Original Article

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Analysis of the Incidence and Risk Factors in the Development of Acute Kidney Injury after Off Pump Coronary Artery Bypass Grafting

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Abstract

Background: Acute kidney injury (AKI) is a serious complication after coronary artery bypass grafting and is associated with a high mortality. The aim of this study was to evaluate the incidence and the risk factors involved in the development of AKI after off pump coronary artery bypass grafting (OPCAB). **Subjects and Methods:** A retrospective analysis of 1378 adult patients who underwent OPCAB in Sapthagiri Institute of Medical Sciences and Research Centre during a one-and-a-half-year period was done. AKI was defined as an increase in creatinine more than 0.3 mg/dl or a decrease in urine output less than 0.5 ml.kg.hr for 6 hrs. The data relevant to the risk factors were collected and analysed using chi square test. **Results:** The overall incidence of AKI was 18.2%. The independent risk factors that were associated with AKI were increasing age, pre-operative chronic kidney disease, diabetes mellitus, left ventricular dysfunction, low mean arterial blood pressure and the need for intra-aortic balloon pump. **Conclusion:** AKI was common after OPCAB. Pre-existing renal dysfunction, diabetes mellitus, left ventricular dysfunction, advanced age, low mean arterial blood pressure during the intra operative period and the need for intra-aortic balloon pump were identified as the risk factors for the development of AKI after OPCAB.

Keywords: Acute kidney injury, Coronary artery disease, Graft

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Introduction

Acute Kidney injury (AKI) developing in the post-operative period is among the most serious complications in patients who undergo coronary artery bypass grafting (CABG).[1–3] The incidence of AKI after coronary artery bypass grafting as reported in various studies varies between 1-30%.[4] Of the patients developing renal failure around 2% require temporary renal replacement therapy.[4] The development of acute kidney injury is associated with an increased short term and long-term mortality.[5,6] In the setting of CABG, the pathogenesis of AKI is multifactorial, the major contributors being impaired autoregulation due to disturbances in hemodynamics during surgery and increased systemic inflammatory response triggered by the surgery.[7–9]

The need for cardiopulmonary bypass (CBP) is eliminated by Off Pump Coronary Artery Bypass surgery (OPCAB) which in turn leads to a decreased incidence of systemic inflammatory response and decreased haemolysis which is thought to decrease the incidence of AKI after OPCAB.[10]

This study was done to evaluate the incidence of AKI and to assess the risk factors in the occurrence of acute kidney injury after Off Pump Coronary Artery Bypass Grafting. The mortality rate among the subgroup of patients who developed AKI after OPCAB was also analysed.

Subjects and Methods

A retrospective study was done on all consecutive patients admitted for OPCAB in the Sapthagiri Institute of Medical Sciences and Research Centre for a one-and-a-half-year period, between 1st October, 2019 till 30 th April, 2021.

Patients who were taken on cardiopulmonary bypass during surgery, patients who had a simultaneous valve repair or replacement procedure during surgery were excluded from the study.

Acute Kidney Injury (AKI) was defined on the basis of KDIGO criteria [Table 1].

AKI is defined by Kidney disease Improving Global outcomes (KDIGO) definition as an increase in serum creatinine of more

than 0.3 mg/dL within 48 hrs of observation or 1.5 times the baseline serum creatinine value which is presumed to have occurred within 7 days or a reduction in urine volume below 0.5ml/kg/hr for at least 6 hrs.

The following risk factors were analysed – age, gender, history of diabetes operative chronic kidney disease (defined as S Creatinine > 1.5 mg/dL for at least 3 months), hypotension (Defined as a systolic blood pressure less than 100 mm Hg), requirement of Intra-aortic Balloon pump (IABP) either in the pre op period or immediate post-operative period, need for emergency surgery, prior CABG and left ventricular dysfunction on Echocardiogram (defined as an ejection fraction -EF less than 35%).

The need for dialytic support was evaluated.

The primary end point evaluated was the development of AKI during the immediate post-operative period of 1 week. The secondary end points that were analysed was the need for dialytic support in the AKI group and the mortality rate.

All the pertaining data relevant to the study was sourced from the patient records, intensive care unit records and electronic data. The data included the pre-operative medical records, intra operative records and the data during 1-week post-operative stay.

Statistical analysis

Continuous variables were expressed as medians with interquartile range or median ± standard deviation. Categorical variables were expressed as percentages.

The significant predictors of development of AKI after OPCAB were determined by univariate and multivariate logistic regression analysis.

Chi square test was used to compare the AKI group and the non-AKI group

Value of <0 05 was taken as statistically significant

All statistical analysis were performed with SPSS software (version 20.0).

Results

A total number of 1662 patients underwent off pump coronary artery bypass surgery during the time period from 1^{st} October, 2019 to 30^{th} April, 2021 during the one-and-a-half-year period.

Exclusion after application for the criteria selected in the study and the lack of relevant data on electronic database and on medical records resulted in 1378 patients available for the study.

The baseline characteristics are reported in [Table 2].

The median age of the patients was 60 years with a standard deviation of 8.82. Of the 1378 patients analysed, 216 were females (15.7%) and 1161 males (84.3%).

The incidence of acute kidney injury as defined by the KDIGO criteria in these patients undergoing OPCAB was 18.21%, corresponding to 251 patients.

Total of 31(2 2% patients needed dialytic support

Left Ventricular dysfunction as defined by an ejection fraction of less than 35% on pre-operative echocardiogram was observed in 240 patients (17.4%).

Diabetes mellitus is observed in 819 patients (59.5%).

3% of patients who underwent OPCAB had pre-existing chronic Kidney disease (CKD

6 patients (0.4%) had history of previous cardiac surgery and 22 patients were taken up for surgery on an emergency basis (1.6%).

The mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) in the study population was 137- and 79-mm hg respectively.

The mean arterial pressure (MAP) of the study group was 98.7 mm hg.

12 patients needed Intra-Aortic Balloon Counter Pulsation (IABP) for hemodynamic support in the peri operative period (0.9%).

[Table 3] shows the comparison of the clinical and demographic characteristics of patients with and without AKI.

[Table 4] Shows the Risk factor assessment for the development of AKI after OPCAB.

Discussion

From the statistical analysis as shown in table 3, in the patients who developed AKI after OPCAB, were mostly elderly, with a mean age more than 60 years compared to non-AKI group in which patients were younger which was statistically significant ($p<0.001$).

Dialysis requirement was needed in only 31 patients (12.4%) of the 251 patients who developed AKI. The main indications for dialytic therapy were the unresponsiveness to loop diuretics or the development of uremic complications, which was similar to the data published in other studies.[11,12] The majority of the patients who developed AKI was managed by conservative measures which included careful fluid and electrolyte management along with optimisation of hemodynamic and therapeutic measures which included the judicious use of diuretics.[13,14]

Left ventricular dysfunction as defined by a pre-operative echocardiography finding of an ejection fraction (EF) of

Table 1: Kidney Disease Improving Global Outcome (KDIGO) criteria for AKI

Kidney disease: improving global outcome (KDIGO)- diagnosis and staging of AKI		
Satge	**S Creatinine**	**Urine output**
Stage 1	1.5-1.9 x baseline OR increase in serum creatinine >0.3 mg/dL above baseline	<0.5 ml/kg/hr for 6-12 hrs
Stage 2	2-2.9 x baseline	<0.5 ml/kg/hr for 12hrs
Stage 3	3 times baseline OR increase in serum creatinine >4 mg/dL OR initiation of renal replacement therapy	<0.3 ml/kg/hr for 24 hrs OR Anuria for 12 hrs

Table 2: Demographics and clinical profile of the study population (n=1378)

Parameters	No. of patients (n=1378)
Age (years), mean (SD)	60.33 (8.82)
Gender Male Female	1161 (84.30) 216 (15.70)
Incidence of AKI	251 (18.21)
Preoperative creatinine, mean (SD)	1.11 (0.51)
Postoperative creatinine, mean (SD)	1.29 (0.74)
Dialysis requirement	31 (2.20)
Left ventricular dysfunction	240 (17.40)
Preoperative CKD	156(11.3)
Diabetes mellitus	819 (59.50)
Previous Cardiac surgery	6 (0.40)
Emergency surgery	22 (1.60)
SBP*(mmHg), mean (SD)	137.15 (20.80)
DBP ** (mmHg), mean (SD)	79.48 (24.81)
MAP *** (mmHg), mean (SD)	98.70 (19.96)
IABP**** Requirement	12 (0.90)
Data shown as n (%), unless otherwise specified.	

SBP*- Systolic Blood Pressure, DBP**-Diastolic Blood Pressure, MAP***- Mean Arterial Pressure, IABP ****- Intra Aortic Balloon Pump CKD – Chronic kidney disease.

less than 35% was statistically associated with an increased risk of development of AKI after OPCAB.AKI is thought to develop in this subset of patients as a result of multiple mechanisms which include reduced perfusion pressures, renal ischemia, sympathetic overactivity, activation of the renin angiotensin aldosterone system with subsequent worsening of renal ischemia.[15–17]

Patients with diabetes mellitus accounted for nearly 60 % of the study population (59.5%). Of the patients who developed AKI after OPCAB, nearly 69.7%, corresponding to 175 patients were diabetic. This was shown statistically as an important risk factor in the development of AKI.The increased association of AKI secondary to diabetes is postulated to be due to decreased renal reserve, endothelial injury and impaired renal perfusion.[18,19]

22 patients (1.6%) of the total underwent OPCAB as an emergency procedure. The risk of developing AKI was significantly high if the patient underwent an emergency procedure.

Of the 1378 patients, 6 patients (0.4%) had a history of previous cardiac surgery. A previous history of cardiac surgery was not found to be associated with an increased risk of AKI after OPCAB in our study.

Pre-existing chronic kidney disease (CKD) was observed in 156 patients (11.3%). The presence of CKD was significantly associated with the development of AKI after OPCAB ($p<0.001$). This finding was clearly in tandem with similar findings published in other studies.[20–23]

Table 3: Comparison of demographic and clinical profile of patients with or without AKI after OPCAB

Characteristics	AKI (n=251)	No AKI (n=1127)	Chi square (χ^2) value and p value
Age (years), mean (SD)*	62.22 (8.48)	59.92 (8.85)	P<0.001
Gender Male Female	224 (89.20) 27 (10.80)	937 (83.20) 189 (16.8)	χ^2=5.693 p=0.16
Preoperative creatinine, mean (SD)*	1.38 (1.04)	1.06 (0.26)	p<0.001
Postoperative creatinine, mean (SD)*	2.18 (1.32)	1.10 (0.29)	p<0.001
Urine output decreased meeting AKI criteria	222 (88.4)	1126 (99.9)	χ^2=126.703 p <0.001
Dialysis requirement	31 (12.4)	0 (0)	χ^2=142.395 p <0.001
Preoperative CKD	150(96,1)	6(0.03)	χ^2= 140.87 p<0.001
Left ventricular dysfunction	88 (35.1)	152 (13.5)	χ^2=66.298 p <0.001
Diabetes mellitus	175 (69.7)	644 (57.2)	χ^2=13.365 p <0.001
Previous Cardiac surgery	2 (0.8)	4 (0.4)	χ^2=0.925 p=0.301
Emergency surgery	1 (4.4)	11 (1.0)	χ^2= 15.141 p=0.001
SBP (mmHg), mean (SD)*	132.52 (22.84)	138.19 (20.21)	p<0.001
DBP (mmHg), mean (SD)*	75.39 (12.63)	80.39 (26.73)	p<0.001
MAP (mmHg), mean (SD)*	94.43 (14.87)	99.65 (20.81)	p<0.001
IABP requirement	7 (2.8)	5 (0.4)	χ^2=13.079 p=0.002

Data shown as n (%), unless otherwise specified. * Mann Whitney U test is used for statistical analysis. CKD Chronic Kidney disease DBP, diastolic blood pressure; IABP, intra-aortic balloon pump; MAP, mean arterial pressure; SBP, systolic blood pressure.

Table 4: Assessment of Risk factors in the development of AKI after OPCAB

Parameter	Odds Ratio (OR)	95% confidence interval (CI)	p value
Age (years)	1.005	0.971-1.040	0.78
Sex	1.673	1.090-2.569	0.18
Left ventricular dysfunction	3.459	2.536-4.719	**<0.001**
Diabetes mellitus	1.723	1.284-2.312	**<0.001**
Preoperative CKD	4.367	1.788-15.678	**<0.001**
Previous Cardiac surgery	2.255	0.411-12.380	0.337
Emergency surgery	4.646	1.991-10.840	**<0.001**
SBP (mmHg)	1.020	1.001-1.039	0.04
DBP (mmHg)	0.998	0.965-1.032	0.89
MAP (mmHg)	1.031	1.019-1.043	**<0.001**
IABP requirement	6.438	2.026-20.453	**<0.001**

CKD Chronic Kidney disease DBP, diastolic blood pressure; IABP, intra-aortic balloon pump; MAP, mean arterial pressure; SBP, systolic blood pressure.

The Mean arterial pressure (MAP) was found to be significantly lower in patients with AKI and was associated with an increased risk of development of AKI (p<0.001).

The need for Intra-aortic Balloon pump (IABP) closely correlated with with lower MAP in patients who developed AKI and was also found to be a statistically significant risk factor in the development of AKI after OPCAB.

The risk factors for the development of AKI after cardiac surgery has been extensively reviewed.[24] The risk factors can be classified as pre-operative, intraoperative and post-operative. The preoperative risk factors include non-modifiable risk factors like age, race and gender and the pres-

ence of other co morbidities like – Chronic kidney disease, Diabetes mellitus, cardiac failure and chronic obstructive pulmonary disease. Some studies have found an increased risk of AKI in females. However, our study did not find any gender associated risk of development of AKI after OPCAB.

Genetic predisposition to AKI is being described in which two new loci in chromosomes 3p and 7p are found to have an increased incidence of AKI.[25] Other modifiable risk factors include administration of nephrotoxic medications like angiotensin converting enzyme inhibitors, angiotensin 2 receptor blockers and nephrotoxic antibiotics like aminoglycosides. These medications can lead to alteration in renal autoregulation or development of acute interstitial nephritis. Exposure to radiocontrast dye in the immediate pre-operative period is also associated with an increased risk of AKI.[26]

Intraoperative risk factors which have been described to contribute to AKI include ischemic injury, ischemia reperfusion injury, cardiopulmonary bypass and inflammation.

Homolysis of the red blood cells (RBC's) occur during cardiopulmonary bypass (CPB) which results in the release of haemoglobin which subsequently gets deposited in the renal tubules causing acute tubular necrosis. This is potentiated by the additional toxic effects of iron.[17]The use of OPCAB thus avoiding cardiopulmonary bypass is theoretically helpful in preventing AKI when compared to on pump coronary artery bypass grafting.

The use of on pump CABG is associated with increased levels of pro inflammatory cytokines which leads to increased mortality and complications which include AKI. A meta-analysis of 33 Randomised clinical trials (RCT's) by Cheungpasitporn et al,[27]showed a decreased risk of AKI following OPCAB. This was however contraindicated by the CORONARY trial – a large multicentric RCT, in which there was no difference in the incidence of AKI between on pump CABG and off pump CABG.[28] Tissue injury during surgery, pre-existing left ventricular dysfunction and operative trauma can lead to activation of the immune system, this leads to the production of pro inflammatory cytokines and free radicals which leads to tubular injury.

Post-operative factors which have been implicated in the development of AKI include nephrotoxic medications, hemodynamic instability and systemic inflammation.

The development of anaemia in the peri operative period is also thought to be contributory in the development of AKI by causing ischemic insult to the renal tubules.[29,30]

The limitations of our study were a retrospective analysis, there was no long term follow up of the patients and being a single centre study.

Conclusion

To summarise, we analysed the incidence of AKI in our patients undergoing Off pump coronary artery Bypass Grafting and the risk factors associated with the development of AKI.

The incidence of AKI as defined by the KDIGO guidelines in our study was 18.2 %.

Increasing age, presence of preoperative chronic kidney disease, diabetes, left ventricular dysfunction, need for emergency cardiac surgery, low mean arterial pressure and the need for Intra-aortic balloon pump were identified as significant risk factors for the development of AKI after OPCAB.

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