

Original Research Article

Pre-operative and peri operative predictors of acute renal failure after cardiac surgery

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ABSTRACT

Background: Acute kidney injury (AKI) is one of the most serious complications during the postoperative period of cardiac surgery. Multiple variables predict the ARF after cardiac surgery. Objective of this study was to evaluate the significance of pre and peri-operative variables which may help in predicting the chances of developing ARF after cardiac surgery.

Methods: This study was an observational, prospective study conducted among patients who were scheduled to undergo open heart surgery under cardiopulmonary bypass.

Results: In total, 50 patients who underwent open-heart surgery, ARF was seen in 5 patients, with the incidence rate of 10%. Acute renal failure was present in one patient with ejection fraction <35, 2 patients had ejection fraction between 35 to 50 and 2 patients with ejection fraction >50. It was seen in 4 patients with 1-2 hrs of cardiopulmonary bypass and in 1 patient with >2 hrs of cardiopulmonary bypass. ARF was also seen in 4 patients with hematocrit between 22-26% and in 1 patient with >26%.

Conclusions: The study provided a clinical variable score that can predict ARF after open-heart surgery. The score enhances the accuracy of prediction by accounting for the effect of all major risk factors of ARF.

Keywords: Acute renal failure, Cardiac surgery, Cardiopulmonary bypass, Open heart surgery, Outcome

INTRODUCTION

Cardiac surgery is viewed as one of the great medical advances of the 20th century. However, the procedure is not without complications and one of them is renal complication. Acute kidney injury (AKI), previously known as acute renal failure, after cardiac surgery is one of the most serious complications during the postoperative period leading to poor quality of life, increased length of hospital stay, cost of care mortality and morbidity.¹ Although the overall mortality rates after cardiac surgery are low (2-5%), the incidence of post-operative AKI varies from 1% to 30%. It is associated with strikingly high mortality rates ranging between 37 to

63% compared to zero to 4.3% in case of normal preoperative renal function.^{2,3}

Although attempts to prevent or to treat kidney injury have been met with limited success, the clinical setting of cardiac surgery offers an exciting opportunity to improve patient outcomes in kidney injury, as it is a setting where renal injury could be anticipated, and pre-operative renal risk assessment is possible. The epidemiological data, however, overwhelmingly support that AKI is an independent risk factor for postoperative death, and that the risk for mortality is proportional to the degree of severity of kidney injury.

The risk for kidney injury is influenced by demographic factors, pre-operative comorbid disease burden, type of surgical procedure, intra-operative events, and post-operative complications. Additionally, >70% disease in the left main coronary artery, history of cardiac surgery, emergency surgery, or pre-operative use of intra-aortic balloon pump (IABP) also predict the risk for AKI.^{4,5} Among types of surgery, coronary artery bypass grafting (CABG) is considered low-risk for the development of post-operative AKI compared with valve surgery, combined CABG and valve procedures, or other procedures such as aortic repairs.

Thus, accurate prediction of probability of developing acute renal failure provides an opportunity to develop strategies for early diagnosis and treatment. Identifying patients who are at high risk for developing acute renal failure after cardiac surgery before the procedure may help not only to provide a more detailed informed consent but also to focus on a specific cohort in which new preventive treatments can be studied. This study was undertaken to evaluate the significance of pre and perioperative variables which may help in predicting the chances of developing acute renal failure after cardiac surgery.

METHODS

The present study was an observational, prospective study conducted in the department of Cardiothoracic and vascular surgery of Indira Gandhi Medical College, Shimla, for period of 22 months (March 2012 to December 2013). The study was conducted after obtaining permission from institutional ethics committee and department of Cardiothoracic and vascular surgery. Study population: The participants considered in this included those patients who were scheduled to undergo open heart surgery under cardiopulmonary bypass at our institution. They were recruited in to the study with following inclusion and exclusion criteria.

Inclusion criteria

- Patients >18 years of age
- Scheduled to undergo Open heart surgery under cardiopulmonary bypass

Exclusion criteria

- Pre-existing renal dysfunction requiring renal replacement therapy
- Pre-operative dialysis
- Mechanical ventilation

The parameters that were analyzed preoperatively as possible predictors of acute renal failure were age, race, gender, weight, history of congestive heart failure; severe left ventricular dysfunction (ejection fraction <35%); preoperative use of intra-aortic balloon pump; emergency surgery; history of chronic obstructive pulmonary disease

requiring medical therapy; diabetes mellitus, preoperative serum urea and creatinine (mg/dl), electrolytes, types of cardiac surgery, including coronary artery bypass graft, valve surgery, combined coronary artery bypass graft and valve procedures, and other complex cardiac surgeries for congenital heart disease.

The following parameters were considered as Intraoperative risk factors: aortic cross clamp time, cardiopulmonary bypass (CPB) time, urine output during intraoperative period, hematocrit and number of inotropes that was required.

The following parameters were monitored postoperatively for assessing renal function, serum urea and creatinine (mg/dl), electrolytes, arterial blood gas analysis and urine output, inotropic requirement that was analyzed at 24 hrs, 36 hrs, 48 hrs and 72 hours.

Patient were defined as having, acute kidney injury if there is an increase in serum creatinine level to 2.0 mg/dL or a 2-fold increase compared with the preoperative baseline serum creatinine level.

All patients received a standard premedication of morphine, 0.1 mg/kg administered 1 hour before surgery. All patients received a standard premedication of morphine, 0.1 mg/kg administered 1 hour before surgery.

For the purposes of this analysis, acute renal failure was defined as a rise of more than 50% above baseline in serum creatinine on the postoperative day 1 to 3.

Statistical analysis

Data was entered in Microsoft excel sheet and was analyzed with the same. Descriptive statistics were used to present the data. Categorical variables presented as numbers and percentages. Continuous variables presented as mean and standard deviations.

RESULTS

During the study period of 22 months, 50 patients underwent open-heart surgery and were included in study for analysis. The average age of participants in our study was 44 years (range 18 to 70 years) with 32 males and 18 females (Table 1). Acute renal failure was seen in 5 patients, with the incidence rate of 10%. Congestive heart failure was seen in 6 patients (Table 2). Majority of patients i.e. 76%, had ejection fraction >50. Acute renal failure was present in one patient with ejection fraction <35, 2 patients had ejection fraction between 35 to 50 and 2 patients with ejection fraction >50 (Table 3). Among the all the enrolled patients, 14 underwent CABG, Valve replacement was done in 22 patient, 13 patients underwent surgery and one patient underwent Bentall's procedure for CHF (Table 4). Pre-operative creatinine was <2 mg/dl in 49 patients and ≥2 mg/dl in one patient. None of the patient required preoperative inotropes.

Table 1: Basic demographic characteristics.

Basic demographic characteristics			
		No of participants	Percentage
Gender	Male	32	64
	Female	18	36
	Total	50	100
Weight (Kg)	<50	20	40
	50-80	30	60
	>80	0	0

Table 2: Clinicopathological condition.

Clinical condition	No of participants	ARF	Normal
CHF present	6	2	4
CHF absent	44	3	41

Table 3: Ejection fraction among study participants.

Ejection fraction	No of participants	ARF	Normal
<35	4	1	3
35-50	8	2	6
>50	38	2	36

Table 4: Type of surgery.

Type of surgery	No of participants	ARF	NORMAL
CABG	14	0	14
VALVE	23	5	18
CHD	13	0	13

Aortic clamp was applied for <1 hr in 14 patients, 1 to 2 hrs in 29 patients and >2 hrs in 7 patients. ARF was seen in patients where aortic clamp was applied for 1 to 2 hrs. Cardiopulmonary bypass time less than 1 hour in 4 patients, 1-2 hours in 28 patients and >2 hrs in 18 patients. ARF was seen in 4 patients with 1-2 hrs of cardiopulmonary bypass and in 1 patient with >2 hrs of cardiopulmonary bypass (Table 5).

Hematocrit was <22% in 2 patients, between 22-26 % in 14 patients and above 26 in 34 patients. ARF was seen in 4 patients with hematocrit between 22-26 % and in 1 patient with >26%. All the 50 patients had urine output more than 2ml/kg/min (Table 6). Intraoperatively 49 patients required one inotrope and one patient required 2 inotropes. Out of those 49 patients, 5 patients had postoperatively acute renal failure (Table 7). Postoperatively, 4 patient had acute renal failure at 24 hours, 2 patients at 36 hours and 3 and 2 patients at 48 and 72 hours respectively. Post operatively all patients had urine output at 1-3ml/kg/min upto 72 hrs. Postoperatively at 24 hours 42 patients required 1 inotrope, 5 patient required 2 inotropes, 3 patients required 3 or more

inotropes. At 36 hours 26 patient's required single inotrope and 2 patients required 2 ant 48 hours 2 patients required single inotrope. 5 patients who had acute renal failure 4 required single inotrope and one patient required 3 inotropes (Table 7).

Table 5: Procedure during surgery.

Aortic clamp time			
	No of participants	ARF	Normal
Aortic clamp time (hours)			
<1	14	0	14
1-2	29	5	24
>2	7	0	7
Cardiopulmonary Bypass Time (hours)			
<1	4	0	14
1-2	28	4	24
>2	18	1	17

Table 6: Laboratory findings.

		No of participants	ARF	Normal
Hematocrits (%)	<22	2	0	2
	22-26	14	4	10
	>26	34	1	33
Urine output (ml/kg/min)	<1	0	0	0
	1-2	0	0	
	>2	50	5	45

Table 7: Intraoperative and postoperative findings.

Number of inotropes required intraoperatively			
Number of inotropes required	No of participants	ARF	Normal
1	49	5	44
2	1	0	1
>2	0	0	0
Creatinine (mg/dl)			
Duration (Hrs)	Normal	>50%	>2 time
24	46	-	4
36	48	-	2
48	47	1	2
72	48	2	-
Number of inotropes required (post operatively)			
Duration (Hrs)	1	2	3 or more
24	42	5	3
36	26	2	0
48	4	0	0
72	0	0	0
Number of blood transfusion required (Post operatively)			
Number of blood transfusion	Number of participants	ARF	Normal
1	17	3	14
2-3	25	2	23
>3	8	0	8

In our study group 17 patients were given one blood transfusion, 25 patients were given 2 to 3 blood transfusion, 8 patients were given more than 3 blood transfusion. 3 patients out of 17 had post operatively acute renal failure, 2 patients out of 25 transfused 2 to 3 blood unit had postoperatively acute renal failure (Table 7). Post operatively urea was 50 mg/dl or less in 40 patients, between 51-80 mg/dl in 7 patients and more than 80 in 3 patients. One patient with urea less then 50mg/dl

and 2 patients each with urea between 51-80 mg/dl and above 80 mg/dl have postoperatively acute renal failure. Postoperatively aminoglycosides and NSAIDS was used in 43 patients and not used in 7 patients and acute renal failure was found in 2 patients using aminoglycosides and NSAIDS and 3 patients not taking NSAIDS and aminoglycosides. Post operatively arterial blood gas and serum potassium analysis was mostly in normal range in all patients in the study group (Table 8).

Table 8: Post-operative parameters.

		No of participants	ARF	Normal
Urea mg/dl	≤50	40	1	39
	51-80	7	2	5
	>80	3	2	1
Post-Operative aminoglycosides and NSAIDS used	Yes	43	2	41
	No	7	3	4
Postoperative potassium	Normal	50	5	45
	Raised	-	-	-
Post operatively arterial blood gas	Normal	50	5	45
	Abnormal	--	-	-

DISCUSSION

ARF is one of the most serious complications after cardiac surgery; the occurrence of ARF strikingly magnifies the risk for postoperative death.^{2,4} Preoperative renal risk stratification provides an opportunity to develop strategies of early diagnosis and intervention. The present study provides clinical factors to predict ARF after open-heart surgery and validates these factors in a comparable population.

Few studies have addressed this issue. Chertow and colleagues were among the first to develop a risk algorithm to predict postoperative ARF.² This analysis involved a large multicenter cohort of patients (n=43,642) who underwent cardiac surgery from the Veterans Administration health system. The risk algorithm was subsequently assessed by Fortescue and colleagues in a smaller cohort of patients (n =8797).⁶ This analysis did not include high-risk cardiac surgical procedures such as valve surgery. Both of these analyses excluded patients with severe preoperative renal dysfunction (creatinine >3 mg/dl). The present analysis includes most of the major risk variable of ARF. Which are applied to evaluate the accuracy of the ARF in two randomly selected patients-one with and one without ARF. Thus, the present study enhances the accuracy of prediction by accounting for the interaction of all major risk factors by order of their degree of association with postoperative ARF.

In an earlier study, they identified the independent predictors of ARF after open-heart surgery. In addition to

confirming the traditional risk factors in a large cohort of patients (n=24, 660), earlier study identified female gender as an independent risk factor of postoperative ARF.⁷ In our study the total number of males were 32 and the total number of females were 18. The mean of age of patients was 44 years, range between 18 to 70 years. Postoperatively 2 male and three female had acute renal failure. Which is comparable with other studies. According to Mehta and colleagues and Aronson S. and colleagues' female sex is one of the risk factors for AKI.^{7,8}

Renal functional reserve starts to fall after the third decade; GFR decreases approximately 10% per decade, and by the seventh decade more than 50% of individuals will have a GFR that meets the criteria for CKD (60 mL/min). Elderly patients are susceptible to many forms of ARF because the aging kidney loses functional reserve and the ability to withstand acute insults is compromised. Older patients may have a reduced ability to cope with reduced circulation. Female sex predicts a lower baseline hematocrit and smaller blood volume, increasing the risk of extreme hemodilution and transfusion during cardiac surgery. Other cause can be due to modulating effect of sex hormones on renal physiology and response to ischemia and reperfusion changes.⁹ Women have higher prevalence of predisposing risk factor compared to men including advanced age diabetes and hypertension.¹⁰⁻¹² Mangano CM et al. have shown that the proportion of patients who develop renal dysfunction increases with advancing age. There is a 10% incidence in those in their

60s, that rises to 25% in the 80-year-and-above older age group.³

In our study group one patient below 50 kg and 4 patients between 50 kg to 80 kg had postoperatively acute renal failure. Intra-aortic balloon pump (IABP) was not used in our study to perform surgeries for the listed patients. According to Thakar CV, Chertow GM and Wijeyesundera and colleagues use of an IABP is a risk factor for the development of post cardiac surgery ARF. IABP could facilitate ARF if limb ischemia and rhabdomyolysis develop.^{13,2,14}

Congestive heart failure was present in six patients out of fifty in the study group. Out of those six patients two had acute renal failure. Rahamanian and colleagues and Aronson S et al. described congestive heart failure as a risk factor for the development of post-surgery ARF.^{15,8} Lohr et al. found that both "congestive heart failure" (CHF) and systolic blood pressure less than 110 mmHg were associated with mortality.¹⁶ Lien and Chan found that "heart failure" influenced survival in a retrospective analysis of 58 patients in case of ARF.¹⁷ Lohr and colleagues found that standard AKI risk factors include patients' characteristics such as reduced left ventricular function.¹⁶ According to Chertow GM, Thakar CV, Wijeyesundra DN and Rahmanian PB and colleagues low ejection fraction is a risk factor for post cardiac surgery acute renal failure.^{2,13-15}

The effects of diabetes mellitus on postoperative renal failure may be the result of renal parenchymal disease, such as glomerulonephritis. Out of 50 patients, only 2 patients were diabetic and post operatively acute renal failure was not seen in either of them. Lohr et al. found that AKI risk factors include patients' characteristics such as diabetes and elevated preoperative serum glucose.¹⁶ According to Brown JR and Palomba H and colleagues diabetes is a risk factor for ARF.^{18,19} Chronic obstructive pulmonary disease was not present in any patient in our study. Lohr and colleagues found that AKI risk factors include patients' characteristics such as advanced obstructive pulmonary disease.¹⁶ Chertow, Rahamanian and colleagues have also noted it as a risk factor.^{2,12} Type of surgeries is also noted as risk factor for post cardiac surgery ARF. According to Chertows, Palambo and Thakar.^{2,19,13} According to Cleveland Score, CABG + Valve surgery carries higher risk than valve surgery performed alone, and CABG performed alone carry the least risk.¹³ But according to Mehta Score, CABG carries lesser risk than Aortic Valve alone which carries lesser risk than Mitral valve alone which carries lesser risk than Aortic valve + CABG whereas Mitral valve + CABG carry highest risk of postoperative renal failure.⁷

According to Thakar and colleagues and Fortescue EB et al., the duration of aortic cross clamp time is also a risk factor for ARF.^{5,6,13} Previous studies have hinted that there likely exists a linear relation between the duration of CPB and the development of AKI. Mangano et al.

reported that CPB lasting more than 180 minutes was an independent risk factor for postoperative renal dysfunction.³ Boldt and colleagues showed that patients with CPB times longer than 90 minutes had more pronounced kidney damage than patients with CPB times less than 70 minutes as assessed by sensitive kidney-specific proteins.²⁰ Conlon and associates in their study involving 2,848 patients who underwent cardiac operation, observed a linear relationship between duration on bypass and ARF.²¹ Eriksen BO et al. also noticed relationship between duration of cardiopulmonary bypass and acute renal failure.²²

Preoperative anemia contributes to kidney injury by reducing renal oxygen renal delivery, worsening oxidative stress, and impairing hemostasis. It impairs renal medulla, where the normal partial pressure of oxygen in the renal tissue is very low. For example, the incidence can be reduced by optimising the haematocrit to between 21% and 25% and by optimising oxygen delivery. In general, because hemodilution has a salutary effect on perfusion there is theoretical decrease in micro circulatory flow with hematocrit above 30%.²³ Studies have suggested that there is a correlation between the lowest hematocrit (usually less than 21%) and incidence of AKI.²⁴⁻²⁶

More than two inotropes postoperatively have been associated with acute renal failure according to Aronson S and Palomba H et al.^{8,19} Excessive peri and postoperative blood transfusion is associated with acute renal failure according to Stafford-Smith M, and Newman MF.²⁷ According to Garella S and Matarese RA, nonsteroidal anti-inflammatory drugs inhibit the production of prostaglandins that prevent regional vasoconstriction in the kidney and are well-known nephrotoxins.²⁸ Except in cases of massive overdose, NSAIDs produce renal dysfunction only in patients with co-existing renal hypo perfusion or vasoconstriction. Aminoglycosides are postoperative risk factor for ARF according to Hock and Anderson.²⁹ The urine output is a very rarely studied variable in publications concerning ARF after cardiac surgery, although, urine output is more sensitive to changes in renal function than biochemical markers. However, it is far less specific except when severely decreased or absent; the changes in urine output often occurs long before biochemical changes are apparent. Urine output criteria for ARF is studied by Lopes JA and colleagues.³⁰

Even small increase in serum creatinine levels (0.5 mg/dL) after surgical intervention are associated with high mortality, longer length of hospitalization, and higher hospital costs. Mehta and Grab observed that AKI with even small changes in sCr level during hospitalization was associated with an independent long-term risk of death.⁷ None of the studies have evaluated urea as a risk factor for postoperative acute renal failure. Outcomes among patients with non-dialysis-dependent renal disease have been less well studied. This translates

into two major limitations related to clinical research. First, it limits the ability of most of the epidemiologic studies to identify independent predictors of ARF, as a result of inadequate power (i.e. number of patients). Second, it impedes the development of clinical studies that pertain to early diagnosis and intervention in ARF by necessitating the enrollment of a large number of patients. This underscores the importance of risk stratification in clinical settings where renal injury can be anticipated. The present study involves a large cohort of patients, sufficient to generate and validate a score that incorporates multiple independent risk factors, despite the low event rate of ARF.

The frequency of ARF ranged between 0.4 and 22% across the risk categories. It should be noted that the overall frequency of ARF was 1.8%, so the risk categories allow identification of subgroups of patients who have lower- as well as higher-than-average risk for developing ARF. This can be a valuable tool used to randomize patients in clinical trials of ARF. It is known that dialysis dependent patients undergoing heart surgery are at an increased risk for perioperative morbidity and mortality. Mortality rates have ranged from 8% to 30% in this group of patients, with morbidity ranging from 10% to 60%.^{1,2,7,13}

A weakness of the present study is that the data are derived from a single center. The model needs to be tested prospectively at multiple centers to substantiate its broad applicability. However, unlike other studies, it does include the single largest cohort of patients that is well represented by differences in gender, race, and all types of cardiac surgical procedures. Inherent to the observational study design is the limitation that it establishes association and not causality. Thus, it would be incorrect to justify a change in clinical decision making regarding open-heart surgery as a result of the risk for ARF on the basis of any such analyses.

Nevertheless, it can improve individual patient care by allowing us to identify accurately patients who have a greater likelihood of developing ARF. It should be noted that the proposed scoring model predicts severe form of ARF defined by requirement of dialysis. Although less severe degrees of renal dysfunction (defined arbitrarily) may portend a risk for worse outcomes, the clinically relevant threshold of renal dysfunction after cardiac surgery remains unclear. Our rationale to choose this definition was based on clinical relevance and, more important, because ARF that requires dialysis after cardiac surgery has been unequivocally associated with mortality.

CONCLUSION

The study provided a clinical score validated in our population of patients that predicts ARF after open-heart surgery. The score enhances the accuracy of prediction by accounting for the effect of all major risk factors of ARF.

In addition, the score identifies patients who have a lower- as well as a higher than- average risk for ARF. This increases the clinical utility of the score in improving both individual patient care and by providing a vital tool in planning future clinical trials of early diagnosis and intervention in ARF.

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