative renal failure requiring dialysis. In addition, patients with prolonged intubation and pulmonary complications tend to have higher co-morbidities and higher EuroSCORE predisposing them to a higher risk of ARF requiring dialysis [12].

Patients requiring CCRT post cardiac surgery have a higher mortality (43% vs. 2%, $P<0.0001$) and prolonged hospital stay (mean 22 vs. 8 days, $P<0.0001$) than controls. The high mortality in the dialysis group has been reported to be the result of dialysis-induced effects on inflammatory and immune responses, haemodynamic instability and visceral ischaemia [13]. This will ultimately lead to increased hospital costs and increased hospital bed usage together with the increased emotional distress to patients and their families. The ability to predict such patients will be useful as preventative measures can be planned and commenced at a reasonably earlier stage to prevent such a complication.

Patients with the above risk factors should be managed aggressively in the first instance. Specific measures among these high-risk patients should include adequate hydration (pre- and intra-operatively), maintenance of adequate cardiac output (through adequate filling and inotropic support), the use of continuous infusion of mannitol, frusemide and dopamine [14] and early institution of haemofiltration postoperatively [15]. By applying such measures, a dramatic decrease in mortality and morbidity could be expected in these high-risk patients.

In conclusion, we have identified some of the risk factors predisposing patients with normal preoperative renal function undergoing cardiac surgery to the risk of developing ARF requiring CRRT. By doing so, early preventative measures can be planned ahead in order to achieve a better outcome and a more efficient use of hospital and intensive care resources.

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