Original Article

Influence of time interval between coronary angiography to off-pump coronary artery bypass surgery on incidence of cardiac surgery associated acute kidney injury

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ABSTRACT

Background and Aims: Cardiac surgery associated acute kidney injury (CSA-AKI) is serious complication after cardiac surgery. The time interval between coronary angiography (CAG) to coronary artery bypass surgery (CABG) is proposed as modifiable risk factor for reduction of CSA-AKI. The aim of this study was to assess influence of time interval between CAG to off-pump CABG (OPCABG) on incidence of CSA-AKI. **Methods:** This was a retrospective observational study of 900 consecutive OPCABG patients who were classified into 2 groups based on time interval between CAG and OPCABG: ≤7 days or longer. **Results:** The incidence of CSA-AKI was 24% (214/900) by Kidney Disease: Improving Global Outcomes (KDIGO) definition. The incidence of CSA-AKI was not significantly different in two groups (22% in >7 days groupvs. 28% in ≤7 days group, $P = 0.31$). The factors independently associated with CSA-AKI were: Age (OR 1.04; $P = 0.002$), baseline creatinine (OR 1.99,; $P = 0.03$), moderate LV dysfunction (OR 1.64,; $P = 0.007$) and blood transfusion (OR 3.3,; $P < 0.001$), but not the time interval between CAG and OPCABG. The incidence of CSA-AKI was highest in patients with creatinine clearance (CC) <50 mL/min when OPCABG was performed ≤7 days of CAG (16/38; 42%, OR 2.7, 1.4-5.4; $P = 0.005$) compared to lowest incidence of CSA-AKI in patients with CC >50 mL/min and OPCABG performed >7 days of CAG (114/543; 21%). **Conclusion:** This study demonstrated that there is no increased incidence of CSA-AKI if OPCABG is performed ≤7 days of CAG; but we recommend to postpone OPCABG for seven days if CC is <50 mL/min and there is no urgent indication for OPCABG in order to reduce incidence of CSA-AKI.

Key words: Cardiac surgery-associated acute kidney injury, off-pump coronary artery bypass, coronary angiography

Access this article online

Website: www.ijaweb.org

DOI: 10.4103/ija.IJA_770_18

Quick response code

INTRODUCTION

The incidence of cardiac surgery-associated acute kidney injury (CSA-AKI) can vary from approximately 9% to 40%, depending on the definition used. This is potentially devastating complication after cardiac surgery and mortality after routine coronary artery bypass grafting (CABG) surgery can increase from less than 1% to 20% when moderate CSA-AKI develops. The risk factors are multiple, and the etiology

How to cite this article: Borde DP, Asegaonkar B, Apsingekar P, Khade S, Khodve B, Joshi S, *et al*. Influence of time interval between coronary angiography to off-pump coronary artery bypass surgery on incidence of cardiac surgery associated acute kidney injury. Indian J Anaesth 2019;63:475-84.

and pathogenesis is complex and only partially understood.[1] To improve diagnosis and ultimately improve outcomes, there is a need for a single definition of AKI for practice, research, and public health, hence Kidney Disease: Improving Global Outcomes (KDIGO) guidelines have been proposed.[2]

Unfortunately, many of the risk factors for and injuries that cause CSA-AKI are not modifiable. The time interval between coronary angiography (CAG) to CABG is one such proposed modifiable risk factor. American Heart Association guidelines on CABG recommended that, in patients with preexisting renal dysfunction, a delay of surgery after CAG may be reasonable until the effect of radiographic contrast material on renal function is assessed (Class II b, level of evidence B).[3] There is limited and conflicting evidence on this topic as far as off-pump CABG (OPCABG) is concerned, with some studies suggesting increased incidence of CSA-AKI with shorter interval between CAG and OPCABG[4] but not others.[5,6] It must be appreciated that performing a randomised controlled trial on this topic is very difficult, as randomization process would unnecessarily place patients in a potential risk condition for CSA-AKI.

To obtain further evidence, authors tested the hypothesis, whether there is any influence of the timing between CAG and OPCABG on incidence of CSA-AKI.

METHODS

This was a retrospective observational study of data collected at a tertiary care level hospital from January 2014 to October 2017. The institutional review board approved the study with waiver of consent. All consecutive isolated OPCABG patients operated during study period were included for analysis in the study. Exclusion criteria were: intraoperative conversion to on pump CABG, non- availability of exact date of CAG, preoperative dialysis dependent patients, patients operated by minimally invasive thoracotomy approach and patients who underwent re-exploration and/or repeat CAG in immediate post-operative period.

The authors documented demographic variables, which included: patient's age, gender, and body mass index. Also various significant co-morbidities like hypertension, diabetes, chronic obstructive pulmonary disease (defined by X-ray and clinical criteria); cerebrovascular disease (neurological deficit more than 24 h), peripheral artery disease, (defined as stenosis of 1 or more peripheral arteries with more than 50% occlusion of the vessel lumen except the cerebral and carotid artery) and anemia were noted. Preoperative renal function was assessed by serum creatinine values and, an estimated creatinine clearance (CC) as measured by Cockraft-Gault formula. Preoperative echocardiography and CAG findings were also documented. For every patient, EuroSCORE II was calculated and documented.[7] The timing of CAG was documented as calendar days from performance of CAG to OPCABG. Patients who had undergone CAG at outside facilities were also included in the analysis.

At authors' institute, all the patients coming for CABG are operated by off-pump approach unless contraindicated. Single cardiac surgical team operated upon all patients by midline sternotomy. Perioperative management, anaesthetic and surgical techniques were standardised as per institutional practice. A fast track anaesthetic technique typically comprised of intravenous fentanyl (5-10 mcg/kg), midazolam (0.05-0.3 mg/kg), propofol/etomidate, inhaled sevoflurane or isoflurane, and intravenous vecuronium as muscle relaxant. Standard monitoring included 5-lead electrocardiogram, pulse oximetry, end tidal CO_2 measurement, radial or femoral arterial pressure, pulmonary artery catheter, and trans esophageal echocardiography. Antibiotics prophylaxis consisted of Cefuroxime 1.5 gm. and Amikacin 500 mg. Amikacin was replaced by Ciprofloxacin 500 mg if patients had preoperative renal dysfunction as defined by preoperative creatinine more than 1.5 mg/dL or CC <50-mL/min. After midline sternotomy, and conduit harvest as per surgeon preference, systemic heparinization was achieved with 200 IU/Kg body weight to maintain activated clotting time of more than 300 seconds. The surgical team as per severity of lesion decided the sequence of grafting. Post grafting, heparin was neutralised by protamine. The perioperative fluids were mainly balanced salt solution, Ringer's lactate or normal saline and in case of severe hypovolemia colloids were used (maximum dose 50 mL/kg/day). Packed red blood cell transfusion was indicated when haemoglobin value was less than 7 g/dL; when patient was bleeding and or haemodynamically unstable transfusion trigger was haemoglobin value was less than 8 g/dL.

The primary end point was the difference in impact of the timing between coronary angiography and surgery on CAS-AKI development. Postoperative CSA-AKI was defined according to KDIGO criteria using the maximal change in serum creatinine during the first seven postoperative days compared with the pre-operative baseline values.[2] It was defined by either of the following: an increase in creatinine by 0.3 mg/dL or greater within 48 hours or an increase in creatinine 1.5 times baseline or greater, which was known or presumed to have occurred within the prior 7 days. AKI also was staged for severity according to the following criteria: stage 1 an increase in creatinine by 0.3mg/dl or greater or to 1.5 to 1.9 times the baseline.; stage 2 an Increase in creatinine to 2.0 to 2.9 times the baseline; and stage 3: Increase in creatinine to 3.0 or more times the baseline or increase in creatinine 4.0 mg/dL or greater or initiation of renal replacement therapy (RRT).

A urine output criterion was not used, as there was frequent use of diuretics in perioperative period, which would make it unreliable.

Patients were classified into 2 groups based on the patient's time interval between CAG and OPCABG: ≤7 days or longer. This cutoff was based on a previous report suggesting that after being exposed to contrast, renal function usually returns to preexisting levels within 7 days.[8]

All of the data in the study were presented as either mean ± SD for continuous variables or numbers and percentages for categorical variables. Measurements of baseline demographic and clinical characteristics, intra-operative and post-operative characteristics, and postoperative outcomes were compared across time interval categories using the analysis of variance model and the x2 test in univariate analysis.

Univariate logistic regression analysis was used to identify demographic, preoperative laboratory, and coronary angiographic factors significantly associated with CSA-AKI development. Variables with a *P* value <0.01 in univariate logistic regression analysis were included in the multivariable logistic regression analysis by the stepwise selection method to determine independent factors for CSA-AKI. Adjusted odds ratios (OR) with 95% CI were also calculated. Another multivariable regression analysis was run for mortality as end point to evaluate impact of CSA-AKI on mortality. A subgroup analysis was conducted for patients with preoperative CC <50 mL/min or more with CAG to CABG time ≤7 days or longer and OR with 95% CI were calculated. All reported *P* values are two-sided, and values of *P* less than 0.05 were considered statistically significant. Data manipulation and statistical analyses were performed using SPSS version 16.

RESULTS

A total of 994 consecutive isolated OPCABG patients were considered for the study. 94 patients were excluded as per exclusion criteria as; intraoperative conversion to on pump CABG (n = 32), exact date of CAG being not available (n = 25), pre-operative dialysis dependent patients (n = 3), incomplete data set (n = 26), patients operated by minimally invasive thoracotomy (n = 6) and patients who underwent coronary angiography in immediate postoperative period (n = 2). Thus, final analysis included 900 patients.

In all, 900 patients were classified into 2 groups based on the patient's time interval between CAG and OPCABG: ≤7 days (n = 210) or longer (n = 690). The baseline demographic and clinical characteristics, intraoperative and postoperative characteristics, and postoperative outcomes are demonstrated in Table 1. Two groups were comparable in most of the aspects expect that, there were less number of patients with significant left main disease in >7 days groups compared to ≤7 days group (9.7% vs. 21.9% P < 0.01). The overall incidence of CSA-AKI by KDIGO definition was 24% (214/900). Majority of the patients who developed CSA-AKI were having Grade 1 CSA-AKI 22% (n = 196); few were having Grade 2 CSA-AKI, 1.5% (n = 14) and only 0.5% (n = 4) patients suffered from grade 3 CSA-AKI. The incidence of CSA-AKI was not significantly different in 2 groups (22% in >7 days groups compared to 28% in ≤7 days group, P = 0.31).

The factors independently associated with CSA-AKI on multivariate analysis were: age (OR 1.04 CI 1.01-1.05; P = 0.002), baseline creatinine (OR 1.99, CI 1.01-3.7; P = 0.03), moderate LV dysfunction (OR 1.64, 1.1- 2.4; P = 0.007) and blood transfusion (OR 3.3, 1.9- 5.6; P < 0.001) but not the time interval between CAG and CABG [Table 2].

EuroSCORE II (OR 1.3, CI 1.4- 1.7; P = 0.01) and CSA-AKI (OR 5.7, CI 1.4-23.3; P = 0.02) were independently associated with mortality as shown in multivariable regression analysis as demonstrated in Table 3.

There were 182 (20.2%) patients with baseline CC <50 mL/min. Table 4 demonstrates subgroup analysis

Table 1: Baseline characteristics, demographics, co-morbidities; intraoperative and postoperative variables				
	Total (*n*=900)	CABG >7 days after CAG (*n*=690)	CABG ≤7 days after CAG (*n*=210)	*P*
Preoperative				
Age (years)	60±9	60±9	60±10	0.72
Female Gender	192 (21.3%)	150 (21.7%)	42 (20%)	0.36
Height (cm)	161±8	161±8	162±8	0.16
Weight (kg)	63±11	63±11	64±11	0.06
Body mass index (kg/m²)	24.4±3.5	24.3±3.5	24.6±3.4	0.28
Hypertension	612 (68%)	464 (67.2%)	148 (70.5%)	0.42
DM	402 (44.7%)	281 (44%)	94 (44.8%)	0.81
COPD	177 (19.7%)	141 (20.3%)	36 (17.4%)	0.07
CVA	18 (2%)	14 (2.02%)	4 (1.9%)	0.97
PVD	13 (1.4%)	10 (1.4%)	3 (1.4%)	0.61
Anaemia	323 (35.8%)	239 (34.6%)	84 (40%)	0.28
Recent (<90 days) myocardial infarction	251 (27.8%)	189 (27.3%)	62 (29.5%)	0.6
NYHA Class				
II	413 (46%)	319 (46.2%)	94 (44.8%)	0.14
III	482 (53.5%)	369 (53.5%)	113 (53.8%)	
IV	5 (0.5%)	2 (0.3%)	3 (1.4%)	
Baseline Creatinine (mg/dL)	1.05±0.26	1.08±0.27	1.05±0.22	0.84
EF				0.68
Good (>50%)	414 (46%)	309 (44.8%)	105 (50%)	
Moderate (31-50%)	423 (47%)	331 (48%)	92 (44%)	
Poor (21-30%)	59 (6.5%)	47 (6.8%)	12 (6%)	
Very Poor (<20%)	4 (0.5%)	3 (0.4%)	1 (0.5%)	
Pulmonary Hypertension				0.91
Moderate	133 (15%)	102 (14.8%)	31 (14.8%)	
Severe	5 (0.6%)	4 (0.6%)	1 (0.5%)	
Mitral Regurgitation				
Mild	257 (28.5%)	201 (29%)	56 (26.6%)	0.39
Moderate	15 (1.5%)	14 (2%)	1 (0.5%)	
No. of Coronaries Diseased				0.28
1	25 (2.8%)	17 (2.5%)	8 (3.8%)	
2	134 (15%)	99 (14.3%)	35 (16.6%)	
3	741 (82.2%)	574 (83.2%)	167 (79.6%)	
Left Main >50%	113 (12.5%)	67 (9.7%)	46 (21.9%)	<0.01
EuroSCORE II	2.6±1.8	2.6±1.8	2.5±1.9	0.74
Intraoperative				
No. of grafts				0.37
1	38 (4.2%)	25 (3.6%)	13 (6.2%)	
2	239 (26.5%)	182 (26.3%)	57 (27.1%)	
≥3	623 (69.3%)	483 (70.1%)	140 (66.7%)	
Perioperative Transfusions				0.28
No	832 (92.4%)	639 (92.6%)	193 (92%)	
1-2	62 (6.8%)	46 (6.6%)	16 (7.5%)	
≥3	6 (0.8%)	5 (0.8%)	1 (0.5%)	
Postoperative				
In- hospital mortality	9 (1%)	7 (1%)	2 (1%)	0.94
Postoperative Stroke	5 (0.6%)	4 (0.6%)	1 (0.5%)	0.86
Postoperative prolonged ventilation (>24h)	18 (2%)	14 (2%)	4 (1.9%)	0.92
CSA-AKI (KDIGO)				0.31
No	686 (76%)	538 (78%)	151 (72%)	
Yes	214 (24%)	155 (22%)	59 (28%)	
Grade 1	196 (22%)	142 (20.5%)	54 (25.6%)	
Grade 2	14 (1.5%)	11 (1.6%)	3 (1.4%)	
Grade 3	4 (0.5%)	2 (0.3%)	2 (1%)	

DM–Diabetes Mellitus; COPD–Chronic Obstructive Pulmonary Disease; CVA–Cerebrovascular Accident; PVD–Peripheral Vascular Disease; NYHA–New York heart association; EF–Ejection Fraction; CAS-AKI–cardiac surgery associated acute kidney injury; KDIGO–Kidney Disease: Improving Global Outcomes

Table 2: Univariate and multivariate regression logistic regression analysis with CSA-AKI as end point

Variable	Univariate logistic regression		Multivariate Logistic Regression	
	OR (Lower- Upper 95% CI)	*P*	OR (Lower- Upper 95% CI)	*P*
Age	1.04 (1.02-1.06)	<0.01	1.04 (1.01-1.05)	0.002
Female gender	0.84 (0.57-1.2)	0.37		
Hypertension	0.96 (0.69-1.2)	0.80		
DM	0.88 (0.64-1.2)	0.4		
COPD	1.13 (0.77-1.65)	0.53		
CVA	1.62 (0.6-4.3)	0.34		
PVD	0.96 (0.26-3.5)	0.95		
Anemia	1.27 (0.93-1.75)	0.13		
Baseline Creatinine	2.45 (1.37-4.4)	0.003	1.99 (1.07-3.7)	0.03
CC >85	Ref			
Moderate CC (50-85)	1.2 (0.77-1.8)	0.43		
Severe CC (<50)	1.63 (1.14- 2.3)	0.03	Variable removed from the model as it is derived from age and creatinine	
Recent MI	1.1 (0.75-1.5)	0.73		
NYHA II	Ref			
III	0.95 (0.7-1.3)	0.48		
IV	2.1 (0.34-12.7)	0.43		
No. of vessels	1.2 (0.85-1.7)	0.3		
Left Main disease (>50%)	0.96 (0.59-1.6)	0.85		
EF Good (>50%)	Ref			
Moderate (31-50%)	1.8 (1.3-2.5)	<0.01	1.64 (1.1-2.4)	0.007
Poor (21-30%)	1.4 (0.7-2.6)	0.33	1.2 (0.6-2.4)	0.6
No PH	Ref			
Mod PH	1.5 (0.98-2.3)	0.05		
Severe PH	0.85 (0.09-7.6)	0.9		
No MR	Ref			
Mild MR	1.74 (1.2-2.4)	0.002	1.4 (0.9-2.04)	0.66
Mod MR	4.5 (1.5-13.5)	0.008	3.4 (1.02 - 11.6)	0.07
CAG- CABG interval≤7 days	1.32 (0.93-1.9)	0.13		
Blood transfusion	Ref			
None				
1-2 units	3.4 (2.02-5.8)	< 0.01	3.3 (1.9-5.6)	<0.001
> 2 units	18.2 (2.1-153)	< 0.01	13.9 (1.5-128.1)	0.02
EuroSCORE II	1.12 (1.02-1.2)	0.02		
No. of grafts	1.1 (0.92-1.4)	0.25		

OR–Odds' ratio; CI–Confidence interval; DM–Diabetes mellitus; COPD–Chronic Obstructive Pulmonary Disease; CVA–Cerebrovascular accident; PVD–Peripheral Vascular Disease; CC–Creatinine Clearance; NYHA–New York heart association; EF Ejection fraction; PH–Pulmonary Hypertension; MR–Mitral regurgitation; MI–Myocardial infarction

Table 3: Multivariate Analysis - Effect of CSA-AKI on in- hospital mortality

Variable	OR (Lower- Upper 95% CI)	*P*
CSA-AKI	5.7 (1.4- 23.3)	0.02
EuroSCORE II	1.3 (1.1- 1.7)	0.01

of CC <50 mL/min or >50 mL/min with CAG to CABG interval ≤7 days or longer. The incidence of CSA-AKI was highest in patients with CC <50 mL/min when CABG was performed ≤ 7 days of CAG (16/38, 42% with OR 2.7 CI 1.4-5.4; $P = 0.005$) as compared to lowest incidence of CSA-AKI in patients with CC >50 mL/min and CABG performed > 7 days of CAG (114/543, 21%). The group CC <50 and CABG within 7 days of CAG was associated with higher grades of CSA-AKI with incidence of grade 2 and grade 3 injury being 5.3% and 2.6%, respectively. The calculated power of the study (for α error of 0.05) was 0.82.

DISCUSSION

The main findings of the study are: The risk of CSA-AKI is not different if the interval between CAG and OPCABG is ≤7 days or longer, but the incidence of CSA-AKI is significantly high in patients with CC <50 mL/min when CABG was performed within 7 days of CAG (16/37, 42% with OR 2.6 CI 1.3-5.2; $P = 0.005$); the factors independently associated with CSA-AKI are age, baseline creatinine, moderate LV dysfunction and perioperative transfusion; and CSA-AKI is independently associated with mortality in patients undergoing OPCABG.

Table 4: Subgroup Analysis of CC <50 mL/min or CC >50 Ml/min with CAG- OPCABG interval ≤7 days or longer

	CC>50 mL/min		CC<50 mL/min	
	>7 days interval (*n*=543; 60.3%)	≤7 days interval (*n*=175; 19.4%)	>7 days interval (*n*=144; 16%)	≤7 days interval (*n*=38; 4.2%)
CSA-AKI- Yes	114 (21%)	43 (24.6%)	41 (28.55)	16 (42%)
Grade 1 CSA-AKI	108 (20%)	41 (23.4%)	34 (23.6%)	13 (34.2%)
Grade2 CSA-AKI	5 (0.8%)	1 (0.6%)	6 (4.2%)	2 (5.3%)
Grade 3 CSA-AKI	1 (0.2%)	1 (0.6%)	1 (0.7%)	1 (2.6%)
OR (C.I.)	Reference	1.23 (0.82-1.8)	1.5 (1-2.27)	2.7 (1.4-5.4)
P	-	0.32	0.06	0.004

CSA-AKI is one of the most important complications after cardiac surgery, as it associated with increased perioperative and long-term mortality as well as poor quality of life (QOL) after cardiac surgery.[9-12] In our study also, CSA-AKI was an independent risk factor for mortality. So, any intervention which can reduce the incidence of CSA-AKI will also most likely influence mortality. There are various risk factors that predispose patients for CSA-AKI. Most of them are not modifiable. Hence, it is imperative to concentrate on modifiable risk factors for CSA-AKI.

One of the proposed modifiable risk factor for CSA-AKI is time interval between CAG and cardiac surgery. It was one of the earliest studies by Del Duca *et al.*,[13] which proposed that cardiac surgery performed within 5 days of CAG is an independent risk factor for CSA-AKI. There are various studies since then available on this topic.[4-6,13-29] There is marked heterogeneity in patient population, definition of CSA-AKI used, incidence of CSA-AKI and time interval used to assess impact of CAG timing on CSA-AKI; hence it is not surprising that the results are also different in these studies as mentioned in Table 5.

Until now, there is no consensus about safe time interval between CAG and cardiac surgery in order to minimise risk of CSA-AKI. It must be appreciated that, performing a randomised controlled trial on this topic is very difficult, as randomization process would unnecessarily place patients in a potential risk condition for CSA-AKI. Hence, we should perform more observational studies to come to reasonable conclusion.

A recent meta-analysis of 9 studies concluded that, a time interval of 1 day or less between CAG and on-pump cardiac surgery was significantly associated with increased risk of AKI.[30] But, The impact of time interval between CAG and CABG can be different in patients undergoing on pump or OPACBG. Kim *et al.*,[6] in their study demonstrated that a shorter interval between coronary angiography and surgery influenced the occurrence of acute kidney injury in patients undergoing on-pump CABG, but not an independent risk factor in patients who undergo OPCABG.

There are limited studies on impact of time interval between CAG to surgery in patients undergoing OPCABG.[4-6,28,29] There are 2 studies which support that shorter time interval between CAG and OPCABG (<24 hours as per study by Zhang[4] and <5 days as per study by Ji[28]) is an independent risk factor for CSA-AKI. Remaining three studies do not support the hypothesis.[5,6,29] Our study also demonstrates that there is no increased incidence of CSA-AKI if OPCABG is performed within seven days of CAG. It should be noted that, CSA-AKI was not defined by majority of the previous studies by KDIGO; which is most acceptable definition in contemporary practice.

Previously, Lee and co-workers[5] demonstrated that in 1364 patients undergoing OPCABG was not related to time interval between CAG and surgery, and that there was no difference of this time interval in patients with preserved or reduced renal function assessed by CC. In contrast, our study demonstrated that patients with CC <50 mL/min who undergo OPACBG within 7 days of CAG are at significantly increased risk of CSA-AKI (16/38, 42% with OR 2.7 CI 1.4-5.4; $P = 0.004$). Patients with reduced baseline renal function are independently at increased risk for CSA-AKI, if in this high-risk group shorter time to recover from CAG induced renal injury may make them prone for CSA-AKI.

So, based on our study findings, we recommend to postpone OPCABG for seven days in order to reduce incidence of CSA-AKI, if CC is <50 mL/min and there is no urgent indication for OPCABG. It is proposed earlier as well that one could capitalise on this delay by addressing other preoperative variables such as anemia management, glucose management, coagulopathies, infections, and other issues which can impact have on CSA-AKI.[24]

Table 5: Published studies assessing impact of CAG- Cardiac Surgery interval on CSA-AKI

Author & Journal	Year of Publication	Country	*n*	Patient group	CSA-AKI criteria	CSA-AKI Incidence (%)	CAG to cardiac surgery duration categories	Conclusion	Impact of interval on CSA-AKI Y/N
Del Duca; Ann Thorac Surg[13]	2007	Canada	649	Cardiac surgery on CPB	creatinine by 25%/ Dialysis	24	< 5 days &> 5 days	Catheterization within 5 days of surgery is a risk factor for AKI	Y
Brown; Mayo Clin Proc[23]	2007	USA	226	Valve surgery	STS	1.8	Same day CAG and surgery	In properly selected patients, same day CAG is safe	N
Ranucci; Am J Cardiol[20]	2008	Italy	423	Elective cardiac surgery	STS	5.7	CAG on day of surgery vs. Others	Cardiac surgery within 24 hours of CAG increases AKI	Y
Hennessy; J Thorac Cardiovasc Surg[15]	2010	Canada	1287	Valve surgery	STS	6.6	CAG within 24 hours vs. Others	CAG within 24 hours of valve surgery is significantly associated with AKI	Y
Kim; Korean J Anesthesiol	2010	Korea	110	OPCABG	AKIN	16	≤2 days vs. > 2 days	CAG within 2 days doesn't affect AKI	N
Kramer; Ann Thorac Surg[16]	2010	USA	668	Elective adult cardiac surgery	AKIN	45	Same admission vs. later admission	CAG and cardiac surgery in same admission increase risk of AKI	Y
Medalion; J Thorac Cardiovasc Surg[17]	2010	Israel	395	CABG	creatinine by 25%/ in GFR ≤60mL/ min	13.6	≤ 1 day; 1-5 days; > 5 days	CABG should be delayed for 5 days in patients who received high contrast dose	Y
Greason; Ann Thorac Surg[24]	2011	USA	1413	AVR	AKIN	23.4	Same vs. more than 1 day	In properly selected patients, CAG can be performed on same day of AVR	N
Mehta; Circulation[18]	2011	USA	2441	CABG	creatinine >50%	17.1	Days 0,1; day 2; day3; day4; day≥5	Risk of AKI is inversely and modestly related to time interval between CAG and CABG	Y
Ji; Circ J[30]	2012	China	307	OPCABG	AKIN	16.6	≤ 5 days; > 5 days	Beginning OPCABG early after CAG increases risk of AKI	Y

Contd...

Table 5: Contd...

Author & Journal	Year of Publication	Country	*n*	Patient group	CSA-AKI criteria	CSA-AKI Incidence (%)	CAG to cardiac surgery duration categories	Conclusion	Impact of interval on CSA-AKI Y/N
McIlroy; J Cardiothoracvascanaesthesia[25]	2012	USA	644	Elective cardiac surgery	AKIN	21.9	≤ 1 day; 2-7 days; >7 days	In appropriately selected patients cardiac surgery can be performed within 1 day od CAG	N
Baloria; Asian Cardiovasc Thorac Ann[19]	2012	India	749	Cardiac surgery on pump	creatinine by 25%	15	0-3 days; 4-6 days; >6 days	AKI has definite relationship with CAG to cardiac surgery interval	Y
Ansderson; J Thorac Cardiovasc Surg[26]	2012	USA	285	Elective proximal Aortic Surgery	RIFLE	31	1-3 days; ≥ 4 days	CAG within 1-3 days of elective proximal aortic surgery is safe	N
Ko; European Heart Journal[27]	2012	USA	2133	Elective cardiac surgery	AKIN and RIFLE	32%AKIN; 18% RIFLE	≤ 3 days; > 3 days	Risk of AKI is not influenced by CAG to cardiac surgery duration	N
Ranucci; Ann Thorac Surg[20]	2013	Italy	4440	Cardiac Surgery	AKIN	21.7	On the day of cardiac surgery vs. later	Surgery on same day of CAG significantly increases AKI	Y
Zhang; AM J Cardiol[4]	2013	China	1513	OPCABG	AKIN	34.9	≤ 24 hours; 24-48 hours; 48-72 hours; >72 hours	OPCABG performed within 24 hours is an independent risk factor for AKI	Y
Lee; Ann Thorac Surg[5]	2013	Korea	1364	OPCABG	AKIN	28.7	≤ 1 day; day2; day3; day 4; day≥5	Risk of AKI is not related to time between CAG to OPCABG	N
Mariscalo; Int J Cardiol[21]	2014	Italy	2504	Cardiac Surgery	RIFLE	9	≤ 1 day; >1 day	Delaying surgery beyond 24 hours seems justified only in combined valve and CABG surgery	Y
Kim; J Thorac Cardiovasc Surg[6]	2016	Korea	2371	On pump and OPCABG	KDIGO	40.7	≤ 7 days; >7 days	CAG to CABG interval is not independent risk factor for AKI in OPACBG but important in on pump CABG	N

Contd...

Table 5: Contd...

Author & Journal	Year of Publication	Country	*n*	Patient group	CSA-AKI criteria	CSA-AKI Incidence (%)	CAG to cardiac surgery duration categories	Conclusion	Impact of interval on CSA-AKI Y/N
Dayan; Asian Ann Cardio ThoracAnn[22]	2017	Urugway	1044	Valve surgery	AKIN	28.4	≤ 3 days; 4-7 days; ≥ 8 days	Hospital mortality is higher with decreased renal function who undergo surgery within 3 days after CAG	Y

CSA-AKI–Cardiac surgery associated acute kidney injury; STS criteria–Defined as creatinine levels of >2.0 mg/dL and 2 times the preoperative value; AKIN (acute kidney injury network) criteria–Absolute increase of ≥0.3 mg/dL or a relative increase of≥50% in serum creatinine from baseline value within 48 h after surgery, or requiring post-operative haemodialysis; RIFLE–Risk, Injury, Failure, Loss of function, End-stage renal disease) criteria, 50% increase in peak postoperative Creatinine over baseline. KDIGO–Kidney Disease: Improving Global Outcomes

Our study population had comparatively less number of patients in ≤7 days group as compared to previous studies. There can be various reasons for it; most of the patients who undergo CAG in our setup are loaded with antiplatelet medications like clopidogrel/ticagrelor so surgical team has to wait for at least 5 days; many of the CAGs are performed at outstation facilities and referral of patients to our unit may add to time and patients have to wait for insurance clearance from authorities. Also, the groups were significantly different in another aspect. Patients who were operated within 7 days had more significant LMCA disease, which is why the surgeons did not wait more than 7 days in the case of those patients.

At the same time, our study has some notable limitations. First and foremost being related to retrospective single center nature of this study. Secondly, we didn't have exact details of CAG procedure as many of the studies were performed at outstation facilities. But Lee *et al.*[5] have proved that amount and type of contrast media used has no impact on CSA-AKI when adjusted for other confounding factors. Nevertheless, there is need to perform a prospective study on this topic with detailed analysis of contrast type and dose. Thirdly, we didn't use urine output as criteria used in KDIGO definition. Lastly, although one of the important factors for development of CSA-AKI, we didn't have complete information on perioperative intravenous fluids. At the same time, some of our patients have received amikacin as perioperative antibiotic, which can influence incidence of CSA-AKI.

CONCLUSION

Our study demonstrated that there is no increased incidence of CSA-AKI if OPCABG is performed within seven days of CAG; but we recommend to postpone OPCABG for seven days after CAG if CC is <50 mL/min and there is no urgent indication for OPCABG.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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