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Acute Kidney Injury (AKI) After Cardiac Surgery: Incidence, Risk Factors and Outcome

(Research Article)

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Abstract

Background: *Acute kidney injury (AKI) occurs in up to 30% of patients who* undergo cardiac surgery and *is* associated with substantial morbidity and mortality. There is very limited data regarding the post cardiac surgery AKI from *India.*

Materials and methods: *All consecutive patients who underwent cardiac surgeries at Amrita Institute of Medical Sciences and Research, Kochi, Kerala, from May 2008 to April 2010 were included in the study. Postoperative AKI was defined as >25% change in serum creatinine corresponding to a 20% reduction in Cockroft-Gault GFR from baseline within one week* after surgery.

Results: *1146 (males:952; females:194) patients, aged 18-82 years (mean 55.90; SD:11.15) were included in the study. The nature of surgeries and patient number were; CABG (on pump:841, off pump: 73), CABG with valve surgery (32), valve surgery (158) and ASD repair (42) respectively. The overall incidence of AKI was 25.7 % & incidence was highest (53.1 %) in combined CABG with valve surgery and lowest (4.8 %) in ASD repair. Dialysis requiring AKI (AKI-D) was seen 2.1 % of all patients & was highest following (6.25 %) in combined CABG and valve surgeries and none required dialysis after ASD repair. The overall in hospital mortality rate in study was 2.2 % and was highest (50 %) in those with AKI-D.*

Conclusions: Cardiac surgery is associated with a *high risk for AKI. The incidence of AKI and AKI-D was 25.7 and 2.1%, respectively. Presence of AKI, increased the morbidity and mortality, especially in those with AKI-D.*

Keywords: *AKI, AKI-D, cardiac surgery.*

INTRODUCTION

Acute kidney injury (AKI), depending on the specific definition, occurs in up to 30% of all patients who undergo cardiac surgery. [1-8] The development of AKI is associated with a higher morbidity and mortality due to a more complicated hospital course, and a higher risk for infectious complications. [1-8] Even minimal changes in serum creatinine that occur in the postoperative period are associated with a substantial decrease in survival. [8] Despite advances in bypass techniques, intensive care, and delivery of hemodialysis, morbidity and mortality associated with AKI have not markedly changed in the last decade. [1-8] There is limited data regarding AKI after cardiac surgery from India. [6,7]

AIMS AND OBJECTIVES

Our objective was study the incidence of AKI following all cardiac surgeries and its effect on hospital stay and in-hospital mortality. Our secondary objective was to assess the effect of pre-operative, intra-operative and post-operative factors on incidence of AKI.

METERIALS AND METHODS

All consecutive patients undergoing cardiac surgeries from May 2008 to April 2010 at Amrita Institute of Medical Sciences and Research, Kochi, Kerala, were included in this prospective study. The patients undergoing re-operations (within 30 days) and those with chronic kidney disease stage 5 on renal replacement therapy (hemodialysis or continuous ambulatory peritoneal dialysis) were excluded. Postoperative AKI was defined as >25% change in serum creatinine corresponding to a 20% reduction in Cockroft-Gault GFR from baseline within one week after surgery, similar to an earlier study. [9] Data analysis was done using SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA). Two tailed, *p* value < 0.05 was considered as significant. Patients needing renal replacement therapy (RRT) were managed with hemodialysis and the method (CVVHD-continuous venovenous hemodialysis, SLED- sustained low efficiency dialysis or conventional hemodialysis) was chosen as per hemodynamic status.

The presumptive risk factors for AKI were divided into pre, intra and post-operative factors to analyze their association with its incidence. The Pre-operative risk factors were, age, gender, body mass index (BMI in Kg/m2), presence of insulin requiring diabetes mellitus (DM), left ventricular ejection fraction (LVEF) <35%, congestive heart failure, as per Framingham criteria (CHF), chronic obstructive pulmonary disease (COPD), use of intra-aortic balloon pump (IABP), nature of surgery, preoperative renal disease & serum creatinine levels. The intra-operative factors were, duration of cardiopulmonary bypass (CPB), mean CPB flows, perfusion pressures (mean), urine volume during CPB. The post-operative factors were, need for prolonged inotropic support, IABP, urine output, creatinine profile, indication for dialysis, number of dialysis, days on ventilator, duration of ICU and hospital stay.

Cardio pulmonary bypass system: Terumo Sarns 8000, Soma Technology, Inc., USA - A modular heart lung machine was used in all patients who underwent on-pump surgery, with pulsatile flow. Blood cardioplegia delivery system by Medtronic (BCD - Myotherm) was used in on-pump surgeries.

RESULTS

A total of 1146 (males:952; females:194) patients, aged 18-82 years (mean 55.90; SD:11.15) were included in the study. The nature of surgeries and patient number were; CABG (on pump:841, off pump: 73), CABG with valve surgery (32), valve surgery (158) and ASD repair (42) respectively.

Incidence of AKI and its relation to type of surgery

The overall incidence of AKI was 25.7 % (295 out of 1146 patients) using the definition as >25% change in serum creatinine from baseline within 1-week post-surgery (Table-1). The incidence of AKI varied according to the type of surgery (Table-1). The incidence rates of AKI were; 4.8, 17.1, 27.24 and 53.1 % after atrial septal defect (ASD) repair, valve surgery, coronary artery

bypass grafting (CABG) and combined CABG with valve surgery, respectively (Table-1).

Dialysis requiring AKI (AKI-D) was seen 2.1 % (24 out of 1146) of all patients (Table-1). The incidence of AKI – D also varied according to type of surgery (Table-1); it was 1.3, 2.2 and 6.25 % after valve surgery, CABG and in combined CABG with valve surgeries, respectively. None of the patients developed AKI-D after ASD repair. The indications for dialysis were presence of one or combinations features like; anuria/oliguria, pulmonary edema, fluid overload, biochemical abnormalities (hyperkalemia, dilutional hyponatremia) and uremic encephalopathy.

Risk Factors Associated with AKI

Risk factors found to be associated with increased incidence of acute kidney injury are divided into pre-operative (Table 2), intra-operative (Table 3) and post-operative (Table 4) factors.

Pre-operative risk factors

The incidence of AKI was higher (27.2 %) in patients aged > 40 years (1049 subjects, mean: 58.28 years) than those aged ≤ 40 (97 subjects, mean:30.16 years) (10.3 %). The incidence of AKI was higher in males (26.57%) than females (21.64%); but the difference was not statistically significant. The mean BMI (Kg/m2) was 23.82 and 23.94 in subjects with AKI and without AKI respectively; the difference was not statistically significant. The incidences of AKI in patients with and without COPD were 16.67% (6 out of 36) and 26.03% (289 out of 1110) respectively, but the difference was not statistically significant (p:0.284).

The patients with CHF pre-operatively had higher (44.8 %) incidence of AKI than those without CHF (24.7 %) with an odds ratio (OR) 2.41 for AKI. Patients with LVEF ≤ 35 % and insulin requiring diabetes mellitus (DM) had higher incidence of AKI, 50 % (OR 3.04) and 34.1 % (OR 2.18) respectively, than those with LVEF > 35 % and without insulin requiring DM. The presence of pre-operative renal disease and serum creatinine more than 1.2 mg /dl also increased the incidence of AKI to 72 % (OR 8.85) and 62 % respectively. The incidence of AKI was 17.6 % in patients with preoperative serum creatinine was < 1.2 mg/dl. Pre-operative renal disease (based on clinical/laboratory or Imaging criteria) was found in 6.5 % of patients and the most common was diabetic nephropathy (90 %), followed by primary glomerular disease (5 %), urolithiasis (2.5 %), and renal artery stenosis (2.5 %).

Emergency surgery was done in 9 patients (CABG:8, MVR redo:1) and incidence of AKI were 44.44 % (4 out of 9) and all 4 required hemodialysis. Five patients (CABG:4, MVR:1) who had previous cardiac surgery underwent redo CABG (4) and redo MVR (1) with incidence rate of AKI of 60 % (3 out of 5) and all 3 required hemodialysis. One patient required pre-operative IABP and was managed without hemodialysis for AKI in post-operative period.

Intra-operative risk factors

The incidence of AKI and AKI-D in subjects undergoing on-pump surgeries was 25.39 % (272/1071) and 2.15 % (23/1071) respectively. The incidence of AKI and AKI-D in subjects undergoing off-pump (75 subjects) surgeries was 30.67 % (23 out of 75) and 1.33 % (1 out of 75) respectively. The difference in incidence between on-pump and off-pump surgeries was not statistically significant. The subjects were categorized into two groups of CPB time ≥ 100 mins (414 subjects; mean CPB time:126.76) and < 100 mins (657 subjects; mean CPB time:67.81) for analysis. The incidence of AKI was significantly higher (29.7 % vs. 22.8 %) in patients in whom CPB time was ≥ 100 minutes. The subjects were categorized into 2 groups mean CPB pressure (mmHg) of < 50 (81 subjects; mean: 45.25) and ≥ 50 (990 subjects; mean:57.20). The incidence of AKI in subjects mean CPB pressure of < 50 and ≥ 50 mmHg were 19.75 % (16 out of 81) and 27.83 % (256 out of 990) respectively; the difference was statistically insignificant (p:0.22). There was no statistically significant difference in incidence of AKI based on mean CPB flow (<3 or ≥ 3 L/min/1.73m2), urine volume during CPB (< 400 or ≥ 400 ml) and number of grafts during CABG (≤ 3 vs. > 3).

Post-operative risk factors

The patients were categorized into two groups on the basis of serum albumin (≥ 3 & <3 g/dl) on 1st post-operative day. The incidence of AKI and AKI-D was 17.76 % (27 out of 152) and 0.66 % (1 out of 152) respectively, in patients with serum albumin of ≥ 3 g/dl. In subjects with serum albumin (<3gm/dl) the incidence of AKI and AKI-D was 26.96 % (268/994) and 2.31 (23 out of 994), respectively. The effect on serum albumin on incidence of AKI and AKI-D was statistically significant. The requirement for prolonged post-operative inotropic support (>48 hours) and IABP support also increased the incidence of AKI to 81.8 % (OR 14.6) and 65.2 % (OR 5.6) respectively.

Effect of AKI on morbidity and mortality

The mean duration of hospital stay in patients without AKI, with AKI (not requiring RRT) and AKI-D were 11.27, 13.27 and 27.04 days, respectively. The difference in duration hospital stay and its relation to the incidence of AKI was statistically significant (Table-4). Need for prolonged hospital stay (>10 days) was seen in 79.16 % (19 out of 24), 57.19 % (155 out of 271) and 37.13 % (316 out of 851) in patients with AKI-D, AKI (not requiring RRT) and no AKI, respectively. The overall in-hospital mortality rate in study was 2.18 % (25 out of 1146). (Table 4) The mortality rates were, 0.47 (4 out of 851), 3.32 (9 out of 271) and 50 % (12 out of 24) in those without AKI, AKI (not requiring RRT) and AKI-D, respectively. Majority (76.14%, 206 out of 271) of the patients with AKI (not requiring RRT) had recovered from AKI at the time of discharge.

The modality of RRT was chosen based on hemodynamic status of the patient; those on inotropes (2 or more), IABP, arrhythmias were started on CVVHD, those on single inotrope, MAP >90 mmHg, no arrhythmias were started on SLED and those patients stable hemodynamics, without inotropes were started on conventional hemodialysis. Hence, the survival rate in patients who underwent only CVVHD (as they were unfit to undergo SLED or conventional hemodialysis due to hemodynamic instability) was least, followed by those undergoing CVVHD initially followed by SLED or conventional HD after improvement in hemodynamics. (Table 5) The survival rates were better in those undergoing and SLED or conventional HD initially due to better hemodynamic status. (Table 5) Among the patients having AKI-D, 3 (12.5%) were discharged to continue hemodialysis, 3 (12.5%) had mild renal insufficiency and 6 (25%) had normal renal parameters (Table 5).

Table 1: Type surgery of surgery and incidence of AKI and AKI-D

		Surgery					Total
		CABG on pump n (%)	CABG off pump n (%)	CABG + Valve n (%)	Valve only n (%)	ASD repair n (%)	
Gender	Males	753	70	21	91	17	952
	Females	88	3	11	67	25	194
Age in years (Mean)		58.55	59.19	60.98	45.42	34.07	55.90
AKI	No	615	50	15	131	40	851
	Yes	226 (26.9)	23 (31.5)	17 (53.1)	27 (17.1)	2 (4.8)	295 (25.7)
Patient with AKI needing RRT		19 (2.25)	01 (1.36)	02 (6.25)	02 (1.26)	00	24 (2.1)
Total		841	73	32	161	42	1146

Table 2: Pre-operative risk factors for AKI						
Parameter		Patients without ARF (*n* - 851)	Patients with ARF (*n* - 295)	P value (2- sided)	OR	95 % CI
Females		152	42	0.176 *	0.763	0.527 to 1.106
Congestive heart failure		16	13	0.029 *	2.406	1.143 to 5.064
LVEF < 35 %		23	23	< 0.0001 *	3.044	1.681 to 5.513
Preoperative IABP		00	01	-	-	-
COPD		30	06	0.248 *	0.568	0.234 to 1.379
Insulin requiring DM		335	173	< 0.0001 *	2.184	1.668 to 2.860
Previous cardiac surgery		02	02	-	-	-
Emergency Surgery		05	04	-	-	-
Surgery type	Valve surgery only	131	27	< 0.0001 **	-	-
	Valve + CABG	15	17			
	Other cardiac surgeries	705	251			
Preoperative creatinine (mg/dl)	< 1.2	772	165	< 0.0001 **	-	-
	1.2 to 2.1	79	127			
	> 2.1	00	03			
* Fisher's Exact test ** Pearson Chi-Square test						

Table 3: Intraoperative risk factors for AKI						
Parameter		Patients without ARF (n - 851)	Patients with ARF (n - 295)	P value (2- sided)	OR	95 % CI
On pump surgeries		799	272	0.339 *	1.299	0.780 to 2.163
CPB time > 100 min		279	118	0.014 *	1.428	1.079 to 1.890
Mean CPB flow < 3.0 (l/min/1.73m2)		63	16	0.461 **	-	-
Mean CPB Pressure < 50 (mmHg)		65	16	0.22 **	-	-
Urine volume during CPB < 400 ml		219	71	0.677 **	-	-
CABG (Number of grafts)	≤ 3	223	89	0.817 *	0.967	0.716 to 1.307
	> 3	457	175			
* Fisher's Exact test ** Pearson Chi-Square test						

Table 4: Post-operative risk factors for AKI and effect of AKI on hospital stay and mortality					
Parameter	Patients without ARF (n - 851)	Patients with ARF (n - 295)	P value (2- sided)	OR	95 % CI
Sr. Albumin < 3.0 g/dl (1st POD)	764	278	0.025 *	0.573	0.314 to 0.319
Prolonged Postoperative Inotropic support (> 48 hours)	08	36	< 0.0001 *	14.647	6.723 to 31.908
Postoperative IABP	08	15	< 0.0001 *	5.645	2.368 to 13.456
Hospital stay > 10 days	316	174	< 0.0001 *	2.435	1.858 to 3.191
Death	04	21	< 0.0001 *	16.229	5.523 to 47.689
* Fisher's Exact test					

Table 5: Modality of RRT and its effect on renal recovery and mortality					
Mode of RRT	Number of patients	Renal function recovered	Discharged with mild renal failure	Discharged to continue HD on OP basis	Expired
CVVHD only	3	00	00	00	03
CVVHD + SLED/ Conventional HD	4	00	00	01	03
SLED/ Conventional HD only	17	03	06	02	06
Total	24	03 (12.5 %)	06 (25 %)	03 (12.5 %)	12 (50 %)

DISCUSSION

The incidence of AKI and AKI-D were 25.7 and 2.1% respectively, using the definition as >25% change in serum creatinine from baseline within 1-week post-surgery. The incidence of AKI and AKI-D were highest (53.1 and 6.25 %) in combined CABG with valve surgery and lowest (4.8 and 0 %) following ASD repair. The indications for dialysis were presence of one or combinations features like; anuria/oliguria, pulmonary edema, fluid overload, biochemical abnormalities (hyperkalemia, dilutional hyponatremia) and uremic encephalopathy. The incidence of AKI varied from 1 to 30 % based on the criteria for AKI. [1-8] The incidence of AKI was 17.2 % following CABG in which a defining criteria, was similar to the present study. [9] The incidence of AKI – D has been reported in 0.7 to 3.3 % in different studies, consistent with our study. [1, 5, 10, 11] The highest risk group included combined CABG and valvular surgery with an incidence of AKI of 4.6% and AKI-D of 3.3%. [10, 11] The incidence of AKI-D in the present study was similar to earlier studies. [1,5, 10,11]

Other risk factors found to be associated with increased incidence of AKI in our study were age more than 40 years, congestive heart failure, LVEF ≤ 35 %, insulin requiring DM, presence of pre-operative renal disease, preoperative serum creatinine >1.2 mg /dl, emergency surgery and redo surgery (CABG or valve). Pre-operative kidney disease was found in 6.5% of patients and the most common was diabetic nephropathy (90 %). Among the intra-operative risk factors statistically significant association was found with CPB time. There was no statistically difference in

incidence of AKI based on mean CPB pressure, mean CPB flow, urine volume during CPB, on-pump vs. off-pump surgery and number of grafts during CABG. Postoperative factors associated with increased the incidence of AKI were hypoalbuminemia (<3gm/dl), requirement for prolonged post-operative inotropic support and use of IABP.

Several studies have examined the risk factors associated with the development of AKI after CPB. In almost all studies, certain risk factors have been repeatedly associated with an increased risk for AKI. [2-4, 6-7, 13-15] These include female gender, age more than 50 years, reduced left ventricular function, presence of congestive heart failure, diabetes mellitus, peripheral vascular disease, preoperative use of an intra-aortic balloon pump, COPD, the need for emergency surgery, and an elevated preoperative serum creatinine. This last factor is perhaps the most predictive, with the risk for AKI-D approaching 10 to 20% in patients with a baseline preoperative creatinine 2.0 to 4.0 mg/dl. [13-19] In patients with a preoperative creatinine >4.0 mg/dl, the risk for AKI-D rises to 25 to 28%. [13-15] Several other risk factors have been identified but are more controversial and, thus, individually they do not play as prominent a role in determining the risk for AKI. In aggregate, however, these factors may be important and potentially modifiable. These include factors specifically related to the bypass procedure itself, such as duration of CPB [16-18] and on- versus off-pump coronary artery bypass surgery [19-24].

The mean duration of hospital stay in patients without AKI, with AKI (not requiring RRT) and AKI-D were 11.27, 13.27 and 27.04 days, respectively. Need for prolonged hospital stay was observed in majority of patients with AKI and AKI-D. The overall in-hospital mortality rate in study was 2.18 %. The mortality rate was least (0.47%) in patients without AKI and was highest in those with AKI-D (50%). The survival rate in patients who underwent only CVVHD was least, followed by those undergoing CVVHD initially and SLED or conventional HD after improvement in hemodynamics. Majority (76.14%) of the patients with AKI (not requiring RRT) and minority (25%) of those with AKI-D had recovered from AKI at the time of discharge.

Earlier studies have shown that even small rises (0 to 0.5 mg/dl) in serum creatinine are associated with significant higher mortality (2.77 fold). [5, 8] In patients who require dialysis, the mortality is uniformly high in all studies and averages 60 to 70%. [1-8] In study by Chertow et al. [5] AKI-D was an independent determinant of the risk for death with an odds ratio of 7.9. The results of present study correlates with studies by Chertow et al, [5] and Lassnigg et al, [8] which that, even with minimal rise in serum creatinine increases mortality risk and the risk was highest in AKI-D category of patients. In one of studies; development of post-CPB AKI was an independent factor for long-term mortality. [9] The present cohort need follow-up to assess the effect of AKI on long term mortality.

Newer markers for AKI

There are no ideal laboratory markers to monitor renal function available for routine clinical practice. Hence, serum creatinine is the most the commonly used marker even today. Besides, serum creatinine, which is a blood marker, the other blood markers like the Cystatin C, Plasma Interleukin 6 (IL 6) and Interleukin 10 (IL 10) and urinary biomarkers like Neutrophil Gelatinase Lipokalin (NGAL), Interleukin 18 (IL 18), Kidney Injury Molecule 1 (KIM 1), Liver fatty acid binding protein (LFABP), hyaluronic acid are being extensively investigated for early detection of AKI. [25-28]

Limitations

The effect of pre-operative hemoglobin level, proteinuria, and the lowest hematocrit during cardiopulmonary bypass were not part of the study. The effect of crystalloids vs. colloids in priming of the pump, effect of blood replacement or fluid replacement protocols were not studied. The effect of post-operative pain management protocols and its effect on AKI were not assessed, however none of the study patients received NSAIDS for pain

for during the hospital stay. We have only done univariate analysis and not the multivariate analysis. The selection bias for off-pump vs on-pump might have played a role in influencing the incidence of AKI. None of the new markers for early detection of AKI were studied in addition to serum creatinine due their prohibitive cost and un-availability.

CONCLUSIONS

Cardiac surgical procedures are associated with a high risk for AKI with an overall incidence of was AKI and AKI-D of 25.7 and 2.1 %, respectively. The incidences of AKI and AKI-D were highest (53.1 and 6.25 %) in combined CABG and valve surgery and lowest (4.8 and 0 %) following ASD repair. Of the subset of patients with AKI; especially those requiring dialysis have increased rate of morbidity (increased hospital stay and requirement of long term dialysis) and mortality (50 %). The survival rate in patients who underwent only CVVHD was least, followed by those undergoing CVVHD initially and SLED or conventional HD after improvement in hemodynamics.

The factors which increased the risk for AKI were age more than 40 years, reduced left ventricular function (≤ 35 %), and presence of congestive heart failure, insulin requiring diabetes mellitus, an elevated preoperative serum creatinine (> 1.2 mg/dl) and preexisting renal disease, combined CABG and valve surgery and CPB duration ≥ 100 minutes. Postoperative factors associated which increased the incidence of AKI were hypoalbuminemia (<3gm/dl), requirement for prolonged post-operative inotropic support and IABP.

There was no statistically significant difference in incidence of AKI based on gender, presence of COPD, mean CPB flow, mean CPB pressure, urine volume during CPB, on-pump vs. off-pump surgery and number of grafts during CABG.

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